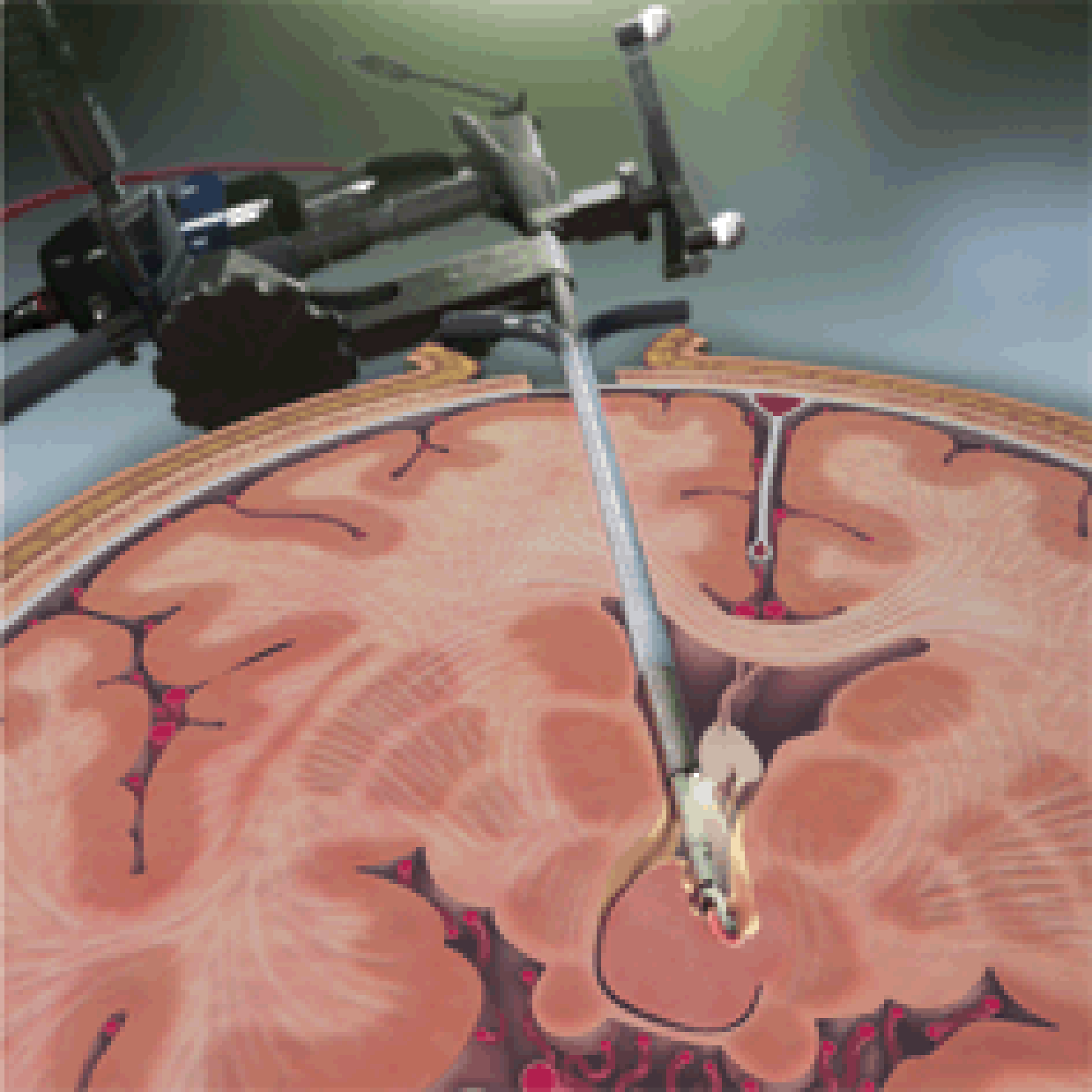

Introduction

Management of hypothalamic hamartomas: progress due to alignment of the stars

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The February 2011 issue of *Neurosurgical Focus* is devoted to a discussion of the recent explosion of information regarding the management of a rather rare birth defect that can have devastating effects on children and adults. The actual prevalence of hypothalamic hamartoma (HH) cannot yet be estimated because the clinical presentation of patients is so variable, and until very recently the diagnosis was extremely difficult. Some patients are minimally symptomatic, and it must be presumed that there are many in this group as well as a significant number of asymptomatic patients in whom the diagnosis is not made.

Historical Perspective of HH

Before approximately 1990, little was known about HH. For the most part a diagnosis was made when imaging studies showed very large lesions thought to be brain tumors within and below the third ventricle. Surgical exploration and biopsy revealed that these masses were composed of normal neuronal elements and glia, and a clear interface between the mass and the native hypothalamus could not be established. The relationship between HH and both isosexual precocious puberty and epilepsy was known, but until the 1980s there were no reports of surgical management except for the abovementioned biopsy.

Between 1990 and 2000, case reports on the successful surgical management of HH began to surface. These reports presumably reflected the increasing availability of contemporary imaging techniques. The first CT scanner was installed in the US in 1973. Typical of these reports was an early publication by Machado and colleagues[8] from the Hospital for Sick Children in Toronto. They reported the case of a child with refractory epilepsy surgically treated via the pterional approach. The patient had an excellent outcome, including freedom from seizures and no postoperative morbidity. Interestingly, these authors noted that they found a mass lesion within the hypothalamus, and its consistency and color were indistinguishable from the native hypothalamus. They stated that the entire mass was removed without difficulty. How these authors decided where to stop the resection was unclear from the operative description; however, the take-home message was that seizures in the context of HH are definitely related to the lesion itself and can be treated or ameliorated by surgical removal of the mass.

There are 2 types of HH and they overlap significantly. Sessile HH lesions with broad-based attachments to the hypothalamus, especially within the third ventricle, are primarily associated with epilepsy and especially with gelastic seizures. On the other hand, HHs that cause isosexual precocious puberty are more likely to be pedunculated lesions that "hang" below the tuber cinereum. Surgical strategies for the latter were more understandable, and soon thereafter the successful treatment of precocious puberty by removing the lesions began to be reported.[1,11,18] In the US, this form of treatment has fallen from favor with the development of effective hormonal management. In China, however, it remains the treatment of choice because of the difficulty in obtaining and affording the hormonal analogs.[7]

Development of Modern Approaches to the Surgical Management of HH

The past decade has seen a dramatic increase in the understanding and management of HH, especially in terms of intractable epilepsy. These advances relate to the synchronous development of the technology needed for the safe and effective treatment of lesions in critical areas of the brain and without physically demonstrable borders between the offending lesion and critical areas of the brain such as the hypothalamus. By the turn of the millennium, three major technological advances blossomed. Once considered in the realm of science fiction, but by that time fully realized, these three advances were MR imaging, neuronavigation, and the Internet.

Before the mid-1980s, only very large HHs could be diagnosed. To do so usually required the injection of a dye used for myelography and careful observation of the basal cisterns. All but the largest of these lesions were missed. With the development of MR imaging technology, particularly with multiple sequences, HHs that were only a few millimeters in diameter could be diagnosed within the third ventricle in patients with signs of precocious puberty or gelastic epilepsy.

This new information, plus the knowledge gained from the few published case reports, led to the thought that surgical removal might be appropriate for selected patients with HH. Before that time the standard approach to the hypothalamus was via a pterional or orbitozygomatic approach. Through these approaches, it was difficult or impossible to remove or disconnect the part of the mass that lay within the third ventricle, even after the lamina terminalis was opened.

The group from Melbourne, Australia, including neurosurgeon Dr. Jeffrey Rosenfeld and epileptologist Dr. Simon Harvey, explored the possibility of attacking HHs from above by using a transcallosal interforniceal approach. In 2003 they reported on their first 12 cases utilizing this approach with encouraging results.[4] A year later their series had increased to 45 cases.[17] The personal history associated with this set of accomplishments is highlighted in the first article in this issue by Rosenfeld.

At the same time, many families affected by the ravages of HH were desperate for information. Essentially all were told that, yes, the problems their loved ones faced were due to the HH but that nothing could be done surgically to help them. At this point, the Internet was available to facilitate international communication. Several families affected by HH established a website, which served to form a support group and announced new findings. This website discovered the advances of the Melbourne group, and its membership became aware that there was indeed hope for treatment. As a result, a significant number of patients were referred to Australia for treatment. The group there collected a large series of patients in a very short period, allowing validation of the surgical approach and its value in improving the quality of life of individuals affected by HH.

The final technological advance needed was the general availability of frameless stereotactic neurosurgery known as neuronavigation. A neurosurgeon removing an HH sees tissue that looks just like normal brain. The ability to identify the HH-brain interface depends on the subtle differences in signal intensity seen on MR imaging and shown by the navigation system. The surgical view is through the microscope, utilizing the endoscope or stereotactic equipment for Gamma Knife or the implantation of radiofrequency electrodes.

Multiple strategies are now available for the surgical management of HH. It is possible to tailor the treatment plan for each affected individual. It is increasingly clear that multiple surgical approaches or approaches from various trajectories, supplemented with Gamma Knife treatment, may be needed to safely treat large HHs causing both the behavioral abnormalities, which are the rule rather than the exception, and the seizure disorder.[12,19]

Aside from open craniotomy for HH, several other approaches are of value. Regis and his colleagues from Marseilles have shown that in selected patients good results can be expected from Gamma Knife therapy.[14,15] Delalande and Fohlen have been continuing advocates for the resection of HHs within the third ventricle by using the endoscope to remove or disconnect the lesions.[3,13] The idea that these lesions can be managed using the quicker and somewhat safer option of endoscopic removal was suggested to me by Dr. Jung Uhn Choi at a neuroendoscopy meeting in Naples in 2003. Although I do not use this approach exclusively, I have found that most HHs within the third ventricle are excellent candidates for this type of excision.[2,9,16] Radiofrequency obliteration and stimulation of the mamillothalamic tract have also proved useful in the management of HHs associated with intractable epilepsy.[5,6,10]

Within this collection of works, there is a general discussion by Wait et al. of the surgical strategies that have proved useful in the management of HHs at the Barrow Neurological Institute and a review by Pati et al. of patients who have needed subsequent surgery for this lesion. There is also a discussion of the dreaded complication related to the hypothalamus that has previously been associated with the resection of large craniopharyngiomas. That complication is the severe cyclical problems with sodium metabolism that can occur when dealing with giant HHs. This complication is frustrating, and the fact that it has only followed the resection of giant HHs has led us to consider staging the surgery for the largest of these lesions; see the article by Abla et al.

Conclusions

At a very few centers the concurrence of technology has resulted in the ability to treat a relatively large number of patients with HH. The result has been a rapid and dramatic increase in our knowledge base of this disorder and in the improvements in outcomes in these patients. A great deal of credit for this progress goes to the individuals and families who have refused to accept that there was no hope for improvement. They have shown profound courage in dealing with these difficult problems. For their stories and more information about this amazing community, I refer you to the following website: www.hopeforhh.org. *(DOI: 10.3171/2011.2.FOCUS.Intro)*

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The evolution of treatment for hypothalamic hamartoma: a personal odyssey

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The prognosis for patients with hypothalamic hamartoma has improved dramatically over the last 20 years, for 3 main reasons. First, because of improved understanding of the anatomy and pathophysiology of these varied lesions. Second, due to advances in brain imaging and refinements in microsurgery, including the anterior transcallosal interforniceal approach, endoscopic, and skull-base approaches. And third, because of increasing experience with stereotactic radiosurgery, interstitial radiotherapy, and radiofrequency lesioning. Patients with hypothalamic hamartoma should be managed in comprehensive epilepsy centers where the treatments are individualized and concentrated in the hands of surgeons who can perform the full range of surgery, including approaches to the third ventricle. Total seizure-freedom rates of 52% to 66% have been achieved with surgery. *(DOI: 10.3171/2010.11.FOCUS10244)*

Key Words • **hypothalamic hamartoma** • **radiosurgery** • **gelastic epilepsy**

Hypothalamic hamartomas frequently cause intractable epilepsy with frequent gelastic and other mixed seizure types, intellectual disability, appalling behavioral disturbance with severe temper tantrums, and precocious puberty. Resection of the HH may cure the seizures and result in dramatic improvements in behavior, concentration, and the ability to learn new information. These children are given the chance to lead a relatively normal life and their parents are overjoyed to see this transformation in their child. A neurosurgeon could receive no greater reward.

Prior to the development of successful surgery for HH, the prognosis for these children was abysmal because the resulting epilepsy is particularly resistant to antiepileptic drugs and these patients frequently experience a relentlessly deteriorating clinical course. The seizures may occur every few minutes or even virtually continuously in those who are severely affected. This creates an epileptic encephalopathy that results in serious cognitive decline.[5,18] Formerly, these children eventually became a complete burden on their parents, and family dynamics often became dysfunctional. Many of these children had a shortened lifespan and required institutional care. Successful intervention for these children has evolved, particularly in the last 20 years, and it is the purpose of this review to examine the factors responsible for this transformation. This paper reflects a personal view and does not attempt to exhaustively review and synthesize all the series of patients with HH reported in the literature, but instead attempts to focus on the principal developments in the field as observed from a personal perspective over this extended time period.

Mixed seizure patterns in patients with HH often electrically localize to the cortex. Because of this localization, frontal corticectomies and temporal lobectomies were performed without achieving control of the seizures. We identified examples of these patients in our series.[17,33] The HH was not always noted on CT, particularly if it was small, and it was only after the introduction of MR imaging that the presence of the HH and its enormous anatomical variations were appreciated in these patients with intractable epilepsy.[3,12] It is also challenging to diagnose gelastic seizures in infants. Some of these infants may be diagnosed with gastroesophageal reflux[36] or colic. In some patients Lennox-Gastaut syndrome may be due to HH, but misdiagnosed.[22]

The Development of Surgery for HH

Before the mid-1990s there was a legitimate fear of HH surgery because of the location of the hamartoma, the uncertainty that the epilepsy was emanating from the hamartoma, and the chance of hypothalamic damage and serious complications or death caused by surgery to remove the HH. Neurosurgeons were generally reluctant to remove a lesion from the hypothalamus. The first

Abbreviation used in this paper: HH = hypothalamic hamartoma.

reports of surgery for HH were those of Northfield and Russell,[25] who described 2 patients in 1967 who underwent subfrontal approaches for precocious puberty. The first lesion was probably pedunculated. The second lesion was 2 cm in diameter and attached to the tuber cinereum. Patients with central precocious puberty usually have pedunculated HHs attached to the infundibulum or tuber cinereum.[7] In the French literature in 1969, Paillas et al.[26] reported the case of a 14-month-old child with epilepsy who underwent 2 operations, the first via a transsylvian approach with removal of the temporal pole, and the second operation a subtemporal approach to excise an HH. Interestingly, these 3 hamartomas were diagnosed using air encephalography.

The literature on HH before the 1990s contained many individual case reports and small series with limited follow-up, and thus there could be no confidence that surgical treatment was regarded as an evidence-based standard. The surgery was often unsuccessful with lower epilepsy control rates compared with other types of epilepsy surgery,[21,33] and serious complications and deaths were reported.[33] Therefore, very few patients were referred by neurologists to neurosurgeons for surgical treatment.

The reasons for the successful transformation of the treatment of HH were first, improved definition of the exact anatomy and relationships of the HH observed on multiple projections on MR images;[12] second, the realization that the HH was not a significant intrinsic structural element of the hypothalamus, but was a discrete lesion fused to the hypothalamus, which could be safely removed or disconnected in many patients; and third, increasing refinement of microsurgical techniques aided by intraoperative stereotactic navigation. In conjunction with the evolution of the surgery for HH was the increasing application of stereotactic radiosurgery.[28] Further treatment options for HH are radiofrequency lesioning[15,19] and interstitial radiotherapy with ^{125}I,[32,34] but the sample sizes reported are smaller and these treatments are not freely available.

It took some time for the realization and proof that the seizures were emanating from the HH itself and rapidly spreading to the cortex.[5,13,16] There are multiple possible routes by which seizures spread from the HH into adjacent and remote parts of the brain. One pathway is that the seizures spread directly through the mammillary body to the thalamus and beyond via the mammillothalamic tracts,[13] so that disconnection of the HH from the mammillary body has become one of the key goals of the disconnection surgery. Sessile HHs are attached to one or both mammillary bodies.[12] Hypothalamic hamartoma is a model for human subcortical epilepsy, secondary epileptogenesis, and epileptic encephalopathy.[18] The frequent seizures in these children may cause an epileptic encephalopathy with cognitive and behavioral decline. This encephalopathy tends to resolve following resection or disconnection of the HH.[18] The best results from treatment of the HH will likely result if the treatment occurs before the evolution of the seizure pattern into a widespread secondary generalized epilepsy. Once this secondary epilepsy is established, removal of the HH will not be likely to eliminate the generalized seizures, which may be independently generated in the cortex.

The Royal Children's Hospital Experience

Hypothalamic hamartoma is a rare, usually sporadic condition that we initially estimated to occur in approximately 1 person per million of the population, based on the number of patients who were referred to Royal Children's Hospital from within Australia. However, with greater clinical recognition and improved diagnostic capability using MR imaging, the incidence of HH is currently reported to be about 1 in 200,000.[6] Advances in the treatment of patients with HH could not have occurred without a strong multidisciplinary team approach within the setting of a comprehensive epilepsy program, in this case led by the pediatric neurologist Dr. Simon Harvey. These complex patients require an extensive preoperative workup, which has been described previously.[13,17,33]

The first patient we operated on for HH and gelastic epilepsy at Royal Children's Hospital presented in 1996. The exophytic component of the lesion, attached to and extending below the hypothalamus, could be debulked via a subfrontal approach, but a significant component of the lesion was still present within the cavity of the third ventricle and was attached to the medial walls of the hypothalamus on the postoperative MR image. It was clear that an approach from below could never remove this component completely or safely and that epilepsy control would probably remain poor if a significant component of the lesion remained attached to the hypothalamus. A transcallosal approach would enable exposure of this component of the HH and permit excision with what we surmised would result in better control of the epilepsy with acceptable morbidity. The next patient who presented with a sessile intrahypothalamic and intraventricular hamartoma causing intractable epilepsy had the transcallosal approach performed with success. The initial transcallosal experience in 5 patients at the Royal Children's Hospital resulted in 3 patients who were seizure-free and 2 with only occasional, brief gelastic seizures with reduced antiepileptic drugs. There were marked improvements in behavior, school performance, and quality of life in these 5 patients. Follow-up ranged from 9 to 37 months (mean 24 months).[33]

There was clearly a need for a detailed prospective analysis of a sizable series of patients with HH, including a detailed description of the epilepsy, the type and extent of the surgery, the postoperative course, the endocrine function including risk of diabetes insipidus, thirst center dysregulation, weight and appetite changes, and effects on vision, mood, and behavior. The degree of control of the epilepsy and an adequate length of follow-up were prime concerns. Neuropsychological outcome including memory function were also of interest. Many previous case reports and series had relatively short follow-up durations. We expanded our initial series to 29 cases by 2003;[17] 52% were seizure-free, and 24% had a > 90% reduction in seizure frequency after a mean follow-up of 30 months (range 12–70 months). These results were later replicated at the Barrow Neurological Institute.[23] In

2002, Palmini et al.[27] reported on 13 patients who underwent surgery for HHs from 3 centers, 12 using a frontotemporal approach and 1 using an endoscopic approach. Delalande and Fohlen[9] reported on 17 patients in 2003 who underwent surgery for HH (14 transsylvian and 9 endoscopic approaches). We subsequently reported our epilepsy findings,[13,17] endocrine findings,[14] and MR imaging findings.[12] There was a wide variation in the size and position of HH, and the attachments and relations of the HH were also described.[12]

We were able to acquire a relatively large series of patients with this rare condition because the families of these children developed their own website called HHugs (http://www.hhugs.com/) which informed them about what treatments were available around the world along with some analysis of the medical literature, and in doing so empowered them to make decisions about the treatments they wished to pursue. We were surprised when patients came from the United Kingdom, US, Europe, Tanzania, and even Mongolia. This response demonstrates the powerful force-multiplying effect of the internet on the way medicine is now practiced, especially for patients with rare disorders. There are now 250 families who are members on this site.

The goal of surgery is to resect and/or disconnect the hamartoma from the adjacent hypothalamus and to preserve the mammillary bodies (which may be malpositioned and deformed), mammillothalamic tracts, tuber cinereum, and hypothalamic nuclei. The spread of seizures occurs in part via the mammillary body. The surgery should ideally be performed before the onset of secondary generalized epilepsy and has been achieved endoscopically in infants as young as 13 months.[24]

There was concern that the standard transcallosal interforniceal approach would, of necessity, retract and injure both fornices and cause a significant rate of permanent short-term memory disturbance. We therefore refined the standard transcallosal interforniceal approach to a more anterior trajectory with a more restricted access passing between the columns rather than between the bodies and commissure of the fornices where they are close, flattened, and partially fused and where more retraction would occur.[30,31] Although we could not test the memory and cognitive function of the very young children, the rate of short-term memory deficit in our series was 48.3% (14 of 29 patients) in the early postoperative period, which decreased to 13.8% (4 of 29) in the longer term. It should be noted that that early patients in the series underwent the standard transcallosal approach.[17] Ng et al.[24] reported 3 (8.1%) of 37 patients had permanent short-term memory deficit following endoscopic resection for HH. We believe this disability may be acceptable if the terrible consequences of the HH abate following the surgery.

After the successful anterior interforniceal transcallosal surgery on a 4-year-old boy with HH from Phoenix, Arizona, Dr. Spetzler and Dr. Rekate kindly invited me to demonstrate the technique at the Barrow Neurological Institute. I was also invited to demonstrate this surgery at Shands Hospital, University of Florida, Gainesville; in Singapore; at Radcliffe Infirmary, Oxford, United Kingdom; and at Dana Children's Hospital, Tel Aviv Medical Center, Israel.

A recommended pathway to refine a surgical technique or approach is to use a fully equipped microsurgical laboratory and dissect cadaver specimens injected to clearly display arteries and veins. I did not have this facility available at the time of refining the transcallosal interforniceal approach, but the anatomy of the more targeted anterior, transcallosal, interforniceal approach could be studied in detail with the support of Dr. Spetzler and Dr. Rekate in the anatomy laboratories of the Barrow Neurological Institute. Dr. Siwanuwatn, a Barrow Neurological Institute fellow at the time, conducted the detailed anatomical studies.[35] Dr. Rekate and Dr. Spetzler and the comprehensive epilepsy team at Barrow Neurological Institute have performed operations on more than 100 patients with HH.

The Endoscopic Approach

The endoscopic approach to HH was initially reported in the literature mixed with reports of the open approach.[9,27] Rekate et al.[29] reported the early outcome of 44 patients with normal-sized ventricles who underwent endoscopic surgery. Fourteen patients had complete endoscopic removal of the HH, and there was total control of seizures in 13 of these patients. This investigative group reported prospectively on the endoscopic approach in 37 consecutive patients with HH.[24] Mean follow-up of these patients was 21 months (range 13–28 months). Twelve patients underwent a complete excision, 18 were seizure-free, and 26 had more than a 90% reduction in seizures. Postoperative stay using this approach was reduced compared with the open transcallosal approach. The complications in this study were short-term memory loss in 3 patients and small thalamic infarcts in 11 patients.[24] Ng et al.[24] concluded that the endoscopic approach is a safe and effective treatment for seizures and is comparable to the transcallosal approach, but recovery time is shorter. Rekate et al.[29] have defined the indications for the endoscopic approach. The ability to approach the HH unilaterally via the foramen of Monro and not disturb the fornix on both sides is an advantage compared with the open midline transcallosal approach.

Discussion

There have been extraordinary advances in scientific knowledge concerning the genetics,[37] histopathology,[8] and ultrastructure[4] of HH, the electrical properties of the neurons in HH,[11,20] and the molecular correlates of central precocious puberty[7] in HH. These discoveries have advanced our understanding of the pathogenesis and clinical features of HH and informed the treatment of these complex patients.

The advantage of the open transcallosal or transventricular endoscopic approach compared with the skull-base approach is the direct visualization of the HH and its main attachments to the hypothalamus, including the mammillary bodies. A wider angle of view is likely to be obtained with the transcallosal compared with the

endoscopic approach. While it is our opinion that the intrahypothalamic, third ventricular hamartoma should be approached from above, the subfrontal and/or transsylvian approach is indicated for primary surgery on HHs in which the lesion is pedunculated or exophytic and parahypothalamic, attached to the base of the hypothalamus extending laterally beyond the floor and the vertical axis of the third ventricle and inferiorly into the basal cisterns.[10] Although the third ventricle may be entered via the lamina terminalis, the view of the entire HH is generally restricted with this approach and there may be problems from frontal lobe retraction and vascular injury. Where the approach from above has not been able to remove or disconnect an inferior extension, the approach from below may also be required at the same session or delayed as a second stage.[1] The orbitozygomatic craniotomy is the preferred approach in these cases because of the minimization of retraction of the brain and the flat- or upward-angle trajectory to the lesion. Abla et al.[1] performed the orbitozygomatic approach in 10 patients and reported 40% of patients were seizure-free, 40% attained > 50% seizure reduction, and 66% attained seizure freedom when there was a total or near-total excision of the HH. Ng et al.[23] found that 100% resection correlated with better seizure control.

Stereotactic radiosurgery has an established and important role in primary and secondary treatment of patients with HH.[28,30] The epilepsy control rates are not as high as with open surgery. There is also a latency period for the epilepsy control to be achieved. Potential injury to surrounding structures including the optic pathways and chiasm is a concern, but the risk to memory is lower compared with open surgery. We have recently reported a significant risk of memory deficit following transcallosal surgery in the older adolescent and adult patients with HH.[2] Therefore, stereotactic radiosurgery may be the preferred treatment option for the older adolescent or adult patients with HH and with intact memory and milder epilepsy, or in select patients with bilateral mammillary body attachment. Stereotactic radiosurgery may also have a role in treating residual HH in patients with ongoing epilepsy.[32]

Treatments offered for patients with HH should be individualized because there is such an enormous range of clinical, electroencephalographic, and radiological features. The epilepsy surgeon should be familiar with the transcallosal, endoscopic, and extended skull-base approaches. This surgery is quite different from other types of (pediatric) epilepsy surgery. Stereotactic radiosurgery and other minimally invasive procedures are less intrusive options that should also be considered.

Future research in patients with HH could be directed to improving medical therapy; better defining the ideal age for surgery; better defining the selection of cases for surgery, radiosurgery and other treatments; and the selection of the most efficacious surgical options with the least risk. Reporting detailed long-term follow-up for substantial cohorts of patients with HH will also be of great interest.

Conclusions

It has been a privilege to have experienced the transformation of the treatment of children with HH over the past 20 years, from what was believed to be a virtually untreatable condition to the current situation in which these children have been given a chance to experience a normal life. The best outcomes will be achieved with the management of these patients by an experienced multidisciplinary team in comprehensive epilepsy centers in which there is a sizeable volume of patients in all their variety. The epilepsy surgeon should be well versed in all the approaches to these complex lesions.

Disclosure

The author reports no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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Surgical approaches to hypothalamic hamartomas

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Object. Hypothalamic hamartomas (HHs) are devastating lesions causing refractory epilepsy, rage attacks, social ineptitude, and precocious puberty. Microsurgical and/or endoscopic resection offers an excellent risk/benefit profile for cure or improvement of epilepsy.

Methods. The authors reviewed a prospective database maintained during the first 7 years of the Barrow Hypothalamic Hamartoma program. They describe and illustrate their surgical methods, and they review data from several previous publications regarding surgical outcome.

Results. To date, the authors have performed surgery in 165 patients for symptomatic HHs. Patients underwent an endoscopic, transcallosal, or skull base approach, or multiple approaches. Twenty-six patients (15.8%) required more than 1 treatment for their HH.

Conclusions. Microsurgical and endoscopic resection of symptomatic HHs are technically demanding but can be performed safely with excellent results and an acceptable risk profile. Meticulous attention to the subtleties of surgical management helps optimize outcomes. *(DOI: 10.3171/2010.11.FOCUS10250)*

Key Words • hypothalamic hamartoma • endoscope • microsurgery • epilepsy

Hypothalamic hamartomas are rare CNS nonneoplastic lesions composed of hyperplastic neural tissue[3,24] associated with 2 patterns of presentation. The Delalande classification classifies HHs based on size, and amount of and laterality of attachment to the hypothalamus.[4] Children with HHs that are significantly attached to and involved with the hypothalamus become symptomatic with gelastic seizures (Delalande Types II, III, and IV). These lesions are usually resistant to medication and if left untreated devolve into more sinister epileptic patterns as the child grows.[21,23] Furthermore, children with these lesions may develop problems with social interaction, including frequent rage attacks. In contrast, Delalande Type I HH can cause central precocious puberty and may be treated medically with excellent results.[4] This type of HH seldom manifests with epilepsy or behavioral problems, and microsurgical excision tends to be curative.[5,14]

The Barrow Hypothalamic Hamartoma Program was established late in 2003. Thus far, we have treated many patients with HH.[1,3,5–10,13,15–21,23,25] The goal of this manuscript is to describe, in a single, free, online, easily accessible publication, the current methods of resection and to share pitfalls and pearls that we have learned during the process. The approaches used can be classified as endoscopic, transcallosal, or skull base. We also review data previously published by our group on the outcomes and complications associated with this challenging group of patients. This project is ongoing and continues to accrue data.

Abbreviations used in this paper: ACA = anterior cerebral artery; GKS = Gamma Knife surgery; HH = hypothalamic hamartoma.

Methods

Between late 2003 and late 2010, the Barrow Hypothalamic Hamartoma Program has treated 165 patients with a symptomatic HH. The patients have come from many states and countries. The program operates under the approval of the institutional review board of St. Joseph's Hospital and Medical Center, Phoenix, Arizona. A team of physicians, including neurosurgeons, epileptologists, neuroradiologists, and endocrinologists, reviews each case. Each patient is also thoroughly reviewed by each specialty, and their cases are presented at the monthly HH conference to obtain a consensus on the appropriate treatment. Data from each patient are cataloged in a prospective fashion, and portions have been reported in several publications.[1–3,5–10,15,17–21,23,25] In especially instruc-

tive or unusual cases, pre- and postoperative imaging studies, surgical videos, intraoperative photographs, and other appropriate data are also cataloged. We reviewed selective cases treated at different times to evaluate our methods, to share surgical pearls and surgical pitfalls, and to obtain an understanding of how our surgical approaches have evolved over time.

Operative Techniques

We have used 3 approaches to address HHs: transventricular endoscopic, transcallosal, and skull base approaches. No single approach is the best approach or is appropriate in all cases. Adequate treatment requires individualization of the approach based on a patient's age and condition, on the anatomy of the HH, and on the surgeon's experience. It is becoming increasingly clear that a 1-stage approach to all HHs is probably inappropriate. We often plan a staged approach depending on the extent of resection or disconnection achieved with the initial treatment, the patient's symptomatic response to the initial treatment, and the willingness of the patient and family to undergo further treatment. Stereotactic radiosurgery, either as a stand-alone treatment or treatment for postoperative residual HH, is now included in the treatment paradigm for appropriate patients.[2]

Endoscopic Resection

Endoscopic resection is preferred as the stand-alone surgical treatment for small Type II HHs and as a stage in the treatment of small Type III HHs.

Stereotactic guidance is required in these cases for 3 reasons. First, the entry point is chosen based on using the trajectory views provided by the stereotactic software. Second, the trajectory of resection is determined by tracking the end of the endoscope and again, using the trajectory views to best estimate the course of the HH/normal hypothalamus interface (Fig. 1C). Third, endoscopic entry into a small ventricle is often aided by stereotaxy. The entry point is determined by finding the point on the scalp that is intersected by a line drawn from the anterior edge of the side of HH attachment to the hypothalamus and the anterior edge of the contralateral Monro foramen. This is easily done using the trajectory views provided by the stereotactic software. Thus, a right-sided HH will be approached from the patient's left side.

Once the entry point is chosen, a generous bur hole is made, and the dura is coagulated and opened. The pia is also coagulated and opened. We then place a peel-away sheath into the brain along the appropriate trajectory and stop just short of the ventricle. Most patients do not have hydrocephalus, and blindly placing a sheath in a small ventricle is challenging. Once the sheath is placed, we use a stereotactic-tracked 30° endoscope and endoscopic visualization to advance the tip of the scope into the ventricle.

Once the ventricle is entered, gentle irrigation is infused to induce mild ventriculomegaly and the sheath is advanced over the endoscope until it is just inside the lateral ventricle. Placement of the sheath in the ventricle relieves the ventriculomegaly and leaves a small space within which to work. The choroid plexus and anatomy of the ventricular venous system guide the endoscope through the Monro foramen and into the third ventricle. Care must be exercised to avoid forcefully impinging the fornix at the anterior margin of the foramen. While the tip of the endoscope is in the third ventricle, the fornix is not visible. The entry point is chosen as described above because the fornix will not tolerate anterior "windshield wiping" of the endoscope. Gentle posterior "windshield wiping" movements are better tolerated but should be minimized.

Once the third ventricle has been accessed, gentle irrigation will separate the walls enough to provide a clear view of the anterior and posterior margins of attachment. The endoscope is secured in place using a robotic manipulator arm (Fig. 1B). We then obtain microelectrode recordings in the HH for research purposes.[10] A distinct cleft or indentation marks the border of the HH attachment to the hypothalamus (Fig. 1A). Using this cleft as the starting point, we use the stereotactic trajectory view to determine the angle the disconnection will follow.

The resection begins by using a grasper through the working port of the endoscope. We start at the posterior edge of the HH and work anteriorly. This cycle is repeated until the pial surface on the deep side of the HH is reached. As the disconnection proceeds deeper, the remaining disconnected HH falls away medially from its hypothalamic attachment. We resist the temptation to pull out large chunks of the HH as it is disconnected. Doing so makes the interface swing laterally and increases the difficulty in disconnecting the most inferolateral attachment. Once the HH is disconnected, it is grasped and the endoscope/grasper complex is removed from the ventricle in one piece. If the HH is too large to fit through the foramen, it is morcellized before it is removed. Irrigation

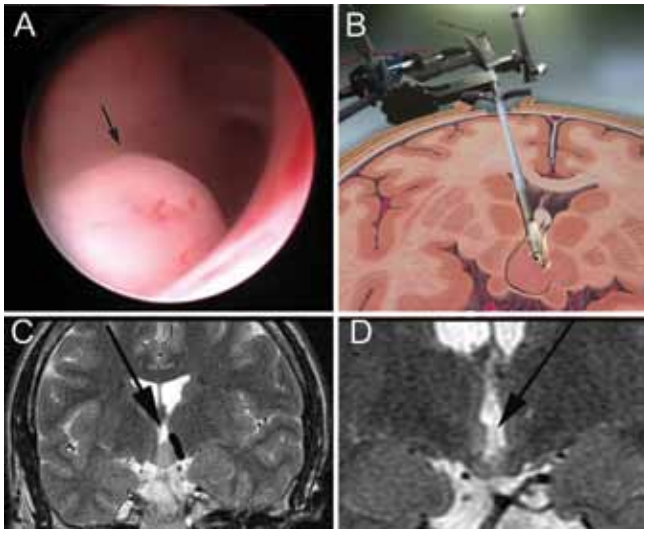

Fig. 1. A: Endoscopic view of a Type II HH through the right Monro foramen. The attachment to the left hypothalamus is easily distinguished *(arrow)*. **B:** Illustration depicting the surgical arrangement of the stereotactic-tracked endoscope, robotic endoscope arm, and angle of dissection down the wall of the hypothalamus. (Reprinted from "Hypothalamic hamartoma." **Barrow Magazine 17:**12–13, 2005. Used with permission from Barrow Neurological Institute.) **C:** Preoperative coronal T2-weighted MR image showing a 1-cm Type II HH with the angle of dissection *(arrow)* and intended cleavage plain *(black line)*. **D:** Postoperative MR image confirming complete resection of the HH *(arrow)*.

with or without coagulation is used to stop any bleeding. A ventriculostomy catheter is typically left in place and removed the next day.

One surgical pearl needs to be emphasized: the HH cannot reliably be distinguished from the hypothalamus based on the difference in the color or consistency. Hence, such cues cannot be relied on to guide resection. It is best to think of the resection as a straight-line disconnection guided by the initial angle determined by stereotaxy and proceed down that line until the deep pia/arachnoid surface is reached. By not breaching the pia/arachnoid surface, deeper structures such as the optic tract and perforating vessels remain beyond the reach of the instruments. Breaching this surface and damaging the perforating arteries can result in small infarctions of the basal ganglia and internal capsule. Such infarctions are often, but not always, clinically silent.[21]

If any part of the HH is positioned superior to the mammillary body, the disconnection must be shallow over the mammillary body to avoid its injury. However, many of these patients are so clinically and socially impaired that clinically significant damage to a mammillary body or fornix would not be evident. For this reason, it is reasonable to be more aggressive in pursuing resection or disconnection and in tolerating damage to relieve epilepsy in severely affected patients.

Transcallosal Resection

The transcallosal, interseptal, interforniceal approach is the preferred approach for large HHs with a significant intraventricular component located superior to the level of the optic tracts. This approach can be used alone to treat large Type II lesions. Many Type III and IV lesions require a staged approach. If the lesion is entirely medial to the line of sight down the wall of each hypothalamus, then a large Type III or IV lesion can be disconnected during 1 operation. In young patients (< 6 years old) and in patients with a small residual cavum septum, the leaves of the septum pellucidum are easily separated (Fig. 2). This feature facilitates safe separation of the fornices. As the patient ages, the interforniceal dissection becomes more difficult.

In most cases, the HH is primarily attached to 1 side of the hypothalamus. This side is placed up. If an equal bilateral attachment is present, we place the dominant hemisphere up. We use a large shoulder bolster to position all patients undergoing interhemispheric approaches in the semilateral decubitus position. The head is turned so that the falx is parallel to the floor, and the head is tilted up approximately 45° (Fig. 3A). This position requires considerable rotation, flexion, and side bending of the neck. We monitor somatosensory evoked potentials during positioning of all patients to ensure that aggressive positioning does not compromise the patient.

The incision is planned using stereotactic guidance to avoid large frontal bridging veins. In general, we plan a coronal incision placed just behind the hairline that allows two-thirds of the sagittal dimension of the craniotomy to be anterior to the coronal suture and two-thirds of the coronal dimension of the craniotomy on the dependent side of the head. We place bur holes directly on the sinus at either end of the exposure and turn a craniotomy with the footplate cutting away from the sinus. The dura is opened in a U-shaped flap based on the sinus and tacked back. Care is exerted to avoid taking large bridging veins or cutting into large venous lakes.

Microsurgical dissection of the dependent hemisphere from the falx is straightforward. The cingulate gyri can be densely adherent, and dissection may be difficult. If clean dissection is impossible we prefer to go through the nondominant cingulate rather than damage both cingulate gyri. Both pericallosal arteries are identified and separated widely. We place cotton balls at the deep anterior and posterior limits of our dissection to keep the hemispheres separated.

Using stereotactic guidance with the microscope at the highest magnification and gross anatomical clues, we perform the callosotomy with the aid of a small dissector. It is key to be exactly in the midline as one proceeds (Fig. 3C). If the midline dissection is performed at high magnification, a blue-gray line representing the interforniceal space can be appreciated. It is easier to enter this space anteriorly. After entry, gentle dissection is continued posteriorly and inferiorly until the roof of the third ventricle is encountered. As the roof of the third ventricle is approached, the fornices will be on either side of the dissection.

Continuing the dissection into the third ventricle and separating the internal cerebral veins posteriorly gently separates the fornices. It is important to maximize the transforniceal working space so that the fornices will not be damaged during HH removal. The choroid plexus of the third ventricle posteriorly and the anterior commissure should be clearly visualized (Fig. 3D). We place a re-

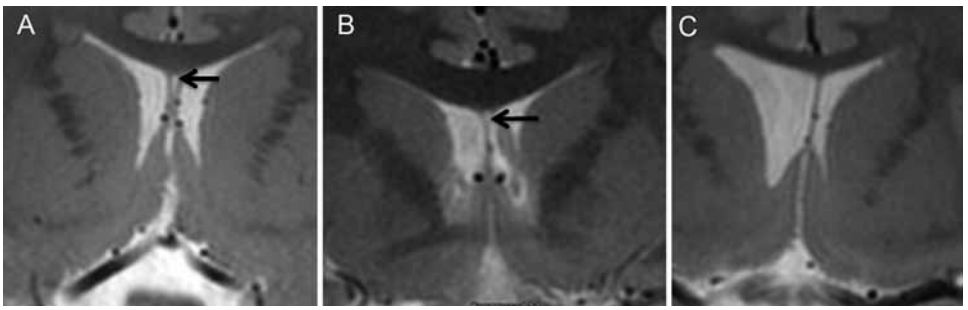

Fig. 2. Coronal T2-weighted MR images obtained in patients with an HH requiring transcallosal resection. In 2 patients **(A and B)**, signal from the CSF *(arrows)* is visible between the leaves of the septum. There is no discernible signal from CSF in the third patient **(C)**. Interseptal interforniceal dissection is thought easier in patients with a discernible signal from CSF in the septum.

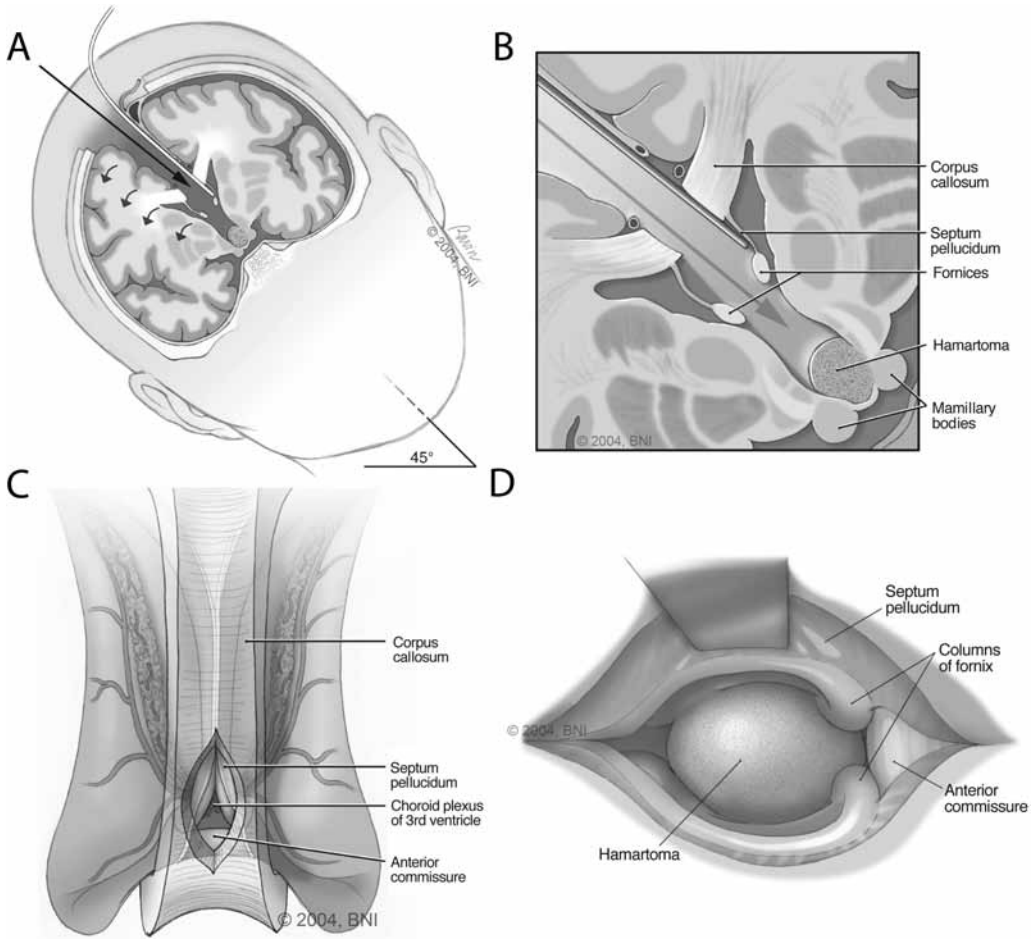

Fig. 3. A: Illustration of the appropriate head positioning *(upper left)* and use of gravity to retract the "downside" hemisphere during the transcallosal approach. **B:** Close up showing the excellent line of sight afforded large Type II lesions and the proximity of the fornices to the inferior septum. **C:** The callosotomy must be precisely midline and start anteriorly to arrive at the interseptal space. **D:** Once the fornices have been separated, the anterior commissure and the entire HH-hypothalamus interface should be visible. Reprinted from Ng T et al: **BNI Quarterly 20:**13–17, 2004. Used with permission from Barrow Neurological Institute.

tractor against the falx extending inferiorly onto the "upside" leaf of the septum (Fig. 3C). A cottonoid is trapped under and extended beyond the retractor tip to gently elevate and protect the "upside" fornix.

Tumor resection proceeds by centrally debulking with an ultrasonic aspirator. Next, the upside HH-hypothalamus interface is dissected using a combination of ultrasonic aspiration, dissection, and suction. Stereotactic guidance is used to plan the angle of dissection. Great care is taken to identify the piarachnoid membrane on the deep and lateral surface of the HH. This should be inferior to the level of the optic tract. Once a piarachnoid plane is identified, it can be followed 360° to disconnect the HH completely. Posteriorly, the mammillary bodies can be differentiated from the HH by their lighter color. The perforating arteries of the basilar and posterior cerebral arteries are adjacent to the deep and lateral surfaces of the HH. They can be avoided by careful subpial dissection and leaving the pia intact. The same is true anteriorly for the infundibulum and laterally for either optic tract.

It is a long reach to the inferior margin of large Type III and IV HHs and often requires working at the tips of the microsurgical instruments with a reduced amount of control. If we are unsure of the safety of further removal, we stop the removal and will often leave the HH in situ. If the inferior portion can be easily dissected from the piarachnoid on its deep surface, we remove it (Fig. 4). We typically leave a closed ventriculostomy in the resection cavity and remove it the next day.

Skull Base Approaches for Resection

Several skull base approaches to Type I, III, and IV HHs are used. We have performed variations of the orbitozygomatic, pterional, supraorbital eyebrow, and recently subtemporal approaches. Each approach has distinct advantages and disadvantages. Currently, we favor the modified orbitozygomatic craniotomy to maximize working space and light, minimize brain retraction, and to achieve as low and lateral of an angle as possible to lesions with bilateral attachment. For lesions with ipsilateral attachment, the supraorbital eyebrow approach is sufficient. Recently we had 1 patient with a temporal arachnoid cyst, which offered a perfect working corridor to approach an HH with bilateral attachment.

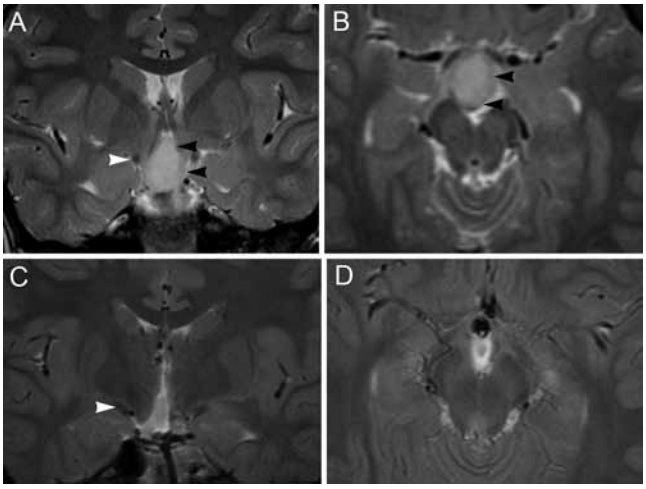

Fig. 4. Preoperative **(A and B)** and postoperative **(C and D)** T2-weighted MR images of a large Type II HH completely resected via the transcallosal approach. The HH is hyperintense *(black arrowheads)* compared with the normal surrounding structures including the optic tract *(white arrowheads)*.

The patient is positioned with the ipsilateral shoulder elevated with a sandbag, the head rotated, and the neck extended so that the ipsilateral malar eminence is placed directly up. In the case of eyebrow incisions and supraorbital craniotomies, the nose is placed directly up and the incision is placed in the superior margin of the eyebrow. For others, a standard behind-the-hairline incision is performed.

The key to successful visualization of the inferior hypothalamus, mammillary body, optic tract, and pituitary stalk is achieving a very flat or even upward-looking trajectory. This trajectory is best obtained through a supraorbital craniotomy by extradural drilling of the ridges formed by the orbital part of the anterior skull base. In the case of the orbitozygomatic approach, it is performed by removing the orbital rim and orbital roof.[11] The modified orbitozygomatic approach and a complete sylvian fissure dissection allow the most lateral and upward angle for disconnection of lesions with bilateral attachments (Fig. 5).

Standard subfrontal dissection and wide splitting of the proximal sylvian fissure are performed. In a stepwise fashion, the internal carotid artery is dissected along its course until at least 1 cm of both the ACA and middle cerebral artery are free. Likewise, the ipsilateral optic nerve is followed posteriorly dissecting the chiasm and ipsilateral optic tract as it passes just lateral to the hypothalamus. To follow the optic tract back requires working in the opticocarotid window and in the window above the internal carotid artery bifurcation above and posterior to the ACA. The tumor emanating from the hypothalamus should be evident at this point.

Great care is taken to dissect posteriorly any perforators from the middle cerebral artery, posterior cerebral artery, and posterior communicating arteries from the tumor capsule. The capsule is coagulated and incised. Intratumoral debulking is performed using ultrasonic aspiration, suction, and dissectors. Once debulked, the superior margin of the tumor is defined by incising the capsule immediately inferior to the optic tract.

Working along the superior margin is challenging and is blind medial to the lateral edge of the optic tract. We have found down-pushing microsurgical curettes to be helpful in transecting the hamartoma from the hypothalamus while watching the tract to ensure that it is not tractioned downward.

The posterior resection margin should be the mammillary body if it is not involved in the hamartoma. It is difficult to see and may only be evident as the intratumoral resection proceeds and space is developed enough to "feel" the ipsilateral mammillary body with a dissector or to see it via the endoscope. If it is involved (evident from the MR images), the disconnection will proceed until it is encountered. The mammillary body is a slightly lighter color than the hamartoma and usually can be distinguished with maximal magnification of the microscope. It is easier to see and to avoid the ipsilateral mammillary body than the contralateral mammillary body.

Anteriorly, the stalk should be visualized and avoided. The resection should continue medially until the third ventricle is entered. If the hamartoma is bilateral, dissection continues until the contralateral pia is reached. A pial plane separates the HH from the contralateral optic tract. As long as this plane is respected, the optic tract will not be injured. At this point, the tumor is usually disconnected from the hypothalamus.

The remaining inferior "lump" can be resected in a subpial fashion to protect the contents of the prepontine cistern beyond the piarachnoid layer. The same tenets discussed under *Transcallosal Resection* apply to the remaining disconnected portion of the HH.

Again, it is important to remember that a HH cannot be distinguished from normal hypothalamus under microsurgical view. Only the abnormal anatomy that it forms allows the surgeon to determine where to stop resection. Careful evaluation of the patient's preoperative MR imaging study and use of intraoperative stereotactic guidance help clarify the aforementioned limits of resection.

Results

Surgical Procedures

Of the 165 patients with symptomatic HHs, 14 underwent skull base approaches as their initial surgery. Of those 14 patients, 3 required a second approach (endoscopic disconnection of residual HH). Fourteen patients underwent GKS as their initial treatment.[2] Three of these patients had subsequent endoscopic approaches. Ninety patients underwent endoscopic approaches as their initial surgery. Seven patients had additional procedures (GKS for residual HHs in 5, orbitozygomatic craniotomy in 1, and transcallosal approach in 1).

Forty-seven patients initially underwent a transcallosal approach. Eleven patients required subsequent procedures (GKS for residual tumor in 1, orbitozygomatic craniotomy in 3, a second contralateral transcallosal approach in 2, and endoscopic approach in 4). Of the 165 patients, 26 (15.8%) required more than 1 procedure. Twenty-two patients required 2 procedures, 3 patients required 3 procedures, and 1 patient required 4 procedures.

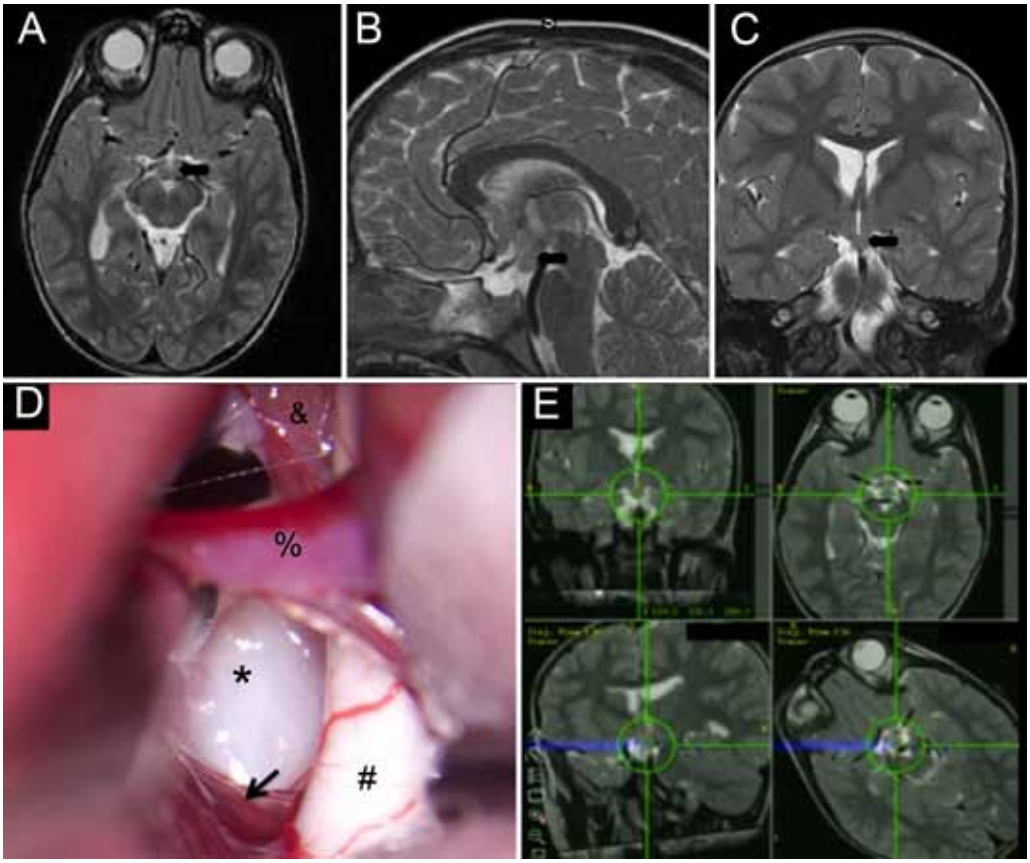

Fig. 5. A–C: Preoperative T2-weighted MR images of a small Type I HH *(arrows)* with bilateral attachment. This required a low, lateral trajectory to safely address each connection and was completely resected from a right modified orbitozygomatic approach. **D:** High-magnification view of the operative site demonstrating the tight working space but excellent view of the hamartoma *(asterisk)*, infundibulum *(ampersand)*, ACA *(percentage sign)*, optic tract *(number sign)*, and perforating vessels *(arrow)* swept posteriorly. Most of the operation takes place superior and posterior to the ACA. However, the anterior portion of the HH is addressed by moving the ACA posteriorly and working anterior to it. **E:** Stereotactic illustration *(lower right)* of the angle of attack. The *blue lines* represent the working trajectory.

Outcomes

Updated epilepsy outcome data for our entire series will be reported in a future publication. Previously, however, we published data on the first 26 patients undergoing a transcallosal approach.[20] The mean postoperative follow-up interval was 20.3 months (range 13–28 months). Fourteen patients (54%) were completely seizure free, and 9 (35%) had at least a 90% improvement in total seizure frequency. Parents reported postoperative improvement in the behavior of 23 patients (88%) and in the cognition of 17 patients (65%). Transient postoperative memory disturbances occurred in 15 patients (58%), but persisted in only 2 (8%). Two patients (8%) had persistent endocrine disturbances that required hormone replacement therapy (diabetes insipidus and hypothyroidism in 1 each).

In the first 37 patients who underwent endoscopic resection,[21] 18 (48.6%) were seizure free at last follow-up (median 21 months, range 13–28 months). Seizures were reduced in 34 patients (91.9%). The mean postoperative stay was shorter in the patients undergoing endoscopy than in the patients undergoing transcallosal resection (mean 4.1 days vs 7.7 days, respectively; $p = 0.0006$). The main complications were permanent short-term memory loss in 3 patients and small thalamic infarcts in 11 patients (9 were asymptomatic).

Of the 10 patients who underwent an orbitozygomatic craniotomy for HH,[1] 4 (40%) are seizure free and 4 (40%) have had more than a 50% reduction in seizures. One patient had no significant change in seizure frequency, and another patient died unexpectedly 2.8 years after surgery. Residual complications included diabetes insipidus, poikilothermia, visual field deficit, and hemiparesis in 1 patient each. Eight families (80%) reported improved quality of life.

Discussion

Initially, attempts at surgical cure of epilepsy for patients with HH were largely unsuccessful and had a high complication rate.[12,22] Individualizing the approach based on the anatomy of the HH and frequently using several approaches in a single patient allowed seizure-free rates of more than 50% in patients treated in the first half of our series. By following the surgical procedures we have outlined above, we aim to improve the outcomes for patients undergoing surgery for these difficult lesions (Table 1).

TABLE 1: Simplified treatment paradigm at Barrow Neurological Institute indicating the first approach recommended for HHs based on their type and size*

HH Type	Approach to Small Lesions	Approach to Large Lesions
Type I	orbitozygomatic GKS	orbitozygomatic
Type II	endoscopic GKS	transcallosal
Type III	endoscopic ± orbitozygomatic GKS	transcallosal ± orbitozygomatic
Type IV	not applicable (Type IV = giant)	staged approach: address primary component first

* Gamma Knife surgery may also be used for more complex or giant lesions as salvage therapy after debulking/disconnection, and GKS may be considered for small Type I lesions, although to date no Type I lesion has been found suitable at the center. Reprinted with permission from Abla et al: **J Neurosurg (Suppl) 113:**207–214, 2010.

The difficulties encountered in early reports of small series of patients are likely the natural and inevitable results of the "learning curve." One purpose of this manuscript is to share the technical nuances that we have learned, sometimes painfully, during the accrual of a large patient population.

We counsel patients and families that their initial treatment may be the first of multiple treatments to achieve the safest, most efficacious outcome. We favor superior approaches to HHs with a significant hypothalamic attachment. Endoscopy is the preferred method but its use is limited by the size of the third ventricle. Larger lesions are more difficult to disconnect completely using the endoscope. However, patients undergoing endoscopic approaches have shorter hospital stays, and fewer complications than open transcallosal approaches.[21]

Factors favoring a transcallosal interforniceal approach include young age (children tolerate transcallosal resection better than adolescents and adults), a bilateral HH attachment, and large lesions that fill or nearly fill the third ventricle. The presence of a residual cavum septum, helping to minimize manipulation and traction on the fornix, is also favorable for transcallosal resection.

Factors favoring transventricular endoscopic resection include small HH lesions, unilateral attachment, and generously sized ventricles. Type II lesions with a unilateral attachment are ideal for an endoscopic approach from the contralateral ventricle.

At our institution, GKS is used to treat small lesions distant from radiosensitive structures in patients with higher cognitive function. The patient must have a stable clinical picture that will allow time for the effects of radiosurgery to occur without further deterioration. Patients must not be severely affected by epilepsy at the time of treatment.

Often, patients harboring HHs are so devastated by severe epilepsy and frequent rage attacks that they are essentially noncommunicative and, other than interactions with their caregivers, socially isolated. In such cases, damage to a fornix is seldom a clinically significant side effect or even detectable. In this situation, cure of epilepsy is the goal regardless of any potential damage to the fornix or of endocrinological problem from manipulation of the hypothalamus.

Conclusions

The use of 1 or more surgical approaches in appropriately selected patients with symptomatic HHs can provide excellent results. Cure or control of seizures and improvement in quality of life are seen in a large majority of patients. Complications occur at an acceptable rate and can be minimized by a thorough understanding of the complex regional anatomy and anatomical considerations specific to each approach.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Wait, Rekate. Acquisition of data: Wait, Abla, Nakaji, Rekate. Analysis and interpretation of data: Wait, Abla, Rekate. Drafting the article: Wait, Killory. Critically revising the article: Abla, Nakaji, Rekate. Reviewed final version of the manuscript and approved it for submission: Rekate.

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Repeat surgery for hypothalamic hamartoma in refractory epilepsy

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Object. Hypothalamic hamartomas (HHs) often cause pharmacoresistent epilepsy, incapacitating behavioral abnormalities, and cognitive decline. Surgical intervention offers the patient the best opportunity of seizure resolution, which occurs in approximately 50%–60% of patients, and improvement in both cognitive and behavioral difficulties. For those in whom the initial operation has failed, further medical treatment options remain quite limited, whereas, in some cases, a second surgery may improve seizure outcome. The authors retrospectively reviewed their surgical cases to document the success rate and complications of reoperations in patients with HHs.

Methods. Data were obtained from the HH epilepsy surgery database at the Barrow Neurological Institute between 2003 and 2010. Surgical treatment consisted of open and endoscopic procedures, as well as radiosurgery. Demographic details, seizure history, presurgical evaluation, and postoperative follow-up data were evaluated.

Results. In the last 7 years, 21 (13%) of 157 patients underwent reoperation after an initial epilepsy operation. The initial surgical approach in the 21 patients included: endoscopic (8 patients [38%]), transcallosal (8 patients [38%]), orbitozygomatic (3 patients [14%]), and radiosurgery (2 patients [10%]). Of the 8 patients who initially underwent endoscopic resection, repeat procedures included: radiosurgery in 4 (50%), an orbitozygomatic approach in 2 (25%), repeat endoscopy in 1 (12.5%), and a transcallosal approach in 1 (12.5%). Repeat procedures after an initial transcallosal resection included: endoscopic resection in 2 (25%); radiosurgery in 1 (12%); an orbitozygomatic approach in 2 (25%), and repeat transcallosal surgery in 3 (38%). Predominant seizure types that recurred after the first surgery were gelastic seizures, complex partial seizures, and tonic-clonic seizures. Magnetic resonance imaging in all patients prior to reoperation demonstrated either residual HH and/or connection with the mammillary bodies. Review of patients with more than 6 months of follow-up since the last surgery showed greater than 90% reduction in seizures in 4 patients (19%) and by 50%–90% in 10 patients (48%). Two patients were seizure free, and in 5 patients (24%) there was no change in seizure frequency. Following reoperation, none of the patients had any worsened behavioral issues such as increased rage attacks or disruptive violent behavior. New postoperative complications after reoperation included hemiparesis, thalamic stroke (asymptomatic and symptomatic), hyperphagia, and panhypopituitarism.

Conclusions. Reoperation should be considered in selected patients with HH in whom initial epilepsy surgery fails because more than half the patients have significant reductions in seizure. *(DOI: 10.3171/2010.11.FOCUS10248)*

Key Words • **hypothalamic hamartoma** • **gelastic seizures** • **repeat surgery**

Hypothalamic hamartomas are rare nonneoplastic developmental lesions arising from the tuber cinereum and inferior hypothalamus. They can be identified incidentally in association with precocious puberty alone or with a syndrome of intractable epilepsy, disruptive behavior, and intellectual deterioration.[3] The epilepsy syndrome associated with HH usually begins in early childhood with gelastic seizures and continues, later on, with a generalized epileptic encephalopathy characterized by other types of seizures (complex partial seizures with or without secondary generalization, tonic-clonic seizures, tonic seizures, and drop seizures). Predominantly gelastic seizures, but also other types, are extremely refractory to antiepileptic drugs. Studies report more than 95% of these seizures are refractory to medical treatment.[6] Because of this epilepsy syndrome's high degree of pharmacological resistance, different surgical and radiosurgical treatment options have been advocated to resect or disconnect HHs with varied success. The rationale for the resection was based on electrophysiological and functional imaging data that demonstrate that the hamartoma itself is intrinsically

Abbreviations used in this paper: HH = hypothalamic hamartoma; TAIF = transcallosal anterior interforniceal.

epileptogenic and propagates generalized seizures through mamillothalamic pathways.[5] In accordance with this, different resective treatments have demonstrated that seizures can be arrested and that improved behavior and cognitive function are possible.[13] Debate still continues whether HH disconnection offers any benefit over, or is even comparable to, complete resection. The choice of surgical technique for resection is often dictated by the specific surgical anatomy of each HH lesion. Most importantly, this choice depends on the size and location of the base of attachment and whether the majority of the tumor lies below the third ventricle or within it.

The surgical management of HHs associated with gelastic seizures has been shown to be an effective strategy that results in seizure resolution in approximately 50%–60% of patients; the remainder of patients have experienced significant improvement in seizure burden, associated symptoms, and quality of life.[2] For those in whom the first surgery fails, further medical treatment options remain limited; at times, a second surgery may improve seizure outcome. We retrospectively reviewed our surgical cases to document the success and complications of reoperation after a failed first surgery. Our intention was to identify possible factors associated with poor seizure control and to improve selection criteria for reoperation. Information reviewed includes preoperative clinical history, electrophysiological data, MR images, operative procedures, follow-up clinical data, and complications.

Methods

Review of Clinical Database

All patients included in this study had refractory epilepsy and symptomatic HH, and were referred to our institution. This series includes all patients who underwent different types of resection and radiosurgery between October 2003 and January 2010. A minimum of 6 months of follow-up review was an inclusion criterion. During the study period, 157 patients underwent different resective surgeries and radiosurgery. Twenty-one (13%) of the 157 patients underwent 25 surgical procedures after the first epilepsy surgery. Indications for repeat surgeries included persistent or recurrent seizures, postoperative MR imaging suggestive of incomplete resection, and/or an initial operation that was aborted because of intraoperative complications. Prior treatment for epilepsy associated with HH before referral to our institute included temporal lobe resection, partial frontal lobe resection, and corpus callosotomy in one patient each; two patients had undergone implantation of vagus nerve stimulators. This study was approved by the hospital institutional review board.

Classification of Hypothalamic Hamartoma

The Delalande and Fohlen Classification was used to describe HH.[4] This instrument consists of 4 descriptors: Type I has a horizontal implantation plane and may be lateralized on one side (parahypothalamic), Type II has a vertical insertion plane and resides in an intraventricular location (intrahypothalamic), Type III is a combination of Types I and II, and Type IV includes all giant hamartomas.

Preoperative Evaluation

Presurgical evaluation comprised detailed history, examination, and assessment of electroencephalograms, brain MR images, and neuropsychological test results when feasible. Endocrinological assessment was done only when there were clinical features suggestive of endocrine abnormalities. All patients were imaged in a 1.5- or 3.0-T MR imaging unit (General Electric). At least 3 antiepileptic drugs had failed in all cases before the patient was considered for repeat surgery. All patients were examined preoperatively by an epileptologist. Results of all studies were reviewed, and the choice of the specific treatment modality was made at a multidisciplinary HH conference composed of a dedicated pediatric neuroradiologist, pediatric neurosurgeons, pediatric epileptologists, pediatric endocrinologist, and neuropsychologist.

Preoperative and Postoperative Imaging

Preoperative and postoperative MR images were used to determine the size of the HH, surface area of the base of attachment, HH type according to Delalande Classification, site of attachment, extent of resection, amount of disconnection, and possible surgical complications. Preoperative and postoperative imaging sequences used for tumor-volume measurement included volumetric T2-weighted coronal and sagittal images and a T1-weighted axial spoiled gradient echo image. Preoperative and postoperative HH lesion volumes were calculated by summation of manually measured regions of interest (area of region of interest × slice thickness) on sequential, contiguous coronal T2-weighted images by using Voxar 3D imaging software (DR Systems). Likewise, pre- and postoperative surface areas of the base of HH attachment (for the purpose of determining the percentage of surgical disconnection of HHs in patients with residual postoperative HH tissue) were determined by summation of surface area (linear measurement of base of attachment × slice thickness) on contiguous coronal T2-weighted image slices. All patients underwent routine diffusion-weighted imaging and apparent diffusion coefficient imaging.

Neuropathology

Resected specimens were reviewed by a neuropathologist. Histopathological examination showed subependymal tissue composed of disorganized glial and neuronal elements consistent with hypothalamic hamartoma.

Follow-Up

In addition to the follow-up interview conducted by our neurologist and endocrinologist, long-term follow-up was maintained via telephone and email contacts. A self-reported questionnaire querying change in seizure frequency was used by patients and family members.

Results

Characteristics of the Patient Population

At the last clinic visit, the median age of the 13 male and 8 female patients was 19 years (range 11 months–41

years). All patients had refractory epilepsy associated with HH and at least 3 antiepileptic drugs had failed to resolve seizures. The median age of patients at epilepsy onset was 1.5 years (range birth–29 years); the mean lifetime duration of epilepsy prior to the first HH resection was 12.2 years (range 1–30 years). The initial seizure type in 19 patients (90.5%) was gelastic. Prior to HH resection, all patients had gelastic seizures. The other 2 common types of seizure were complex partial (in 17 cases [80.9%]) and generalized tonic-clonic (in 12 cases [57.1%]). In patients with a given seizure type, the mean seizure frequency of gelastic seizures was 30 per day, that of complex partial seizures was 26 per day, and that of generalized tonic-clonic seizures 2 per day. Three patients' seizures were described as "rage attacks," which constituted an emotional and anger outburst lasting for a few minutes. Two patients in this series had episodes of status gelasticus and had emergency resection; the details have been published elsewhere.[9,10] Status gelasticus is defined as a prolonged cluster of gelastic seizures (that is, those lasting > 20–30 minutes, a duration similar to that for status epilepticus) but does not necessarily involve loss of awareness between seizures. Patients were taking a mean of 4 antiepileptic drugs prior to repeat surgery. Three patients had previously undergone implantation of a vagus nerve stimulator. One patient had previously undergone a temporal lobectomy and another had undergone biopsy of the HH.

Distribution of cases among different types of HHs per Delalande and Fohlen Classification[4] is as follows: 2 with Type I Delalande lesions, 14 (66.6%) with Type II, 4 with Type III, and 1 with Type IV Delalande lesion. The median volume of the 21 HHs at the time of the initial operation was 1.27 cm^3 (range 0.77–15.6 cm^3).

Seventeen patients (81%) had mental retardation (based on full-scale IQ or estimated development quotient < 70). Age-appropriate Wechsler Scales (including the Wechsler Adult Intelligence Scale, 3rd edition, and the Wechsler Intelligence Scale for Children, 3rd or 4th edition) were used in neuropsychological testing. Behavioral problems, including rage attacks, were noted in 14 patients (66.7%). Three patients (14.3%) had a history of central precocious puberty. Alterations in electroencephalography ranged from focal to multifocal sharp waves, and bilateral spikes and spike-wave discharges with a variable degree of synchronicity.

Types of Surgical Intervention

In the last 7 years, 21 (13%) of 157 patients underwent reoperation after the first epilepsy surgery. The initial surgical approach in the 21 patients included the following: endoscopic (8 patients [38%]), transcallosal (8 patients [38%]), orbitozygomatic (3 patients [14%]), and radiosurgery (2 patients [10%]) (Fig. 1). Of the 8 patients with initial endoscopic resection repeat procedures, 4 (50%) underwent radiosurgery, 2 (25%) underwent orbitozygomatic surgery, 1 (12.5%) underwent repeat endoscopy, and 1 (12.5%) underwent a transcallosal approach. Reoperation in patients who had already undergone the transcallosal approach included the following procedures: endoscopy (2 patients [25%]); radiosurgery (1 patient [12%]); orbitozygomatic (2 patients [25%]), and repeat transcallosal resection (3 patients [38%]). All 3 patients in whom the initial approach was orbitozygomatic underwent further endoscopic resection. Two patients who had received radiosurgery also underwent endoscopic resection.

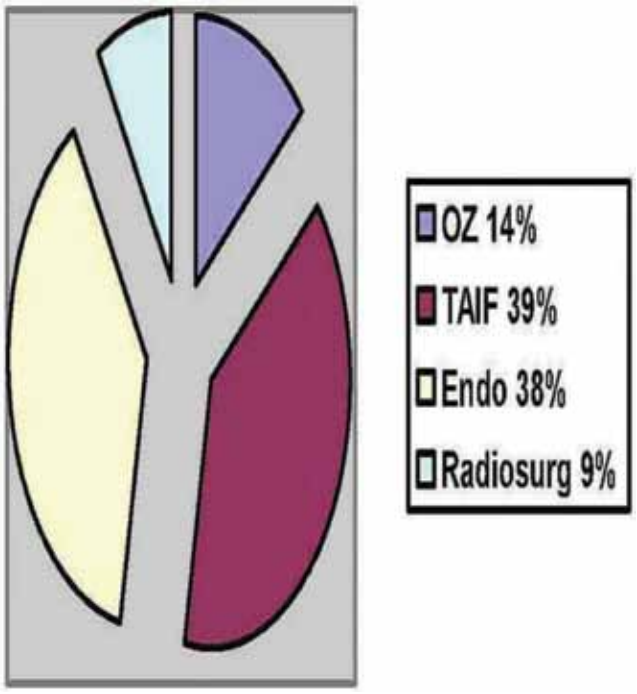

Fig. 1. Surgical approaches in the 21 reoperated patients with HHs. Endo = endoscopy; OZ = orbitozygomatic; Radiosurg = radiosurgery.

Seizure Outcome

At last follow-up after the last surgery (median 9 months, range 6–21 months), 2 patients were seizure free. Seizures were reduced more than 90% in 4 patients (19%) and by 50%–90% in 10 patients (48%). In the 5 patients (24%) who reported no change in seizure frequency, 2 had behavioral improvement with resolution of rage attacks. None of the patients reported worsening of seizures; no patients suffered worsening behavioral issues (for instance, increased rage attacks or disruptive violent behavior). Parental perception of their child's overall postoperative behavioral functioning compared with the preoperative baseline functioning suggested improvement in 18 (85%) of the patients. The results are further detailed in Tables 1 and 2.

Complications

The mortality rate in this multiple-surgery series was 0%. The most common adverse event was transient diminished short-term memory, which was noted in 13 patients (62%) after the first surgery. Typically this deficit would last less than 2 weeks, with ongoing improvement to baseline functioning. In 3 patients, although gradual improvement from the immediate postoperative short-term memory deficit was noted, we observed residual difficulties in short-term recall compared with baseline. New postoperative complications after reoperation included: transient hemiparesis (1 case) without MR imaging infarcts, thalamic

TABLE 1: Summary of the patients and their surgical outcomes*

Patient Data				Seizure Type & No. Affected (%)				Outcome After Repeat Op (%)		
Total No.	Males	Median Age at Seizure Onset (yrs)	Median Age at 1st Op (yrs)	Gelastic	Complex Partial	GTC	Atonic/Tonic/ Myoclonic	Seizure Free	>90% Seizure Reduction	50%–90% Seizure Reduction
21	13	1.5	13	19 (90.4)	17 (80.9)	12 (57)	10 (47)	2 (10)	4 (19)	10 (48)

* Unless otherwise specified, values reflect the number of patients. Abbreviation: GTC = generalized tonic-clonic seizure.

stroke (asymptomatic in 3 cases and symptomatic 1 case), hyperphagia (5 cases), and panhypopituitarism (2 cases). Four patients had hypernatremia following the second surgery, 1 of whom required short-term desmopressin acetate therapy. In one patient, a headache developed due to communicating hydrocephalus, which resolved after placement of a lumboperitoneal shunt.

Discussion

The results from this cohort indicated that repeat surgery in patients with HH-associated refractory epilepsy resulted in improvement in seizure burden. In individual patients, this was accompanied by neuropsychological and behavioral improvement. The results also demonstrate the relative safety of repeat surgery in HH patients with refractory epilepsy. Prior to this study there was a paucity of evidence in the literature on outcome of repeat surgeries in HH for refractory epilepsy. This study demonstrates the importance of reevaluating patients with persistent seizures after first surgery and encouraging further resection when residual tumor is present and patients are neurologically deteriorating or are debilitated by the seizures and associated symptoms. The surgical approach to the lesion should be tailored to each case. No single approach is best for every patient.

Historically, epilepsy surgery in general has been directed toward the total removal of the seizure focus. Because electrophysiological studies have demonstrated the intrinsic epileptogenicity of HHs, based on our previous experiences and the experiences at other centers, surgical (transcallosal/endoscopic/orbitozygomatic)[1,10,11] or radiosurgical[14] intervention offers the best chance for seizure resolution. Resection or Gamma Knife irradiation of the HH tissue often reduces the seizure frequency and intensity. However a minimum of several months must elapse

TABLE 2: Patient information and seizure outcome following surgeries*

Case No., Sex	Age at Seizure Onset (yrs)	Age at 1st Op (yrs)	Delalande & Fohlen Class	1st Op	% Resection After 1st Op	% Disconnection After 1st Op	Subsequent Ops	Seizure Outcome at Last FU
1, F	2	27	III	endoscopy	100	100	OZ	seizure free
2, M	0.6	1.2	III	TAIF	100	0	TAIF	seizure free
3, F	1.5	12	II	endoscopy	22	100	OZ	>90% seizure reduction
4, F	6	30	II	radiosurgery	NA	NA	endoscopy	>90% seizure reduction
5, M	2	5	II	OZ	100	100	endoscopy	>90% seizure reduction
6, M	12	17	IV	TAIF	88	76	radiosurgery, OZ	>90% seizure reduction
7, M	0.5	2	II	endoscopy	88	84	endoscopy	50–90% seizure reduction
8, F	0.3	18	I	TAIF	22	100	TAIF	50–90% seizure reduction
9, M	3	15	II	radiosurgery	NA	NA	endoscopy	50–90% seizure reduction
10, F	17	17	II	endoscopy	95	69	radiosurgery	50–90% seizure reduction
11, M	2	11	II	TAIF	75	40	TAIF	50–90% seizure reduction
12, F	0.6	13	II	endoscopy	90	83	radiosurgery	50–90% seizure reduction
13, M	0.4	1.8	II	TAIF	100	100	OZ	50–90% seizure reduction
14, M	1.5	7	III	endoscopy	51	0	TAIF	50–90% seizure reduction
15, M	0.4	4	II	TAIF	75	90	OZ	50–90% seizure reduction
16, M	29	30	II	endoscopy	80	0	radiosurgery	50–90% seizure reduction
17, M	1	14	II	TAIF	69	64	endoscopy	no change in seizure frequency
18, M	0.4	2	I	OZ	100	100	endoscopy	no change in seizure frequency
19, F	3	27	II	TAIF	58	67	endoscopy	no change in seizure frequency
20, M	0.1	5	II	endoscopy	18	0	radiosurgery	no change in seizure frequency
21, F	0.5	2	III	OZ	74	91	endoscopy	no change in seizure frequency

* FU = follow-up; NA = not applicable; OZ = orbitozygomatic approach.

before significant improvements can be seen with radiosurgery, a feature considered disadvantageous compared with surgery.[8] Multiple surgical approaches and techniques have been used to resect HHs, and of these 2 have emerged as the most popular: the TAIF approach and the endoscopic resection. The seizure-free outcomes following both of these surgeries are comparable. The choice of surgical approach is based on the specific anatomical features of each HH lesion. The surgical approach to the lesion should be determined individually for each case to minimize morbidity. No single approach is best for every patient. As described previously, our center has adopted and published outcomes following endoscopic and transcallosal approaches[10,11] as well as following orbitozygomatic and radiosurgical approaches.[1] Numerous patients in this study underwent both open surgery and endoscopic procedures. Debate exists as to whether complete resection or anatomical disconnection is necessary to cure patients, and the results from the literature have not settled this debate.[12] Complete disconnection and resection were achieved in 5 patients. In 2 of these patients greater than 90% decrease in seizure burden was achieved, in another 2 seizure frequency decreased by 50%–90%, and in 1 no change in seizure frequency occurred. However, all of these patients had a subjective improvement in behavior.

The most common adverse effect was transient diminished short-term memory, which was noted in 13 patients (62%). This is comparable to prior published studies suggesting short-term memory loss in 50%–60% of patients.[7] Endocrine abnormalities were reported in other studies including asymptomatic hypernatremia with polyuria, overt diabetes insipidus requiring vasopressin therapy, hypothalamic obesity, or panhypopituitarism. Four of our patient had postoperative hypernatremia following the second surgery; one of them required desmopressin acetate therapy for a short time.

We are encouraged by the parental perception of overall cognitive and behavioral changes after surgery. The potential for improvement in neurobehavioral functioning after repeat surgery for HH resection requires additional study before drawing firm conclusions. In light of recent developments in surgical technique, our bias is for earlier surgery in patients with hypothalamic hamartomas associated with epilepsy. Earlier surgical intervention in those symptomatic cases that present during infancy may avoid the deterioration of seizures and possibly the decline in cognitive and psychiatric functioning that is seen in many of these patients. With experience, we are resecting larger volumes using an endoscopic technique, but in general it is difficult to achieve total resection or disconnection when a mass is greater than 1.5 mm in largest diameter. In general each individual patient should be evaluated in a multidisciplinary meeting involving neurosurgeon, neuroradiologist, and neurologist to decide on the safest approach for resection of the HH.

Conclusions

Repeat surgery of HHs associated with epilepsy has been demonstrated to be an effective strategy resulting in decrease in seizure burden in more than half of the patients. In addition, many patients have experienced subjective improvements in behavior and cognitive functioning following surgery. The results also demonstrate the relative safety of repeat surgery in HHs with refractory epilepsy. Prior to this study there has been a paucity of reports in the literature on the outcome of repeat surgeries in HH patients with refractory epilepsy. This study demonstrates the importance of reevaluating patients with persistent seizures after a first surgery and encourages further resection when residual hamartoma is present and patients are debilitated by the seizures and associated symptoms.

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Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Pati, Ng. Acquisition of data: Pati. Analysis and interpretation of data: Pati. Drafting the article: Pati, Abla, Ng. Critically revising the article: all authors. Reviewed final version of the manuscript and approved it for submission: Abla, Ng. Study supervision: Rekate, Ng.

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Deep brain stimulation for the treatment of drug-refractory epilepsy in a patient with a hypothalamic hamartoma

Case report

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Hypothalamic hamartomas (HHs) are developmental malformations associated with a range of neurological problems, including intractable seizures. There is increasing evidence of the epileptogenicity of the hamartoma and of the inhomogeneous distribution of the epileptic abnormalities within the malformation. The management strategy for treatment and results differ according to the insertion plane and the extension of the malformation into the hypothalamus. Cases characterized by extensive involvement of the hypothalamus are particularly challenging.

The authors describe the case of a patient with drug-resistant epilepsy and a large hypothalamic hamartoma with an extensive area of attachment. The patient underwent implantation of 2 deep brain electrodes. The intraoperative recording showed a synchronous interictal epileptic discharge in the left temporal lobe and on the left side of the lesion. The patient was treated with chronic high-frequency stimulation. No side effects due to the stimulation were reported. At 18 months' follow-up, a reduction in complex partial seizure frequency was reported, but no significant reduction in overall seizure frequency was noticed ($p = 0.14$, t-test).

The authors report on neurophysiological studies of the relationship between HH and epilepsy, and also discuss the literature on chronic high-frequency stimulation, including its rationale and the results of chronic stimulation of various targets for the treatment of drug-resistant epilepsy due to HH. *(DOI: 10.3171/2010.11.FOCUS10241)*

Key Words • hypothalamic hamartoma • deep brain stimulation • invasive monitoring • gelastic seizure

Hypothalamic hamartomas are rare developmental malformations associated with a range of neurological and endocrine disturbances, including seizures resistant to antiepileptic medications, cognitive and psychiatric disorders, and precocious puberty.

There is strong evidence that patients with HH and drug-resistant epilepsy benefit from resection or disconnection of the HH, but resective surgery can lead to hypothalamic disturbances, visual field deficits, motor deficits, and thalamic infarcts.[27,40] Disconnection by transventricular or transcallosal endoscopic approach has a good outcome and fewer complications than resective surgery.[1,8,14,24] There is also strong evidence that radiofrequency and Gamma Knife surgery may lead to complete seizure control with limited morbidity.[3,9,15,16,29,31,33,40,42]

The Grenoble group hypothesizes that seizures arising from the HH spread to the cortex through the mamillothalamo-cingulate tract. Kahane et al.[17] also demonstrated that chronic stimulation of the hamartoma induced a complete disappearance of interictal spikes recorded from the hamartoma and from scalp EEG, with reappearance when the stimulation was interrupted.

We report the case of a patient with an HH and drug-resistant epilepsy treated with high-frequency chronic stimulation by implantation of 2 deep brain electrodes within the malformation.

Abbreviations used in this paper: ANT = anterior nucleus of the thalamus; DBS = deep brain stimulation; EEG = electroencephalography; HH = hypothalamic hamartoma; MTT = mammillothalamic tract.

Case Report

History and Presentation. This 31-year-old right-handed woman was admitted to our hospital for presurgical evaluation for drug-refractory epilepsy associated with an HH.

Epilepsy onset was at 13 years of age with a secondary generalized tonic-clonic seizure during sleep. A few weeks later the patient developed gelastic and complex focal sei-

zures characterized by a pleasant thoracic aura followed by loss of contact, with staring, bilateral gestural, oroalimentary, and deambulatory automatisms. In the postictal phase, a language disturbance was reported. Seizure duration ranged between 20 and 60 seconds; the frequency reported was 3–7 episodes per month, often in clusters of 3–4 successive seizures. Phenobarbital, carbamazepine, vigabatrin, and levetiracetam were not effective in controlling the seizures. The patient's relevant personal and family medical histories were otherwise unremarkable.

Examination Findings. The results of general and neurological examinations at hospital admission were normal. The patient's body mass index was 25. The results of a routine blood analysis and a complete hormonal assessment were within the normal range.

The EEG was characterized by normal background activity and interictal epileptic abnormalities in both temporal lobes, with prevalence on the left side. The abnormalities were increased by sleep. A complex focal seizure was recorded: the ictal discharge was characterized by theta-delta rhythmic recruiting activity recorded on the left temporal lobe.

Magnetic resonance imaging showed a retrochiasmatic lesion extending to the anteroinferior part of the third ventricle with a wide insertion into the hypothalamus. The 25-mm lesion was hypointense in T1-weighted images and hyperintense in T2-weighted images, without contrast enhancement (Fig. 1).

A complete ophthalmological examination and neuropsychological and psychiatric assessments were performed. All results were normal.

After the presurgical evaluation, resective surgery was refused by the patient. At that point, palliative DBS was proposed and accepted. Informed consent was obtained.

Operation and Postoperative Course. Implantation of the DBS electrodes was performed after induction of general anesthesia. Four-lead DBS electrodes (Medtronic DBS lead 3389, 4 contacts 1.27 mm in diameter, 1.5 mm long, spaced by 0.5 mm) were placed bilaterally by stereotactic technique (Leksell G frame) (Fig. 2).

Intraoperative EEG recording was performed using scalp electrodes and within the lesion using the DBS electrodes (Fig. 3). Synchronous interictal epileptic discharges were recorded from the left temporal lobe and the left side of the lesion. The maximum amplitude of the spikes was observed on the distal contacts of the left DBS electrode (contacts 0–1-2) and on the F7 and T3 scalp electrodes. No interictal epileptic abnormalities were recorded from the right side of the hamartoma.

No early or delayed surgical complications were observed. The postoperative CT scan revealed correct placement of both electrodes within the hamartoma (Fig. 2).

Two days after surgery chronic bilateral unipolar stimulation was started with the following parameters: (case positive; 0–1-2 negative) 90 μsec, 130 Hz, 0.3 V.

The patient maintained a seizure diary for accurate pre- and postoperative seizure frequency evaluation.

Follow-up visits, performed every 3 months, included

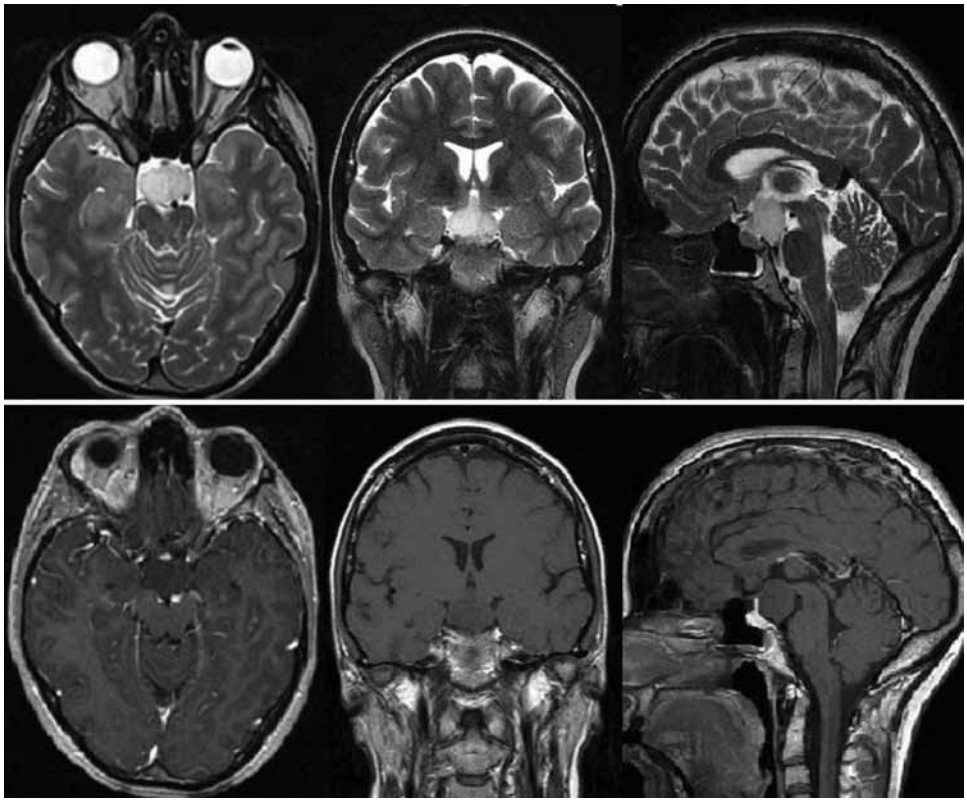

Fig. 1. Preoperative axial, coronal, and sagittal MR images showing the hamartoma with an extensive area of attachment to the hypothalamus. The malformation was hyperintense in T2-weighted images **(upper)** and hypointense without enhancement in T1-weighted images obtained after Gd administration **(lower)**.

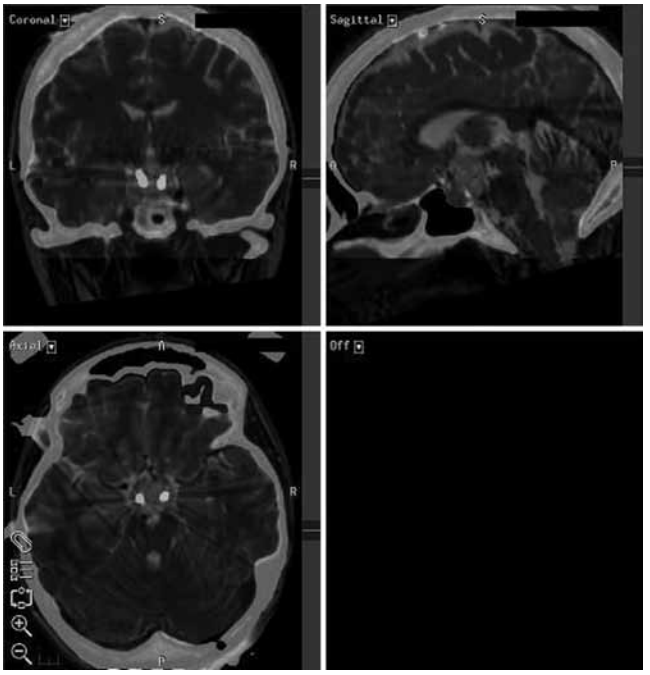

Fig. 2. Postoperative brain CT scan merged with preoperative MR imaging (T2-weighted images) showing the position of the electrodes within the malformation.

body mass index assessment, routine blood studies, complete hormonal assessment, neurological and psychiatric examination, and basal EEG. Within the 1st year after surgery, the amplitude of stimulation was increased at each visit. An amplitude of 2 V was reached at the last follow-up visit without any side effects. No behavioral, endocrinological, or neurological abnormality or abnormal increase in weight was observed at any of the follow-up visits.

After a follow-up period of 18 months, the patient and the family reported a reduction in intensity and frequency of the complex partial seizures. Nevertheless, analysis of the patient's seizure diary did not reveal a significant reduction in overall seizure frequency (complex partial and

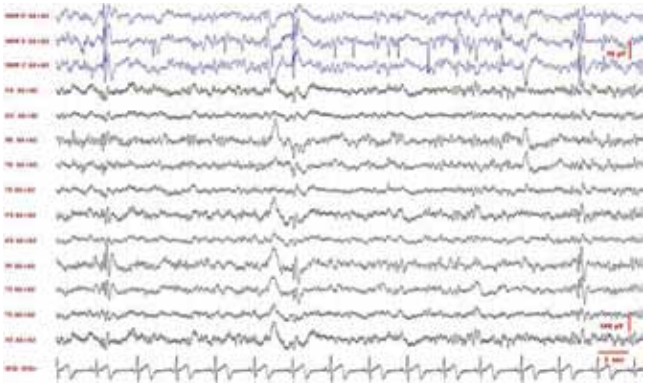

Fig. 3. Simultaneous scalp and intrahamartoma (left side) EEG recording (referential montage, bimastoid reference, lacking frontal and central leads for surgical reasons). Spikes of elevated voltage are evident on the traces from the hamartoma leads (mainly HAM 1'). When the epileptiform abnormalities are more diffused in the hamartoma, the abnormalities are also synchronously observed on the scalp temporal leads with highest amplitude on F7 and T3.

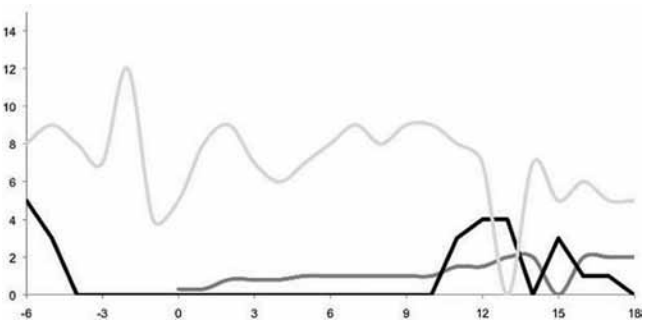

Fig. 4. Graph demonstrating pre- and postoperative seizure frequency and the relationship of postoperative seizure frequency to the amplitude of stimulation. The x axis indicates time in months (surgery at Month 0); the y axis indicates seizure frequency and amplitude (V). Within the 1st 10 months of stimulation, a reduction in complex partial seizures was noticed but there was no significant lowering in overall seizure frequency ($p = 0.14$, Student t-test). The *black line* indicates complex partial seizures; the *light gray line*, gelastic seizures; and the *dark gray line*, amplitude of stimulation.

gelastic seizures; $p = 0.14$, Student t-test) (Fig. 4). At 10 months after initiation of stimulation, the onset of reappearance of complex partial seizures was noticed, and at 15 months a hardware failure occurred (the pulse generator spontaneously switched off).

Discussion

Recently, an increasing number of papers dealing with epilepsy in children or adults with HH have been published.[2,5,6,11,13,18,25,26,28,30] Our case confirms that the epilepsy syndrome observed in adults with HH is different from the catastrophic epilepsy that develops in childhood. When epilepsy begins later, learning and behavioral problems are fewer, gelastic seizures are less prominent, and the epilepsy syndrome is usually restricted to 1 or 2 partial seizure types.[22,34,35,41]

The majority of the cases of hamartoma reported were drug refractory, and the resection or disconnection allowed good results and a low complication rate, if surgery was tailored to the anatomical characteristics of the individual patient. According to the classification proposed by Delalande and Fohlen,[7] which categorized HHs into 4 types, surgical outcome is good in patients with Types I, II, and III (Type I, horizontal insertion plane, lesion may be unilateral; Type II, vertical insertion plane and intraventricular location; and Type III, combination of Types I and II), but not good (low rate of seizure freedom) in patients with so-called giant hamartomas (Type IV).

The cognitive, behavioral, and hormonal conditions of our patient were normal, and according to the Delalande classification, the hamartoma was classified as Type IV; a less-invasive treatment, different from resective or disconnective surgery, such as DBS, was suggested.

Invasive neurophysiological studies on the relationship between hamartomas and epilepsy are few and inconclusive. Reports of chronic high-frequency stimulation for the treatment of HH are also limited. Deep brain stimulation surgery is a minimally invasive procedure that allows the perioperative recording of epileptoge-

nicity of the hamartoma, and permits the mapping, by stimulation, of the "symptomatogenicity" of the malformation. In the series of 5 patients with HH reported by Kahane et al.,[17] the scalp EEGs showed diffuse interictal and ictal abnormalities; in 4 out of 5 cases the predominant side of the EEG abnormalities was ipsilateral to the activity recorded within the hamartoma. One patient in the series underwent chronic high-frequency stimulation with an unclear reduction of seizure frequency as well as weight gain that reduced when the stimulation was stopped (Table 1).[17] The neurophysiological data reported by the Grenoble group were confirmed by our case, which showed interictal epileptic abnormalities in both temporal lobes, with prevalence on the left side, and an ictal discharge arising in the left temporal lobe. In addition, our intraoperative study showed abundant epileptic activity within the hamartoma with the maximum amplitude of the spikes on the left DBS electrode, synchronous with the epileptic abnormalities recorded from the left temporal scalp EEG.

In line with the experience of Munari and Kahane, our data confirm the epileptogenicity of the hamartoma and the nonhomogeneous distribution of the epileptic abnormalities within the malformation.[17,23] Moreover, the symptoms elicited by stimulation of the malformation demonstrated a specific distribution of the epileptogenic areas within the epileptic foci.[17,23] In the 2 cases reported by Khan et al.,[19] the EEG findings were not reported, and the unilateral stimulation was effective in reducing the seizure frequency in both cases. This study demonstrates indirectly the findings of Munari and Kahane and their colleagues, and confirms the role of the invasive study for the correct mapping of the epileptic network of the hamartoma.

Waldau et al.[39] performed a histopathological study of an HH that had been resected from a pediatric patient with gelastic seizures. The lesion showed only rare, randomly distributed neurons, suggesting that a few solitary neurons in an HH can drive epilepsy.

The rationale for DBS is based on an inhibitory effect on the epileptogenic zone achieved by stimulation of deep brain structures connected with the cortex. As a matter of fact, seizure control could be obtained by activation of all the epileptogenic neurons with supramaximal stimulus intensity. The target of stimulation could be a deep brain structure or a fiber tract connected with the majority of the neurons in the epileptogenic zone.[21] The corpus callosum and the fornix could be this kind of target. The fornix connects the hippocampus with the hypothalamus and the mammillary tract; moreover, it is strongly connected with the homologous contralateral fornix. Based on this concept, 2 patients with medically intractable epilepsy secondary to HH were successfully treated by means of unilateral DBS of the MTT. In both patients, the electrode was placed ipsilateral to the hamartoma.[19] One patient with complex partial seizures remained seizure free 14 months from surgery; the other patient suffering from gelastic and complex partial seizures showed a seizure frequency reduction of greater than 80%. Both patients had an improvement in their quality of life with the ability to attend full-time school activities.

Among the deep brain structures, the ANT, which

TABLE 1: Summary of the 5 cases reported in the literature*

Authors & Year	Age at Onset, Sex	Sz Type	Sz Freq	Preop Cognitive Status	Delalande Class	Target	Electrode Placement	Age at Op (yrs)	Stimulation Parameters	Results	Side Effects	FU (mos)
Kahane et al., 2003	infant, F	CPS & gelastic	30/mo	no cog decline	NR	HH	3 covering entire HH	30	130 Hz, 90 µsec, 0.5 V; 185 Hz, 60 µsec, 0.1 V	increase in Sz freq	weight gain, headaches	12
Savard et al., 2003	2 yrs, M	gelastic, CPS w/ or w/o generalization, & drop attacks	daily	mod impairment, aggressive behavior	NR	HH & lt ANT	1 in lt ANT, 1 HH placement not specified	41	NR	no gelastic Szs, rare CPS, persistence of drop attacks	NR	12
Khan et al., 2009	8 yrs, M	CPS	3/wk	cog decline	3	MTT	1 on rt side	16	140 Hz, 90 µsec, 3 V (2 min on, 1 min off)	Sz free	none	21
	15 mos, F	CPS & gelastic	daily gelastic Szs & 3 CPS/wk	cog decline	4	MTT	1 on lt side	13	140 Hz, 90 µsec, 3.5 V (2 min on, 1 min off)	80% reduction in Sz freq	none	13
present case	13 yrs, F	gelastic & CPS	10/mo	normal	4	HH	bilat	31	130 Hz, 90 µsec, 2.1 V	no sig reduction in Sz freq	none	18

* cog = cognitive; CPS = complex partial seizure; freq = frequency; FU = follow-up; mod = moderate; NR = not reported; sig = significant.

lies on the mammillo-thalamic-cortical pathway, could be considered as a target of DBS for the treatment of hamartoma-related seizures.[43] Literature data showed that the hamartoma and the MTT are more effective targets than the ANT. Direct stimulation of the hamartoma permits a direct effect on the epileptogenic focus; the lower threshold of excitation and the smaller volume make the MTT suitable for epilepsy control.[15,19] However, high-frequency stimulation of the ANT inhibits the spreading of interictal and ictal activity originating from hippocampal foci or from the hamartomas placed on the anterior hypothalamus; these data are supported by the work of Savard et al.,[32] who obtained good results by simultaneous stimulation of the ANT and their patient's hamartoma. The patient was previously treated with callosotomy to control disabling seizures, with disappointing results. After combined stimulation of the 2 targets, disappearance of gelastic seizures and an impressive reduction of partial complex seizures were obtained, without any effects on seizures with falls.

After 18 months of stimulation, our patient had not obtained a significant reduction in overall seizure frequency; to establish the ideal parameter of stimulation and to avoid side effects due to hypothalamic stimulation, a longer follow-up period is mandatory. Moreover, the efficacy of unilateral stimulation (ipsilateral to the left electrode that recorded the interictal activity) rather than bilateral stimulation should be tested. According to Khan et al.,[19] investigation of stimulation parameters and a higher amplitude could be also considered.

The effect of neuromodulation on deep brain nuclei[4,10,12,20,36–38,43] exerts seizure control by anterograde or antidromic stimulation or inhibition of the cortex,[21] but no conclusive data on the ideal parameters for stimulation are known. The experience reported by Kahane et al.[17] demonstrated seizure induction with frequency parameters ranging between 1 and 50 Hz. Velasco et al.[36] reported on scalp-EEG synchronization followed by a recruiting response with a stimulation of 6–10 Hz to the centromedian thalamic nucleus, and spike wave complex discharges and typical absence with stimulation at 3 Hz. These results were reported with both uni- and bilateral stimulation.[4]

In conclusion, DBS is a safe and reversible procedure that could be suggested in difficult cases in which resective and disconnective surgery have a low rate of success and high morbidity. In addition, the use of DBS facilitates the collection of outstanding neurophysiological data. It could also be indicated when disconnective or resective surgery has failed, and could be considered as the first surgical option when the patient is neurologically and endocrinologically intact with a normal cognitive status.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Marras. Acquisition of data: Deleo. Analysis and interpretation of data: Rizzi, Villani. Drafting the article: Marras. Critically revising the article: Rizzi, Villani, Messina, Cordella, Franzini. Reviewed final version of the manuscript and approved it for submission: Franzini. Statistical analysis: Deleo. Administrative/technical/material support: Rizzi, Messina. Study supervision: Marras, Villani.

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Long-term outcome after emergency resection of hypothalamic hamartomas for status gelasticus

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Object. Gelastic seizures are epileptic events characterized by bouts of laughter. They are rare and mostly associated with hypothalamic hamartomas (HHs). Status gelasticus, a rare form of status epilepticus, is defined as a prolonged cluster of gelastic seizures (> 20–30 minutes) without necessarily involving loss of awareness between seizures. Emergency resection of the hamartoma is highly effective in these situations and should be considered as early as possible. The authors retrospectively reviewed their surgical cases to document the success, complications, and long-term follow-up after emergency resection of HHs for status gelasticus.

Methods. The authors report on a retrospective case series from a single tertiary care center. Three patients who presented with status gelasticus underwent emergency resection of HHs. Demographic details, seizure history, medical treatment, and postoperative follow-up data were evaluated. Long-term follow-up (minimum 2 years) data were obtained either from the last clinic visit notes or via telephone and e-mail contacts. The institutional review board at St. Joseph's Hospital approved this study.

Results. In the last 7 years, of 157 patients who underwent HH resection, the resection was performed on an emergency basis for status gelasticus in 3 cases. At emergency surgery, these 3 patients ranged in age from 9 months to 3.5 years. All of the patients were boys. Delalande and Fohlen Type II, III, and IV lesions were present in the 3 patients. Surgical approaches for resection of HH included an orbitozygomatic, transcallosal anterior interforniceal approach and endoscopic resection. Status gelasticus was terminated following emergency surgery in all cases, and 1 patient was seizure free. Postsurgical complications included, in 1 case, a small right thalamic infarct with mild transient left hemiparesis, which completely resolved within 2 days. Within 2 years of their original surgery, 2 patients underwent further elective surgeries (endoscopic resection and radiosurgery for persistent symptomatic seizures). Follow-up since their most recent surgery ranged from 8 months to 2 years. Two patients were seizure free and 1 patient had greater than 50% reduction in seizures.

Conclusions. Status gelasticus associated with HHs can be successfully terminated by emergency resection of the HH. Long-term follow-up in the present series suggests good seizure freedom results or at least greater than 50% reduction in seizures, although repeat operations were necessary. *(DOI: 10.3171/2010.12.FOCUS10249)*

Key Words • hypothalamic hamartoma • gelastic seizure • status gelasticus • status epilepticus

Gelastic seizures are epileptic events characterized by bouts of laughter and were first described by Trousseau in 1877.[18] The conscious state may not be impaired, although this is often difficult to assess, particularly in young children. Gelastic seizures have been related classically with HHs, which are rare congenital malformations of the inferior hypothalamus and tuber cinerum.[5] Status gelasticus has been defined as a prolonged cluster of gelastic seizures (that is, for more than 20–30 minutes, a duration similar to that of status epilepticus), but without necessarily involving loss of awareness between seizures.[10] These extremely frequent to near-continuous gelastic seizures fully impair the patient and family. Gelastic seizures, especially status gelasticus, are characteristically refractory to medical treatment, and hence emergency resection is often the only option. We have previously published a single case report demonstrating the success of emergency resection of the HH for status gelasticus,[11] retrospectively reviewed our (HH) surgical database, and identified patients who underwent emergency resection for status gelasticus. Immediate postoperative complications and long-term prognoses were studied to evaluate the utility of emergency resection of HHs for status gelasticus.

Abbreviations used in this paper: GKS = Gamma Knife surgery; HH = hypothalamic hamartoma.

Case Reports

Since 2003, 157 patients have undergone HH resection for epilepsy at our center; 1 or more of these 4 approaches have been used: transcallosal anterior interhemispheric, orbitozygomatic, endoscopic resection, or GKS. Only patients who had emergency surgery for status gelasticus

were included in the study. Demographic details, seizure history, presurgical evaluation, medical and surgical management of status gelasticus, and postoperative and long-term follow-up data were evaluated. Management of status gelasticus and presurgical evaluation were conducted by a team that included dedicated pediatric neuroradiologists, pediatric neurosurgeons, pediatric epileptologists, pediatric endocrinologists, and neuropsychologists. The Delalande and Fohlen Classification was used to describe HH.[3] The Delalande and Fohlen Classification consists of 4 lesion types: Type I has a horizontal implantation plane and may be lateralized on 1 side (parahypothalamic), Type II has a vertical insertion plane and resides in an intraventricular location (intrahypothalamic), Type III is a combination of Types I and II, and Type IV includes all giant hamartomas.[3]

In addition to the follow-up interview conducted by our neurologist and endocrinologist, long-term follow-up was maintained via telephone and email contacts. A self-reported questionnaire about change in seizure frequency was used by the patient and family members.

In the last 7 years, of the 157 patients in whom an HH was resected, 3 underwent emergency resections for status gelasticus. Age at time of emergency surgery ranged from 9 months to 3.5 years. All of the patients were boys. Delalande and Fohlen Type II, III, and IV lesions were present in the 3 patients. Emergency surgical approaches for resection of HH included orbitozygomatic, transcallosal anterior interforniceal approach, and endoscopic resection. Status gelasticus was terminated following emergency surgery in all 3 cases. Postsurgical complications included, in 1 case, a small right thalamic infarct with mild transient left hemiparesis, which completely resolved within 2 days. In the next 2 years, 2 patients underwent elective endoscopic resections and 1 underwent radiosurgery for symptomatic seizures associated with the HH. Long-term follow-up ranged from 8 months to 2 years. At last follow-up, 2 patients were seizure free and 1 patient had greater than 50% reduction in seizures. A summary of the 3 cases is shown in Table 1.

Case 1

History and Examination. This 2.5-year-old boy was transferred to our institution from another hospital via air ambulance for further management of status gelasticus. He was a developmentally normal child in whom gelastic seizures began at age 4 months. He had seizures that were typical and consisted of laughing, crying, and violent behavior in the form of slapping and extreme thirst—he would ask for water and drink ferociously. A Delalande and Fohlen Type II HH was subsequently diagnosed on brain MR imaging. His gelastic seizures were brief and lasted for 60–90 seconds. In the course of time, these seizures increased in frequency, and over the following 6-week period, a seizure occurred every 5 minutes. They even persisted during his sleep. Pharmacotherapy with levetiracetam, acetazolamide, and lorazepam failed to terminate these near-continuous gelastic seizures.

Operation and Postoperative Course. His status gelasticus was finally resolved after emergency resection of the HH. The surgical approach was the transcallosal anterior interhemispheric approach, which has been described in literature.[12] Postoperatively, he had small right-sided thalamic stroke with mild transient left hemiparesis that completely resolved within 2 days. The pre- and postoperative MR images confirmed a 67% disconnection and 58% resection. His seizure frequency was reduced by more than 90%.[11] Twelve months after surgery, he had brief episodes of gelastic seizures every 2 weeks. Levetiracetam therapy was continued during that time. Eighteen months postsurgery, he had an episode of viral illness that increased the frequency of gelastic seizures to every week. He was further evaluated by our team and was deemed appropriate for further resection. He underwent endoscopic resection of the residual HH. No new postoperative complications were present. At the last clinical follow-up, which was about 3 years after the initial emergency resection and 12 months after his most recent resection, he was seizure free. He has had no further rage attacks or violent behavior.

Case 2

History and Examination. This 3.5-year-old boy was referred to our institution for further management of status gelasticus. He had mildly delayed milestones, achieving speech and walking status at 16 months of age. At 2 years of age, he talked in brief phrases and had infrequent rage attacks. He had 3 seizure types (gelastic, atonic, and atypical absence) that had started shortly after birth. At 20 months of age, the patient was diagnosed with refractory epilepsy related to a giant (Delalande and Fohlen Type IV) bilaterally attached HH. He had undergone 2

TABLE 1: Patient information and long term seizure outcome following emergency surgery for status gelasticus*

Case No., Sex	Age at Seizure Onset (mos)	Seizure Type	Delalande & Fohlen Class	1st Op	Emergency Op for Status Gelasticus	Immediate Complications	Subsequent Ops	Seizure Outcome at Last FU
1, M	4	gelastic	II	NA	TAIF	rt-sided thalamic stroke	endoscopic	seizure free
2, M	w/in 1st wk of birth	gelastic, atonic, atypical absence	IV	rt OZ, lt OZ	endoscopic	none	NA	seizure free
3, M	w/in 2nd wk of birth	gelastic, tonic, complex partial	III	NA	lt OZ	none	endoscopic; GKS	50–90% seizure reduction

* FU = follow-up; NA = not applicable; TAIF = transcallosal anterior interforniceal; OZ = orbitozygomatic approach.

prior HH resections at another institution; both were orbitozygomatic resections, 1 from the right at 22 months of age, and the other from the left 9 months later. The second surgical procedure was complicated by the development of hydrocephalus requiring ventriculoperitoneal shunt placement. The first surgery resulted in complete cessation of the atonic seizures and marked reduction of the atypical absence seizures. The second operation stopped the residual atypical absence seizures, but the gelastic seizures persisted even after both operations and, in fact, worsened to status gelasticus. His gelastic seizures were described as strained, painful laughter often associated with flatulence for about 15 seconds (maximal 30 seconds) without loss of awareness. He was having gelastic seizures every 5–10 minutes. Four antiepileptic medications (clonazepam, acetazolamide, carbamazepine, and levetiracetam) were unable to terminate these near-continuous gelastic seizures. Twenty-four-hour video electroencephalographic monitoring captured numerous gelastic seizures (> 100).

Operation and Postoperative Course. He underwent endoscopic resection of the residual HH as described previously[13] without any complications. Postoperatively, his status gelasticus was resolved. Follow-up MR imaging showed only a trace of residual HH tissue "floating" in the tuber cinereum. Eight months postoperatively, the patient remained seizure free while taking 1 antiepileptic drug, with significantly improved behavior and cognition.

Case 3

History and Examination. This 9-month-old boy was referred to our institution for further management of status gelasticus. He had severe developmental delay and was impaired cognitively. He had 3 seizure types (gelastic, tonic, and complex partial) that had started within the 2nd week of birth. The brief episodes of gelastic seizures were increasing in frequency to almost 1 every 10–12 minutes in the preceding 2 weeks. He had been diagnosed at 5 months of age with refractory epilepsy related to a Delalande and Fohlen Type III HH. He also had a prominent left frontotemporal arachnoid cyst. None of the antiepileptic medications had ever significantly helped his seizures.

Operation and Gamma Knife Treatment. The patient underwent emergency HH resection via a left orbitozygomatic approach as described previously,[1] and arachnoid cyst fenestration (2-stage procedure) (Fig. 1) His near-continuous gelastic seizures were reduced by greater than 50%. However, he continued to have at least 2–3 brief episodes daily. The patient was treated with 3 antiepileptic medications (levetiracetam, clonazepam, and carbamazepine). In the next 2 weeks, he had further endoscopic resection of the residual HH. Postsurgery MR imaging brain confirmed a 48% disconnection and 67% resection. Complication after the endoscopic resection included a right internal capsule infarct that resulted in left-sided weakness. His gelastic seizures were resolved completely, and he remained seizure free while taking 2 antiepileptic medications (levetiracetam and clonazepam) for the next

Fig. 1. Case 3. **Upper:** Coronal T2-weighted brain MR images obtained shortly after left orbitozygomatic resection of most of the HH (with drain tube in situ) and before arachnoid cyst fenestration. *Arrow* points to residual HH tissue on the right. **Lower:** Coronal T2-weighted brain MR image obtained after arachnoid cyst fenestration with resultant relief of mass effect. The residual HH is shown by the *arrow*.

2 months. Seven months after surgery, he started to have clusters of complex partial seizures every 2–3 weeks, which were not well controlled by 4 antiepileptic medications (levetiracetam, clonazepam, carbamazepine, and zonisamide). He was again evaluated by our team and underwent GKS at the age of 20 months. At the last clinic follow-up, almost 15 months after the emergency resection, his seizures were reduced by greater than 50%. His present seizures are complex partial seizures that consist of crying and then unresponsiveness for a few seconds.

At the time of this draft, the plan was to admit the patient to our epilepsy-monitoring unit for further presurgical evaluation.

Discussion

These cases illustrate the potential value of emergency resective lesional epilepsy surgery in patients with a form of status epilepticus (status gelasticus secondary to HHs). Gelastic (that is, laughing) seizures represent one of the hallmark features of the HH. They can be associated with little or no change in consciousness, particularly early in the clinical course. They are typical and automatic repetition of laughter without pleasure and appear to be forced pathological laughter. Patients with gelastic seizures that are associated with the intrahypothalamic form of HH usually present at an early age and are often the first seizure type. Tassinari et al.[17] reported a mean age of onset of 2.8 years, with seizures occurring in more than one-third of patients. In addition, these seizures have been reported to occur on the 1st day of life, as illustrated in Case 2.[16] The frequency of status gelasticus in patients with HH remains unknown. Our small series of patients would suggest that it tends to present in young patients. Recent electrophysiological studies have clearly demonstrated the intrinsic epileptogenicity of the HH and its direct association with induction of gelastic seizures.[6,8,9] SPECT studies have demonstrated hyperperfusion within the hamartoma itself during gelastic seizures.[2,4] The authors of 2 recent studies performed ictal fluorodeoxyglucose-PET scanning in patients with intractable gelastic seizures associated with HHs.[14,15] They demonstrated a large circumscribed hypermetabolic region within the location of the HH, representing localized intense epileptiform activity. Resection of the HH successfully terminated the status gelasticus in all of our cases despite their not remaining seizure free. This suggests that emergency surgical intervention is the best option for terminating intractable, near-continuous gelastic seizures and improving cognitive function. Complete and sustained seizure control with medications alone is achieved in fewer than 5% of patients with intrahypothalamic HH and epilepsy. Medications are often described as lacking efficacy against gelastic seizures.[7]

In all 3 of our cases, multiple operations appeared to help the patients by reducing seizure frequency and improving overall cognitive and behavioral functioning. None of the antiepileptic drugs were able to terminate status gelasticus. A number of different surgical approaches have been developed and advocated for resection of the HH lesions. The surgeon should choose among these approaches based on the specific anatomical features of each HH lesion. No single approach is best suited for every patient, as evident in our illustrated cases. All 3 patients had different types of HH and underwent emergency resection in which 3 different surgical approaches successfully stopped the status gelasticus. In addition, the repeat surgical procedures, which resulted in seizure freedom in 2 patients, were distinctly different from the initial operation (or operations, as in Case 2). The reason multiple procedures were necessary was the difficulty or impossibility of safely removing the entire HH due to its location, attachment, and size in a single approach and procedure. In general, the aim is to completely remove the HH; if this is not possible, disconnection should be the goal, and, if necessary, repeat surgery (via a different approach) can be performed. The results in our 3 cases also illustrate the merit of different surgical approaches for emergency resection.

In summary, we present immediate and long-term outcomes following emergency surgery of HHs for status gelasticus. Status gelasticus can be successfully terminated by emergency resection of the HH. Long-term follow-up in our small series resulted in seizure freedom in 2 patients and greater than 50% reduction in seizures in 1 patient, although a "more complete" repeat resection was necessary.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Ng, Pati, Abla, Rekate. Acquisition of data: Pati, Rastogi. Analysis and interpretation of data: Pati, Rastogi. Drafting the article: Pati, Rastogi. Critically revising the article: Ng, Abla, Rekate. Reviewed final version of the manuscript and approved it for submission: Ng, Abla.

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Syndrome of alternating hypernatremia and hyponatremia after hypothalamic hamartoma surgery

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Object. In this paper, the authors' goal was to describe the occurrence of alternating hypernatremia and hyponatremia in pediatric patients who underwent resection of hypothalamic hamartomas (HHs) for epilepsy. Hypernatremia in patients after pituitary or hypothalamic surgery can be caused by diabetes insipidus (DI), whereas hyponatremia can occur due to a syndrome of inappropriate antidiuretic hormone, cerebral salt wasting, or excessive administration of desmopressin (DDAVP). The triphasic response after surgery in the pituitary region can also explain variations in sodium parameters in such cases.

Methods. One hundred fifty-three patients with HH who underwent surgery were enrolled in a prospective study to monitor outcomes. Of these, 4 patients (2.6%) were noted to experience dramatic alterations in serum sodium values. The medical records of these patients were identified and evaluated.

Results. Patients' ages at surgery ranged from 1.2 to 6.0 years. All patients were girls. Two patients had Delalande Type IV lesions (of 16 total Type IV lesions surgically treated) and 2 had Type III lesions (of 39 total Type III lesions). All patients had a history of gelastic seizures refractory to medication. Seizure frequency ranged from 3 to 300 per day. After surgery, all patients experienced hypernatremia and hyponatremia. The largest fluctuation in serum sodium concentration during hospitalization in a single patient was 53 mEq/L (range 123–176 mEq/L). The mean absolute difference in maximum and minimum sodium values was 38.2 mEq/L.

All patients exhibited an initial period of immediate DI (independent of treatment) after surgery followed by a period of hyponatremia (independent of treatment), with a minimum value occurring between postoperative Days 5 and 8. All patients then returned to a hypernatremic state of DI, and 3 patients still require DDAVP for DI management. A second occurrence of hyponatremia lasting several days without DDAVP administration occurred in 2 patients during their hospitalization between periods of hypernatremia. One patient stabilized in the normal range of sodium values prior to discharge from rehabilitation without the need for further intervention. At last follow-up, 3 patients are seizure-free.

Conclusions. Severe instability of sodium homeostasis with hypernatremia and hyponatremia is seen in up to 2.6% of children undergoing open resection of HH. This risk appears to be related to HH type, with a higher risk for Types III (2 [5.1%] of 39) and IV (2 [12.5%] of 16) lesions. Here, the authors describe alternating episodes of hypernatremia and hyponatremia in the postoperative period following HH surgery. Management of this entity requires careful serial assessment of volume status and urine concentration and will often require alternating salt replacement therapy with DDAVP administration. *(DOI: 10.3171/2010.12.FOCUS10235)*

Key Words • hypothalamic hamartoma • diabetes insipidus • syndrome of inappropriate antidiuretic hormone secretion • serum sodium concentration

The relationship between postoperative hyponatremia and hypernatremia has been well described in a prospective study investigating the causes of both entities, either alone or in combination, following pituitary surgery.[12] Those authors found that, following pituitary surgery, DI was responsible for hypernatremia, and suggested that CSW rather than SIADH was responsible for hyponatremia, evidenced by hypovolemic states for both of these abnormalities (DI and CSW) that are at opposite ends of the sodium spectrum. Two other studies suggested that SIADH causes most cases of postoperative hyponatremia after transsphenoidal pituitary surgery.[14,19] Diabetes insipidus has been previously demonstrated after HH surgery.[1,3,9,10] In 1 study of patients with HH, hypernatremia (> 145 mEq/L) was found in 26 of 29

Abbreviations used in this paper: ADH = antidiuretic hormone; ANP = atrial natriuretic peptide; CSW = cerebral salt wasting; DDAVP = desmopressin; DI = diabetes insipidus; HH = hypothalamic hamartoma; SIADH = syndrome of inappropriate ADH.

patients, and 55% of these patients developed hypernatremia greater than 150 mmol/L.[3] Following surgery in the pituitary region, the sequential occurrence of CSW and SIADH has been previously demonstrated to occur in the same patient.[5,12,18] However, fluctuations in serum sodium levels resulting in sequential development of hypernatremia and hyponatremia have not been previously described following HH surgery; this entity is in line with other water electrolyte disturbances experienced after surgery in this region.

Here, we demonstrate alternating hypernatremia and hyponatremia following resection of some of the largest HHs at our center. Four patients presented here all exhibited sodium values both above and below the normal value ranges. All HHs were treated surgically and all were Delalande Type III or IV.

Methods

Since 2003, 153 patients have been treated surgically at our center for epilepsy due to HHs with 1 or more of the following approaches: transcallosal anterior interhemispheric interforniceal, orbitozygomatic, or endoscopic resection of HH. Nineteen HH lesions have been treated using Gamma Knife surgery. Patients are evaluated preoperatively by a multidisciplinary team including epileptologists, endocrinologists, and neurosurgeons for appropriate selection of treatment modality based on patients' symptoms, as well as MR imaging and video electroencephalography findings. Patients are prospectively enrolled and observed after surgery with data collection in a secure, proprietary database following informed consent under protocols approved by the institutional review board of the Barrow Neurological Institute at St. Joseph's Hospital and Medical Center. Follow-up is obtained with surveys, office visits, and telephone calls at regular intervals.

Patients are evaluated preoperatively and postoperatively for endocrinopathies including weight gain and DI by a pediatric endocrinologist (R.E.J.), seizure outcome, behavioral changes, and cognitive/developmental as well as short-term memory capacities. Four patients to date have been identified who experienced large fluctuations in their sodium values during hospitalization and for up to several months after surgery in nearly all cases.

Results

Four patients are included in this report. Data related to seizure frequency, seizure type, and seizure onset and other symptoms are shown in Table 1. None of the patients had preoperative DI, CSW, or SIADH and none were taking DDAVP before surgery. Data involving the hospital course and outcomes as they relate to seizure control, sodium levels, and other endocrinopathies are given in Table 2.

Patients' sodium values, urine specific gravities, baseline (dry) weight and nearly daily weights, and urine input and output values were monitored during their hospitalization, most of which took place in an ICU setting. The patients' laboratory values of the above-stated parameters are shown graphically in Figs. 1–4, which correspond to the patients in Cases 1–4. Desmopressin administration is also shown.

All patients immediately went into DI after surgery and required at least 1 dose of DDAVP intranasally. All patients then went into a hyponatremic state that lasted at least 4 days and persisted without DDAVP administration; that is, this occurrence was not iatrogenic. In Case 4, the hyponatremia improved and overshot the normal sodium range by Day 4, but the level returned to a hyponatremic state and hit the nadir value around Day 7 after surgery (Fig. 4). In Case 4, hyponatremia occurred several times for shorter periods later in the hospitalization, but the effect was likely iatrogenic and related to DDAVP (Fig. 4). Another patient experienced a prolonged second decrease, with a second hyponatremic state occurring between Days 14 and 18 after surgery (Fig. 2, Case 2). In this patient, as well as the patient in Case 4 and in all patients between Days 4 and 8, hyponatremia occurred independent of ongoing DDAVP administration.

Urine specific gravity, urine output, and daily weights were used in the management of sodium hemostasis (Figs. 1–4). However, weight and daily fluid output were found to be unhelpful in differentiating hyponatremia due to CSW from low sodium due to SIADH. Weights were not particularly helpful, and they were not measured consistently in our patients. All 4 patients did eventually weigh more than they did at baseline, which would indicate that their volume status at the end of hospitalization was not depleted. Volume status would be expected to be on the

TABLE 1: Preoperative characteristics: seizures and symptoms*

Case No.	Age (yrs), Sex	Age at Seizure Onset (mos)	No. of Seizures/Day	No. of AEDs at Op	Seizure Type	Symptoms
1	5.6, F	4	3–12	3	gelastic, grand mal, tonic	precocious puberty, developmental delay, rage
2	1.2, F	2	50–300	2	gelastic	precocious puberty, developmental delay†
3	6.0, F	1	5–10	3	gelastic, secondary complex partial	developmental delay, rage‡
4	3.3, F	1	8–12	2	gelastic, complex partial	precocious puberty, mild developmental delay, rage

* AEDs = antiepileptic drugs.

† As assessed postoperatively. The patient was too young preoperatively for symptom assessment.

‡ This patient exhibited mild mental retardation and short-term memory loss.

TABLE 2: Hospitalization and follow-up data related to seizure control and sodium homeostasis*

Case No.	Type (max length)	Approach	Na Value Range (mEq/L)	Symptoms From Hyponatremia (seizure or aLOC)	DDAVP Continued on Discharge	LOS (days)	FU (mos)	Seizure Outcome, Medication	Sodium Outcome	Other Endocrine Outcomes
1	IV (2.9 cm)	transcallosal	124–150	yes	no	16	2	seizure free; taking 3 AEDs	resolved before discharge from rehab	hyperthermia to 38.9°C during hospital stay
2	III (2.1 cm)	endoscopic transventricular	125–160	yes	yes	26	30	10–20 gelastic/day; taking 2 AEDs	6 mos of Na swings; Na stable on DDAVP	significant weight gain
3	III (2.1 cm)	transcallosal	123–176+†	no	yes	21	41	seizure free; taking 1 AED for mood	Na fluctuated for 3 mos; DDAVP 0.1 mg bid (last sodium value 146 mEq/L)	hyperthermia to 39.8°C during stay; increased appetite/weight gain (improving)
4	IV (3.6 cm)	transcallosal	121–160	yes	yes	27	41	seizure free; taking 1 AED	Na level hovers ~150 mEq/L; DDAVP 0.05 mg once nightly	hyperthermia during hospital stay, temperature remains slightly elevated; weight gain/aggressive behavior toward food

* aLOC = altered level of consciousness; FU = follow-up; LOS = length of stay; rehab = rehabilitation.

† This value was obtained outside the normal analytical range.

Fig. 1. Case 1. Sodium concentration **(A)** in mEq/L, urine specific gravity **(B)**, daily fluid intake *(solid line)* and daily fluid output *(dashed line)* in ml **(C)**, and weight in kg **(D)**. The values on the x axes indicate the postoperative days. The *asterisk* in panel **A** represents the time of administration of DDAVP. Time zero for sodium concentration represents baseline sodium level. Time zero for weight represents baseline dry weight.

dehydration end of the spectrum had patients experienced both DI (which they did) and CSW (characterized by a low volume state) without periods of SIADH. This was not the case; SIADH was more likely occurring. In most of the patients, except the one in Case 4, fluid intake and urine output were closely matched. In Case 4, although demonstrating fluid output greater than fluid input for the majority of the stay, the patient managed to gain weight. This raises the concern or limitation that fluid and weight measurements in the ICU are not always completely accurate or reliable in predicting volume status.

Most patients exhibited long-term impairments in the ability to regulate water and electrolytes, continued to have central DI, and remained on DDAVP at last follow-up. One patient had resolution of the fluctuating sodium prior to discharge and did not require DDAVP postoperatively (Case 1). There were also several other associated endocrine disturbances including hyperphagia and hyperthermia (Table 2). Three of the 4 patients with these sodium perturbations experienced permanent injury and continued to have DI. Three of the patients had undergone transcallosal surgery, and at surgery, a very aggressive resection was obtained in all 3, with the percentages of resection based on volumetric calculations totaling 92%,

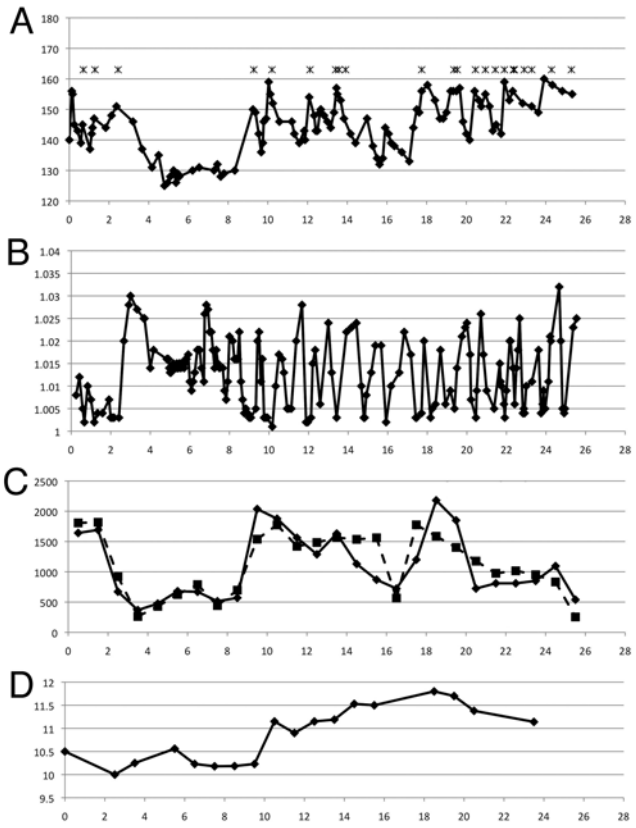

Fig. 2. Case 2. Sodium concentration **(A)** in mEq/L, urine specific gravity **(B)**, daily fluid intake *(solid line)* and daily fluid output *(dashed line)* in ml **(C)**, and weight in kg **(D)**. The values on the x axes indicate the postoperative days. *Asterisks* in panel **A** represent the time of administration of DDAVP. Time zero for sodium concentration represents baseline sodium level. Time zero for weight represents baseline dry weight.

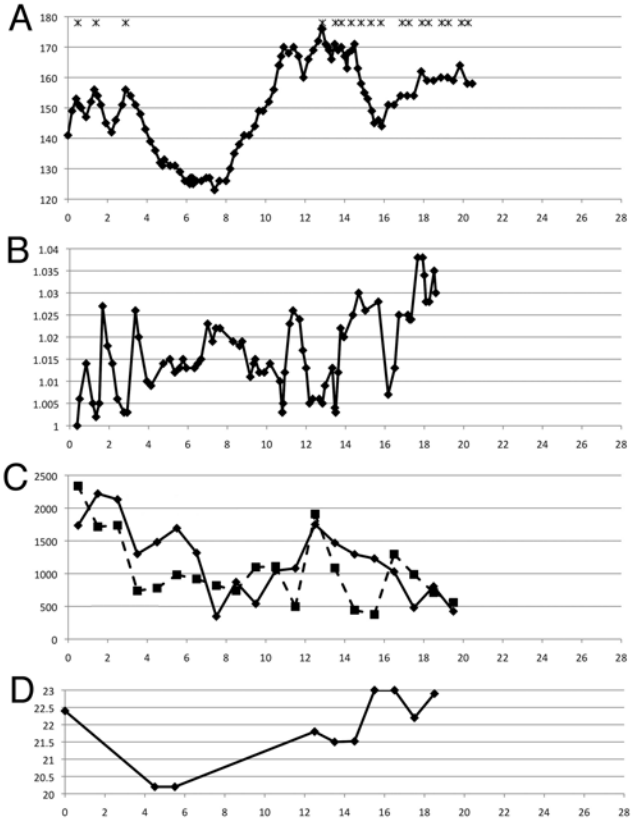

Fig. 3. Case 3. Sodium concentration **(A)** in mEq/L, urine specific gravity **(B)**, daily fluid intake *(solid line)* and daily fluid output *(dashed line)* in ml **(C)**, and weight in kg **(D)**. The values on the x axes indicate the postoperative days. *Asterisks* in panel **A** represent time of administration of DDAVP. Time zero for sodium concentration represents baseline sodium. Maximum sodium value was outside the range of recordable values of the laboratory test at its peak (> 176 mEq/L). Time zero for weight represents baseline dry weight.

99%, and 100% of lesion volume. The remaining patient (Case 2) underwent endoscopic surgery aimed at disconnection only.

Illustrative Case

Case 4

Presentation and Examination. This 3-year-old girl presented to our institution for management of a giant HH. Preoperatively, she had experienced 8–12 gelastic seizures per day since the 1st month of life. She had mild cognitive delay with expressive language being the most affected capacity on baseline neuropsychological and cognitive testing. She also exhibited behavioral symptoms including rage attacks and premature menarche at 16 months of age (treated with Lupron).

Operation. The patient underwent surgery via a transcallosal anterior interforniceal approach. Her HH is one of the largest lesions treated to date, with a maximum length of 3.6 cm and a volume of 20.4 cm^3 (Fig. 5). The lesion extended outside the third ventricle into the prepontine cistern directly adjacent to the basilar artery. Surgery proceeded uneventfully with the aid of stereotactic neuronavigation and intraoperative MR imaging; no additional resection took place after intraoperative MR imaging. The lesion was nearly totally resected (99%) (Fig. 5). Afterward, she was immediately extubated and taken to intensive care.

Postoperative Course. The patient experienced few postoperative neurological deficits after surgery and had minimal verbal output for the first 72 hours. She said "no" on Day 3 after surgery but remained aphasic for most of her hospitalization; at times, she would communicate, sometimes verbally, with her parents. She had left hemiparesis/neglect, which improved within the first few weeks after surgery. Anisocoria was present initially, but both pupils were reactive and her anisocoria resolved slowly during her stay. She maintained minimal eye contact with the examiner but would follow simple commands. On postoperative Day 7, she experienced an approximately 3-minute spell of lip-smacking and right-sided tonic posturing. She experienced several more seizures during the same day, which were attributed to hyponatremia given that these did not resemble her preoperative seizure semiology. She also was believed to experience an altered level of consciousness during hyponatremia with bouts of lethargy. Later during

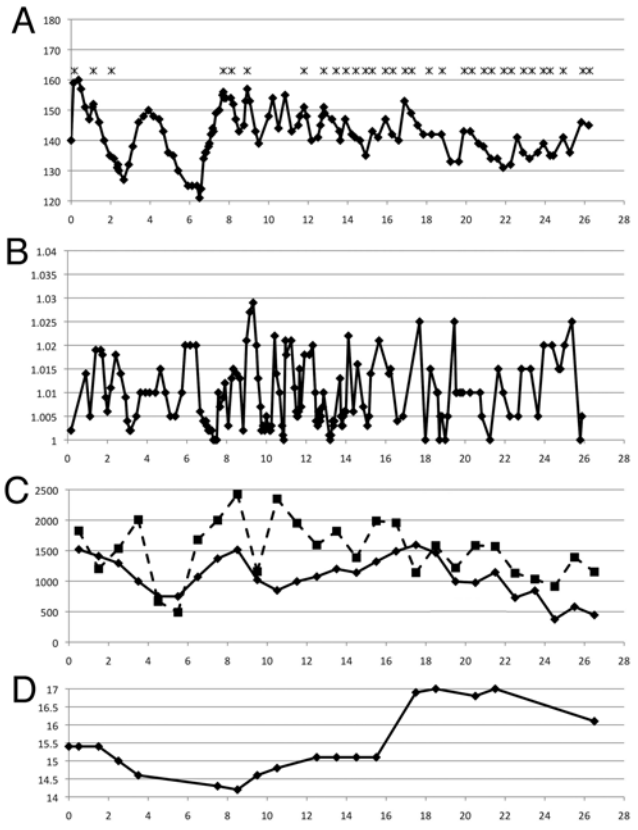

Fig. 4. Case 4. Sodium concentration **(A)** in mEq/L, urine specific gravity **(B)**, daily fluid intake *(solid line)* and daily fluid output *(dashed line)* in ml **(C)**, and weight in kg **(D)**. The values on the x axes indicate the postoperative days. *Asterisks* in **A** represent the time of administration of DDAVP. Time zero for sodium concentration represents baseline sodium. Time zero for weight represents baseline dry weight.

her hospitalization, once she was no longer hyponatremic, she also experienced staring spells but no overt seizures.

The patient's sodium values and other parameters are documented in Fig. 4. On postoperative Day 9, the sodium value returned to 152 mEq/L. Desmopressin was given intranasally and orally for all measured sodium values greater than 150 mEq/L. Generally speaking, our regimen starts with 2.5 μg of DDAVP intranasally, and we will increase this dose up to 10 μg intranasally if needed on a 1-time basis. Once patients are placed on standing DDAVP orders, we will administer doses between 50 and 100 μg orally twice daily. The patient was discharged 27 days following surgery after readmission to the pediatric ICU from a regular ward. She required DDAVP frequently throughout her hospitalization but did not receive any between Days 2 and 9, at which point she experienced 2 episodes of hyponatremia with a hypernatremic state in between. After her 2nd week of hospitalization, she continued to suffer from DI and required twice daily oral DDAVP, which at 2 points caused her to become hyponatremic. At the same time, she experienced central neurogenic hyperthermia during her hospitalization and required antiinflammatory medication on several occasions.

Fig. 5. Case 4. Sagittal T2-weighted MR images. **Left:** Preoperative image illustrating a giant HH *(arrow)* with components both inside and outside the third ventricle. **Right:** Postoperative image showing gross-total resection of this previously identified giant HH with a small rim of residual lesion anteriorly *(arrow)*.

After discharge from the hospital, this patient remained in neuro-rehabilitation for 1 month for ongoing physical therapy and then transferred to a subacute care center closer to home. She continued to have variations in her sodium measurements for several months. Her parents weighed every diaper and also measured all fluid intake to assist in managing her volume status, recording these in a spreadsheet. She required a peripherally inserted central catheter for intravenous medication and fluids upon returning to her home state.

At present, the patient is seizure free and is taking DDAVP 0.05 mg orally once nightly. She has experienced mild short-term memory loss since the surgery, and her language abilities remain slightly delayed, although she is in the 1st grade now and participates in all activities. She continues to undergo speech and language therapy. Her parents continue to maintain mild fluid restriction of free water to avoid precipitous decreases in her sodium levels. She undergoes blood sampling every 3 months now, and her sodium values hover above 150 mEq/L. She has not had a sodium value of less than 140 mEq/L in 2 years. Her appetite has been reported by her parents as insatiable, which triggers aggressive behavior related to taking food from others.

Discussion

It has been reported that DI can develop after pituitary region surgery in up to 75% of cases[7,8,12,15,17] and after transsphenoidal surgery in 10%–44% of cases,[4,6,12] whereas hyponatremia can occur in up to 35% of cases after surgery of pituitary region lesions.[12,13]

The management of hypernatremia and hyponatremia following pituitary or hypothalamic region surgery can often be complex and dependent on several variables. Following these types of surgeries, it is generally accepted that hypernatremia develops in response to decreased circulating levels of ADH in a process known as central DI. This can be caused by a lack of ADH secretion (after the appropriate stimulus) following such surgery and likely occurs from surgical disruption of the supraoptic and paraventricular nuclei of the hypothalamus, pituitary stalk, or posterior pituitary. We believe that one explanation for this effect in pediatric patients (such as those who have undergone HH surgery) involves the smaller circulating volume, perhaps evidenced by large shifts in serum sodium concentrations with minimal shifts in intake or output of fluids or

salts. It is also possible that HH is a secretory tissue, and removal results in deficits of hypothalamic-pituitary axis endocrine function responsible for normal sodium homeostasis, resulting in DI.

In contrast to hypernatremia, there are numerous etiologies for postoperative hyponatremia. Hyponatremia in this setting can be due to overzealous ADH administration (via DDAVP medication), a coinciding SIADH secretion caused by operative trauma,[2,12,13,16] or CSW, which is a state characterized by hypovolemia and poor resorption of sodium in the kidney. A prior report regarding pituitary surgery found that combined DI and hyponatremia proceeded with hypernatremia on the 1st–3rd postoperative days followed by hyponatremia during postoperative Days 7.5–10.[5] Another study reviewed (in rats) the so-called triphasic response that occurs after pituitary stalk sectioning: DI, followed by hyponatreria, and DI again.[16] These authors suggested, as did others, that leakage of vasopressin from damaged hypothalamiconeurohypophysial tracts and the posterior pituitary causes an "isolated second phase" (hyponatremia).[5,16] In other studies, hyponatremia has been previously shown not to be associated with high levels of ADH but rather associated with elevated ANP, thought to have a role in CSW, after pituitary region surgery.[12,18]

What likely happened in these 4 patients after resection of these very large tumors, most of which were removed aggressively, is a similar occurrence to the triphasic response. However, it is unclear and not possible to say with certainty that the hyponatremic states that occurred with the lowest values of sodium between Days 5 and 8 was due to CSW or SIADH. Whether high circulating ADH levels due to release from injured posterior pituitary cells caused SIADH in these patients as shown in the triphasic response in rats or high circulating values of ANP caused CSW is unknown here. More likely is that SIADH occurred given the overall weights of the patients when comparing discharge with baseline weight. Also, 2 additional periods ("double-dip") of hyponatremia cannot be explained by iatrogenic causes (that is, administration of DDAVP) in 2 of the 4 patients. One patient, in addition to experiencing a second decrease in sodium below the normal range, did have 2 hyponatremic episodes later during hospitalization that were attributable to DDAVP, likely from routine twice daily administration.

Management

We have not routinely measured urine osmolalities, urine free sodium, or fractional sodium excretion to evaluate hyponatremia and hypernatremia. We also have not measured central venous pressure in these young patients as a way of determining volume status, which may be more invasive and add an unnecessary risk. In contrast to extensive testing used by other authors in a prospective investigation into the causes of aberrations in sodium physiology after pituitary region surgery,[12] our management is described below. Those authors measured ADH levels, ANP levels, central venous pressure, creatinine clearance, free water resorption, fractional sodium excretion, and daily sodium output. They focused on central venous pressure as an indicator of the fluid volume resuscitation needed. They used free water resorption as a barometer to dictate DDAVP administration and used fractional sodium excretion as a way to monitor sodium replacement.

At our institution, patients are routinely monitored for hypernatremia or hyponatremia with serum sodium measurements every 6 hours, or more frequently when sodium values are more volatile. Input and output fluid parameters are measured hourly for urine output, oral intake, intravenous fluid intake, and other output such as emesis or bowel movements.

When patients are hypernatremic, in the setting of large amounts of dilute urine (specific gravity < 1.005) and sodium values are greater than 150 mEq/L, we place them on a regimen of DDAVP and encourage free water intake.

For patients who are hyponatremic, the management is more difficult and involves the assessment of volume status. Cerebral salt wasting requires vigorous salt replacement, whereas SIADH requires fluid restriction.[11] Fluid restriction, however, as well as diuretic use in symptomatic patients, was suggested by 1 group as the sole treatment of hyponatremia occurring after pituitary surgery if the sodium level is less than 130 mEq/L (given that their group believed it to be a form of SIADH).[5] The same group suggested that hyponatremia is the more troublesome of the 2 extremes and could lead to significant morbidity and mortality if untreated but also warned that 1 patient developed acute renal failure during a period of fluid restriction during a hyponatremic state (sodium level of 127 mEq/L).[5]

In addition to restricting fluid, we have used diuretics and saline replacement for treating hyponatremia. Saline replacement, however, is not without risk and can have iatrogenic consequences just as DDAVP can. Overaggressive treatment of hyponatremia can lead to central pontine myelinosis with correction of sodium too quickly. Correction of sodium at a rate of not more than 1 mEq/L every 2 hours has been our institutional goal. In those patients who can tolerate oral intake, salt tablets are also prescribed. Central pontine myelinosis was not observed in this cohort of patients.

Complications Associated With Hyponatremia

Two areas of concern related to hyponatremia include the development of seizures and the development of altered level of consciousness presumably due to cerebral edema and increased intracranial pressure. For this reason, if we have to err outside the normal range, we prefer for patients to be slightly hypernatremic rather than hyponatremic. We treated 3 patients who experienced seizures during their hyponatremic periods; 1 of these 3 patients also experienced a decreased level of consciousness. The patient in Case 1 experienced seizures within 48 hours of surgery of a tonic seizure semiology during a period of hyponatremia. Tonic seizures and gelastic seizures were part of her preoperative seizure semiology. The patient in Case 2 developed seizures during hyponatremia on postoperative Day 6 that were similar to previous gelastic seizures but also had episodes of staring to the right, with right nystagmus and left arm rhythmic movement followed by emesis. Seizures for the patient in Case 4 are described previously.

As stated, volume status in children (or adults) may

not be easy to quantify;[12] assessing the latency of peripheral capillary refill can be useful in demonstrating dehydration but remains a crude measurement. More invasive evaluations in children such as central venous pressure testing were forgone in our management. We recorded daily weights and measurements of input and output of fluids in these patients. Although they are also crude measures of volume status, these values can potentially predict a deficit or surplus in a patient's volume status, helpful in differentiating between salt wasting and SIADH. Daily weights, however, can be inconsistent or unreliable as can a reliable quantification of exact fluid input and output measurements.

The potential volatile nature of volume status in children, given a smaller circulating fluid volume, lends a possible explanation as to why the alternating values of high and low serum sodiums can occur so quickly in young patients; our impression is that small fluid shifts in children could potentially result in large changes in serum sodium (or other osmolality) values. A prior study found a trend for water electrolyte disturbances to tend to occur in younger patients but did not address the mechanism and suggested rather that it may occur since patients with hormone-producing pituitary tumors tend to be younger.[5]

Conclusions

We have shown that sequential alterations in hyponatremia and hypernatremia, previously demonstrated in pituitary region surgery, can occur in the largest of HHs. Careful management of this entity requires frequent assessment of sodium values, urine-specific gravity, and volume status. The determination of the cause of hyponatremia can be further demonstrated with laboratory testing of circulating ADH and ANP levels. The sodium homeostasis derangements demonstrated here seem to mimic the triphasic response; however, additional periods of hyponatremia independent of DDAVP administration that occurred here suggest that there is more to the phenomenon than is currently understood. A syndrome of alternating hypernatremia and hyponatremia after HH surgery seen here requires further investigation into the exact cause of hyponatremia occurring after HH surgery. It appears to be independent of DDAVP administration, but whether it is CSW, SIADH, or another possible abnormality related to removal of HH lesional tissue is not known. Although an HH often causes a pathological state of seizures, it potentially could serve a secretory role in normal physiological sodium homeostasis.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Abla, Ng. Acquisition of data: Abla, Kerrigan. Analysis and interpretation of data: Abla, Wait, Forbes, Ng. Drafting the article: Abla, Ng. Critically revising the article: Abla, Forbes, Kerrigan, Ng. Reviewed final version of the manuscript and approved it for submission: all authors. Statistical analysis: Abla, Kerrigan, Ng. Administrative/technical/material support: Abla, Wait, Forbes, Pati, Kerrigan, Ng. Study supervision: Abla, Kerrigan, Ng.

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Giant solid-cystic hypothalamic hamartoma

Case report

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Hypothalamic hamartomas are rare lesions for which different classification schemes have been proposed. The authors report on an exceptionally large solid-cystic hamartoma that led to hydrocephalus, precocious puberty, and intractable gelastic seizures. They discuss potential mechanisms of the development of hypothalamic hamartomas. *(DOI: 10.3171/2011.1.FOCUS10240)*

Key Words • **hypothalamic hamartoma** • **giant hypothalamic hamartoma** • **hydrocephalus**

Hypothalamic hamartomas are rare nonneoplastic lesions originating from the tuber cinereum or mammillary bodies. They often present in early childhood with either precocious puberty and/or medically refractory seizures. Gelastic seizures are the hallmark of these lesions, which have been shown to have intrinsic epileptogenicity. Most HHs are sporadic lesions and 10% are part of a multiple malformation syndrome. In 2 large series reported by Freeman et al.[5] and Arita et al.[1] the mean size of the HHs was 19 and 17.9 mm, respectively. Very few cases of giant HHs have been reported.[6,7,10–12] We describe a case of a patient harboring an enormous solid-cystic HH, the size and extension of which seem unique in the literature and potentially raise further questions about the origin of these lesions.

Case Report

History and Examination. This 8-month-old boy presented with enlarged head circumference, precocious puberty, and delayed development. After fetal ultrasound detection of hydrocephalus at 20 weeks age of gestation, fetal MR imaging revealed a solid-cystic mass originating from the floor of the third ventricle, suggesting an HH. At referral, MR imaging revealed a huge solid-cystic HH broadly based on the tuberomammillary region and extending down to the lower clivus, with the cystic component displacing the brainstem and left cerebellar hemisphere. The dimension of the solid component was 2.7 × 4.5 cm (width × height). The cyst further extended through the posterior tentorial notch into the velum interpositum and both lateral ventricles with associated hydrocephalus (Figs. 1, 2A, and 3). Neither the solid nor cystic parts had increased disproportionally to brain growth up to the time of referral.

Operation. We performed a transcallosal partial resection with the aim of decompressing the aqueduct and establishing communication of the cyst through the solid part of the HH to the basal cisterns (Figs. 2B and 4). The abducent nerves were found to be tightly adherent to the lesion. The resection and fenestration of the solid part were restricted to the median portion toward the foramen magnum. Because the patient did not have seizures, we did not attempt a disconnection. The treatment of hydrocephalus seemed successful and the precocious puberty was effectively treated with a gonadotropin-releasing hormone analog (leuprorelin acetate, Takeda Pharma).

Second Operation. One year later, seizures developed that were refractory to medical treatment; the patient experienced frequent gelastic fits and a developmental de-

Abbreviation used in this paper: HH = hypothalamic hamartoma.

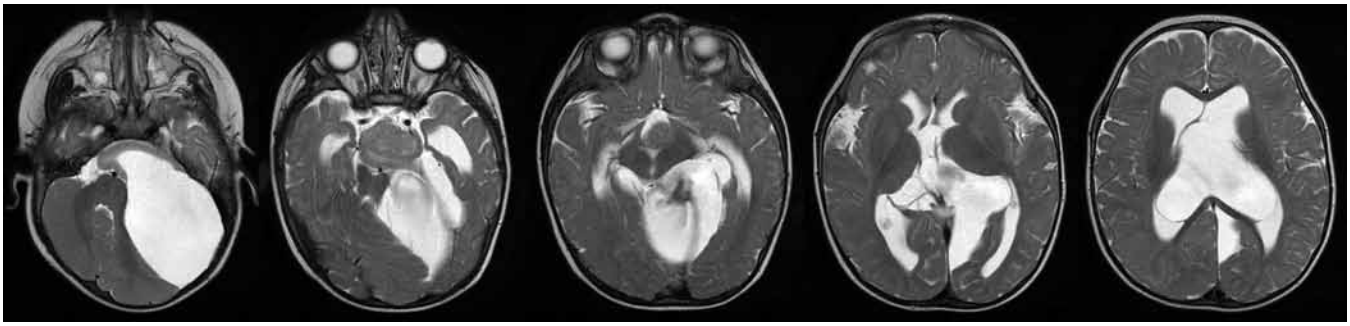

Fig. 1. Axial T2-weighted MR images depicting the large cystic tumor component with space-occupying effect and compression of the left cerebellar hemisphere and dislocation of the brainstem. Also apparent is mild hydrocephalus with widening of the lateral ventricles and the third ventricle.

lay. We decided to undertake a reoperation, transcallosally, with the objective now to disconnect the HH. The dorsal displacement of the brainstem and the hamartoma did not allow a safe total disconnection of the most posterior parts abutting the mammillary bodies (Fig. 2C), but a 50% decrease in seizure frequency was achieved immediately after disconnection. Two weeks after the second operation the boy developed hydrocephalus and a ventriculoperitoneal shunt was inserted.

Postoperative Course and Third Operation. The further development of the boy was quite satisfying and he reached the milestones with a delay of 1–2 months. With increasing seizure frequency 2 years later the boy again experienced a regression in speech development. A third transcallosal operation was performed to complete the disconnection (Fig. 2D). A significant reduction of seizure frequency was achieved (1 episode per month while receiving anticonvulsive medication). The 7-year-old boy still exhibits signs of a severe attention deficit and a delay in speech and motor development. At this time, no additional endocrinological disturbance has been diagnosed.

Discussion

Studies relating to the neuropathology and neurobiology of the HH are limited.[4] Immunohistochemical studies reveal positive staining for neuronal markers, including neuron-specific enolase, synaptophysin, and neurofilament protein, supporting a neuronal phenotype of a great proportion of the cells. A detailed analysis of HH cell characteristics, with respect to the normal hypothalamic cytoarchitecture and immunohistochemistry, demonstrated neuronal elements predominating in most cases and a relative increase in astrocytic elements with increasing age.[4] The hamartomas showed various-sized nodular foci of neurons as well as areas of diffusely distributed pattern. Most HHs are sporadic, and only about 10% are associated with the Pallister-Hall syndrome or other syndromic entities including McKusick-Kaufman syndrome, Bardet-Biedl syndrome, oral-facial-digital syndrome Type 6, and Waardenburg syndrome.[8] The reported prevalence of children and adolescents affected by an HH has been reported to be 1 in 200,000.[2] However, an autopsy study in 1962 demonstrated hamartomatous malformations adjacent to the mammillary bodies in 26 (21.5%) of 121 consecutively investigated brains, indicating that clinically silent HHs may be underreported.[14] No clinical data were reported. The size of these lesions ranged from 0.5 to 1.5 mm in diameter at the base of the lesion. Of note, the authors of the aforementioned study described these lesions as nodules composed of compact and loose glial tissue containing ganglion cells, which were all directly related to a perforating hypothalamic artery.[14]

The mechanism of HH development is still not understood, but several hypotheses exist. One hypothesis is that the hamartoma may result from ectopic localization of otherwise relatively normal cellular elements. This misplacement could be related to defects in cell-cell recognition and cell-matrix interference, which normally guides the cells' neuronal migration along radial glial cells. The absence of the right migratory and proliferation stimuli might lead to an abnormal local brain structure.

A second hypothesis indicates that HH cells are positioned normally but have an abnormal proliferative potential. Immunohistochemical studies focusing on cell lineage may be capable of identifying cells that are themselves intrinsically abnormal, potentially expressing more primitive cell markers, including tumorlike or stem cell–like phenotypes. No data are available at that time to support either of these hypotheses.

At least in our case the large, predominately cystic lesion supports the notion of an abnormal proliferative tumorlike mechanism of origin. Factors determining cystic degeneration include the delicate balance between growth and its perfusion requirements with the underlying angiogenesis. Therefore, an at least temporary highly proliferative phenotype of the hamartoma cells might be the explanation for the large cystic HH in our case. This hypothesis of an ischemic degenerative process was posited by Prasad et al.[12] in a report on 2 giant cystic HHs. In rare cases this proliferative phenotype may persist and result in a hypothalamic hamartoblastoma with more primitive and immature neuronal and glial elements, as described by Clarren et al.[3]

In the postnatal course, the enlargement of the hamartoma is proportional with the normal brain growth, so that the lesion's size does not change in relation to the rest of the brain. This growth pattern is further supported by the observations of a glial predominance with increasing age and a few MIB-1 proliferating glial cells in most of the histologically studied cases by Coons et al.[4] In our

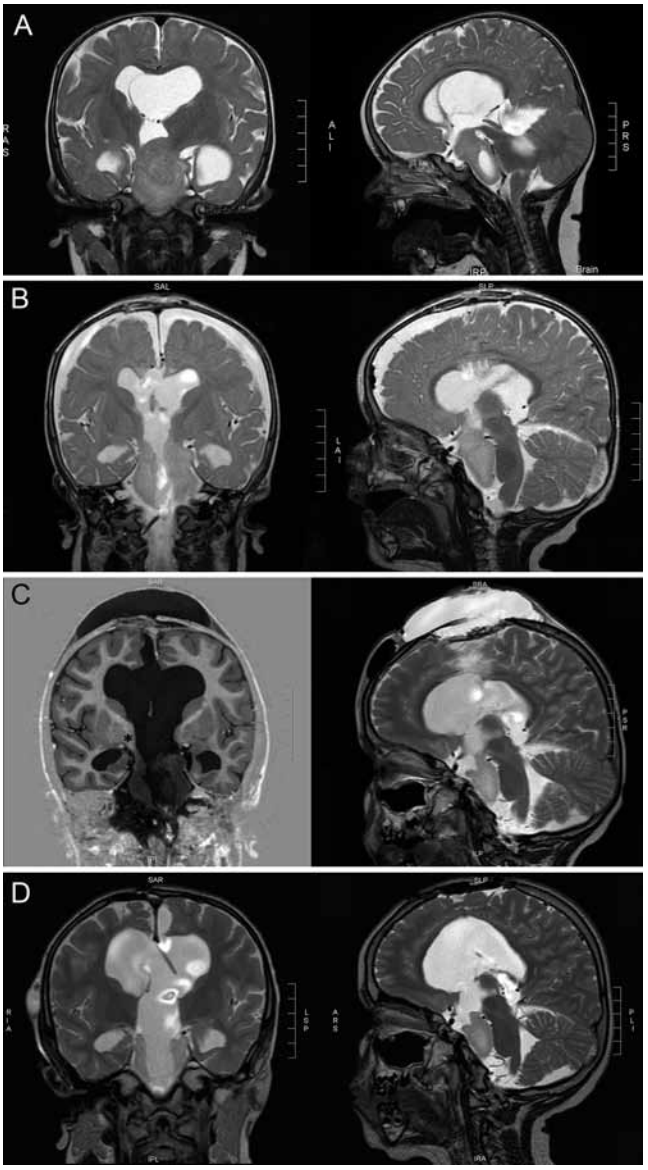

Fig. 2. Coronal and sagittal T2-weighted MR images displaying the solid tumor part as mainly isointense to gray matter–appearing mass, located ventrally to the brainstem. **A:** Images at presentation showing compression of the distal aqueduct by the solid component of the hamartoma anteriorly and the cystic component posteriorly, causing mild hydrocephalus. **B:** Images obtained after the first partial resection, decompression of the aqueduct, and communication of the cyst through the solid part of the HH to the basal cisterns. **C:** Images obtained after second surgery demonstrating right posterior parts of the hamartoma still connected to the hypothalamus *(asterisk)*. **D:** Images obtained after third transcallosal operation demonstrated a completed disconnection.

case the large cystic component may have developed late, as the displaced cerebellum did not exhibit any clear evidence of hypoplasia.

The fact that true HHs never show progression would indicate that these cells only get proliferative stimuli during the proliferative phase of the normal hypothalamic development between the 25th and 41st day postconception,[9] thereby suggesting their developmental vicinity to normal hypothalamic cell lines. The Gli3 transcription

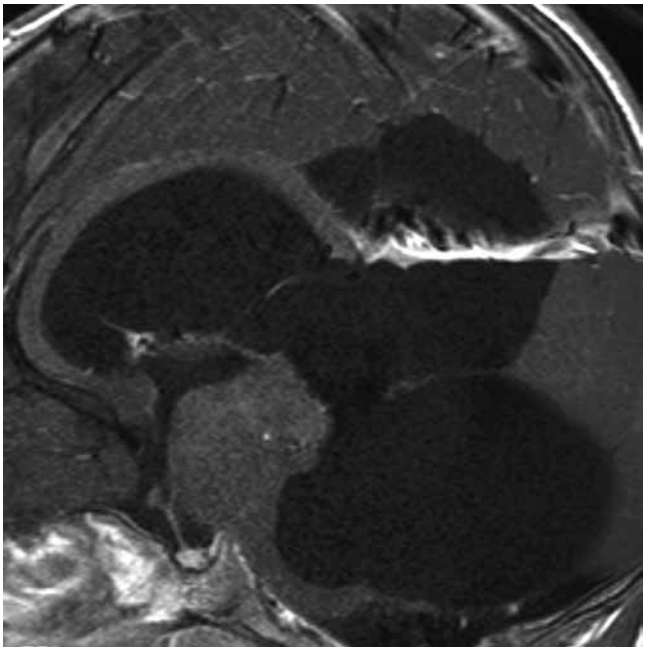

Fig. 3. Sagittal postcontrast T1-weighted MR image. No enhancement is seen; the lesion is isointense to gray matter tissue.

factor gene has been found to be mutated in some patients with HH associated with Pallister-Hall syndrome. With Gli3 being a downstream effector protein of the sonic hedgehog transduction pathway, HH could be related to the spectrum of sonic hedgehog–associated forebrain anomalies.[13]

In addition to immunohistochemical and electrophysiological studies, molecular biology studies of HH will be essential to elucidate the mechanisms of development of these intriguing lesions.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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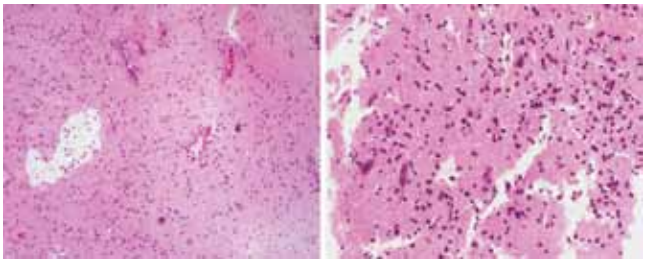

Fig. 4. Hematoxylin and eosin–stained sections of the HH showing dysplastic neurons clustering in nodular foci. Original magnification × 10 **(left)** and × 20 **(right)**.

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Egas Moniz (1874–1955) and the "invention" of modern psychosurgery: a historical and ethical reanalysis under special consideration of Portuguese original sources

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The Portuguese neurologist Egas Moniz (1874–1955) is often regarded as the founder of psychosurgery. He performed the first prefrontal leukotomy in 1935—about 75 years ago—with the help of neurosurgeon Almeida Lima (1903–1985). In contrast to the psychosurgical interventions performed by the Swiss psychiatrist Gottlieb Burckhardt (1836–1907), Moniz's interventions on the white brain substance caught great attention worldwide. As a matter of fact, it was this repercussion that led to the award of the Nobel Prize for Medicine in 1949, an award that is still highly controversial today.

The goal of the present article is to reconstruct the historical background of the first leukotomies, the tangible expert debate since 1935 on the indication and legitimacy of these interventions, and their contemporary and recent (ethical) evaluation. Special focus will be set on the original Portuguese literature, which has been given too little attention thus far in the English-language literature. *(DOI: 10.3171/2010.10.FOCUS10214)*

Key Words • Moniz • Burckhardt • psychosurgery • leukotomy • Portuguese literature • ethical discourse

The term "psychosurgery" describes interventions on the morphologically unobtrusive brain with the goal to exert influence on the psychological experience and behavior. The beginnings of the surgeries, which are regarded as highly controversial today, date back to the second half of the 19th century. It was the Swiss psychiatrist Gottlieb Burckhardt who performed the first psychosurgical interventions at Neuchâtel in 1888.[24,35,37] In the English-language literature, these interventions were hardly taken notice of, but in the German-speaking area, this unequalled advance was often consciously received with disregard.[8,38,51] This was possibly why Burckhardt discontinued the intended surgeries,[12] and it explains why the Portuguese neurologist Egas Moniz is often regarded as the actual founder of psychosurgery.[35] He performed the first prefrontal leukotomy with the help of neurosurgeon Almeida Lima (1903–1985) in 1935. Moniz's interventions met with great response worldwide and led to the award of the Nobel Prize for Medicine in 1949, an award that met strong criticism early on.

Egas Moniz and the Historical Background of Leukotomy

António Caetano de Abreu Freire Egas Moniz (Fig. 1) was born in Avanca, a small village in northern Portugal, in 1874.[16,17,35,40] After attending school, he enrolled at the University of Coimbra in 1891, where he graduated with honors in medicine in 1899, following a 3-year preparatory course.[10] In 1902, Moniz started his university career as lecturer in Coimbra.[9] For the time being, his career reached its peak in 1911 with a call to a newly established chair for neurology in Lisbon.[9] After shortly entering politics (Moniz, among other posts, was Portuguese minister of foreign affairs from 1918 through 1919[50]), he dedicated his time to a series of experiments in the early 1920s, which led to the first performance of cerebral angiography in a patient.[42]

He presented his experiments only a few days after the first successful recording in Paris to an enthusiastic audience. The works concerned led to the first nomination for the Nobel Prize for Medicine in 1928.[7]

Early Experiments

The leukotomy Moniz developed and dedicated his time to in the 1930s, however, caused a much greater stir than the angiography.[45] While outlining preliminary reflections, he attached special importance to Ramón y Cajal (1852–1934), who had discovered the contact connections between nerve cells in a histological specimen in 1888.[31] Moniz[45] assumed that mental disorders originated from synaptic disorders. He described a "fixation of synapses,"[47] which were expressed as "predominant, obsessive ideas" in mentally ill persons, which in turn "absorbed" other mental activities. Similar tendency supposedly existed in healthy persons, for example, when learning an activity that at first

Fig. 1. Photograph of Egas Moniz, date unknown. Source: http://Nobelprize.org.

caused difficulties but could be performed automatically at a later time.[45] In this case, the nerve excitation could be changeable as proven by the experiments of the Russian physiologist Iwan Petrowitsch Pavlov (1849–1936).[45] Pavlov's experiments in dogs and the resulting theory on the "conditional reflexes"[27,34] (classic conditioning) were received worldwide.

Moniz[45] also described the experiments conducted on chimpanzees by Fulton and Jacobson as "extremely valuable." In 1935, the 2 British physiologists had presented the results of their research in London; they had explored the importance of the frontal brain in relation to the ability to solve problems and learning processes.

After a double-sided extraction of parts of the frontal brain, the monkeys were not able to perform certain tasks or to relearn them. As an additional finding, 1 female chimpanzee displayed changes in character. Whereas she had to be forced to enter the experiment cage prior to the operation, she now entered it voluntarily and with interest after the operation on the frontal brain.[28–30,65]

Moniz[46] also recorded experiences with patients who had been wounded during war and had suffered lesions of the frontal brain and who featured, among others, "changes in character and personality." Here, he especially referred to the work of Karl Kleist (1879–1960)[47] and Richard Brickner (1896–1959).[41,43,45–47,49]

The Decision

Based on the reading of specialist literature and on his own experience, Moniz is said to have come to the conclusion that it was necessary to "change the synaptic facilities and also the path which is chosen by the stimuli in their continuous process, in order to change the corresponding thoughts and to force them into other channels. For this reason,… I decided to cut the connecting fibers of the neurons concerned."[43]

Moniz also expressed his thoughts and plans to Barahona Fernandes,[9] who later reported how long Moniz had thought that one could attain an improvement of the illness if the nerve fibers in the depth of the white mass of the frontal lobe were separated surgically.

It is striking how much Moniz retrospectively stressed that he had prepared his decision for a long time to counteract the accusation of an imprudent, hasty, and precipitated action. It is more probable that a speech of the American John Fulton (1899–1960) at a neurology convention in 1935 gave the first and decisive impetus to Moniz's work in this area.[22] Moniz soon instructed his long-time staff member Almeida Lima (1903–1985) to test the procedure on a heterogeneous group of 20 psychiatric patients; they mostly featured clinical pictures such as schizophrenia, cyclothymia, and anxiety neurosis. Moniz would not have been able to perform the surgeries himself as his hands were deformed by gout.[18] Even so, Lima saw himself only as an "instrument handled by the Master."[7,15] Sobral Cid, director of the psychiatric clinic Bombarda in Lisbon, provided Moniz with patients from his clinic for the first surgical trials.[7] Barahona Fernandes[9] was ordered by his "old teacher," as he would call Moniz, to perform a psychiatric evaluation on the first 20 patients who had undergone leukotomy.

The Era of Modern Psychosurgery Through the Conferral of the Nobel Prize (1935–1949)

The surgeries took place under general anesthesia. Ten of the first 20 surgeries were conducted by Lima, who was instructed by Moniz, through injection of alcohol. Later, Moniz and Lima developed an alternative procedure with the leukotome, which consisted of an 11-cm-long cannula with an outer diameter of 2 mm. Five millimeters before the closed, rounded end of the cannula, there was a retractable wire loop. By rotating the wire loop, one could separate part of the white brain substance.[48]

First, the leukotome was inserted 4 cm into the white substance, the wire loop was retracted, and by rotating the instrument against a "résistance typique,"[48] the nerve fiber tissue was cut. When closed, the leukotome was retracted about 1 or 1.5 cm, and the procedure was repeated. This way, lesions were set on both sides in both directions—a total of 8 during the entire surgery.[48]

Moniz's inaccurate description of the technical parameters, lacking angle values and variable depths of insertion, gives us an idea of how different the morphological results of the brain must have been. He presented his results on March 3, 1936 (less than 4 weeks after starting operations), in Paris to an expert audience; a few weeks later, the results were published in the *Bulletin de*

l'Académie de Médecine.[44] In addition, Moniz wrote the monograph *Tentatives operatoires dans le traitement de certaines psychoses*, in which he not only explained the operation method and summarized the results but also documented case descriptions.[48]

If we believe in the summary published by Moniz[48] of the first 20 operations, the results look promising: "35% (seven cases) healed, 35% (seven cases) improved, 30% (six cases) unchanged, no worsening, no cases of death." Categorized according to diagnoses, of the group of 5 cases of "Mélancolie anxieuse," 4 cases resolved and 1 improved. However, of the 7 cases of schizophrenia, only 2 improved and 5 were unchanged. Although undesirable effects arose in almost every intervention, they were only described as temporary. These were, in particular, increased temperature, vomiting, bladder and bowel incontinence, diarrhea, and ocular affections such as ptosis and nystagmus, as well as psychological effects such as apathy, akinesia, lethargy, timing and local disorientation, kleptomania, and abnormal sensations of hunger.[48] Moniz did not admit to having detected a decrease in intelligence and memory performance, whereby it is unclear how he could have come to this conclusion.[48]

Development of Leukotomy

In 1936 and 1937, Moniz published 12 articles on leukotomy in international academic journals. In 1936, he published his monograph and 5 articles in French and Portuguese, in 1937, he published 3 articles in French and 1 each in English, Italian, and German. In addition, an editorial in the *New England Journal of Medicine* referred to Moniz's surgeries in 1936.[5] The number of interventions under the leadership of Egas Moniz amounted to about 100.[18]

Undoubtedly, Moniz's leukotomy belongs to the most respected medical innovations of the first half of the 20th century. Among former advocates of Moniz's method, one person is especially striking: Walter Freeman (1895–1972). Freeman made a substantial contribution to the popularization of Moniz's procedure within the expert community and also conducted several psychosurgical interventions himself. As early as 1937, Freeman and Watts[19,20] reported on 6 patients whom they had surgically treated according to the Moniz method. Walter Freeman and James Watts later modified the method, which was then known by lobotomy and used in many regions of the world until 1955, in particular in the Anglo-American area.[21] Freeman not only increased his own popularity with his works but also the level of awareness of Egas Moniz, whom Freeman referred to as the pioneer of psychosurgery, in a book by Freeman et al.[21] that was published in 1942 and appreciated by Moniz as "magnífico volume" (magnificent work).[41]

In 1948, at the First International Conference on Psychosurgery in Lisbon, the Brazilian delegation was also pleased with the "good results" of Moniz's leukotomy.[68] The delegation reported on more than 200 leukotomies performed in Brazil between 1936 and 1945: 21 of 143 schizophrenic patients had reached "complete or social recovery" after operative treatment according to the Moniz method, whereas only 3 of 46 patients treated with the Freeman parietal lobotomy displayed similar results. The Brazilian Yahn[69] reported further on his leukotomy experiments on a total of 9 children, 2 of whom died of hemorrhages. One is described as "bastante influenciado" (very influenced), 4 others as "parcialmente influenciado" (partially influenced), and 2 as "não influenciados" (not influenced).[36]

The Nobel Prize

The Brazilians were also the ones who recommended Moniz for the Nobel Prize and who generated a proposal for this purpose at the psychosurgical convention. Moniz was awarded the Nobel Prize for Medicine on October 27, 1949,[3] for the "discovery of the therapeutic value of prefrontal leukotomy at certain psychoses." In his laudatory speech, Herbert Olivecrona (1891–1980), member of the professorial staff of the Karolinska Institute, described Moniz's therapeutic procedure as follows: "Many of these patients, in particular the group of schizophrenic, are very difficult patients and often constitute a danger to the persons in their surroundings. Considering that other treatment methods have failed or that after some time there had been a relapse, the immense importance of Moniz's discovery for the problematic issue of psychiatric treatment is understandable."[3]

The news of the Nobel Prize award made headlines around the world. On October 28, 1949, the *New York Herald Tribune* announced, "Dr. Egas Moniz developed a surgical operation on the brain…with brilliant results against such mental illnesses as schizophrenia and paranois."[4] The journal *Nature* made the following statement regarding the award on December 3, 1949: "[Moniz] has demonstrated that skilful intervention may yield a degree of success even in the most serious and advanced cases of psychosis."[2,55]

The Portuguese neurologist had reached the peak of his career. Antunes[7] estimated the number of interventions performed based on their psychiatric indication between 1942 and 1954 in Great Britain to be about 11,000; in the US, it was at least 18,000[23] for the same period of time as was probably closer to 50,000.[7,60] Besides the US and Great Britain, at this time the romance-language and Eastern European countries in particular arose as advocates of psychosurgical interventions, namely Portugal, Italy, France, and Spain, as well as Russia and Hungary.[60]

Leukotomy Under Fire From Critics

As early as the time of the award of the Nobel Prize to Moniz, psychosurgery was already regarded as controversial.[11] For example, Galeano Muñoz und Arana Iñiguez (Uruguay) criticized Moniz's interpretations in 1949: "The principles on which Egas Moniz bases his conceptions are the existence of dynamic automatism to which he assigns a determinated [sic] nervous path. There is nothing to allow such a supposition. Psychological activity is global, not in the excitation processes but also in those of concommittend [sic] inhibition…."[13,52]

The harsh ethical criticism expressed by the German psychiatrist Siegfried Haddenbrock[25] is paradigmatic. In

1949, he turned against the measures of the psychosurgeons by equating leukotomy with a "definitive destruction of the self-confident and free personality of the human being."

Although the award of the Nobel Prize to psychosurgeon Moniz is surprising from today's point of view, it must be seen in the context of its time. Following the world economical crisis and, in many respects, the traumatizing World War I, the number of psychiatric illnesses increased dramatically in many regions of the world. At the same time, there was no effective medication available worldwide, unlike today.

Only during the midcentury was chlorpromazine brought to the market as an effective psychotropic drug, and several years went by to gain sufficient experience with the application of psychotropic drugs (indication, dose, side effects, and interactions). By the time of the award to Moniz, lobotomy appeared to be the only treatment method that promised help in severe cases, although it did not prove to have a curative effect.

Increasing Criticism

The criticism against Moniz's intervention and the decision of the Nobel Prize committee increased quickly after 1949. Despite the often-expressed fundamental reservations about psychosurgical interventions, the technical procedure—that is, that the operations were merely performed by eye—was also discredited. A new stereotactic surgery method was presented in Lisbon as early as 1948, which consisted of a target insertion of the instrument into the brain after prior stereometric determination and calculation of the target area. This procedure allowed the targeting of smaller, more determined brain areas and limiting of lesions of neurosurgical interventions.[1,26] However, this technique underwent a longer period of improvement and propagation; thus, "free" leukotomies and lobotomies dominated until at least the mid-1950s. In the early 1960s at the latest, psychosurgery experienced a withdrawal worldwide, mostly as a result of the increasing number of effective psychotropic drugs. Nonetheless, wherever it was practiced, stereotactic interventions dominated.

In the last third of the 20th century, the fundamental criticism against psychosurgery reached its peak. One such critic was the American psychologist Elliot Valenstein, who discussed Moniz's biography and his first leukotomy operations in his monograph of 1986: He described Moniz's theoretical considerations as "vague and loosely reasoned argument[s]," his approach to a solution as not oriented on theory: "the logic of his arguments was typically weak if not fallacious."[65] Valenstein[65] saw the reason why Moniz hardly faced public criticism in his high reputation as former Portuguese minister of foreign affairs and in his position as founder of cerebral angiography. He also referred to the great hastiness of Moniz in publishing his first results and attributed it to his age: "He was, after all, over sixty, and had not many years left to achieve a place in history."[65] Another reason for Moniz's rush, according to Valenstein, was the competition with other scientists, for example, Maurice Ducoste, who in 1932 injected blood into the frontal brain of his patients as expansion of Jauregg's fever therapy to treat progressive paralysis, or the Italian Ody,[54] who in 1938 was said to have performed operations upon psychiatric indication on the frontal brain months before receiving Moniz's monograph and to have waited with his own publications.[65,66]

The criticism expressed by the British neurologist and author Oliver Sacks is also quite drastic: "[Moniz's] lack of rigor, his recklessness, and perhaps dishonesty were all overlooked in the flush of therapeutic enthusiasm…. Moniz was widely acclaimed as a 'savior' and received the Nobel Prize in 1951 [sic] – the climax…of 'this chronicle of shame'."[59]

With reference to the continuous expert criticism against psychosurgery and its most renowned exponent Egas Moniz, an international initiative for persons affected by psychosurgical interventions and their families was started, which aims for social rehabilitation of persons affected and the disqualification of the Nobel Prize to Moniz by the Stockholm committee. However, this initiative has been mostly unsuccessful thus far.[62]

Conclusions

In retrospect, there are convincing arguments that disavow Moniz's interventions from a clinical and ethical view.

Efficacy and Informed Consent

One must refer to 2 aspects that were hardly considered by Moniz: the medical efficacy of the method and informed consent. It can be demonstrated without a doubt that, according to modern standards, no evidence whatsoever could be shown for the efficacy of leukotomies considering the heterogeneous composition and small number of leukotomized patients in the first operation series, the differing and variable techniques used, and the purely subjective and nonstandardized interpretation of results. In addition, the concluding examinations took place only a few days or weeks after the operation. Midterm or long-term observations over months or years did not occur. Moniz could not or would not report on social or familial integration, the reintroduction to professional life, and a sustainable improvement or healing.

The patient's right to self-determination was not taken into account. Departing from this principle, therapeutic intervention on mentally ill patients could only be performed with the valid consent of the patient or (when decision-making ability was missing) of a legal representative.[53] Nowadays, research on persons without decision-making ability—which would encompass most of Moniz's patients—is bound to strong criteria. Against this background, it is explainable why, for example, an investigative committee of the American Congress recommended in 1974 that psychosurgical measures were not to be used on jailed inmates, on persons with forced hospitalization in psychiatric institutions, on persons with limited legal capacity, or on persons for whom the controlling committee has the impression they are not capable of well-informed consent. Said recommendation, however, allowed for the exception that a legal representative could

consent to an operation if the patient did not deny it at the same time.[1,61] The basis for a consent by the legal representative had to be his or her commitment to consider the interests, wishes, and life plans of the person concerned to the best of his or her knowledge and to make decisions that the patient would have made.[32]

Historical Context

Concepts of health and illness and their ethical evaluation are always subject to the influences of their time and the relating spirit of the time.[57] In view of this, it is not enough to compare the leukotomy operations of the 1930s and 1940s of the 20th century with the interventions exact to the millimeter and minimal invasive possible today and to qualify them prematurely as "coarse"[1] and immature.

It is also not possible to easily apply our modern view of proof of efficacy and informed consent to this time period. In the same way, we cannot deny Egas Moniz's wish to contribute to the healing of chronically ill persons a priori, that is, without closer look at his picture of the patient and his procedure. His reference to the missing therapeutic possibilities of his time (he spoke of "impotência terapeutica"[39]) is true. In the first half of the 20th century, there was an enormous increase in internments into psychiatric institutions; thus, a therapy that promised improvement seemed to be urgent and was therefore gratefully received.

The overcrowding of institutions and the resulting inadequate hygienic conditions quickly led to a spreading of tuberculosis and other infectious diseases. Swayze[63] estimated the mortality of these diseases of manic-depressive patients after a 15-year stay in an institution for the said period to be 17.7% and for patients with dementia praecox at 25%. Effective therapeutic alternatives such as the application of psychotropic drugs were not yet available at that time.[67]

Position Toward the Patients

What was Egas Moniz's perception of the physician-patient relationship? What was his position toward the patients? Moniz[39] wrote a monograph in 1954—a year before his death—in which he stated the different positions that were mostly taken by theologians. Moniz recurred to the opinion of a Jesuit priest named Tesson, according to which the physician had no right to intervention if the patient did not agree to it, even if the family had recommended it. However, if the patient was mentally ill and could not make a decision him- or herself—so the limitation—the family and the physician could make a decision. In this statement, it is not clear whether mentally ill persons were in principle denied the capability of consent and if the authority to decide in these cases was given to the physician or the family or both.

Latent Euphoria?

It is highly interesting to understand how not only the general basic position toward leukotomy but also of the persons responsible changed over time. After initial excitement, which led to the award of the Nobel Prize in 1949, the public criticism against leukotomy reached a temporary peak in the late 1970s.[6,32,33] As a consequence, the pressure to provide justification by its advocates was extremely high. In contrast to this, Moniz and his scientific work have recently been connoted in a positive way, especially in Portugal. As shown by the 50th anniversary of the award of the Nobel Prize to Moniz in 1999 and the edition of the special stamp in his honor, he is highly revered in his country (Fig. 2). At the same time, leukotomy is designated as a procedure of "apparent importance and validity" by individual authors.[64] The latent euphoria transpiring is alarming. On the one hand, the debate of the 1970s is rated as "virtual cessation of psychosurgical procedure,"[56] whereas on the other hand, psychosurgery is currently seen as "probably underutilized"[58] and the modern technique characterized as "minimally invasive and highly selective."[14]

Fig. 2. Portugese stamp from 1974 honoring Egas Moniz.

In light of this, a critical comment made by Feldman and Goodrich[14] strikes a reflective chord: "…economic pressures to decrease the costs of caring for chronically ill patients, may provide an opportunity for psychosurgery to become a more attractive option for the treatment of psychiatric diseases." If the authors are correct in their prediction, medicine and society will indeed be facing new challenges.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: both authors. Acquisition of data: both authors. Analysis and interpretation of data: both authors. Drafting the article: both authors. Critically revising the article: both authors. Reviewed final version of the manuscript and approved it for submission: both authors.

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Abstracts of the 2011 AANS/CNS Cerebrovascular Section Meeting February 2011

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1. Cavernous Malformation Of Brainstem, Thalamus And Basal Ganglia- A Series Of 176 Patients

Paritosh Pandey, MD; Erick Michael Westbroeck; Gary Steinberg, MD, PhD (Stanford, CA)

Introduction: Deep cavernous malformations account for around 9 to 35% of all intracranial CMs.

Methods: Between 1990- 2009, 176 patients were operated by the senior author (GKS) at Stanford University, and were reviewed retrospectively.

Results: There were 176 patients with 179 CMs (75 M, 101 F, 3m–72 years, mean 39.2 years, 20 pediatric). 136 CMs were in brainstem, 27 in basal ganglia, and 16 in thalamus. Cranial neuropathy (51.1%), hemiparesis (40.9%), numbness (34.7% and ataxia (38.6%) were the presenting symptoms. 172 patients presented with clinical hemorrhage. The annual retrospective clinical hemorrhage rate was 5.1%, while the clinical rebleed rate was 31.5%/year. Thirteen patients received previous radiation therapy, 10 had previous surgery. Surgical approach was determined according to proximity to pial/ependymal surface. Postoperatively, 121 patients (68.7%) had no new deficits. The commonest complications were ataxia (21), diplopia (25), hemiparesis (22), and 7th nerve paresis (10). Overall, 34 patients (19.3%) improved, 55 (31.3%) worsened, and 86 (48.9%) remained the same. Follow-up was available in 170 patients (0.5-19 yrs, mean 3.5 years). 105 patients (59.7%) patients improved, 44 (24.4%) remained same and 20 (11.3%) were worse at follow-up attributable to surgery. The mean mRS was 1.6 compared to 2.2 preoperatively. Good preoperative mRS and single hemorrhage were predictors of good outcome. Thirty patients (17%) had poor outcome (mRS 3-6). Only 2 patients (1.8%) in good neurological status preoperatively had poor outcome. Eight patients died at long-term follow-up.

Conclusions: Symptomatic deep CMs can be resected with acceptable morbidity and good results.

2. Effect Of Intracranial Pressure (ICP) Versus ICP Wave Amplitude Guided Intensive Care Management On Acute Clinical State And 12 Months Outcome In Patients With Aneurysmal Subarachnoid Hemorrhage. A Randomized And Blinded Single-Center Trial

Per K. Eide, PhD, MD; Gunnar Bentsen, PhD, MD; Angelika Sorteberg, PhD, MD; Paal Bache Martinsen, MD; Audun Stubhaug, PhD, MD; Wilhelm Sorteberg, PhD, MD (Norway, Oslo)

Introduction: This clinical trial explored the effect on acute clinical state and outcome of mean intracranial pressure (ICP) - versus mean ICP wave amplitude (MWA) guided intensive care management in patients with aneurysmal subarachnoid hemorrhage (SAH).

Methods: A randomized and blinded single-center trial (ClinicalTrials.gov: NCT00248690) enrolled aneurysmal SAH patients during the time period November 2005 - January 2008. Patients were randomized to two different types of management: maintenance of mean ICP <20 mmHg or MWA <5 mmHg. Primary outcome measures were daily acute clinical state according to Glasgow Coma Scale (GCS) in non-intubated patients and outcome in all patients after 12 months as assessed by the Rankin Stroke Score (RSS)

Results: Ninety seven patients were included in the study. The only management modality that differed between the two treatment groups was the volume of CSF drainage during the first week. Both the mean ICP and mean ICP wave amplitude were significantly lower during this week in the MWA group. The GCS during weeks 1-3 was nearly significantly higher in the MWA group (P=0.065). RSS in all patients at 12 months were significantly better in the MWA.

Conclusions: Lowering of mean ICP and mean ICP wave amplitude through extensive CSF drainage during the first week improves outcome at 12 months afteraneurysmal SAH. Management is crucial during the first week and should be aimed at lowering ICP wave amplitude. Thereby the functional outcome of SAH can be improved. There possibly exists a functional penumbra that can be rescued or lost early after an aneurysm bleed.

3. Intracranial Venous Sinus Stenting For Benign Intracranial Hypertension: Clinical Indications, Technique, And Preliminary Results

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Introduction: The cause of pseudotumor cerebri, or benign intracranial hypertension (BIH), is controversial. We report our results from 18 cases of venous sinus stenting (VSS), the largest series in the literature, with specific focus on the rate of technical success, amelioration of the subjective symptom of headache, attendant complications, and radiographic patency on follow-up.

Methods: Review of our prospectively maintained database identified 18 patients who had undergone 19 VSS procedures for the placement of 30 stents in the last 2.5 years. Indications for treatment included a clinical diagnosis of BIH with venographic demonstration of stenosis.

Results: VSS was technically successful in all patients (100%). No patient suffered a permanent complication. Three patients were lost to follow-up. The remaining 15 patients were followed clinically and asked to rate their headache severity on a scale of 1 to 10 both before and after VSS. Overall, 12 patients (80%) qualified their headaches as better after VSS, 2 stated that they were the same, and 1 said that they were worse. Of 14 patients who underwent follow-up angiography, all demonstrated normal patency of the stented segments. In 1 of these patients, stenosis was detected on follow-up in the unstented segment of the sigmoid sinus and jugular bulb.

Conclusions: VSS is highly effective (80%) in ameliorating headache associated with BIH. The procedure is associated with a high rate of technical success (100%), a low rate of permanent complications (0%) and a high rate of stent patency on follow-up angiography (100%).

4. Carotid Endarterectomy Versus Stenting: A Meta-Analysis

Daniel Yavin, MD; Derek Roberts, MD; Micheal Tso, MD; Garnette Sutherland, MD; John H. Wong, MD, MSc (Canada, Calgary)

Introduction: A meta-analysis of randomized controlled trials (RCTs) was conducted to update the available evidence on the safety and efficacy of carotid endarterectomy (CEA) versus carotid artery stenting (CAS) in the treatment of carotid artery stenosis.

Methods: A comprehensive search was performed of MEDLINE, EMBASE, CENTRAL, bibliographies of included articles and past systematic reviews, andabstract lists of recent scientific conferences. For each reported outcome, a Mantel-Haenszel random-effects model

was used to calculate odds ratios (ORs) and 95% confidence intervals (CI). The I2 statistic was used as a measure of heterogeneity.

Results: Twelve RCTs enrolling 6,973 patients were included in the meta-analysis. Carotid artery stenting was associated with a significantly greater odds of periprocedural stroke (OR 1.72, 95% CI 1.20 to 2.47) and a significantly lower odds of periprocedural myocardial infarction (OR 0.47, 95% CI 0.29 to 0.78) and cranial neuropathy (OR 0.08, 95% CI, 0.04 to 0.16). The odds of periprocedural death (OR 1.11, 95% CI 0.56 to 2.18), target vessel restenosis (OR 1.95, 95% CI 0.63 to 6.06), and access-related hematoma were similar following either intervention (OR 0.60, 95% CI 0.30 to 1.21).

Conclusions: n comparison with CEA, CAS is associated with a greater odds of stroke and a lower odds of myocardial infarction. While the results our meta-analysis support the continued use of CEA as the standard of care in the treatment of carotid artery stenosis, CAS is a viable alternative in patients at elevated risk of cardiac complications.

5. Understanding Ischemic Events After Extracranial-intracranial Bypass For Moyamoya

Terry C. Burns, MD, PhD; Nadia Khan, MD; Maziyar Kalani, MD; Elma Tunovic; Raymond Choi; Gary K. Steinberg, MD, PhD (Stanford, CA)

Introduction: EC-IC bypass is a means of providing additional collateral blood supply to patients with Moyamoya disease. Post-operative stroke is a known potential complication of EC-IC bypass. Factors correlating with increased risk of post-operative infarct remain to be determined.

Methods: Intra-operative graft flow data and hemodynamic parameters were reviewed retrospectively and correlated with presence and location of post-operative ischemic lesions on MRI.

Results: From the records of over 780 bypass procedures, we identified 14 adult patients with post-operative infarcts in a predominantly watershed distribution and 22 adult patients with infarcts occurring predominantly within a major vascular territory. A group of 133 patients with verified normal post-operative MRIs served as controls. Flow in the bypass graft, as measured intraoperatively after anastamosis, was significantly higher in patients who developed watershed infarcts (34.56cc/min), than controls (22.83cc/min, $p<0.005$). By contrast, graft flow in patients who developed territory infarcts, was quite similar to controls (22.79cc/min). Intra-operative mean arterial pressure was higher, both before and after anastamosis in patients who developed vascular territory infarcts (91.4, 90.6), compared to controls (82.3, 82.2, $p<0.005$). By contrast, mean arterial pressure in patents who developed watershed infarcts (84.6, 85.5), was not significantly different than controls.

Conclusions: Distinct differences in intra-operative graft flow and blood pressure are observed in patients who develop post-operative watershed infarcts versus vascular territory infarcts, when compared to controls. Attention to such parameters may facilitate the development of management strategies to minimize the risk of post-operative ischemic injury.

6. Impact Of The Infarct Size On The Efficacy Of Neural Stem Cell Transplants In Experimental Stroke Model

Marcel Daadi, PhD; Shijun Hu, PhD; Jill Klausner, BA, MS, BS; Zongjin Li, PhD; Joseph Wu, MD, PhD; Gary Steinberg, MD, PhD (Stanford, CA)

Introduction: The clinical applications of cell transplantation as a therapeutic strategy for brain repair require an in depth understanding of the mechanisms of stem cell-mediated functional recovery. This study was undertaken to longitudinally analyze the reparative potential of cell transplantation therapy in moderate and large strokes.

Methods: Self-renewable and multipotent NSCs were isolated from hESC based on their responsiveness to mitogenic growth factors. For the MR imaging, undifferentiated NSCs were incubated with superparamagnetic iron oxides particles in the presence of Poly-l-lysine. Rats were subjected to middle cerebral artery occlusion for 65 minutes. Labeled cells were suspended at a concentration of 50,000 cell/μl and stereotaxically grafted into the stroke boundary zone, two weeks post stroke.

Results: Graft survival was monitored biweekly using T2-weighted MR imaging for 3 months. Volumetric analysis of the stroke and the NSC grafts in the moderate stoke demonstrated a significant reduction over ten weeks by 73.2+/- 11.7% of the infarct volume in comparison to large infarct ($P<0.001$). Larger infarcts increased in volume by 2.4% over ten weeks. In addition, there was a significant reduction in infarct volume in the NSC-treated group in comparison to vehicle animals with moderate stroke ($P<0.001$). Grafted cells differentiated into neurons astrocytes and oligodendrocytes in the peri-infarct region.

Conclusions: These studies suggest that neural stem cells are more efficacious in moderate than larger infarct and that MR imaging provides reliable means to monitor and analyze in real time the stroke evolution in relation to NSC grafts. Synthetic extracellular matrices may increase grafts efficacy in larger strokes.

7. A Single Center Comparison Of Coiling Versus Stent-assisted Coiling In 90 Consecutive Paraophthalmic Region Aneurysms

Geoffrey P. Colby, MD, PhD; Alexandra Paul, BS; Martin Radvany, MD; Dheeraj Gandhi, MD; Philippe Gailloud, MD; Judy Huang, MD; Rafael Tamargo, MD; Alexander Coon, MD (Baltimore, MD)

Introduction: Aneurysm recurrence is a principle limitation of endovascular coiling procedures, with recurrence rates reported > 30%. The adjunct use of self-expandable stents has revolutionized the treatment of intracranial aneurysms, especially for complex morphologies, wide necks, or unfavorable dome to neck ratios. However, further investigation into the durability and outcomes of stent-assisted coiling procedures is required.

Methods: We retrospectively reviewed the records of a prospective single-center aneurysm database and identified 90 consecutive patients with paraophthalmic aneurysms who underwent coil embolization, 30 of which included stent placement. Patient demographics, aneurysm characteristics, coil packing density, angiographic results (initial and follow-up) were analyzed.

Results: Complete aneurysm occlusion was obtained on initial angiography in 13/30 (43.3%) stented and 19/60 (31.7%) nonstented patients. At = 24 months (mean follow-up 12.8 ± 6.2 months for stented and 12.8 ± 6.6 months for nonstented), aneurysm recurrence occurred in 3/26 (11.5%) stented and 14/39 (35.9%) nonstented patients ($p<0.05$). At longest follow-up (mean 14.5 ± 12.5 months for stented and 37.6 ± 35.3 months for nonstented), aneurysm recurrence occurred in 4/26 (15.4%) stented and 17/41 (41.5%) nonstented patients ($p< 0.03$). There was no statistically significant correlation between recurrence and aneurysm size or coiling packing.

Conclusions: Following endovascular coil embolization of paraophthalmic region aneurysms, recurrence rates at 2 years are significantly lower in patients that had stent-assisted coiling (11.5%) as compared to patients that had coiling procedures without the use of a stent (35.9%). Aneurysm size and coiling packing density did not significantly affect recurrence in our study population.

8. Endovascular Embolization Of Unruptured Intracranial Aneurysms With Onyx HD-500: Modified Technique Using Continuous Balloon Occlusion

Ralph Rahme, MD; Todd A. Abruzzo, MD; Usman Khan, MD; Andrew J. Ringer, MD (Cincinnati, OH)

Introduction: Conventional Onyx HD-500 aneurysm embolization technique involves interrupted cycles of balloon inflation-deflation resulting in 3 to 5-minute periods of parent artery occlusion. This

protects the parent artery from Onyx leakage while minimizing cerebral ischemia. However, intermittent balloon deflation may lengthen procedure time and permit balloon migration causing intimal injury or Onyx leakage. We describe a modified technique using continuous balloon inflation (CBI) under conscious sedation and close monitoring of neurological status.

Methods: Procedure time, angiographic results, and clinical complications were analyzed for all cases of Onyx HD-500 aneurysm embolization using the modified CBI technique performed at our institution between September 2008 and November 2009.

Results: Twenty patients with 21 unruptured saccular aneurysms were treated using this technique. There were 20 internal carotid artery aneurysms (11 paraclinoid, 7 communicating segment, 2 petrous) and 1 vertebral artery aneurysm. Aneurysm size varied from 3 to 20 mm and neck breadth from 2 to 8 mm. Two aneurysms had recanalized following stent-assisted coiling and 1 after previous Onyx embolization. Adjunct coils were used in 3 cases and stent in 1. Complete occlusion was achieved in 18 aneurysms and subtotal occlusion in 3. Mean procedure duration was 168 minutes and fluoroscopy time 42 minutes. Unintentional Onyx leakage into the parent artery occurred in 3 patients, 1 of whom had asymptomatic distal emboli. Delayed parent vessel compromise occurred in 1 case at 5 months. There was no mortality or permanent morbidity.

Conclusion: The modified CBI technique with conscious sedation permits safe and effective Onyx HD-500 embolization of unruptured saccular aneurysms.

9. Brain Oxygen-directed Management In Poor-grade Subarachnoid Hemorrhage Patients

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Introduction: The detection of brain hypoxia is now possible with continuous brain oxygen (PbtO2) monitoring, although treatments to restore brain oxygen have not been well defined. We examined the efficacy of medical interventions employed for the treatment of cerebral hypoxia in aneurismal subarachnoid hemorrhage (aSAH) patients.

Methods: We retrospectively analyzed aSAH patients undergoing PbtO2 monitoring and brain oxygen-directed treatment. Medical treatments per hypoxic episode (PbtO2 less than 20 mmHg) were recorded. Successful treatment was defined as an increase in PbtO2 to 20 mmHg or greater within one hour of intervention.

Results: Seventy-six aSAH patients (53.6 ± 13.2 years; 72% female) underwent 11,341 hours of continuous PbtO2 monitoring. Eight hundred and six hypoxic episodes were identified and treated. Overall, 66% of the hypoxic episodes were treated successfully. Hypoxic episodes occurred despite CPP greater than 60 mmHg in 88% of patients and CPP greater than 80 in 68% of patients. CPP augmentation with phenylephrine or norepinephrine was effective for treating brain hypoxia in 69% and 84% of the episodes, respectively. An increase in the fraction of inspired oxygen through mechanical ventilation was effective for 75% of the hypoxic episodes and airway suctioning for 65% of the episodes. Additional interventions included administration of sedation or analgesia (58% effectiveness), mannitol for reduction of intracranial pressure (56%), normal saline IV bolus (50%), and red blood cell transfusion (50%).

Conclusions: Medical management can successfully treat brain hypoxia in aSAH. Bedside procedures to augment CPP and ventilation are effective treatments for low brain oxygen.

10. A Proposed Grading System Of Brain And Spinal Cavernomas

Juri Kivelev, MD; Aki Laakso, MD, PhD; Mika Niemelä, MD, PhD; Juha Hernesniemi, MD, PhD (Finland, Helsinki)

Introduction: Most cavernomas in the CNS are characterized by benign natural course. Progressive symptoms usually indicate surgical removal. The factors affecting long-term postoperative outcome have previously not been statistically well confirmed. We applied multifactorial analysis of potential risk factors on a large patient series, and utilized the results to propose a simple grading scale to predict outcome.

Methods: We studied 303 consecutive patients with cavernomas treated surgically at our department between 1980 and 2009. Follow-up assessment was performed on average 5.7 years after surgery (range 0.2–36 yrs). The main outcome measure was patients' condition at the last follow-up on Glasgow Outcome Scale (GOS). For statistical analysis, the outcome measure was dichotomized to favorable (GOS 5) and unfavorable (GOS 1-4) outcomes. Binary logistic regression analysis was used to estimate the effect of age, gender, seizures, pre-existing neurological deficits, hemorrhage, size and location of cavernoma on long-term outcome.

Results: Infratentorial, basal ganglia or spinal location and preexisting neurological deficit were only independent risk factors for unfavorable outcome, with relative risks of 2.7 ($p=0.008$) and 3.2 ($p=0.002$), respectively. By assigning one point to both risk factors, we formulated a grading from 1 to 3 based on score from 0 to 2. When applied to our series, the proposed grading system strongly correlated with outcome ($p<0.001$, Pearson's chi-square test). The risk for long-term unfavorable outcome was 13%, 22% and 55% in Grades 1 to 3, respectively.

Conclusions: The proposed grading system showed a convincing correlation with postoperative outcome in surgically treated cavernoma patients.

ELECTRONIC POSTERS

101. Incidence Of Shunt Placement With Clipping Versus Coiling In The Nationwide Inpatient Sample Database 2002-2007

Brian L. Hoh, MD; Dominic Kleinhenz, BS; Yueh-Yun Chi, PhD; J Mocco, MD, MS (Gainesville, FL); Fred Barker II, MD (Boston, MA)

Introduction: Few studies have compared the incidence of ventricular shunt placement for hydrocephalus after clipping versus coiling of cerebral aneurysms.

Methods: The Nationwide Inpatient Sample (NIS) database was used to compare, on a national level, the incidence of ventricular shunt placement following clipping versus coiling of ruptured and unruptured aneurysms. Hospitalizations for clipping and coiling of ruptured and unruptured aneurysms from 2002 to 2007 were collected from the NIS by cross-matching ICD-9 codes for diagnoses of subarachnoid hemorrhage or unruptured cerebral aneurysm with procedure codes for clipping or coiling. The incidence of ventricular shunt placement for hydrocephalus following clipping and coiling was compared using GEE generalized linear models adjusted for patient- and hospital-specific factors.

Results: Of 10899 ruptured aneurysm patients (6593 clipping, 4306 coiling), clipping had similar incidence of ventricular shunt placement (9.3%) compared to coiling (10.5%)(odds ratio = 0.984; 95% C.I. =0.85, - 1.14; p-value = 0.833 after adjustment for patient-specific and hospital-specific factors). Likewise, of 9686 unruptured aneurysm patients (4483 clipping, 5203 coiling), clipping had similar incidence of ventricular shunt placement (0.4%) compared to coiling (0.5%)(odds ratio = 0.763; 95% C.I =0.37, - 1.58; p-value = 0.465 after adjustment for patient-specific and hospital-specific factors). Predictors of shunt placement in ruptured aneurysm patients were age, comorbidity score, admission type, payer, and hospital aneurysm volume. Predictors of shunt placement in unruptured aneurysm patients were comorbidity score and admission type.

Conclusions: Clipping and coiling of ruptured and unruptured cerebral aneurysms are associated with similar incidences of ventricular shunt placement for hydrocephalus.

102. Withdrawn

103. Futile Recanalization After Mechanical Embolectomy For Acute Stroke: Exploring The Mismatch Between Successful Recanalization And Favorable Outcome

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Introduction: Interventions after acute stroke have consistently demonstrated a rate of good outcome that is substantially less than the recanalization rate. We hypothesized that infarction in territory supplied by recanalized vessels is a common occurrence, and is associated with a poor outcome.

Methods: We reviewed a prospectively collected database of acute stroke for patients with anterior circulation large vessel occlusion treated successfully (>TIMI 2) with endovascular intervention. We compared the predicted infarct based on the final angiogram and pre-intervention CTP or MRI with the actual infarct on follow-up imaging. Patients with large infarctions in territories supplied by recanalized vessels were characterized as having futile recanalization. Multivariate analysis was performed on a variety of clinical and procedural variables.

Results: 58 patients with anterior circulation stroke treated with endovascular intervention were evaluated. Angiographically futile recanalization occurred in 45.8%. Fisher exact test revealed futile recanalization was associated with poor outcome as defined as mRS =3. Two predictors, use of any procedural heparinization and use of perfusion imaging, were found to be significant in multivariate analysis.

Conclusion: In patients with acute anterior circulation stroke treated with angiographically successful endovascular therapy, 46% suffered a large infarction in the region supplied by the recanalized vessel. Multivariate analysis showed procedural heparinization and pre-treatment perfusion imaging to predict angiographically nonfutile recanalization. Futile recanalization predicted a poor outcome, and may underlie the mismatch between angiographic outcome and clinical outcome seen in trials of acute stroke. Further studies are needed to explore the no-reflow phenomenon and its contribution to poor outcome in acute stroke.

104. Improving Patient Selection For Endovascular Treatment Of Acute Cerebral Ischemia: A Comparison Of The Houston Iat And Thrive Predictive Scales

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Introduction: Outcome after intra-arterial therapy (IAT) for acute ischemic stroke remains variable, suggesting that improved patient selection is needed to better identify those likely to benefit from treatment. We evaluated the predictive accuracies of the Houston IAT (HIAT) and the Totaled Health Risks in Vascular Events (THRIVE) scores in an independent cohort.

Methods: We reviewed records from Columbia Endovascular Center from 2004 to 2010, and patients with acute ischemic stroke who underwent IAT were identified. The HIAT and THRIVE scores were calculated and the scores' predictive accuracies for good outcome (mRS less than or equal to 3) at discharge were analyzed using Receiver Operating Characteristics (ROC) analysis.

Results: Of 74 patients with complete data, 35% underwent mechanical intervention, 35% had IA thrombolytics, and 30% received a combination of mechanical intervention and IV/IA thrombolytics. With the HIAT score, 69% of low-risk (0 or 1) and 90% of high-risk patients (2 or 3) had poor outcome (p=0.07). Per the THRIVE scores, 46%, 76% and 87% of patients in the low-risk (0-2), medium-risk (3-5), and high-risk (6-9) groups had poor outcomes, respectively (p=0.03). The HIAT and the THRIVE scores demonstrated areas under the ROC curve of 0.616 (p=0.133) and 0.733 (p = 0.003), respectively.

Conclusions: The THRIVE score predicts poor outcome after IAT with reasonable accuracy and may perform better than the HIAT score. Nevertheless, both measures may have significant clinical utility. Further validation is needed in larger cohorts and analysis should account for differences in patient demographics, variation in time-to-treatment, and center preferences on IAT modalities.

105. Analysis Of Hemorrhage Risk Factors In Pediatric Arteriovenous Malformations

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Introduction: Pediatric arteriovenous malformation (AVM) hemorrhage represents a much larger percentage of strokes observed in children when compared to adults. Current data are limited regarding the natural history of pediatric AVMs and any differences from AVMs presenting in adult populations. In this retrospective cohort study, we sought to identify factors associated with hemorrhage in pediatric AVMs.

Methods: Seventy-seven pediatric patients (under 22 years old)

with AVMs were treated at CUMC between 1991 and 2010. The records and imaging studies of each patient were reviewed, and each case was described in terms of the rate of hemorrhage, the demographic characteristics, and the morphological characteristics recorded. Two consecutive logistic regression analyses were performed on the collected data, with variables not found to be significant removed after the first analysis. Variables that remained significant through both tests were considered associated with hemorrhage ($p<0.05$).

Results: 48 (62%) of patients presented with hemorrhage upon admission. Univariate analysis suggested that older age, smaller AVM nidus size, eloquence, and deep drainage were associated with AVM hemorrhage. Multivariate analysis excluded age ($p=0.091$), but nidus size ($p=0.005$), eloquence ($p=0.02$), and deep drainage ($p=0.009$) remained associated.

Conclusion: These results validate that hemorrhage is a common presenting characteristic in pediatric AVM patients. Further, unruptured AVMs presenting with deep venous drainage appear to be associated with hemorrhage and may be best treated aggressively whenever possible. Eloquence and small AVM size are likely to be non-causatively related to hemorrhage. Age remains unclearly related with risk of hemorrhage and merits further study.

106. Incidence Of Seizures After Clipping Versus Coiling In The Nationwide Inpatient Sample Database 2002-2007

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Introduction: It is not clear whether treatment modality (clipping or coiling) affects the risk of seizures after treatment for cerebral aneurysms.

Methods: Hospitalizations for clipping or coiling of ruptured and unruptured cerebral aneurysms were identified in the Nationwide Inpatient Sample Database (NIS) for the years 2002-2007 by cross-matching ICD-9 codes for diagnoses of subarachnoid hemorrhage or unruptured cerebral aneurysm with procedure codes for clipping or coiling of cerebral aneurysms. Clipping versus coiling of cerebral aneurysms were compared for the combined primary endpoint: seizure or epilepsy. The analysis was adjusted for patient-specific and hospital-specific factors using generalized linear models with generalized estimated equations.

Results: There were 10899 hospitalizations for ruptured aneurysms (6593 clipping, 4306 coiling); and 9686 hospitalizations for unruptured aneurysms (4483 clipping, 5203 coiling). For ruptured aneurysm patients, clipping had similar incidence of seizure or epilepsy compared to coiling (10.7% vs. 11.1%, respectively, odds ratio = 0.596; 95% confidence interval = 0.158 - 2.248; $P=0.445$ after adjustment for patient-specific and hospital-specific factors). For unruptured aneurysm patients however, clipping was associated with significantly higher risk of seizure or epilepsy (9.2%) compared to coiling (6.2%) (odds ratio = 1.362; 95% confidence interval = 0.155 - 1.606; $P<0.001$ after adjustment for patient-specific and hospital-specific factors). Development of seizures or epilepsy resulted in significantly longer lengths of stay ($P<0.01$) and higher hospital charges ($P<0.0001$), except in coiled unruptured aneurysm patients in which seizures or epilepsy did not significantly affect hospital charges ($P=0.31$).

Conclusions: In unruptured cerebral aneurysm patients, clipping is associated with higher risk of seizures or epilepsy.

107. Angiographic Staging Of 215 Moyamoya Patients: Defining A New Modified Staging And Correlating Results To Patient Demographics And Clinical Findings

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Background: Moyamoya disease (MMD) is a progressive angiopathy involving the entire circle of Willis. We present a modified staging system quantifying changes in anterior, middle and posterior cerebral arteries. Occurrence of MM collaterals and changes in cervical ICA defined as the "bottleneck sign" were observed and clinically correlated.

Patient Selection: Preoperative cerebral angiographies of 215 moyamoya patients were staged. Mean patient age was 32.5 years, including 22% children, 78% adults, 75% females, 25% males, 31% Asians, 58% Caucasians. Unilateral to bilateral disease ratio was 1:1.8.

Results: Distribution of staging was as follows: Stage 1a: supraclinoid ICA stenosis/occlusion = 12%, Stage 2a: ICA involvement, ACA/MCA stenosis/occlusion = 35%, Stage 3a: A1 and M1 occlusion = 33%, Stage 4a: supraclinoid ICA occlusion (filling to level of ophthalmic artery) = 11%. Stage 1p: focal PCA involvement = 5%, Stage 2p: segmental PCA involvement = 10%, Stage 3p: disappearance of PCA = 2%, Stage 4p: proximal involvement of basilar artery = 3%. In 15% ICA stenosis was present extracranially. This was always associated with Stage 4a of the disease. Typical MM collaterals were observed with Stage 1a-2a, disappearing in Stage 4a. Stage 4a was frequently seen in Caucasians. Females presented often with bilateral and posterior circulation disease. Children presented often with Stage 3a and posterior circulation disease. Stage 2a most commonly correlated to side of presenting TIA and Stroke.

Conclusion: This modified staging system enabled quantification of both anterior and posterior MMD, MM collaterals and changes in extracranial cervical ICA. Relevant correlations with clinical presentations could hence be made.

108. Traditional Intracranial Monitoring Parameters Do Not Ensure Adequate Brain Oxygenation In Poor-grade Subarachnoid Hemorrhage Patients

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Introduction: ICP and CPP management do not always ensure adequate brain tissue oxygen tension in traumatic brain injury. We examined whether ICP and CPP management was associated with adequate brain oxygenation in poor-grade aneurysmal subarachnoid hemorrhage (aSAH) patients.

Methods: We retrospectively analyzed poor-grade aSAH patients that underwent ICP, CPP, and brain oxygen (PbtO2) monitoring. ICP and CPP values were collected prior to PbtO2 monitor insertion and recording. Optimal resuscitation parameters were defined as ICP less than or equal to 20 mmHg and CPP greater than or equal to 60 mmHg. Brain hypoxia was defined as PbtO2 less than or equal to 10 mmHg.

Results: Data from 64 aSAH (54 years; 47 women) patients were examined. Data were collected as part of a prospective observational database. Eighty nine percent of patients had optimal ICP and 94% of patients had optimal CPP. Initial PbtO2 was less than or equal to 20, 15, or 10 mmHg in 66%, 48%, and 28% of patients, respectively. Brain hypoxia was present in 30% of patients with optimal ICP and 28% of those with optimal CPP. In the 57 patients (89%) with both optimal ICP and optimal CPP, PbtO2 was less than or equal to 20, 15, or 10 mmHg in 68%, 53%, and 30% of patients, respectively. Brain oxygen did not correlate with ICP ($r2=0.0169$) or CPP ($r2=0.0001$).

Conclusion: Traditional ICP and CPP management parameters do not always ensure adequate brain oxygen in poor-grade subarachnoid hemorrhage patients. Early brain oxygen monitoring and treatment may help to avoid brain hypoxia.

109. Morbidity And Mortality Of Early Carotid Artery Stenting For The Treatment Of Symptomatic Carotid Stenosis

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Introduction: Carotid artery stenting (CAS) may facilitate early

intervention, which may reduce the risk of recurrent stroke. We report on the short and mid-term results of early CAS.

Methods: A prospective database of CAS procedures was reviewed. Patients with symptomatic moderate to severe carotid stenosis (>60% as measured by NASCET criteria) that were treated within 7 days of a stroke or TIA were evaluated over a three year period. All patients had a follow up carotid ultrasound (US) within 6 months and every 6 months thereafter. Complications were recorded as peri-procedural (<30 days) or long term (between 30 days and last follow up).

Results: 118 patients met inclusion criteria. The average age was 69. The average stenosis as measured by DSA was 83%. The mean and median time to treatment was 2.3 and 2 days respectively. Symptoms included a hemispheric stroke (71%), hemispheric TIA (20%), or an ocular symptom (9%). The average clinical or radiographic follow up was 332 days. No patient had evidence of re-stenosis >50% based on US. No patient required re-treatment. The peri-procedural morbidity and mortality rate was 3.3% and 3.3% respectively. Morbidity was comprised of 3 disabling strokes and one symptomatic parenchymal hemorrhage. The 4 mortalities were caused by a parenchymal hemorrhage, myocardial infarction, and 2 cases of pulmonary failure. There were no major long term complications. Three patients experienced ipsilateral TIA's with complete resolution of symptoms at days 151, 211, and 250.

Conclusion: CAS can be performed early after the diagnosis of symptomatic carotid stenosis with acceptable safety and efficacy.

110. Hospital Acquired Pneumonia In Intracerebral Hemorrhage Associated With Poor Outcome In Patients With Intraventricular Extension

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Introduction: Intraventricular hemorrhage (IVH) after intracerebral hemorrhage (ICH) predicts worse outcomes. Although the pathophysiological explanation is complex, infectious burden has been postulated as a potential cause. We examined the relationship between nosocomial infections in ICH-IVH patients and outcome.

Methods: Patients admitted to the Columbia University Medical Center Neurological Institute with ICH from 2009-2010 were included. Patient data was prospectively collected as part of the ICH Outcomes Project. Logistic regression of dichotomized modified Rankin Scale (1-3 vs. 4-6) as a function of age, sex, pneumonia, urinary tract infection, sepsis, and ventriculitis was performed. Pearson's Chi-square and Mann-Whitney were used to associate and compare means of pertinent clinical variables.

Results: During the study period, 110 patients were admitted with ICH. The median age was 61.5, and 50.4% of patients were male. Concomitant IVH occurred in 50.4% of patients (mean Leroux Score ~7.36). Logistic regression identified only age (p=0.028) and pneumonia (p=0.043) as significant contributors of poor outcome in ICH-IVH. Patients with ICH-IVH had more frequent pneumonia (23 vs. 7, p=0.005). Among patients with IVH, pneumonia was associated with greater Leroux severity Scores (10.1 vs. 5.82, p=0.001). IVH patients with pneumonia had greater rates of poor outcome (p=0.04), while no such association was observed in non-IVH patients.

Conclusions: In patients with ICH-IVH, pneumonia occurred more frequently, was associated with more severe intraventricular bleeding, and resulted in worse outcomes. While ICH patients with secondary IVH may benefit from aggressive airway management and antibiotic prophylaxis, larger studies are needed to elucidate the relationship between pneumonia, IVH, and outcome.

111. Large Case Series Experience With Y-stent Reconstruction: Intermediate-term Angiographic And Clinical Primary Endpoint Analysis

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Introduction: Endovascular surgical reconstruction of bifurcation aneurysms (AN) has presented challenges that can be overcome with the "Y-stent"-assisted coiling technique (Y-SAC). Despite being used for several years, no large case-series safety and efficacy data is available. This led us to review our cumulative 5-yr experience for establishing evidence basis of practice.

Methods: Consecutive intention-to-treat (ITT) cases of bifurcation AN treated with Y-SAC were identified by a prospective case database. Peri-operative [24hr], short-term [30d] technical & clinical [neurologic morbidity & mortality], and intermediate term [3-6 mo] angiographic and clinical primary endpoints were assessed. Combinations of Neuroform (NF) and/or Enterprise (E) were used with a few adapted delivery techniques (e.g. stent transfer into empty microcatheter).

Results: Population- NAN:48; NPTS:45. Age: 32-78 [mean 60]. AN size range: 2-25mm [mean 8.3]. AN locations: BA 27, MCA 10, ACoA 6, ICAterm 4, ICA-PCAfetal 1. Unruptured:ruptured ratio- 44:4. Primary Y-SAC- 37/48 (77%). Stents used: primary- NF,E-26, NF,NF-10, E,E-1; secondary- NF,E-7, NF,NF-4. Primary endpoints- Technical & clinical [24hr]: ITT technical success-100%. Acute in-stent thrombus occurred in 4/48[8.3%], all resolved with iv Tirofiban. Clinical [30d]: neurologic morbidity 4.4%; mortality 0. Clinical [over30d]: mean follow-up 20mos(range 5-67)- mRS 0 (98%), mRS 4 (2%). Angiographic: 8/48(16.7%) required retreatment.

Conclusions: Y-SAC techniques have evolved over a 5-yr period, currently permitting single stage Y-stent SAC with high technical success and very low peri-operative, and 30 day morbidity & mortality. Y-SAC enables technically successful treatment of bifurcation AN that otherwise may not be possible. There remains room for improvement regarding retreatment rates.

112. Progress In The ARUBA Study

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Introduction: ARUBA (A Randomized trial of Unruptured Brain Arteriovenous malformations, NINDS U01 U01 NS051483/ NS51566 www.arubastudy.org) was funded by NINDS to address uncertainties in the literature concerning the future for brain arteriovenous malformations (BAVMs) discovered unruptured. The data for their natural history spans the entire range of lesion complexity and leaves unclear both the rate and severity of hemorrhage and the complication(s) of intervention for those seemed suitable for attempted lesion eradication.

Methods: Randomized Clinical Trial. Those eligible for ARUBA are deemed by the local center as suitable for attempted eradication by any single or combined therapy of endovascular, surgical or radiosurgical method(s). Randomization is to the planned intervention (endovascular, neurosurgical, radiotherapy) or to deferral of intervention awaiting the possible occurrence of hemorrhage. All patients receive standard medical therapy for headache or seizures, should any occur.

Results: By mid-September 2010, the international participants have already randomized 135 of the planned 400 patients. These unruptured cases, entered by the 32 active centers on three continents, (65 in contract, >900 patients screened), have a satisfactory distribution concentrated among Spetzler-Martin grades (I=26%, II=28%, III=34%, IV=19%, V=0).

Conclusion: ARUBA has successfully implemented its protocol and is well on its way to providing evidence for making treatment decisions for unruptured BAVMs. We welcome new centers and encourage more rapid randomization, not only to increase the statistical power, but to expand the scope of possible analyses for subtypes of treatment.

113. Surgical Outcomes Of Sta-mca Anastomosis With Or Without Indirect Method In Adult Onset Moyamoya Disease

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Introduction: The object of this study was to report the clinical features, surgical results, and outcomes of adult moyamoya disease treated with direct anastomosis with or without indirect method at a single institution.

Methods: We retrospectively reviewed medical records and radiologic findings after direct bypass surgery on 82 hemispheres of 76 consecutive patients with adult moyamoya disease from the past 6 years.

Results: The majority of patients were women and the mean age at the time of surgery was 37.1 years (16-62 years). The clinical manifestations included transient ischemic attack (TIA) (45.1%), cerebral ischemia (39%,), cerebral hemorrhage (12.2%), and seizure (3.7%). Of the patients reviewed, direct anastomosis without indirect method was carried in 74.4% of cases, the rest included indirect method. Postoperatively, the patency of the donor artery was confirmed by the computed tomography angiography or trans-femoral cerebral angiography and the patency was good in 98.8%. Postoperative brain SPECT showed increased perfusion in 82.6% of patients who were viewed. Postoperative ischemic complications occurred in 12.2% (10/82) of cases. Overall clinical outcome was excellent in 48.8%, good in 36.6%, fair in 2.4% and poor in 12.2%. Therefore, 85.4% (70/82) of the patients had a favorable clinical outcome (excellent and good).

Conclusions: Direct anastomosis with or without indirect method seems to be effective in adult onset moyamoya disease.

114. 7,8-dihydroxyflavone, A Potent Trkb Agonist, Enhances Stem Cell Mobilization After Stroke

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Background: Increasing levels of circulating Hematopoietic Stem Cells (HSC)/Hematopoietic Progenitor Cells (HPC), bone marrow derived mononuclear cells that promote repair in areas of injury, have been demonstrated to correlate with improved neurological function following stroke. Recent studies have demonstrated that 7,8 Dihydroxyflavone (DHF) is a potent TrkB agonist mimicking Brain Derived Neurotropic. Factor, thus making it a powerful potential tool for treating neurological disorders. Stromal Derived Growth Factor 1-Alpha (SDF1-A) along with its receptor CXCR4 is a potent chemo attractant released by areas of injury. SDF1-A has been shown to mobilize HSC/HPC from the bone marrow and leading to 'homing' of the cells to an area of injury. We investigated the effect of DHF on HSC/HPC function following cerebral ischemia.

Methods: Ischemic damage was induced in adult rats with a peri-MCA injection of Endothelin. The rats were sacrificed at 24 hours post surgery and their bone marrow and blood HSC/HPC enriched using nanoparticles tagged with LIN negative and CD90 markers.

Results: Stroked animals showed an increase in bone marrow production of HSC/HPC versus control animals (31.9±7 versus 2±0.5, $p<0.05$). The mobilization of the HSC/HPC from the bone marrow to the blood was also significantly higher in the stroked animals versus control animals (43±19 versus 3.6±0.3, $p<0.05$). Following stroke, DHF pre-treated HSC/HPC's demonstrated significantly improved migration along an SDF-1 gradient compared to controls (129±1.0 versus 108±1.15, $p<0.05$), despite the fact that DHF alone provided no independent migratory stimulus.

Conclusions: The results suggest that DHF may be a viable compound to facilitate HSC/HPC migration post-stroke.

115. Epsilon Aminocaproic Acid In Angiographically Negative Subarachnoid Hemorrhage Patients Is Safe

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Introduction: Epsilon aminocaproic acid (EACA) is used to reduce the rate of cerebral aneurysm rerupture post rupture and prior to definitive treatment. Some patients with angiographically negative subarachnoid hemorrhage (ANSAH) receive EACA as part of a subarachnoid hemorrhage (SAH) treatment protocol, which may place them at increased risk for ischemic complications.

Methods: We conducted a retrospective study of 454 consecutive subarachnoid hemorrhage patients over a 2 year period under a current protocol for EACA use. Patients were excluded if a source for the SAH was discovered, yielding a total of 83 ANSAH patients. The patients were divided into groups that did or did not receive Amicar. The primary endpoints of the study were ischemic complications, pulmonary emboli, vasospasm, shunt rates, and outcomes.

Results: Statistical Analysis yielded no significant difference in the two arms yielded no significant difference in any of the endpoints; Vasospasm ($p=0.65$), Deep Vein Thrombosis ($p=0.51$), Pulmonary Embolism ($p=1.0$), Stroke ($p=1.0$), Myocardial Infarction ($p=1.0$), Ventriculoperitoneal shunt ($p=0.57$). There was no statistical significant difference in the modified Rankin Scale (mRS) $p=0.30$.

Conclusions: Short term (<72 hour) application of EACA does not result in an increase in adverse events in patients with angioigraphically negative subarachnoid hemorrhage.

116. Clipping Of Previously Coiled Aneurysms - Attempted Formulation Of A Guideline To Assess The Need For Coil Extraction

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Introduction: Surgical clipping of an aneurysm, which has been previously treated with endovascular coil embolization, can be challenging. We sought to evaluate the need for extraction of the coil mass in order to enable clip placement and provide a decision-making rule.

Methods: We identified 11 patients with previously coiled aneurysms who underwent craniotomy and clipping of a aneurysm remnant or recurrence. The median age was 52 years, 7 were female (63%) and 81% were ruptured at the time of the original presentation. The median interval between coil embolization and surgical clipping was 8 months, ranging from 2 days to 72 months. Surgery was necessary secondary to either partial treatment in 37% and coil compaction in 63% of all cases.

Results: Coil extraction was necessary in 4 cases for success-

ful clip placement (37%). The aneurysm volume was 0.393 cc for aneurysms where coil extraction was not necessary and 0.817 cc in aneurysms where the coils had to be at least partially extracted. The mean height of the remnant aneurysm was 1.4 mm and 3.4 mm, respectively.

Conclusions: Clipping of previously coiled can be challenging when extraction of the coil mass is required. We present a series of 11 patients requiring surgical clipping of a remnant or recurrent aneurysm neck after endovascular coiling and discuss features that may predict the need for intraoperative coil extraction. We offer a very simple guideline suggesting that if the height of the remnant aneurysm neck exceeds three times the short diameter of the remnant extraction is not necessary.

117. Anti-platelet Preparation Before Stent Placement: A Review Of 294 Cases From 19 Studies

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Introduction: Stenting in intracranial aneurysms (IA) necessitates dual-antiplatelet therapy administration to reduce thromboembolic (TE) complication risk. We analyzed whether specific dosage and duration of anti-platelet were associated with fewer TE events.

Methods: We systematically reviewed the literature of IA stenting, including only studies with patient characteristics that matched complications to pre-treatment type and analyzed pre-treatment duration and aspirin/clopidogrel dosage. Logistic regression and Chi-Squared tests were performed to compare TE complication rate in different treatment regimens

Results: Two-hundred ninety-four cases were analyzed. Stents were placed in 34 (11.6%) ruptured and 260 (88.4%) unruptured aneurysm patients with TE events in 5/34 and 13/260, respectively. Complication rates with respect to pre-treatment duration, dichotomized at <1 and =1 day, were 2/32 and 16/262 (p=0.974). Dichotomization at 3 (p= 0.845) and 5 days (p=0.168) did not significantly change complication incidence. Most patients (139/294) received pre-treatment 3 to 5 days pre-op. Aspirin dosage varied from 100 to 500mg and clopidogrel from 75 to 300mg. The most used anti-platelet pre-treatment dosage regimen (140/294 patients) was 325 mg aspirin and 75 mg clopidogrel (325/75). We investigated the effect of pre-treatment dosage on complication rate; no significant difference in complication rate was observed in majors groups (300/75, 300/225, 500/300). Of note, in the group with no clopidogrel (325 mg aspirin), 1/3 presented with complications (p=0.051).

Conclusions: Although an indirect evaluation of patients, our study found large variability in anti-platelet regimen. While these results need to be evaluated in a prospective cohort, they suggest lack of clopidogrel preparation may lead to higher complication risk.

118. Long Term Angiographic Follow-Up Of Cerebral Aneurysms Treated By Endovascular Coiling

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Introduction: Recent advancements in endovascular techniques have revolutionized cerebral aneurysm treatment. It is imperative to prove the safety and efficacies of new treatment options during the peri-operative period and in long-term follow-up. We performed long-term angiographic follow-up during the period from January2006 and March2010, in patients who had undergone aneurysm coiling.

Methods: A retrospective IRB-approved chart review on patients who had aneurysm coiling was undertaken. Bare platinum coils were used in all patients. Post-coiling aneurysm occlusion was determined immediately following each procedure. Long term angiographic follow-up was performed in five years or longer. Follow-up cerebral angiography was compared to the intra-operative angiography and long-term efficacy was determined.

Results: Preliminary data include a total of 61 patients. The mean patient age was 44.3 years (ranging from 17-79) and Hunt and Hess grade ranged from 0 to 4. Mean follow-up period was 64 months (ranging 60-88 months). Initial post-coiling angiography showed 100% occlusion in 46 patient (75.4%), and residual filling in 15 patients (24.6%). Follow-up angiography showed 100% occlusion in 42 of 46 patients (91.3%); 4 patients (8.7%) showed recurrence which ranged from 40-90%. In the remaining 15 patients with partial initial aneurysm obliteration, 13 patients showed recurrence ranging from 5-60%; two patients with previous residual filling maintained a stable filling pattern. Mean follow-up period was 64 months(ranging 60-88 months).

Conclusion: Preliminary data indicate that endovascular coiling is both a safe and effective method of treatment for cerebral aneurysm with excellent long term angiographic efficacy, provided complete aneurysm occlusion was achieved during initial coiling.

119. Recovery From Stroke Is Limited Due To Impaired Stem Cell Function Following Treatment With Tissue Plasminogen Activator

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Background: Intravenous Tissue Plasminogen Activator (tPA) is the only FDA approved pharmacological recanalization therapy for stroke, however tPA has been associated with deleterious effects on the blood brain barrier. A potential contributor to vascular integrity and/or repair following stroke are Hematopoietic Stem Cells (HSCs)/ Hematopoietic Progenitor Cells (HPCs). HSC/HPC's have been shown to mobilize to the peripheral circulation from bone marrow in response to stroke. Furthermore, increased levels of HSC/HPCs have been demonstrated to correlate with improved neurological function following stroke. Stromal Derived Growth Factor 1-Alpha (SDF1-A) along with its receptor CXCR4 is a potent chemoattractant released by areas of injury. SDF1-A has been shown to mobilize HSC/HPC from the bone marrow to the blood and lead to 'homing' of cells to an area of injury.

Methods: Animals (n=10) were euthanized 24 hours post ischemia/reperfusion following a murine intraluminal filament model. Infarction was confirmed using TTC staining of the brain. HSC/HPC were harvested and counted, treated with 10nM tPA, and migrated towards SDF1-A. mRNA levels of CXCR4 (SDF1-A receptor) were also assessed.

Results: Mean infarct volume was 43±10%. Pre-treatment with tPA reduced HSC/HPC migratory capability towards SDF1-A (100±1.3% versus 173±1.0%, p<0.05) and reduced expression of CXCR4 from 100±7.9% to 35.8±7.1%, p<0.05). Conclusion: These data indicate that exposure of HSC/HPC's to tPA

abrogates their migratory response to SDF1-A and downregulates CXCR4 mRNA expression. These results suggest that tPA may reduce the ability of the HSC/HPC to home to ischemic brain following stroke and possibly interferes with repair mechanisms associated with HSC/HPC.

120. Treatment Of Cerebral Aneurysms: Regional Trends In The Adoption Of Endovascular Techniques

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Introduction: Endovascular techniques have produced significant change in treatment of ruptured and unruptured intracranial aneu-

rysms, and the increasing number of patients treated may substantially increase health care expenditures. Herein we present geographic variations of growth in endovascular procedures.

Materials and Methods: The National Inpatient Sample was queried with ICD-9 codes for clipping and coiling of ruptured and unruptured cerebral aneurysms from 2002 to 2008. In-hospital mortality, length of stay, total cost adjusted to 2007 equivalents, selected procedure, and regional variation over the course of the study was explored.

Results: 12,588 ruptured cases (7,318 clipped and 5,270 coiled) and 11,606 unruptured cerebral aneurysm cases (5,216 clipped and 6,390 coiled), representing 121,000 aneurysms treated in the study period were found. Endovascular treatment increased from 17.28% to 57.59% for ruptured and 29.70% to 62.73% for unruptured aneurysms ($p<0.00001$). Age, elective status, and comorbidities increased likelihood of endovascular treatment ($p<0.00001$, $p<0.00004$, $p<0.02$). In patients with SAH, endovascular therapy was chosen in urban and academic medical centers more frequently ($p<0.009$, $p=0.05$). In-hospital mortality decreased in all patients ($p<0.000001$) with SAH as greatest predictor of mortality (OR=38.09, $p<0.000001$). Geographically, endovascular techniques concentrated to eastern and western coastal states with substantial variation in the adoption of endovascular techniques (2008: 0-92%).

Conclusion: The NIS database reveals the majority of aneurysms treated endovascularly by 2008. Differences in cost between open and endovascular techniques were likely secondary to greater numbers of SAH patients undergoing endovascular therapy and occurring at urban and academic medical centers. There is substantial regional variation in adoption of endovascular techniques.

121. Endothelial Progenitor Cells Enhance Motor Recovery Following Stroke

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Background: Stroke is the leading cause of disability in the United States resulting in upper extremity motor impairments.

Methods: Male Long-Evans hooded rats (350-420g) underwent stroke surgery using Endothelin-1 induced MCAO. Animals were housed in standard laboratory cages on a 12hour light/dark cycle. Animals were pre-trained to familiarize them with the reaching accuracy task. Trained animals were then divided into 3 groups (controls, n=7; stroke, n=3; stroke with post-reperfusion administered endothelial progenitor cells (EPC's), n=6); The EPC's were enriched from the bone marrow of a separate group of donor rats using LIN negative and CD90 markers. Ten million EPC's were injected into the tail vein immediately following reperfusion. Animals were assessed at 3 and 5 weeks following the surgery for reaching task performance. All assessments were performed in a blinded manner.

Results: Reaching accuracy: Control animals scored a reaching accuracy of 41±8.1% and 46±11% at 3 and 5 weeks, respectively. Stroke decreased this task to 12±21% and 18±28%, respectively ($p<0.05$, compared to controls at both time points). Injection of EPC's following reperfusion led to an increase in reaching accuracy to 27±26% and 32±24%, at 3 and 5 weeks, respectively ($p<0.05$, compared to stroked non-EPC cohort at 5 weeks).

Conclusions: These data suggest that EPC's play a significant role in the amelioration of stroke injury following cerebral ischemia.

122. Hypoxia-inducible Factor-1a Contributes To Brain Edema After Stroke By Regulating Aquaporins And Glycerol Distribution

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Introduction: The present study investigated the role of hypoxia-inducible factor-1a (HIF-1a) and aquaporins (AQP-4 and -9) in regulating brain tissue glycerol and inducing brain edema in a rodent model of stroke.

Methods: Middle cerebral artery occlusion (MCAO) followed by 2 hour reperfusion were performed in male Sprague-Dawley rats (250-280g). The anti-AQP-4, anti-AQP-9 antibody, or 2-Methoxyestradiol (2ME2, an inhibitor of HIF-1a) were given at the time of MCAO. The rats were sacrificed at 1 and 24 hours after reperfusion and their brains were examined for protein expression, glycerol concentration and brain edema. Extracellular and intracellular glycerol concentration of brain tissue was calculated with enzymatic glycerol assay. The protein expressions of HIF-1a, AQP-4 and AQP-9 were determined by Western blotting. Brain edema was measured by brain water content.

Results: Compared to control, significant edema and increased glycerol was observed after stroke. Stroke also enhanced expression of HIF-1a, AQP-4, and AQP-9. Edema was decreased after inhibition of AQP-4, AQP-9 or HIF-1a, respectively. Extracellular glycerol was also decreased after inhibition of AQP-4, AQP-9 or HIF-1a while intracellular glycerol was not, even increased 1 hour after stroke. Inhibition of HIF-1a suppressed the expression of AQP-4 and AQP-9.

Conclusions: HIF-1a plays a role in regulating cerebral glycerol and brain edema formation via a molecular pathway involving AQP-4 and AQP-9. Pharmacological blockade of this pathway in stroke patients may provide novel therapeutic strategy.

123. Hemorrhagic Complications (HC) Following Ventriculostomy Insertion In Patients Treated With Chemoprophylaxis For Venous Thromboembolism (vte)

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Introduction: The reported rate of HC following ventriculostomy (EVD) insertion varies widely, ranging from 0 to 41% depending on several factors. A recent study reported 10% as a reasonable complication rate, with less than 1% of symptomatic hemorrhages. The purpose of this study was to investigate the effect that chemoprophylaxis with low molecular weight heparin (LMWH) or unfractionated heparin (UFH) has on this rate.

Methods: Retrospective chart review of patients admitted to the Neurotrauma ICU at Hartford Hospital requiring EVD insertion over the last two years. Admitting diagnosis, LMWH or UFH use, coagulation profile, platelets, and other demographic and clinical data were recorded. Post-procedure CT scans were reviewed and evidence of new blood along the path of the EVD was noted. Hemorrhage leading to clinical deterioration or surgical intervention was classified as symptomatic.

Results: A total of 148 patients were included. Of these, 86 (58.1%) were treated with LMWH, 47 (31.8%) with UFH, and 15 (10.1%) received no chemoprophylaxis. A total of fourteen patients developed HC related to EVD insertion (9.5%). In the LMWH group, 8/86 (9.3%) patients had HC, while in the UFH group 5/47 (10.7%) and in the no chemoprophylaxis group 1/15 (6.7%) developed HC (Pearson Chi-square 0.223).

Conclusions: The use of LMWH and UFH was overall safe and not associated with increased risk of HC. Chemoprophylaxis prior to EVD insertion was similarly found to be safe. Given the high rate of VTE in this patient population, chemoprophylaxis should be strongly considered. Further prospective studies are warranted.

124. Elevated Body Temperature During Hospital Stay Predicts Higher Mortality After Intracerebral Hemorrhage

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Introduction: Fever exacerbates brain damage, leading to an

increased risk of secondary neuronal injury and mortality in critically ill patients. The influence of fever on outcome after intracerebral hemorrhage (ICH) remains undefined. We sought to evaluate whether elevated body temperature predicts outcome in our ICH population.

Methods: Demographic and clinical data were prospectively collected for 111 patients admitted to Columbia University Medical Center with non-traumatic ICH between February 2009 to August 2010. A logistic regression model was created with mortality as the dependent variable and age, sex, fever (body temperature greater than 38.5°C), leukocytosis (Leukocytes greater than 12.000) and history of infection (HI - defined as documented history of urinary tract infection, pulmonary infection, ventriculitis, and positive blood culture) as predictors. A second model was created for the 58 patients with no HI (52% of population), with mortality as the dependent and age, sex, fever and leukocytosis as independents.

Results: The first model identified fever ($p = 0.011$) and age (p less than 0.001) as predictors of mortality; HI was not significant in the model ($p = 0.167$). Of patients with no HI, 21% presented with fever. Fever ($p = 0.039$) was still a significant predictor of mortality in the second model, along with age ($p < 0.001$).

Conclusion: Fever control is recommended in patients with brain injury, though this paradigm has not been extended specifically to ICH. Our results suggest that history of infection aside, high body temperature could be a marker of severity or a source of further brain damage in ICH patients.

125. Stroke Increases Serum Sdf1-a Levels And Mobilization Of Hematopoietic Stem Cells From The Bone Marrow

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Background: Hematopoietic Stem Cells (HSC)/ Hematopoietic Progenitor Cells (HPC) are known to mobilize from the bone marrow to peripheral blood in response to stroke. HSC/HPC's have been correlated with improved neurological function following stroke. Stromal Derived Growth Factor 1-Alpha (SDF1-A) and its receptor CXCR4 is a potent chemoattractant released by areas of injury. SDF1-A has been shown to mobilize HSC/HPC from the bone marrow followed by 'homing' of the cells to an area of injury.

Methods: Animals underwent a murine intraluminal filament model of focal cerebral ischemia. Animals were divided into 4 groups (n=5 each): 4hrs sham surgery, 4hrs post reperfusion, 24hrs sham surgery, and 24hrs post reperfusion. Neurological deficit score was recorded prior to euthanasia and serum SDF1-A was assessed in all groups.

Results: Serum SDF1-A levels were elevated at 4hrs and 24 hours compared to sham's (107±3.8% and 137 ± 11% versus 100 ± 0.04% and 100 ± 0.06%, respectively; 4hrs vs. sham: P=NS, 24hrs vs. sham: $p < 0.05$). Bone marrow showed increased HSC/HPC production at 4 hrs (106 ± 26%) and significantly higher at 24 hrs (272 ± 35%). Mobilization of the HSC/HPC was slightly higher at 4 hrs (167 ± 26%) and significantly higher at 24 hrs (606 ± 91%; $P < 0.05$). Neurological deficit score at 4hrs and 24hrs post reperfusion were 1.846 ± 0.21 and 2.04 ± 0.178, respectively.

Conclusions: Serum SDF1-A levels significantly increased following cerebral ischemia, leading to increased mobilization of HSC/HPC from the bone marrow to the blood. These data suggests that SDF1-A mobilization of HSC/HPC in response to cerebral ischemia may be a relevant pathway for cerebral injury repair following stroke.

126. Use Of Intracranial Pressure And Brain Tissue Oxygen Monitors To Predict Hyperemic Intracranial Hypertension And Decreased Cerebral Blood Flow Around A Brain Tissue Oxygen Monitor

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Introduction: Brain tissue oxygen (PbtO2) monitors can complement intracranial pressure (ICP) monitors in comatose patients. In this study, we asked whether data obtained from these two modalities could be used to predict the presence of hyperemic intracranial hypertension and regionally decreased perfusion around a PbtO2 monitor, as diagnosed by Xenon-enhanced CT cerebral blood flow studies (XeCTCBF).

Methods: 359 patients (mean age 51 ± 19 years) received PbtO2 and ICP monitors between 2004 and 2010. Hyperemic intracranial hypertension was evaluated on the basis of high clinical suspicion. Compromised perfusion around a PbtO2 monitor was evaluated when mean PbtO2 over 24 hours was less than 20 mmHg (FiO2 40-50%) and failed to increase to 30 mmHg with FiO2 70-100%.

Results: Hyperemic intracranial hypertension was suspected in 4 patients, and confirmed in 2 (average CBF greater than 55 ml/min/100 gm). The mean PbtO2/FiO2 ratio for the 24 hour period preceding the XeCTCBF study was higher in the patients with confirmed hyperemia than those without (86 and 60 vs. 21 and 17). XeCTCBF confirmed decreased regional perfusion (CBF less than 30 ml/min/100 gm) around a PbtO2 monitor in 4/4 patients in whom it was suspected. The average PbtO2/FiO2 ratio for these patients was 13.9 ± 7.9. Perfusion deficits were global in 1 patient, and focal in 3.

Conclusions: Our preliminary results suggest that ICP and PbtO2 monitors may help predict hyperemic intracranial hypertension and decreased perfusion around a PbtO2 monitor. A low PbtO2/FiO2 ratio was associated with decreased perfusion, while higher PbtO2/FiO2 ratios appeared to be associated with hyperemia.

127. Initial Experience With Neuroform EZ Stent On The Treatment Of Wide Neck Cerebral Aneurysms

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Introduction: Initial experience with Neuroform EZ stent on the treatment of wide neck cerebral aneurysms.

Background and Purpose: We report our initial clinical experience, technical considerations, and treatment outcomes using Neuroform EZ stent in conjunction with coil embolization.

Methods: This is a review of 13 patients with a total of 17 wide-neck cerebral aneurysms treated with coil embolization and/or aneurysm neck reconstruction using the Neuroform EZ stent. All bifurcation aneurysms had a dome/neck ratio less than 2mm and/or a neck diameter of greater than 4mm. Fifteen of the aneurysms were located in the anterior circulation and 2 were in the posterior circulation.

Results: Seventeen aneurysms with wide neck were treated in 13 patients. The stent was delivered successfully and without deployment difficulty. Technical complications occurred for 3 patients, including a stretched coil, prolapsed coil, and parent vessel occlusion. Post procedure angiography revealed 3 of 17 treated aneurysms with complete occlusion (Raymond 1), 6 of 17 showed contrast filling of the aneurysm neck (Raymond 2), and 8 of 17 showed contrast filling of the aneurysm sac (Raymond 3).

Conclusion: In comparison to previous generations, Neuroform EZ stent system provided improved anchoring and support in stent delivery to the aneurysm site. This is especially useful when overlap-

ping stents in order to help protect the parent vessel and improve flow diversion away from the aneurysm sac. In the future, it appears this feature will help facilitate better outcomes, decrease complications, and may lower the re-treatment rates for endovascular repair of wide neck aneurysms.

128. Surgical Results Of Unruptured Intracranial Aneurysms In The Elderly (over 70 Years): Single Center Experience In The Past Ten Years

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Introduction: Because the life expectancy has increased with the advancement of medicine, it is imperative to develop specific treatment strategies for intracranial aneurysms in the elderly. The purpose of this study was to analyze clinical characteristics and outcomes of the treatment of unruptured intracranial aneurysms in patients older than 70 years.

Methods: Between May 1999 and June 2010, a total of 48 patients (60 aneurysms) aged 70 years or older (mean age, 72.08 years ± 2.03) were treated with surgical clipping. There were 33 females and 15 males. We performed a retrospective review of a prospective database of elderly patients who underwent treatment with surgical clipping.

Results: There were aneurysms located at the internal carotid artery in 23 cases, in the middle cerebral artery in 22, the anterior cerebral artery in 14, and the superior cerebellar artery in 1. Multiple aneurysms were in nine cases. The sizes of the aneurysms ranged between 3 mm to 17 mm (mean size, 7.38 ± 3.09). Complete clipping was achieved in 91.7% of the cases. Procedure related complications occurred in 12.5% of the cases. Permanent neurological deficits, including death, occurred in 4.2% of the cases. Six-month outcomes were: excellent, 91.7%; good, 4.2%; poor, 2.1%; and death 2.1%.

Conclusions: Surgical clipping of unruptured intracranial aneurysms in this age group is safe and effective.

129. Use Of A Dual Aortic Balloon Occlusion In Severe Refractory Vasospasm Following Aneurysmal Subarachnoid Hemorrhage

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Introduction: Delayed ischemic neurological deficits (DINDs) resulting from cerebral vasospasm remains an important cause of poor outcome after aneurismal subarachnoid hemorrhage (aSAH). The Neuroflo™ dual aortic balloon occlusion device augments the blood flow to the brain by diverting circulation from the lower extremities via supra- and infrarenal aortic balloon inflation. We sought to evaluate our center's experience with the Neuroflo™ device for use in cerebral vasospasm refractory to medical and standard endovascular therapies.

Methods: From 2007-2010, a total of eight patients with severe refractory vasospasm after SAH admitted to our institution underwent aortic balloon occlusion with the NeuroFlo™ device. Patient clinical and treatment data were recorded, and outcome at discharge was assessed with the modified Rankin Scale (mRS).

Results: The mean age of patients was 54 years, and six were female. The median admission Hunt-Hess Grade and Glasgow Coma Scale score were 4 and 11.5, respectively. Six patients underwent multiple treatments of intra-arterial verapamil infusion (median of four treatments) prior to NeuroFlo™ treatment. All patients tolerated the procedure well without significant hemodynamic changes or post-procedural complications, and ICP remained stable with drainage. DIND associated symptoms improved in three patients, while four patients underwent further endovascular intervention for persistent clinical vasospasm. There was one in-hospital death secondary to persistent clinical deterioration despite maximal medical management. Two of the remaining seven patients had good functional outcome (mRS less than 4) at discharge.

Conclusions: The NeuroFlo™ intra-aortic dual balloon occlusion device can be used safely and may be effective as an adjunctive endovascular treatment of refractory cerebral vasospasm.

130. Clinical And Angiographic Outcome In Patients With Completely Occluded Intracranial Aneurysms By Endovascular Coiling: Our Experience

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Introduction: The endovascular approach is being used more frequently to treat ruptured and unruptured intracranial aneurysms. We are presenting long term clinical and angiographic outcome of completely occluded intracranial aneurysms by endovascular approach.

Methods: Patients with intracranial aneurysms which were completely occluded by coiling at our institution between January 2005 and march 2009 were reviewed. Clinical and angiographic data were analyzed. The patients were clinically assessed using the Glasgow Outcome Scale (GOS). Follow up angiographic findings were categorized as: Stable aneurysm with no recanalization, recanalization with a neck remnant, and recanalization with body remnant.

Results: Eighty three aneurysms in 74 patients (15 Males and 59 Females, average age 52.4 years) had complete occlusion post intervention. Treatment by coiling only was used in seventy three aneurysms while stent assisted coiling was utilized in 10 cases. At the last angiographic follow up, (mean 16.3 months), 20 (24%) of the 83 aneurysms demonstrated various degrees of recanalization. The recanalization rate was significantly higher in large aneurysms(more than 10mm) than in small aneurysms (less than 5mm). Clinically, 65(87.8%) of the 74 patients showed good recovery (GOS Score 5), 8 (10.8%)had moderate disability (GOS Score 4), and 1(1.4%) was severely disabled (GOS Score 3). There were no bleeding, rebleeding or procedure related death during follow up.

Conclusions: Complete endovascular occlusion of intracranial aneurysm is certainly effective in preventing aneurismal bleeding. However, recanalization rate, despite being lower when compared to subtotal occlusion, remains an issue. Longer follow up is required.

131. Differences Of Cerebral Vasospasm Following Microsurgical Clipping And Endovascular Coiling Of Ruptured Intracranial Aneurysms

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Introduction: Previous studies have been inconclusive about whether the incidence and severity of vasospasm after low-grade aneurysmal subarachnoid hemorrhage (SAH) is lower in patients who undergo microsurgical clipping versus endovascular coiling. This study examines the incidence and severity of cerebral vasospasm following these treatments.

Methods: This retrospective cohort study reviewed 202 patients admitted to Hartford Hospital from 1998-2009 with the diagnosis of Grade I-III aneurysmal SAH. 101 patients underwent endovascular coiling and 101 patients underwent microsurgical clipping. Both groups were similar in terms of Hunt/Hess grade. We compared the incidence of vasospasm in both groups of patients.

Results: The clipped patients had a 55% incidence of vasospasm versus 28% for the coiled group (p less than 0.001). The coiled group seemed to have a higher requirement for angioplasty (39%) versus the clipped group (25%) but this was not statistically significant (p equals 0.336). When assessing risk factors across the entire cohort and in the coiled group, younger age correlated with a higher incidence of vasospasm (cohort, p equals 0.003; coiled, p equals 0.012), as did Hunt/Hess grade (cohort, p equals 0.048; coiled, p equals

0.004). There were no significant differences between the groups' favorable GOS scores at discharge (87% clipped, 90% coiled) or in mean length of stay (24 days clipped, 22 days coiled).

Conclusions: This study found that patients who underwent microsurgical clipping following low-grade SAH had a higher incidence of vasospasm compared to patients who underwent endovascular coiling and that there was no statistically significant difference in their requirement for angioplasty.

132. Safety And Efficacy Of Endovascular Treatment Of Dural Arteriovenous Fistulas

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Introduction: Dural arteriovenous fistulas (DAVFs) are arteriovenous shunts from a dural arterial supply to a dural venous channel, typically supplied by pachymeningeal arteries. At Thomas Jefferson University, we present 39 patients initially treated by endovascular means. Patients were evaluated to determine whether multi-modality therapy would be necessary or whether strict endovascular therapy would suffice.

Methods: Thirty-nine patients underwent endovascular treatment of DAVFs from 2001-2009. Seventy-nine percent of patients had cortical venous drainage. Number of arterial embolizations, need for transvenous embolization, open surgery, or radiosurgery were all assessed. Normalization of retrograde cortical venous drainage was also reviewed.

Results: The average number of embolizations in all patients was 2.1. Patients were considered completely treated when there was a greater than 95% reduction in DAVF flow. Seventy-one percent of patients had complete treatment of the fistula: 21 by purely endovascular treatment and 7 with endovascular therapy followed by craniotomy. Of the eleven patients who did not have complete treatment, 64% of those had at least 90% obliteration. Three of those with incomplete treatment underwent radiosurgery as the final approach for treatment. The average dose for obliteration was 22 Gy in a single fraction. Of those patients with retrograde cortical venous drainage, 87% had resolution. Sixty-nine percent of these had resolution by endovascular means. In five of these patients, success was only obtained when a transvenous approach was performed.

Conclusion: Endovascular management of DAVFs is a safe and effective method of treating these complex lesions. Based on our data, embolization should be the primary modality for treatment of DAVF.

133. WITHDRAWN

134. Size Of Ruptured Cerebral Aneurysms In A Series Of Aneurysmal Subarachnoid Hemorrhages

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Introduction: The decision to intervene on cases of unruptured aneurysms continues to be a challenge for clinicians. The ISUIA, along with smaller studies have pointed to size as a factor predicting likelihood of rupture. In this study, we retrospectively look at a 45-month period from January 2006 to September 2009 with 203 cases of acute subarachnoid hemorrhage (SAH) at Montefiore Medical Center in Bronx, NY.

Methods: Approval was obtained from the IRB. Radiology dictations for angiograms performed for acute SAH were reviewed from January 2006 to September 2009. The etiology of SAH, aneurysm size, location, presence of multiple aneurysms, and treatment modalities were collected and analyzed

Results: Of the 203 cases of SAH, 143 (70.4%) were due to aneurysmal rupture, 7 (3.5%) were from vasculitis, 3 (1.5%) were from small AVMs, and in 50 (24.6%) cases no pathology was seen on primary and follow-up angiograms. Of the 143 cases of aneurysmal SAH, the mean and median size of ruptured aneurysms was 6.1mm ± 3.4 and 5.0mm respectively. ACOM artery (25.8%), PCOM artery (14.7%), ICA (24.5%), and MCA (21.0%) aneurysms were the most commonly encountered aneurysms. Nearly 20% of patients had multiple intracranial aneurysms. Basilar aneurysms were the largest (7.0mm +/- 6.42mm) on rupture while ACOM aneurysms tended to be smallest (5.5mm +/- 2.89mm).

Conclusions: Forget et al (2001) reported that 85.6% of ruptured aneurysms were <10mm, the size deemed low risk by the ISUIA. Our ruptured aneurysm series show that 91% of ruptured aneurysms are less than 10mm and that the distribution is skewed towards smaller aneurysms. Clinicians should not solely use size in evaluating patients for intervention of unruptured aneurysms.

135. Supply Charges, Fluoroscopy And Procedure Time For Intracranial Aneurysm Embolization: Onyx HD-500 Versus Platinum Coils

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Introduction: Onyx-HD is an approved treatment for wide-necked intracranial aneurysms. There has been concern that the use of this device increases procedure cost and operative duration compared to coil embolization.

Methods: We compared supply charges, fluoroscopy time, and procedure time between patients treated by a single surgeon using Onyx-HD (n = 19) and matched (aneurysm size, location, adjuvant stent) coil treated patients (n = 28).

Results: Overall Onyx cases showed a trend toward lower cost, but this was not statistically significant ($13,940 + 6,429 versus $15,941 + 9,728, p = 0.41). There was a strong trend toward reduced expense when using Onyx alone rather than coiling with stent assistance ($12,125 + 5,718 versus $18,805 + 10,360, p = 0.10) with similar procedure and fluoroscopy times (242 + 46 min. versus 228 + 51 min, p = 0.55 and 44 + 14 min. versus 41 + 16 min, p = 0.65). Small (<10 mm) aneurysms tended to be less expensive to treat with Onyx than coiling ($9,397 + 2,562 versus $11,599 + 5,327, p = 0.21), but procedure time showed a trend to being longer (208 + 27 min. versus 186 + 41 min., p = 0.15) and fluoroscopy times were significantly longer (38 + 7 min. versus 29 + 11 min, p = 0.04). Large (>10 mm) aneurysms involved similar procedure costs ($18,484 + 5,902 for Onyx compared to $19,704 + 11,240 for coiling, p = 0.73), but significantly longer procedure times (304 + 48 min. versus 250 + 57 min, p = 0.02) and longer fluoroscopy times (61 + 12 min. versus 51 + 14 min, p = 0.06).

Conclusion: Our data suggest that Onyx-HD may be a more economic alternative to coiling for small aneurysms, and may involve lower supply charges than coiling performed with stent assistance. However, for larger aneurysms use of this agent incurs significantly longer procedure and fluoroscopy times.

136. Withdrawn

137. Outcomes After Early Decompressive Hemicraniectomy For Ischemic Stroke In Elderly Patients

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Introduction: Recent randomized trials have demonstrated that hemicraniectomy for malignant MCA infarction can lessen mortality and improve functional outcome. There is little data, however, on outcomes after hemicraniectomy for large MCA strokes in elderly patients, as patients over 60 were excluded from the trials.

Methods: We performed a single center retrospective chart review

identifying patients who underwent hemicraniectomy for ischemic stroke from Jan. 2005 to Sept. 2010. Patients greater than 60 who received surgery less than 3 days from their stroke were then selected for analysis.

Results: At our center, 31 patients have undergone hemicraniectomy for MCA infarction since 2005 and 8 patients met the inclusion criteria of our study. Our cohort had a mean age of 67.25, were predominately male (7 of 8), and had an average NIH Stroke Score of 21.6. Our study groups' in-hospital mortality was 50%. In 75% of the in-hospital deaths, aggressive medical care was withdrawn after family decided to change code status. Of the survivors, one was lost to follow-up and the others have all returned for cranioplasty. The survivors' average modified Rankin score was 4.25 and average Glasgow outcome score was 3, indicating severe disability.

Conclusions: Although hemicraniectomy in elderly patients is likely to improve survival after malignant MCA infarct, survivors are left with severe disability. If craniectomy is offered for elderly patients, it should be done only after extensive family discussion with the knowledge that if the patient survives

the hospitalization there is a very high chance of severe disability despite the procedure.

138. Real-world Comparison Of Noninvasive Imaging To Conventional Angiography In The Diagnosis Of Cerebral Aneurysms: A Single-center Experience

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Introduction: Based on numerous reports citing high sensitivity and specificity of non-invasive imaging (eg. CTA or MRA) in the detection of intracranial aneurysms, it has become increasingly difficult to justify the role of conventional angiography (DSA) for diagnostic purposes. We sought to determine the proportion of patients for whom the additional information gleaned from 3D rotational DSA led to a change in treatment.

Methods: We analyzed the medical records of the last 258 consecutive patients referred to a neurosurgeon at Vanderbilt University Medical Center for evaluation of "possible intracranial aneurysm" or subarachnoid hemorrhage. Only those who underwent noninvasive vascular imaging prior to conventional digital subtraction angiography (DSA) were included in the study. For asymptomatic patients without a history of subarachnoid hemorrhage, aneurysms less than 5 mm were typically followed conservatively. Treatment, meanwhile, was generally advocated for patients with unruptured aneurysms that measured 5 mm or larger in greatest diameter. Patient age, medical comorbidities, and aneurysm location also factored into the treatment decision.

Results: In those who underwent CTA or MRA prior to DSA, the plan of treatment was changed in 50/145 (34.5%) and 40/113 (35.4%), respectively, based on new information gleaned from DSA. Vessel loops, infundibuli, and fenestrations were among the most common benign anatomic variants erroneously interpreted as "possible aneurysm" by noninvasive imaging. Additional information about aneurysm size or morphology acquired with DSA was another common reason for changing treatment strategy.

Conclusion: In a "real-world" analysis of patients with intracranial aneurysms, DSA continues to play a role in determining the optimal management strategy.

139. High Glucose Variability Increases Risk Of Death In Patients With Spontaneous Subarachnoid Hemorrhage

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Introduction: High glucose variability is a significant marker for poor outcome in critically ill patients but its influence has not been thoroughly evaluated in patients with intracranial pathology. This study evaluated glucose variability and its influence on mortality in patients with spontaneous subarachnoid hemorrhage (SAH).

Methods: Consecutive adult patients were retrospectively identified. Glucose values were collected for the first 7 days of admission. Variability was calculated as the average change in glucose over time for each patient. Classification and regression tree (CART) analysis was used to determine high versus low glucose variability and adjust for severity of SAH and other confounding variables. Mortality was compared between low and high glucose variability groups

Results: In 64 identified patients the percentage with a Hunt/Hess grade of 3, 4, and 5 was 27%, 31% and 8% respectively. Overall mortality was 16%. CART analysis revealed Hunt/Hess grade and high glucose variability as factors influencing mortality. Average glucose was not a factor. When Hunt/Hess score was 3 or greater, mortality was 37% when glucose variability exceeded 10 mg/dl/hr vs. 4% when it was less than 10 mg/dl/hr (p=.015). When Hunt/Hess score was 2 or less, mortality was 9%. Glucose variability did not influence mortality in this subgroup.

Conclusions: Glucose variability is a significant predictor of mortality in patients with severe spontaneous SAH defined as a Hunt/Hess score of 3 or more. Whether this is a causal relationship or a marker of a more complex pathophysiologic process will require further study.

140. Surgical Trial In Lobar Intracerebral Hemorrhage - Current Status Of STICH II

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Introduction: To date there have been 14 trials of surgery for spontaneous intracerebral haemorrhage. The trials have included different populations with equivocal results but have narrowed down the population of patients that may benefit from surgery to those with lobar intracerebral haemorrhages and no intraventricular haemorrhage. The STICH II trial is due to complete patient recruitment at the end of August 2011.

Methods: This international multicentre randomized trial is being undertaken to establish whether a policy of early surgery improves outcome compared to a policy of initial conservative treatment. Eligible patients have spontaneous superficial lobar haematomas, are within 48 hours of ictus, have a GCS motor score of 5 or more and an eye score of 2 or more. The treating neurosurgeon should be in clinical equipoise over the risks and benefits of both treatments. Telephone or web randomization is available. Patients randomized to early surgery have the haematoma evacuated within 12 hours of randomization. The primary outcome is based on extended Glasgow Outcome Scale at six months.

Results: By the end of August 2010, 97 centres had joined STICH II and 350 patients had been randomized. The patients came from 61 centres in 22 countries from around the world. The patients had a median age of 65 years and a median GCS of 13. Their haematoma had a median volume of 35 ml and a median depth from the cortex surface of 1mm.

Conclusions: It is essential to encourage centres to increase their efforts for one more year. For further information visit: http://research.ncl.ac.uk/stich/.

141. Acute Stroke Intervention In Young Patients And The Role Of Vasodilator In The Revascularization Of The Occluded Artery

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Introduction: Endovascular therapy using intra-arterial is an

option for those who are either a candidate or failed intra-venous thrombolysis . However, a little is known about the age specific outcome. Objective is to describe the radiographic and clinical outcome of young patients (<65 years old) who underwent acute stroke interventional therapy. Also to evaluate the role of intra-arterial vasodilator in recanalization rate.

Methods: Consecutive patients underwent acute stroke intervention from 2007 to 2010 were enrolled. Patients demographic including presenting NIHSS, use of intra-arterial throbmolytic, vasodilator and recannalization rate were recorded. Patients' outcome was measured using Glasgow Outcome Scale (GOS) score in 30 day.

Results: 38 patients with a mean age of 38±14 received intervention, 11 of which are failed intravenous thrombolytic cases. The median NIHSS was 16 (ranges 6-38) and endovascular therapy offered within 8 hours except 5 cases who woke up with stroke. Intraarterial thrombolytic was given in 36, clot retriever device used in 30 and 20 patients received intra-arterial vasodilator (varapamil 15, nitroglycerine 5). Complete and near complete recanalization was observed in 92% and no recanalization in 3 cases. Intra-arterial vasodilator was associated with higher rate of recanalization. 30-days Good outcome (GOS 5 in 11, GOS 4 in 7) was observed in 51%, dependent (GOS 3) 34% and dead (GOS 1) 14%. Poor outcome was associated with high NIHSS and poor recannalization.

Conclusions: Acute stroke intervention in young patient achieves a high rate of recanalization and associated with intraarterial vasodilator. Further study is required to evaluate the role of vasodilator in stroke interventions.

142. Safety Of Use Of Intravenous Tirofiban For Treatment Or Prevention Of Acute Thrombus During Stent-assisted Endovascular Treatment Of Ruptured Intracranial Aneurysm

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Introduction: Use of endovascular stent technique has broadened the applicability of endovascular treatment of intracranial aneurysms. A known complication associated with use of intracranial stents is risk of acute thrombus formation and resultant cerebral infarct. Tirofiban, a non-peptide antagonistof platelet glycoprotein IIb/IIIa receptor, has been used with success in endovascular cardiac procedures. The authors sought to assess safety of use of this agent for treatment or prevention of acute thrombus in the setting of aneurysmal subarachnoid hemorrhage.

Methods: Retrospective chart review was conducted including patients admitted to the University of Iowa Hospitals and Clinics from July 2009 to August 2010 with a diagnosis of subarachnoid hemorrhage from ruptured intracranial aneurysm. Records were reviewed for endovascular treatment with stent-assisted technique, use of Tirofiban, postoperative hemorrhagic and ischemic complications.

Results: Eleven patients were identified with ruptured intracranial aneurysm, treatment with endovascular stent-assisted technique, and use of intravenous Tirofiban immediately after deployment of stent. One patient had an increase in intraparenchymal and intraventricular hemorrhage the day following endovascular treatment. No other hemorrhagic complications were identified in the series. Successful thrombolysis was observed in cases of in-stent thrombosis and no new occurrence of intra-arterial thrombus was observed after infusion of Tirofiban. One patient developed a cerebral infarct during hospitalization.

Conclusions: We present preliminary findings of safety of use of intravenous Tirofiban in the setting of endovascular treatment of a ruptured intracranial aneurysm. Our experience suggests that intravenous Tirofiban may represent a safe means of treating and preventing acute thrombus associated with stent-assisted endovascular treatment of acutely ruptured intracranial aneurysms.

143. The Rate Of Recurrence Of Basilar Artery Bifurcation Aneurysm And Role Of The Morphology Of Aneurysm In Recanalization

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Introduction: Endovascular repair is considered superior to surgical approach for aneurysms located at the basilar artery. However, the actual rate of recurrence of aneurysm and cause of recurrent is not described.

Objective: To identify the incidence of recurrent/recanalization of basilar artery bifurcation aneurysm (BAA) treated endovascularly.

Methods: From 2007 to 2010 consecutive patients who underwent endovascular repair of BAA were enrolled. Patient's demographics including the Hunt & Hess grade, Fished scale, morphology and complications including aneurysm rupture, intracranial hemorrhage or thromboembolic event including recurrent growth of aneurysm were recorded. Additionally, 90-days outcome measurement was obtained using Glasgow Outcome Scale (GOS).

Results: 33 patients with a mean age of 50 ± 14 years required 45 successful procedures to treat 33 BAA. Ruptured aneurysm was present in 15 cases. Wide-necked aneurysms were present in 27 cases, 23 of which required stent-assisted remodeling. BAA recurrence rate was 9/33 (27%), all were wide-necked and multilobulated, and were near10 mm or larger in diameter. There was no incidence of intraoperative rupture of aneurysm or thromboembolic event in our series. Good outcome was observed in 91% (GOS 5 in 29, GOS 4 in 1) and poor outcome was observed in 3 patients (GOS 3 in 3) in ruptured cases. All patients who recanalized had good functional outcome (GOS 5 in 9, mRS 0 in 9).

Conclusions: A high rate of recannalization of aneurysm was observed in BAA; these are wide-necked and multilobulated in nature. Therefore, a very close angiographic monitoring is required for all BAA especially those with wide-necked and multilobulated.

144. Angioplasty And Stenting For The Treatment Of Idiopathic Intracranial Hypertension Associated With Dural Venous Stenosis

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Introduction: Surgical options to prevent visual loss in idiopathic intracranial hypertension (IIH) include optic nerve sheath fenestration (ONSF), lumbar-peritoneal shunt (LPS), and ventriculoperitoneal shunt (VPS). Recently, venous stenting of the stenotic venous sinus has emerged as an alternative treatment modality.

Methods: We retrospectively reviewed all cases of patients treated with dural stents for IIH at our institution. Patients were considered eligible based on the following criteria: A) medically refractory IIH with papilledema and B) dural venous sinus stenosis of the dominant venous outflow system with a gradient of at least 10 mm.

Results: Ten cases (all female; mean 36.5 years) were identified. Technical success was achieved in 100% with no major periprocedural complications. The mean pre-procedural gradient was 19 mmHg, reduced to 3.2 mmHg post-procedure. Headache improved in 6/10 (60%). Papilledema resolved and visual acuity stabilized or improved in 8/8 (100%) patients with formal ophthalmologic follow-up. Among the 8 patients with angiographic follow-up, there were no instances of in-stent stenosis, however, stenosis of approximately 50% immediately distal to the stent was seen in 2/8 (25%).

Conclusions: Venous sinus stenting can be performed with a high degree of technical success and safety with excellent clinical outcomes (including, in our series, stabilization or reversal of visual loss and papilledema in all patients and significant improvement or

resolution of headache in 60%). These results suggest that in properly selected patients with IIH and dural venous sinus stenosis, angioplasty and stenting is a reasonable alternative to ONSF, LPS, or VPS.

145. Safety And Cost Effectiveness Of Step-down Unit Admission Following Elective Neurointerventional Procedures

Boyd F. Richards, DO; J. Brett Fleming, MD; Chevis N. Shannon, DR; Beverly C. Walters, MD; Mark R. Harrigan, MD (Birmingham, AL)

Objective: Post procedure monitoring in a neurointensive care unit (NICU) after neurointerventional procedures is conventional at most centers. However, NICU resources are scarce and costly. An intermediate-care step-down unit may be a safe and cost-effective alternative to the NICU for patients after uncomplicated neurointerventional procedures.

Methods: Retrospective review of 128 consecutive patients over a three year period undergoing elective neurointerventional procedures, including treatment of intracranial aneurysms, tumors, and dural arteriovenous fistulas. Seventy-one patients were admitted to a stepdown unit and 57 patients were admitted to the NICU. Endpoints comprised post-procedural complications, hospital costs, and length of stay. Patients admitted to a step-down unit were compared to patients admitted to a NICU.

Results: Patients admitted to the step-down unit did not have more complications than patients admitted to the NICU. One patient, admitted to the step-down unit, had a neurologic change after the procedure which was immediately recognized by nursing staff and adequately managed. The mean total cost was $19,299 (SD $6,955) for step-down unit patients and $22,716 (SD $8,052) for NICU patients, resulting in a statistically significant cost savings for the patients admitted to a step-down unit of $3,417 ($p = 0.012$). Length of stay averaged 1.32 days for step-down unit patients and 1.50 ($p=0.084$) days for NICU patients.

Conclusions: A step-down unit is a safe and cost-effective alternative to the NICU for patients undergoing elective neurointerventional procedures.

146. Length Of Hospitalization, Morbidities And Complications Of Unruptured Intracranial Aneurysms Treated By Single Surgeon

Myeong Jin Kim, MD (Korea, Republic of, Seoul)

Background and Purpose: Endovascular treatment has become an major tool for the management of unruptured aneurysms, however surgical clipping remains as a novel treatment method for unruptured intracranial aneurysms. To evaluate the roles of the both treatment modalities, we report the difference of outcomes for patients with unruptured intracranial aneurysms treated with either clipping or coiling by single surgeon.

Materials and Methods: From 2008 to 2010, 192 patients were retrospectively evaluated with our aneurysm databases.

Results: In clipping group (88 patients, 46%), there were 3 complications (3.4%), one patient had neurologic deficit due to postoperative hemorrhage. In one patient with giant basilar bifurcation aneurysm, the basilar artery occlusion was performed for flow diversion after procedure resulted in brainstem infarction. In coiling group (104 patients, 54%), there were 5 complications (4.8%). There was an aneurysm rupture during the procedure. There were two symptomatic cerebral infarctions. In two patients who underwent stent-assisted coiling had intra-cerebral hemorrhage not related to the aneurysm at 1 day after the procedure. Surgically clipping, compared with endovascularly coiling, was associated with longer hospitalization(median 11 versus 4 days; $P < 0.0001$).

Conclusion: Both groups had low morbidities and procedure-related complications, but serious complication was occurred in patient who received stent-assisted coiling procedure in treating wide necked aneurysm. Stent-assisted coiling while the patient is on dual anti-platelet medication may be a risk of post-procedural intracranial hemorrhage. Special attention should be given in treating patients who were on dual anti-platelet agent. Giant aneurysm in posterior circulation is still challengeable with either treatment modalities.

147. WITHDRAWN

148. WITHDRAWN

149. Improvement Of Ocular Circulation After STA-MCAmca Bypass In The Internal Carotid Artery Occlusion

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Introduction: The authors examined and analyzed the effect of the STA-MCA bypass for the ocular circulation in the internal carotid artery occlusion.

Methods: The ocular circulation was evaluated by the ophthalmic artery (OphAr) flow and the central retinal artery (CRA) flow using color Doppler flow imaging (CDFI) in ninety-five patients having the internal carotid artery occlusion treated with STA-MCA bypass. OphAr or CRA CDFI provided the information about the flow velocity and peak systolic flow velocity (Vs). The authors also evaluated the chronic ocular ischemic syndrome.

Results: 1) Preoperatively, 77 patients showed reversed OphAr flow, and the other 18 patients showed antegrade OphAr flow. The mean OphAr Vs was -0.28 m/sec, and the CRA Vs was 0.06m/sec. 2) At one month after bypass, 48 patients showed the antegrade OphAr flow. The flow direction of the OphAr flow was corrected significantly. The mean OphAr Vs increased to -0.06 m/sec significantly, and the CRA Vs also increased to 0.08 m/sec significantly. 3) At three months after surgery, 60 patients showed the antegrade flow. The mean OphAr Vs increased to 0.05 m/sec significantly, and the CRA Vs also increased to 0.11 m/sec significantly. 4) Before bypass, fifty-four patients complained of the chronic ocular ischemic syndrome. During the follow-up period (mean: 5.3 years), 30 patients (56%) showed the improvement of the visual symptoms.

Conclusions: In the internal carotid artery occlusion, the ocular circulation improved after STA-MCA bypass according to the OphAr and CRA CDFI examination. Chronic ocular ischemic syndrome also improved during follow-up period.

150. Endovascular Intervention For Salvage Of Extracranial-intracranial Bypass Graft Stenosis

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Introduction: Graft conduit stenosis is an uncommon but important problem which can be encountered following extracranial-intracranial (EC-IC) bypass surgery, and carries significant potential for morbidity and mortality. Angioplasty for graft stenosis (with or without stenting) has been discussed in the cardiothoracic literature extensively, but its application for neurosurgical purposes has not been well documented.

Methods: We retrospectively reviewed cases of EC-IC bypass undergoing endovascular intervention for graft stenosis; a literature search was performed. Diagnosis, pathology, and indications for intervention were reviewed.

Results: Three patients underwent 13 endovascular interventions for EC-IC saphenous vein graft stenosis. The indication for the initial bypass was an unsecured intracranial aneurysm in all cases and an interposing saphenous vein graft was used in all cases. The initial endovascular procedure was needed 10 to 23 weeks after the bypass surgery, a timeframe suggestive of intimal hyperplasia as the

underlying etiology of stenosis. There were nine cases of angioplasty alone, three with stent placement, and one case in which vasodilators were infused. Non-invasive phase contrast quantitative magnetic resonance angiography was effective in predicting graft stenosis. Despite intervention, 2 grafts ultimately occluded, and a third has remained patent only after multiple angioplasties and placement of a drug eluting stent.

Conclusions: Though rare, bypass graft stenosis can occur in the subacute period, and likely represents a flow related venopathy. Given the challenges of re-do bypass surgery, endovascular intervention is an attractive treatment option. Although not uniformly successful, repeated interventions with diligent follow-up may allow for graft salvage.

151. Timing And Mechanism Of Ischemic Stroke Due To Extracranial Blunt Traumatic Cerebrovascular Injury

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Objective: Extracranial traumatic cerebrovascular injury (TCVI) is present in 1-3% of all blunt trauma patients and up to 31% of patients have an associated neurological injury. Although antithrombotic medications are widely used in patients with TCVI, the timing and mechanism of ischemic stroke in this setting has not been defined.

Methods: Prospective study of all patients with TCVI admitted to a Level I trauma center over a 28-month period. All blunt trauma patients with risk factors for TCVI underwent a screening CT angiogram (CTA) on admission. All patients with either an ischemic stroke or a CTA suggesting TCVI had a confirmatory digital subtraction angiogram (DSA). Patients with DSA-confirmed TCVI were treated with aspirin 325 mg daily; all patients were followed during their hospitalization for the occurrence of new ischemic stroke. In addition, 12 patients with TCVI underwent transcranial Doppler examination for microembolic signals.

Results: A total of 112 patients had a CTA suggesting a TCVI; 68 were confirmed by DSA. Overall, eight patients had an ischemic stroke prior to or during admission. Six of the patients had their event prior to diagnosis with CTA; one occurred after diagnosis, and in one it was not clear when the stroke occurred. All patients with ischemic stroke had CT findings indicating an embolic mechanism. Two of 12 (17%) of patients with TCVI had microembolic signals on TCD.

Conclusions: Most ischemic strokes due to TCVI are embolic in nature and occur prior to diagnosis using a CTA screening protocol and treatment with aspirin.

152. The Effect Of First Coil Packing Volume On Total Aneurysmal Fill Utilizing Simple Geometric Models

Prashant S. Kelkar, DO (Southfield, MI); Richard D. Fessler, MD (Detroit, MI)

Introduction: Higher packing density of coiled aneurysms has been shown to have a positive correlation with aneurysm obliteration and diminishing recurrences. Studies have compared coil shapes, lengths, assist devices, and brands attempting to find the ideal milieu to achieve the greatest packing density and the lowest recurrence rates. We add to the literature a small cohort of patients treated with single brand coil embolization attempting to show benefit of higher "first coil" packing ratios, re-demonstrating that preoperative examination of the geometry of an aneurysm and selecting the appropriate coil style impacts the total packing density.

Methods: A retrospective review was done of aneurysms treated with coil embolization utilizing axium coils (ev3). Aneurysm volumes were measured utilizing geometric models. Aneurysm location, size, assist devices used, and outcomes at 3 months if available were noted; coil size/shape/length and number were counted and the percentages of aneurysm fill by the first coil and at completion were calculated.

Results: Aneurysms treated utilizing a solitary coil brand showed no difference in the potential of aneurysm fill of ruptured versus unruptured intracranial aneurysms. When comparing aneurysms of similar volume, those that had first coil packing volumes nearing 15 percent had final embolized aneurysm volumes greater than 30 percent with the least recurrences.

Conclusions: Using preoperative aneurysm models and simple geometric calculations can allow the operator to select the appropriate coils to achieve maximal percentage packing after placement of the first coil, which in turn should produce aneurysms with the greatest embolized volume.

153. Major Recurrence Of Intracranial Aneurysm Following Endovascular Treatment Is Related To Aneurysm Sac Growth, Not Coil Compaction

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Introduction: Coil embolization of saccular intracranial aneurysms is established as a safe and successful treatment option with known risk of recurrence requiring retreatment. The authors sought to review cases requiring retreatment in an attempt to identify factors associated with major recurrence.

Methods: All cases of endovascular treatment of an intracranial aneurysm at the University of Iowa Hospitals and Clinics, Department of Neurosurgery, during a one-year period were reviewed. Cases requiring retreatment were identified. Pretreatment, post-treatment and follow-up angiograms were reviewed. Treatment success was defined as residual aneurysmal filling of less than 10%. Angiographic features, use of intracranial stent, and history of subarachnoid hemorrhage (SAH) were analyzed as potential factors associated with recurrence.

Results: Five recurrences were found in a series of 174 endovascularly treated aneurysms with an average follow-up of 6 months. All recurrent aneurysms had wide neck size. Two cases were unruptured. Four aneurysms were completely occluded angiographically at the end of the initial procedure. Three cases required stent placement - one with neck-spanning configuration, one with Y configuration, and one with Waffle-cone technique. None had rehemorrhaged in the interval to second treatment. All recurrent aneurysms showed stable coil volume and growth of the aneurysm sacs. All retreatments were completed with stent-assisted technique.

Conclusions: Our series suggest that that aneurysm sac growth, not coil compaction, is the cause of a major recurrence of an intracranial aneurysm following successful endovascular treatment. Further follow up is needed to confirm this mechanism.

154. Admission Facility Is Associated With Outcome of Aneurysmal Subarachnoid Hemorrhage

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Introduction: Studies of outcome following subarachnoid hemorrhage (SAH) suggest a temporal relationship between delay in treatment and outcome. No study has compared patients admitted directly versus those transferred acutely to a neurovascular center (NC). We investigated patient outcomes comparing patients initially admitted to a general hospital and subsequently transferred, with patients admitted directly to our NC, a 1000-bed Level 1 trauma tertiary referral center with a neurocritical care ICU, cerebrovascular neurosurgeons and endovascular specialists.

Methods: All aneurismal SAH cases between 2006 and 2008 were identified: 31 patients were admitted directly and 76 patients transferred from general hospitals. Univariate and multivariate analyses evaluated mortality, complications, adverse discharge (other than home) and patient length of stay

Results: Differences in baseline parameters (age, gender, admission GCS, fisher grade) were not statistically significant between the two groups but admission Hunt and Hess Grade 4/5 (29 percent direct; 13 percent transfer) were different. Transferred patients developed vasospasm more frequently (58 versus 32 percent) and delays before surgery (3.9 days vs. 2.4 days). The probability of vasospasm increased with HH grades 4/5 and Fisher grades 3/4 (OR 5.41 [1.44-20.4]) leading to greater in-hospital mortality (OR 7.83 [1.38-44.5]). Length of hospital stay and odds of adverse discharge were also both greater with transferred patients. No differences were identified between surgical and endovascular treatment

Conclusions: SAH patients admitted directly to the NC had better outcomes than those transferred from general hospitals. Patients with typical symptoms should therefore be preferentially directed to neurovascular centers. Factors associated with these disparate outcomes deserve further study.

155. O-glcnacylation Is Increased Within The Stroke Penumbra

Thomas R. Whisenhunt, MD, PhD (Birmingham, AL); Agnieszka Ardelt, MD (Chicago, IL); Jeffrey E. Kudlow, MD; Andrew J. Paterson, PhD (Birmingham, AL)

Introduction: Oxidative stress is a well-documented component of many disease states including cerebrovascular accidents and neuroischemia. O-GlcNAcylation, modifying cytoplasmic and nuclear proteins with O-GlcNAc onto serine and threonine residues, regulates multiple cellular functions including the stress response and cell survival. Specifically, oxidative stress has been shown to company with an elevated level of O-GlcNAcylation and glucosamine induced O-GlcNAc elevation has been shown to be neuroprotective in stroke models. The significance of the current study is to show an increased O-GlcNAc modified state exists within the stroke penumbra.

Methods: Cerebral ischemic insults in rats were performed by unilateral MCA occlusions. Animals were sacrificed and brains were collected for sectioning and imaging at different times after the event. Immunoflourescent microscopy with antibodies specific for the O-GlcNAc modification (RL2 and CTD110) and JNK1 were performed on brain sections using standard techniques for fixation and processing.

Results: Increased fluorescence was seen with both RL2 and CTD110 in all post ischemic sections surrounding the ischemic focus, the penumbra, but not in control sections. No significant difference was apparent between RL2 or CTD110 indicating equal effectiveness between the antibodies in Immunoflourescent analysis.

Conclusions: Here we demonstrate increased O-GlcNAcylation within the stroke penumbra. This correlates studies showing JNK1 and p-JNK within the penumbra with studies showing JNK1 activation is regulated by O-GlcNAcylation. Our data provide a link between O-GlcNAcylation and oxidative stress resistance within the stroke penumbra. This may yield novel therapeutic strategies whereby altering the O-GlcNAc dynamic protects patients suffering from neuroischemic events.

156. Long-term Angiographic Recurrence Of Cerebral Aneurysms Treated With Microsurgical Clipping

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Introduction: The recurrence rate of clipped aneurysms is 1-3% and the actual proportion of these that are symptomatic or require re-treatment is very low. The durability of this procedure has become increasing relevant with advancing endovascular techniques. In this study, we reviewed clipped aneurysms with long-term angiograms to assess aneurysmal re-growth, the natural history of residual aneurysms and the formation of denovo aneurysms.

Methods: From a cohort of patients with ruptured and/or unruptured aneurysms treated with microsurgical clipping between 2004-2007, we included those with 3 year angiograms. In those with a residual on post-operative angiography, we determined if there was progression by comparing the post-operative and 3 year angiograms.

Results: There were 100 aneurysms in 85 patients that showed no evidence of re-growth or re-bleeding. A stable residual neck was demonstrated in 12 patients and 67% of these had complex aneurysms of the middle cerebral artery bifurcation or posterior communicating artery. 83% had a

residual less than 3mm. All were asymptomatic and did not require re-treatment. There was one patient (1%) with a small recurrence (2mm) that did not require intervention and one patient (1%) with a denovo aneurysm.

Conclusions: Microsurgical clipping of aneurysms is a durable treatment with a low rate of recurrence and re-bleeding. In our study, we had one patient with recurrence who was asymptomatic and did not require intervention. Those with residual necks did not show angiographic progression or require

treatment. The rate of denovo aneurysms was small. We plan to compare this with a similar cohort of endovascularly treated patients.

157. Magnetic Resonance Angiography Versus Digital Subtraction Angiography In The Follow-up Of Coiled Intracranial Aneurysms: A Real-world Cost Analysis

J. Brett Fleming, MD; Boyd F. Richards, MD; Chevis N. Shannon, MD; Beverly C. Walters, MD; Mark R. Harrigan, MD, (Birmingham, AL)

Introduction: The conventional method for follow-up of coiled aneurysms is digital subtraction angiography (DSA). Recently, gadolinium-enhanced magnetic resonance angiography (MRA) has been found to be an accurate, less invasive alternative to DSA. The clinical usefulness and cost-effectiveness of MRA, however, has not yet been defined.

Methods: Retrospective review of 76 consecutive patients who underwent coil embolization of an intracranial aneurysm from 2004-2008. MRA was used for routine surveillance imaging 6 months and 18 months after treatment; if the MRA indicated recanalization, then DSA was done for confirmation. The complications and costs of using MRA were compared to a theoretical cohort of patients in whom DSA was used as the only method of imaging over the 18 month period.

Results: Of the 76 patients, 9 required DSA at 6 months and 3 required DSA at 18 months. No patients had a complication from DSA or MRA. No patient had a rupture of the treated aneurysm. The average costs of an MRA and DSA were $5,338 and $7,750, respectively. For the 76 patients, the mean cost of radiographic follow-up per patient using this protocol was $11,899; if DSA had been used for all imaging, the mean cost would have been $15,500. This absolute difference in cost was $3,601 per patient and was statistically significant (p less than 0.0005).

Conclusions: MRA, followed by DSA as necessary, costs less when compared to DSA alone. Furthermore, it is much less invasive and more convenient for patients, making it a useful alternative to DSA.

158. The Use Of Intraoperative Duplex Ultrasonography For The Identification And Repair Of Kinking Stenosis Following Carotid Endarterectomy

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Introduction: Post-endarterectomy kinking of the internal carotid artery (ICA) is one type of residual technical defect that has been

identified with the use of intraoperative duplex ultrasonography (IDUS). The goal of this study was to describe the unique anatomical and hemodynamic characteristics of post-endarterectomy kinks as imaged by IDUS, establish parameters for their intraoperative repair based on these characteristics, and determine the effect of such parameters on long-term postoperative ultrasonographic and clinical outcome in patients undergoing carotid endarterectomy (CEA).

Methods: The electronic medical records and IDUS recordings of all CEA cases performed over a 10-year period by a single neurosurgeon, who uses a selective patching closure method, were retrospectively reviewed to identify and assess cases of post-endarterectomy kinking.

Results: IDUS assisted in the identification of 27/285 cases (9.5%) of post-endarterectomy kinking. The degree of stenosis was significant in 11 cases, leading to immediate correction by distal patch angioplasty. Only two cases experienced asymptomatic 60-79% or greater restenosis within 24 months following surgery. No strokes, neurological symptoms, or deaths related to a cerebrovascular accident occurred during the follow-up period.

Conclusions: Post-endarterectomy ICA kinking appears to be a common technical defect following CEA, with special anatomical and hemodynamic properties that may be overlooked in the absence of IDUS monitoring. Selectively patching kinks based on 1) an abnormal duplex ultrasound appearance, and 2) peak systolic flows greater than 120 cm/sec, corresponding to 41-59% or greater diameter stenosis, leads to long-term resolution of the luminal-filling defect.

159. Epidemiology Of Death From Aneurysmal Subarachnoid Hemorrhage In New Mexico: A Different Perspective

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Introduction: Aneurysmal subarachnoid hemorrhage (SAH) is associated with death in 3.49/100,000 people per year. New Mexico has a unique population consisting of 66 percent Caucasians, 42 percent Hispanics, 10 percent Native Americans, 2 percent Blacks, and 1 percent Asians. Our objective was to determine the epidemiological factors associated with death from aneurysmal SAH in New Mexico.

Methods: A retrospective review of 236 patients who died of aneurysmal SAH from January 1, 2001 to December 31, 2007 was completed. Traumatic SAH was excluded. Data were obtained from the New Mexico Vital Records (Santa Fe, New Mexico). ICD 10 coding was used for cause of death (I60.0-I60.7). Data from the Indicator-Based Online Database was used for census values.

Results: The incidence in New Mexico is 2.96/100,000 per year (national-3.49). The incidence for non-Hispanic Caucasians was 2.70/100,000 people (national-3.39), non-Caucasian Hispanics was 3.39/100,000 people (national-2.71), Native Americans was 2.71/100,000 people (national-2.55), Blacks was 4.62/100,000 people (national-4.56), and Asians was 1.76/100,000 people. Age based data showed incidence of 1.11 and 5.71 in the 35-44 and 65-74 groups, respectively, which are higher than national average.

Conclusions: The incidence of death by aneurysmal SAH in New Mexico is lower than the national average. Death from aneurysmal SAH is higher in Hispanics and Native Americans, and lower in Caucasians, Blacks, and Asians. Further analysis of Native American and Hispanic risk factors needs to be done to better understand these unique trends.

160. Functional Outcome And Quality Of Life Following Decompressive Hemicraniectomy For Malignant MCA Territory Infarction

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Introduction: Decompressive hemicraniectomy (DH) has been shown to reduce mortality in patients with malignant MCA territory infarction (MMCATI). However, many patients survive with moderate-to-severe disability and controversy exists as to whether this should be considered good outcome. To answer this question, we assessed the quality of life (QoL) of patients after DH for MMCATI.

Methods: The outcome of 14 consecutive patients who underwent DH for MMCATI between 2001 and 2009 was assessed using retrospective chart analysis and telephone follow-up in survivors. Functional outcome was determined using Glasgow Outcome Scale, modified Rankin Scale (mRS), and Barthel Index. QoL was assessed using Stroke Impact Scale.

Results: There were 6 men and 8 women with a mean age of 44 years (range 27-57). All patients had reduced level of consciousness preoperatively. Five had dominant-hemisphere stroke. Median time to surgery was 45 hours (range 1- 96). Two patients died and 1 was lost to follow-up. Of 11 survivors, 7 (63.6%) had a favorable functional outcome (mRS<4) after a median follow-up of 27 months (range 1-72). No patient was in persistent vegetative state. Despite impaired QoL, particularly in physical domains, the majority of interviewed patients and caregivers (7 of 8), including those with dominant-hemisphere stroke, were satisfied.

Conclusion: In order to properly evaluate the effectiveness of DH for MMCATI, outcome must be evaluated in terms of QoL as perceived by patients and their caregivers. Most patients report satisfactory QoL despite significant disability. Dominant-hemisphere MMCATI should not be considered a contra-indication to DH.

161. Extracranial Carotid-vertebral Bypass For Endovascular Access To Complex Posterior Circulation Aneurysms: A Novel Management Approach

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Introduction: Endovascular embolization is a desirable treatment option for complex posterior circulation aneurysms, particularly recurrent aneurysms or those in difficult to access surgical locations. However, endovascular access is occasionally prohibited by proximal vertebral occlusion or vessel tortuosity. One strategy in such instances involves creation of an extracranial bypass conduit to the distal vertebral artery (VA). This is a novel strategy to allow for endovascular treatment of aneurysms at high risk for direct surgery.

Methods: Three cases of carotid-VA bypass performed to provide endovascular access to posterior circulation aneurysms were identified. The clinical indications, radiographic characteristics, and outcomes were reviewed .

Results: Indications for bypass were: previously clipped recurrent basilar tip aneurysm; previously coiled midbasilar aneurysm with compaction requiring stent placement; distal intracranial VA aneurysm with iatrogenic vertebral dissection/occlusion after initial coil attempt. In all cases routine endovascular access for primary or stent-assisted coiling was prohibited by vertebral tortuosity. Bypass using interposition saphenous vein grafts were successfully performed to the C1-C2 region of the V2 segment without complications. The bypass was followed by successful endovascular treatment in all cases, 2 - 8 weeks post surgery. In one patient, 2 recurrent treatments through the graft were subsequently performed for coil compaction.

Conclusions: Extracranial carotid-VA bypass can be a valuable tool in the management of complex posterior circulations aneurysms. It is a safe and efficacious technique providing a conduit for repeated access to the posterior circulation in patients with otherwise prohibitive vertebral anatomy.

162. Development Of An Iapplication For Usage At The Bedside To Predict Cerebral Aneurysm Recanalization Risk Estimates Utilizing A Centralized Platform

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Introduction: Application of outcome-predicting models in the clinical setting is a common challenge due to model complexity and availability. The goal of this project is to simplify clinical model application, automate model derivation and improve access to the most up-to-date statistical outcome predictors using a handheld iApplication.

Methods: A modular iApp was developed, where the program constructs itself based on the central server model information every time it is started. To test the platform, a multivariate logistic regression model of the endovascularly coiled aneurysm retreatment probability was made based on 414 patients, as described elsewhere. A simple script language was developed to communicate model information between researchers and the software platform.

Results: The logistic regression model suggests aneurysm size and rupture status, patient age, gender and smoker status to be predictive of retreatment risk. The model was deployed online using the developed script language. On the iPhone, the most up-to-date model was evaluated, where the clinician simply entered the required patient data and pushed "Calculate". As the model evolved (patient number and predictor count changed), the iApp endpoint was not reprogrammed, but it changed based on the current globally deployed model, thus seamlessly providing access to the most up-to-date clinical model of retreatment risk model for coiled aneurysms.

Conclusion: This project proposes a novel approach for streamlining the translation of clinical outcome models into clinical decision-making for determining aneurysm recanalization risk.

163. Surgical And Endovascular Treatment Of Intracranial Aneurysms: A Comparative Analysis Of The Outcome

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Introduction: Because of the improvement of the cerebral MRI in the screening for any neurological disease, the diagnosis of unruptured intracranial aneurysms is becoming much more frequent than in the past. In our study we analyze the results of surgical and endovascular treatment.

Methods: We studied 250 patients harboring 262 unruptured aneurysms. They were treated between 1998 and 2009 at Department of Neurosurgery of the Catholic University, Rome. All the cases were treated by the same neurosurgeon and the same interventional neuroradiologist. A questionnaire was submitted to all the patients one year after the treatment. The scale we obtained ranges from 0 Death to 5 Normal.

Results: 73% of the aneurysm were treated surgically and 27% by endovascular procedure. Based on our scale we documented a 1,69% of mortality rate for surgery and 0 for endovascular treatment. Considering the highest scores (4-5) we found 83% for surgery and 92% for endovascular procedure. A non complete exclusion of the aneurysm at the immediate post-treatment control was documented in 29% of the endovascular group (with a further treatment in the 8% of the cases) and 4% of the surgical one (with no need of a new treatment). A late riperfusion of the aneurysm was found in 9,7% of the endovascular group and in 1,7% of surgical group.

Conclusions: Considering only the data obtained by our scale, the endovascular procedure reaches better results, but if we analyze also the percentage of immediate incomplete exclusion and of the late recurrence, the surgical procedure is more reliable.

164. Management Of Blunt Extracranial Traumatic Cerebro–vascular Injury: A Multidisciplinary Survey Of Current Practice

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Objective: Extracranial traumatic cerebrovascular injury (TCVI) is present in 1-3% of all blunt force trauma patients. Although options for the management of patients with these lesions include anticoagulation, antiplatelet therapy, and endovascular treatment, the optimal management strategy

for patients with these lesions is not yet established. Furthermore, indications for the endovascular treatment of clinically silent lesions are also not established.

Methods: A six-item multiple-choice survey was sent by electronic mail to a total of 11,784 neurosurgeons, trauma surgeons, stroke neurologists, and interventional radiologists. The survey included questions about their choice of imaging, medical management, and the use of endovascular techniques. Survey responses were analyzed according to stated specialty.

Results: Seven hundred eighty-five (6.7%) responses were received. Overall, a total of 325 (42.8%) respondents favored anticoagulation (heparin and/or warfarin), 247 (32.5%) favored antiplatelet drugs, 130 (17.1%) preferred both anticoagulation and antiplatelet drugs, and 57 (7.5%) preferred stenting and/or embolization. Anticoagulation was the most commonly preferred treatment among vascular surgeons (56.9%),neurologists (50.2%) and neurosurgeons (40.7%), whereas antiplatelet agents were the most common preferred treatment among trauma surgeons (41.5%). Overall, 158 (20.7%) of respondents recommended treatment of asymptomatic dissections and traumatic aneurysms, 211 (27.7%) did not recommend it, and 39.4% recommended endovascular treatment only if there is worsening of the lesion on follow-up imaging.

Conclusions: These data demonstrate the wide variability of physicians' management of traumatic cerebrovascular injury, both on an individual basis, and between specialties. These findings underscore the need for multicenter, randomized trials in this field.

165. SUR1 Blockade Reduces Hippocampal Injury And Preserves Spatial Learning In Traumatic Brain Injured Rats

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Introduction: Sulfonylurea receptor 1 (SUR1) plays a key role in various forms of CNS injury, but its role in hippocampal dysfunction after mild-to-moderate TBI is unknown. We studied a rat model of cortical impact TBI to assess the hypothesis that post-injury SUR1 upregulation in the hippocampus is associated with a later deficit in learning.

Methods: Male Long-Evans rats underwent sham surgery and cortical impact calibrated to avoid primary and secondary hemorrhage in the hippocampus. To assess the role of SUR1, a blinded investigator administered vehicle or glibenclamide to injured rats for 1 week. Quantitative immunochemistry, histochemistry, and PCR were carried out to measure SUR1 protein, Abcc8 mRNA, cleaved caspase-3, and fluoro-jade C in the hippocampus at various post-injury timepoints. Morris water maze tasks measured incremental and rapid learning ability.

Results: The transcription factor, specificity protein 1, which regulates expression of SUR1 and caspase-3, was activated in the hippocampus 15 min after injury. Upregulation of SUR1 protein and Abcc8 mRNA were evident by 6 hr. At 2 weeks, the increase in activated caspase-3 in hippocampal place cells of glibenclamide-treated rats was half of that in vehicle-treated rats. At 4 weeks, testing for rapid learning showed significantly better performance in glibenclamide-treated rats, with performance correlating inversely

with fluoro-jade staining for degenerated neurons in the hippocampal hilus.

Conclusion: SUR1 is transiently upregulated in the hippocampus after cortical impact injury despite the lack of overt hemorrhagic contusion to the hippocampus. Glibenclamide, a selective SUR1 inhibitor, significantly improves histological outcome and preserves cognitive performance up to 4 weeks after TBI.

166. Review Of Predictive Values Of Available Balloon Test Occlusion Modalities For Abrupt Carotid Closures

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Introduction: Balloon test occlusion (BTO) of the internal carotid artery (ICA) has proven efficacious for the preoperative evaluation of patients that will or may undergo abrupt ICA occlusion. Numerous modalities and combinations of such have been proposed for optimization of the predictive value of the test reducing the false tolerability rate to 5-20%. Some studies report predictive values ranging between 67-98%, attesting the variability in techniques and modalities. Still there is no consensus as to which methods have the better predictive capability.

Methods: We reviewed our results and the available literature to evaluate and compare the predictive values of the different modalities at hand. Between 2004 and 2010, 12 patients at UT Southwestern, Dallas, underwent carotid closure after tolerating BTO. There were 7 men and 5 women. Ages ranged from 11 to 82 (mean 50 y/o). Three patients had neck cancer, 2 carotid body tumors, and 7 intracranial aneurysms.

Results: Four of these patients presented a stroke. Three of these were related to carotid sacrifice. The predictive value for carotid closure tolerance was 75%.

Conclusions: The importance of chemically or hemodynamically induced stress assessment of the cerebrovascular reserve during BTO may help reduce false tolerability and improve prediction of long-term tolerance of occlusion.

167. Adenosine Induced Flow Arrest To Facilitate "Plug And Push" Technique For Onyx Embolization Of High Flow Intracranial Fistulae

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Introduction: Formation of an Onyx plug around the distal end of a microcatheter is fundamental to the "plug and push" technique required for optimal Onyx penetration of an AVM nidus or occlusion of a fistulous connection. A high flow shunt in a large feeder may make this technique difficult or impossible. We describe the use of adenosine flow arrest to facilitate Onyx plug formation.

Methods: We report the case of a 51 year-old with a large right posterior temporal arteriovenous malformation (AVM) with prominent arteriovenous fistulous components. Occlusion of two of the fistulous connections was challenging because the high flow hindered our ability to form an Onyx plug around the distal catheter tip. Tortuosity of the vessels rendered proximal balloon occlusion hazardous. The high flow was not compatible with safe coil occlusion. We, therefore, used adenosine to induce temporary cardiac arrest while we were injecting the Onyx through the microcatheter.

Results: A plug was successfully formed during flow arrest followed by parent artery occlusion proximal to the draining vein. This technique was successfully utilized during two of the patient's five embolizations.

Conclusions: While adenosine induced flow arrest has been previously described for embolization procedures, the technique of using adenosine to temporarily induce cardiac arrest to safely allow creation of an Onyx plug which facilitates embolization of a high flow arteriovenous fistula has not to our knowledge been previously reported. This technique may render otherwise untreatable shunts amenable to safe occlusion.

168. Microsurgical Clipping Of Previously Coiled Intracranial Aneurysms: The Northwestern Experience

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Background: The surgical clipping of intracranial aneurysms previously treated with endovascular coils is a treatment modality for patients with incomplete treatment, recanalization, and/or recurrent aneurysm growth. We present our institutional experience with these complex lesions, addressing the technical nuances, safety and outcomes.

Methods: A retrospective review of the patient records at Northwestern Memorial hospital was performed for patients with a history of aneurysm coiling who underwent microsurgical clipping of that same lesion.

Results: Eight patients were identified. The mean age was 55. The mean latency time between coiling and clipping was approximately 200 days. Fifty percent of the aneurysms were in the anterior communicating artery, and 75% were less that 10mm in size. The mean aneurysm size was 5.5mm. The majority of aneurysms (87.5%) had a history of rupture. The most common indication for clipping was the present of a remnant (50%) followed by new growth on follow up imaging (37.5%). Temporary clipping was employing in half the cases, while coil extraction was not performed. All lesions demonstrated obliteration on follow up imaging. There was one complication of the development of a posterior fossa hematoma requiring evaculation.

Conclusions: Microsurgical clipping of previously coiled aneurysms can be performed with a high obliteration rate as well as low morbidity and mortality in well selected cases. The fact that the procedure is technically complex highlights the importance of patient selection, and ensuring that sufficient neck will be present at the time of clipping. Pre-operative planning should include discussion of alternatives, including bypass.

169. Intravenous Heparin In The Setting Of Acute Cerebral Ischemia. A Prospective Cohort Safety Study

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Introduction: Heparin was amongst the first drugs to be tested for the treatment of acute cerebral ischemia. As minimal benefit has been demonstrated, its use has fallen by the wayside with the advent of thrombolytics and mechanical thrombolysis that have a greater impact. Currently, there is no safety profile for intravenous heparin infusion in patients with acute cerebral ischemic events who are not candidates for intravenous tissue plasminogen activator thrombolytics.

Methods: Over the course of two years, patients not treated with iv thrombolytics were enrolled in a prospective database who received intravenous heparin at admission. Demographics, co-morbidities and adverse events were recorded in a prospective fashion. Qualitatively, early bleeding rates, hospitalization complications, subsequent cranial surgeries and medicinal changes were analyzed. Quantitatively, correlations were sought between patient outcomes based upon length of stay.

Results: 200 patients were enrolled in the cohort. 3.38% patients had hemorrhagic conversion of their stroke and similar number of patients encountered GI bleeding. Overall, in 85.81% of the patients, no adverse events were recorded.

Conclusions: Our results indicate a safe profile of intravenous

heparin administration in patients in the setting of acute cerebral ischemia who are not candidates for intravenous thrombolysis. The low rates of hemorrhagic complications balances well against earlier reports and further analysis as well as outcome data will determine more clinical efficacy in justification of its use.

170. Transient Pupillary Dilatation Following Local Papaverine Application in Intracranial Aneurysm Surgery

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Introduction: Isolated cases of transient pupillary changes after local intra-cisternal papaverine administration during aneurysm surgery have been reported. The goal of this study was to analyze the prevalence of this phenomenon and to examine if additional intra-operative techniques or drugs might contribute to this effect. A discussion of the potential mechanism of this drug-induced effect, as well as a literature review, are presented.

Methods: We retrospectively analyzed 10 consecutive cases of ruptured and unruptured anterior circulation aneurysm clippings performed by a single surgeon (R.D.) at our institution from January to May 2010 in which local papaverine was applied to alleviate vasospasm. All patients were burst-suppressed prior to temporary clipping. In all cases, intra-operative indocyanine green (ICG) angiography and no intra-operative cerebral angiography was performed to assess real-time vascular branch patency and confirm aneurysm occlusion.

Results: We observed either bilateral or ipsilateral pupillary dilation in the immediate post-operative period in three of the 10 (30%) patients who received papaverine. In all cases, immediate post-operative computed tomography disclosed no structural reason for the pupillary dilation, and pupillary changes resolved within several hours.

Conclusions: As intraoperative ICG angiography is increasingly utilized to evaluate the results of aneurysm clipping instead of the more time-consuming conventional intra-operative angiography, the short-term pupillary effects of local papaverine application may be observed with greater frequency. Mechanistically, the onset and resolution of pupillary changes is consistent with the half-life of papaverine and supports a local anesthetic action of papaverine on the oculomotor nerve.

171. Technique Nuances For Superficial Temporal Artery Dissection

Clemens M. Schirmer, MD (Springfield, MA); Carlos David, MD (Burlington, MA)

Introduction: Dissection of the superficial temporal artery (STA) is often required in preparation for a bypass procedure or in cases where the creation of a bypass maybe an option. Traditionally dissection of the STA involves a direct cutdown on the artery after marking the course of the artery on the skin with the help of a Doppler ultrasound probe. We demonstrate a technique that allows rapid and safe harvesting of the superficial temporal artery (STA) graft in preparation for a bypass procedure.

Methods: A total of 37 cases underwent craniotomies for creation of 14 synangiosis (38%) or Extracranial-Intracranial STA to MCA (middle cerebral artery) bypass (23 cases, 62%). The STA was dissected using a blunt malleable brain retractor, which is inserted into the subgaleal plane directly over the STA, allowing for creation of a linear incision and concurrent protection of the STA in its bed. Either CT- or catheter-based angiography was used to evaluate the patency postoperatively.

Results: All 37 STA vessels were dissected without complications or injury to the graft vessel. There was no mortality the sole complication was a superficial wound breakdown in a synangiosis case. Postoperative angiography demonstrated patency in all but one case (97%).

Conclusions: We describe a method that takes advantage of the position of the STA superficial to the temporal fascia to allow rapid, safe and efficacious dissection. The incision is linear and easier to manage and close. In our series there were no technical complications related to the dissection of the STA.

172. Acute Spontaneous Occlusion Of Contralateral Intracranial Ica And/or Mca After Sta-mca Bypass In Moyamoya Resulting In Major Stroke

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Introduction: Occlusion of contralateral ICA and/or MCA after bypass surgery for moyamoya is rare and has not been reported. Four patients who suffered immediate postoperative spontaneous occlusion of ICA and/or M1 segment after STA-MCA bypass are presented.

Patient Selection: Four hundred and thirty two moyamoya patients underwent 729 cerebral revascularization procedures over 19 years. Aim of surgery was always to perform direct STA-MCA bypass. Only in absence of suitable donor/recipient vessel was indirect revascularization performed. Clinically symptomatic side with more angiographically advanced disease stage was operated first.

Results: In 3 patients who underwent direct left sided STA-MCA bypass, complete occlusion of previously stenosed contralateral supraclinoid right ICA was observed postoperatively. One patient showed postoperative occlusion of previously stenosed contralateral right M1 segment and progression of supraclinoid ICA stenosis. These changes were accompanied with acute clinical deterioration within the first 24 hours after surgery and new infarcts in the respective vascular territories. Cerebral angiography revealed progression of disease from isolated stenosis to complete ICA occlusion in 1 patient, right M1 stenosis and ICA-A1 stenosis to complete ICA occlusion in 2 and from stenosis of right ICA-M1 bifurcation with additional A1 stenosis to complete occlusion of supraclinoid ICA in another. All bypasses were patent. No intra- or perioperative technical or anesthesiological complications were observed.

Conclusion: Acute changes in cerebral blood flow and pressure patterns at site of previous contralateral stenosis may result in vessel occlusion after STA-MCA bypass in moyamoya causing major strokes.

173. Indocyanine Green Videoangiography Guided Microsurgical Resection of Type 2 And Type 4 Spinal Arteriovenous Malformations

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Introduction: Indocyanine Green Videoangiography has been shown to be a useful adjunct in many cerebrovascular procedures. Previous reports document ICG's usefulness in the treatment of type I spinal dural fistulas. We have applied ICG to the microsurgical treatment of spinal type II and IV arteriovenous malformations (AVMs). In both type II AVMs and type IV spinal fistulas, ICG allowed for early and correct identification of arterial feeders, nidus/fistula localization, and assessment of treatment. We believe that ICG guided resection of these lesions reduces risk and allows for safer resection.

Methods: We reviewed all cases of laminectomy for spinal AVM resection over the past three years. ICG guided resection of spinal AVM type II and IV was performed in 8 patients. After administration of ICG, the feeding vessels and fistulous connections were identified and coagulated. Results were verified with intraoperative angiography.

Results: By giving ICG prior to resection, the angio-architecture

of these complex lesions was further delineated. In type II spinal AVM's, ICG allowed for the correct and early localization of arterial feeders and nidus localization. In type IV spinal AVM's, ICG correctly differentiated the fistulous connection from arterial feeders and arterialized veins. This early and accurate identification allowed precise resection and minimized trauma to the surrounding spinal cord. Findings on ICG videoangiography correlated with preoperative and intraoperative angiography.

Conclusions: ICG provides accurate identification of the nidus and fistulous connections in type II and IV spinal AVMs. By performing ICG videoangiography prior to resection of the nidus or fistula, spinal cord injury can be avoided.

174. Safety Of Early Endovascular Catheterization And Intervention Through EC-IC Bypass Grafts

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Introduction: The safety and feasibility of catheterizing recently created cerebral bypass grafts is not well described. However, the graft may be the only viable endovascular route to subsequently treat intracranial pathology.

Methods: Five patients undergoing repeated endovascular interventions through the graft in the acute post-operative period following extracranial-intracranial (EC-IC) bypass are presented. Results, complications, and technical nuances are discussed.

Results: Fourteen endovascular procedures were performed post EC-IC bypass for ruptured aneurysms (n=4) and posterior circulation ischemia (n=1). In three patients, the superficial temporal artery (STA) stump was connected to the intracranial circulation via an interposition saphenous vein graft (SVG). In the fourth, a long SVG was used to bypass the common carotid to the middle cerebral artery (MCA). The fifth patient underwent an STA to MCA bypass. The time interval from surgery to endovascular intervention spanned 2 to 18 days, and the indication was intracranial vasospasm in all patients. One case involved angioplasty of the proximal anastomosis on postoperative day 14. All other interventions entailed proximal access of the bypass conduit for intra-arterial infusion of vasodilators. Significant vasospasm of the STA itself was encountered in 2 patients during endovascular manipulation; both were treated with intra-arterial nitroglycerine. There were no cases of anastomotic disruption.

Conclusions: Endovascular catheterization and intervention involving a recent EC-IC cerebral bypass is reasonable. The main limitation in our series was catheter-induced vasospasm involving the STA. A vein graft appears to be the better option in patients with subarachnoid hemorrhage who may require subsequent endovascular intervention for vasospasm.

175. WITHDRAWN

176. Risk Assessment Of Major Adverse Events Associated With Various Anti-platelet Regimens For Stent-assisted Coil Embolization

Hayashi Morito, MD; Minako Hayakawa, MD; John C. Chaloupka, MD (Iowa City, IA)

Introduction: There remains little consensus regarding best clinical practice for adjunctive anti-platelet therapy for stent-assisted coil embolization(SAC) of aneurysms(AN). In particular, large case series experience correlating frequency of major adverse events(MAE) with various pre, peri-& post-operative regimens is lacking.

Methods: Consecutive "virgin" saccular AN treated by SAC were identified by a prospective database. Standardized perioperative[24hr], short-term[30d], and intermediate term [3-6 mo] primary clinical endpoints, defined as neurologic morbidity & mortality from ischemic stroke(IS), indeterminate neurologic deficits(IND), and hemorrhagic stroke(HS) were assessed. Stratified groupings were created from a matrix of factors and analyzed for risk of MAE: ASA, clopidigrel (CLO), tirofiban (TIR); pre-, peri-, or post-regimens; pre-regimen duration; low vs. high loading CLO; rupt vs. unruptAN; in-stent-thrombosis(IST);&MAE from IS, IND,&HS.

Results: 265 patients / 290 AN met entry criteria. Mean age-59. Female/Male-2.4. Unrupt:rupt. AN-241:49 (17%). Cumulative permanent neurologic morbidity 3.4%, mortality, 0.7%. 141/290 (49%) had 3-5d pre-ASA, 43/290 had no pre-ASA or CLO (14.8%). Preventive TIR used in 7/290 (19.7%) [48/241unrupt.& 9/49rupt.], and reactively for IST and/or IS in 20/290(6.9%)[8 unrupt.,12 rupt.]. No acute HS associated with TIR. MAE rates were statistically significant in the following: i. 3-5d pre- ASA &CLO, ANunrupt.vs. same day CLO loading (any dose),ANunrupt. [5%vs.14%;p-0.04],ii. >3d pre-ASA&CLO, ANunrupt.vs.same day CLO(any dose), ANrupt. [5%vs.19.4%;p-0.002],&iii. No pre-ASA or CLO,ANunrupt. vs.ANrupt. without TIR prevention [0%vs.38%;p-0.04].

Conclusions: MAE was most strongly associated with: i. ANrupt., ii. ANrupt.& no preventive TIR, and iii. ANunrupt. same day loading CLO[any dose]. Conversely, the lowest MAE [all causes] was associated with pre-ASA&CLO for 3-5d. TIR use was common(~27%) in our series, associated with lower MAE-IS & IND in ANunrupt.& rupt., and no risk of peri-HS.

177. The Spectrum Of Management Practices In Aneurysmal Subarachnoid Hemorrhage: A Survey Of American Neurointerventionists

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Background: There is an astonishing variety of management practices for non-traumatic subarachnoid hemorrhage (ntSAH) across neurovascular centers of excellence in the United States. We sought to design a survey which would highlight areas of controversy in the modern management of ntSAH and identify specific areas of interest for further study.

Methods: A questionnaire on management practices in ntSAH was formulated using a popular web-based survey tool (SurveyMonkeyTM, Palo Alto, CA) and sent to endovascular neurointerventionists and cerebrovascular physicians who manage a high volume of these patients annually. Two-hundred

questionnaires were delivered electronically and, over a period of three months, 81 physicians responded, representing a cross-section of neurovascular centers of excellence from around the country.

Results: On average, the responding interventionists in this survey each manage approximately 100 patients with subarachnoid hemorrhage annually. Fifty-five percent (55%) reported using steroids to treat patients with ntSAH. Only 20% of the respondents ever use intrathecal thrombolytics in ntSAH. Over 90% of responding physicians administer nimodipine to all patients with ntSAH. Forty percent (40%) selectively administer anti-epileptic drugs to patients with ntSAH. Several additional questions were posed regarding the methods of detecting and treating vasospasm, as well as indications for CSF diversion in patients with hydrocephalus.

Conclusion: This survey illustrates the great variety of treatment practices for patients with ntSAH and underscores the need for further study.

178. A Proposed Classification For The Immediate Angiographic Results Following Onyx HD-500 Embolization Of Intracranial Aneurysms

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Introduction: Onyx HD-500 is being increasingly used in the endovascular management of intracranial aneurysms. Preliminary

experience using this liquid embolic agent has shown promising results in terms of high rates of complete occlusion and low rates of long-term recanalization, even in large and wide-neck aneurysms. However, there is little information as to what constitutes an optimal and desirable immediate angiographic result. We devised a simple angiographic classification scheme based on the pattern of parent artery and aneurysm neck reconstruction and correlated it with the results of short-term angiographic follow-up.

Methods: We graded initial angiographic results (IARs) in 25 cases according to the amount of ectopic Onyx found outside the target aneurysm: A - none; B - hat-brimming; C1 - ectopic, non flow-limiting; C2 - ectopic, flow-limiting; and D - embolic. We correlated initial angiographic grade with angiographic outcome at 6 months and 1 year.

Results: IAR was graded A in 7 cases, B in 5, C1 in 9, C2 in 3, and D in 1. Aneurysm recurrence was observed on 6-month angiography in 2 cases, both grade A. Delayed parent vessel compromise occurred in 2 cases, both grade C2. Another grade C1 case developed symptomatic clot on the ectopic Onyx during post-hemorrhagic vasospasm.

Conclusion: Aneurysm recurrence was more common in patients with IAR grade A, while parent vessel compromise was more common in patients with IAR grade C. Prospective validation is necessary to determine if our grading scheme shows robust correlation with long-term angiographic results.

179. Detachment Force Less With Steel-reinforced Catheters Than Nitanol-reinforced Catheters When Used In Liquid Embolization Of Intracranial Aneurysms

Scott D. Simon, MD (Richmond, VA); Adam S. Reig, MD; Dennis Velez, MD; Robert A. Mericle, MD (Nashville, TN)

Introduction: The biomechanical behavior of the nitanol-reinforced and steel-reinforced catheters approved for use in liquid embolization of intracranial aneurysms is poorly understood. We performed biomechanical laboratory testing and examined our clinical experience in order to identify clinical situations in which one catheter might have an advantage over the other.

Methods: 4 Echelon-10, 4 Echelon-14 and 2 Rebar-14's (eV3 Inc, Irvine, CA) were tested for detachment force from an Onyx HD 500 (eV3 Inc, Irvine, CA) 28mm deep fundus aneurysm model. All catheters were new and untested. Results were statistically compared using ANOVA tests.

Results: The average detachment force for the Echelon-10, -14, and Rebar -14 were 97.6, 76.825, 62.6 grams, respectively (p=0.023). [Figure 1] The reasons for these differences are both the increased elasticity and the presence of ridges on the tip of the nitanol-reinforced catheters.

Conclusions: The lower detachment force of the steel-reinforced catheter make it ideal for liquid embolization, but the stiffness required to achieve this makes it less desirable for accessing smaller aneurysms safely or navigating tortuous anatomy. The smallest nitanol-reinforced catheter should generally be avoided unless it is the only catheter that can access an aneurysm because of small size or tortuous anatomy. In such cases, the higher detachment force suggests a stent should be in place to prevent the cast from being destabilized.

180. Dissecting Aneurysms Of The Posterior Cerebral Artery: Current Endovascular/surgical Evaluation And Treatment Strategies

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Introduction: Posterior cerebral artery (PCA) aneurysms are rare, comprising 1 - 2% of all intracranial aneurysms. To date, most clinical series are heterogeneous in nature with relatively few reports of isolated PCA dissecting aneurysms. Because their evaluation and treatment pose a unique clinical challenge, we report our recent experience in nine consecutive patients with PCA dissecting aneurysms.

Methods: We conducted a retrospective review of nine consecutive patients with PCA dissecting aneurysms from November 2003 to February 2010. Their hospital charts and follow-up records were reviewed and summarized.

Results: We identified six male and three female patients ranging in age from 7 months to 69 years (medium age: 53 years). None had any associated trauma. Four patients presented with subarachnoid hemorrhage. Three presented with intraventricular/intracerebral hemorrhage. The remaining two presented with headache and acute onset of right-sided numbness respectively. Four patients underwent endovascular embolization. Two patients underwent surgical clipping. The remaining three patients were medically managed and followed conservatively. The dissecting aneurysms involved P1 (two), P1-2 junction (one), P2 (four), and P2-3 junction (two). At a mean follow-up of 3 months, six patients had excellent functional outcome with Modified Rankin Score of 0 or 1. The remaining three patients who presented in deep coma did poorly (one death and two with severe disabilities).

Conclusions: PCA dissecting aneurysms pose a unique clinical challenge. Many issues, such as predicting the necessity of bypass, remain unresolved. Angiographic evaluation and current endovascular/surgical management strategies are discussed.

181. Angiographic Closure Devices: A Retrospective Review Of Angioseal Versus Mynx

David Krieger, MD, MS; Pascal M. Jabbour, MD; L Fernando Gonzalez, MD; Aaron S. Dumont, MD; Robert H. Rosenwasser, MD, FACS; Stavropoula I. Tjoumakaris, MD (Philadelphia, PA)

Introduction: Recent advancements in endovascular surgery have introduced several closure devices for the femoral ateriotomy site. Two of the more commonly used devices are the AngioSeal (St. Jude Medical) and the Mynx (AccessClosure), both of which decrease time to hemostasis and expedite post-procedure ambulation. In this study, we retrospectively investigated closure efficacy, associated pain, and complications of each closure device.

Methods: A retrospective patient database was created with 80 patients who had undergone diagnostic cerebral angiography. Post-procedure groin hematoma and pain (quantified on a ten point scale) were monitored over six hours following closure. Other complications investigated were lower extremity vascular compromise and infection at the groin site.

Results: For the 80 patients, 44 received an AngioSeal and 36 received a Mynx. Post-surgical pain at the groin site was found in 4 cases (9%) in the AngioSeal group (range 2-5 on pain scale), and 3 cases (8%) in the Mynx group (range 3-5). No intravascular injury or occlusion was found in either group. The Mynx group had one superficial hematoma that resolved spontaneously. There were 2 cases of infection (6%) in the Mynx group and none in the AngioSeal group (p equals 0.20 by Fisher's test). The patients with infected groin sites presented within two weeks of the procedure, and required hospital re-admission.

Conclusions: In this retrospective study, Mynx and AngioSeal are equally effective closure devices for femoral arteriotomy. Pain incidence and severity were similar between the two groups. However, the Mynx device was associated with a delayed local infection at the groin site.

182. Increased Packing Volumes Of Endovascular-treated Intracranial Aneurysms Correlates With Reduced Aneurysm Recurrence

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Introduction: Aneurysm recurrence following endovascular repair

is a major consideration. We hypothesized that decreased aneurysm recurrence is associated with increased coil packing volumes, and that lower packing volumes are associated with aneurysmal recurrence. Therefore we correlated aneurysm packing volumes with aneurysm recurrence.

Methods: We studied 61 sequential aneurysm patients admitted to a University Hospital from 2007-2010. Fifteen were excluded for incomplete data or pseudo-aneurysm. The remaining 46 patients with a total of 55 aneurysms were placed into two groups: Group A included 38 patients without aneurysm recurrence whereas Group B included 8 patients with recurrence. Aneurysms were categorized according to presentation, location, shape, coil type and number, and immediate angiographic outcomes. Aneurysm packing volume percentages were determined for each aneurysm using AngioCalc, an online program for cerebral aneurysm analysis.

Results: Aneurysm locations were: AcoA (18), ICA (4), Cavernous ICA (3), Paraclinoid ICA (1), Ophthalmic ICA (6), Hypophyseal ICA (2), Supraclinoid ICA (4), PCoA (7), MCA (3), A1 ACA (2), Pericallosal ACA (1), P1 PCA (1), PICA (1), and Basilar Apex (2). Analyses of these 55 aneurysms revealed similar average volumes between Group A (442.59 microliter) and Group B (428.65 microliter). The average packing volume percentages were markedly different: Group A averaged 25.66 per cent, whereas Group B averaged 12.03 per cent.

Conclusion: We conclude that aneurysm packing volumes of about 25 per cent are associated with reduced aneurysm recurrence when compared to aneurysm packing volumes of about 12 per cent.

183. Advanced Neuroimaging Revolutionizes Diagnosis And Prognosis Of Delayed Cerebral Ischemia After Subarachnoid Hemorrhage.

Gregory Kapinos, MD, MS (New York, NY)

Introduction: Randomized clinical trials use dissimilar criteria to define vasospasm (VSP), delayed infarcts and delayed cerebral ischemia (DCI) after aneurysmal subarachnoid hemorrhage.

Methods: We systematically reviewed the last twenty years of English medical literature for the input of multimodal neuroimaging in characterizing VSP and DCI. In the form of question-answer, we condensed the recent qualitative and quantitative data suggesting a role for structural, sonographic, angiographic, diffusion, perfusion, permeability, vasoreactivity, flow heterogeneity and metabolic imaging, in helping clinicians comprehend VSP/DCI.

Results: What constitutes acute brain injury (ABI)? Non-contrast CT, DSA, CTP, MRP, DWI, T2, permeability, metabolic and spectroscopic studies demonstrate cerebral insult due to global transient hypoperfusion, pial microthrombotic events, blood-brain-barrier disruption, global vasogenic edema and rarely, ultra-early vasospasm. Can we quantify ABI and correlate its severity to neurological presentation, development of DCI and predict outcome? Acute non-contrast CT, CTP, MRP, DWI and T2 can quantify the injury, classify patterns of infarcts and edema and this correlates to neurologic,

cognitive and functional outcomes. Can perfusion imaging in the acute/subacute phase detect VSP/DCI earlier than TCD, DSA/CTA or clinical exam? Three studies support qualitative analysis of perfusion defects for early detection of DCI. Ten studies found thresholds accurately diagnostic for VSP/DCI. Quantifying the depth of hypoperfusion is entertained by three studies to help decision about medical perfusion optimization vs. angioplasty. One study of admission CTP found a threshold predicting subsequent DCI.

Conclusions: A breadth of robust neuroimaging data elucidates ABI, predicts DCI, delineates categories for the multifaceted VSP/DCI and refines prognostic significance with therapeutic implications.

184. Minipterional Approach for Anterior Circulation Aneu–rysms

Khaled M. Aziz, MD, PhD; Raymond M. Sekula, MD; Mohammed Hammad, MD, PhD (Pittsburgh, PA)

Introduction: Mini-pterional craniotomy is a modification of the standard pterional (frontotemporal) Craniotomy. It provides the same microsurgical exposure as the standard frontotemporal approaches.

Material and Methods: We analyzed the relation between the sphenozygomatic suture and the marginal tubercle of the frontal process of the zygoma 60 dried skulls. Minipterional craniotomy was performed in 10 cadaveric specimens. The approach was utilized to clip 35 MCA. Meta-analysis of the English language literature on "endovascular coiling of MCA aneurysms".

Results: The marginal tubercle was hiding the sphenozygomatic suture when it is > 8mm, it required drilling to enhance the exposure. Anterior to posterior sub-periosteal dissection and retraction of the temporalis muscle, and avoiding cuts along the origin of the muscle allows excellent cosmetic outcome. All 35 aneurysms were successfully clipped without morbidity or mortality through a 3.5 to 4 cm bone flap. Literature revealed 591 coiled MCA aneurysms with an average follow-up period of 18 months. Complete occlusion 59%, recanalization 19%, morbidity 11%, and mortality 4%.

Conclusion: Minipterional approach is an excellent option to approach anterior circulation aneurysms. The minimally invasive access allows minimal soft tissue trauma, smaller bony opening, less pain, and excellent cosmetic outcome.

185. Utility Of Antibiotic Use With The Starclose Vascular Closure Device

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Introduction: To determine if antibiotics are necessary to administer when using the StarClose Vascular Closure Device during diagnostic angiograms, or aneurysm coiling.

Methods: A total of 193 cases using the vascular closure device, Starclose, were retrospectively reviewed at one institution from March 2007 to June 2009. These 193 cases included both diagnostic angiograms and aneurysm coilings, all of which were accessed through the femoral artery and closed with a StarClose device. A retrospective review of cases using the StarClose device was evaluated for wound infections in patients receiving prophylactic antibiotics and patients who did not receive antibiotics. The antibiotics given to the group that received prophylactic antibiotics include ancef, or clindamycin if the patient had a penicillin allergy. The decision to give antibiotics, or not was completely physician dependent.

Results: Out of the 193 patients, 56 were given antibiotics and 137 were not. There was no report of a superficial or deep infection in either group. There were a total of 64 coiling procedures performed and 20 of those received antibiotics. The other 129 cases were diagnostics angiograms in which 36 received antibiotics.

Conclusions: Based on this retrospective review, antibiotics do not seem to be necessary when using the StarClose Vascular Closure Device.

186. The Relative Importance Of Each Factor Within The Spetzler-Martin Grading System

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Introduction: The five point Spetzler-Martin (SM) AVM grading system assigns points for location, deep venous drainage and size. It

is widely-held that size primarily determines SM grades. We hypothesized that size does not necessarily correlate to increased SM grade. We analyzed 31 AVMs and assessed the relative importance of each factor within the SM grading system.

Methods: We examined 31 consecutive patients presenting to a University Hospital from 2007-2010 for endovascular treatment of AVMs. Neuroendovascular-trained physicians confirmed SM grades from cerebral angiograms. X-knife, a stereotactic radiosurgery-planning program, calculated AVM volumes from stacked MRI AVM nidal tracings. Reference to angiograms increased tracing accuracy.

Results: A total of 31 AVMs were classified: SM I (6), SM II (11) and SM III (14). Average grade I nidal volumes were 1.70 milliliter, grade II were 4.33 milliliter, and SM grade III were 5.89 milliliter. Analysis showed grade I's were 100 percent non-eloquent, superficial, and under 3cm. SM grade IIs were 54.5 percent eloquent, 36.3 percent with deep drainage, and 81.8 percent were under 3cm. For SM grade III, 100 percent were eloquent, 55.6 percent had deep drainage, and 42.9 percent were under 3cm.

Conclusion: For low SM grade AVMs, lesion size did not differ statistically. Instead, eloquent location was the most significant factor in delineating between low SM grade AVMs. However, eloquence and venous drainage were influential in delineating between low SM grades. As SM grade increases, the presence of deep venous drainage significantly increased. Eloquent location was the most significant factor in delineating between low SM grade AVMs.

187. Modified Subtemporal Approach For Intracranial Aneurysm Surgery: Partial Postero-superior Petrosectomy

Bernard R. Bendok, MD, FACS; Rudy J. Rahme, MD; H. Hunt Batjer, MD, FACS; Andrew J. Fishman, MD (Chicago, IL)

Introduction: The subtemporal route is an established corridor for clipping of aneurysms of the upper basilar artery and for accessing lesions in the vicinity of the interpeduncular and ambient cisterns. The standard technique however, has limited degree of surgical freedom, visualization, and may require significant temporal lobe retraction. We present a technical modification, which optimizes the surgical access port by introducing a partial postero-superior petrosectomy to the subtemporal craniotomy.

Subjects and Methods: Detailing of modified surgical technique. In addition, we retrospectively reviewed our experience with this approach in 3 clinical cases.

Results: Improved angle of view is achieved by the addition of a postero-superior petrosectomy which removes all not functional bone from the mastoid antrum to the sigmoid transverse junction. The superior petrosal sinus is the limit of dissection. The additional space provided dramatically increases the subtemporal exposure. Additional room can be achieved by a zygomatic osteotomy, external auditory meatus skeletonization and decreasing the profile of the intracranial infratemporal fossa floor. The middle ear and hearing apparatus as well as the ossicles and hearing can be fully preserved. Reconstruction with abdominal fat is well tolerated as the anatomic defect created is minimal.

Conclusion: The partial postero-superior petrosectomy when added to a subtemporal craniotomy provides a substantial improvement surgical freedom and view of the upper basilar artery and its adjacent structures. The additional time required is minimal in experienced centers. The extended dissection does not result in significant anatomic nor functional deficits.

188. Lumbar Drain In Unruptured Aneurysm Surgery; Is It Helpful

Anu Bedi, PA-C; Brian Bolinger, DO; Amir R. Dehdashti, MD (Danville, PA)

Introduction: Lumbar drain has been used in intracranial procedures including ruptured aneurysms to improve brain relaxation. The use of LD in unruptured aneurysms(UA) surgery has never been evaluated.

Methods: Forty patients with UAs underwent surgical clipping via pterional or orbitozygomatic approach during 18 months period. They were assigned to receive LD(Group A)or not (Group B). Exclusion criteria were SAH and aneurysms for which other approaches were used. The ease of surgical dissection (easy vs. difficult), degree of brain relaxation (none vs. moderate or significant) and the need for retractor use were evaluate.

Results: There were 49 aneurysms in 40 patients. All aneurysms were in the anterior circulation except for two posterior circulation. Seven patients had prior SAH with previously treated aneurysm at other locations. Thirty-two patients underwent pterional and 8 had OZ craniotomy. In the group A(20patients-Mean40ccdrainage), the surgical dissection was easy in 16, the brain relaxation was moderate or significant in 15 and no retractor was used at all in 16. In the group B(20patients), these numbers were 15,16 and 14 respectively. The difference between the two groups was not significant. There was one complication of intracranial hypotension in group A which resolved by bed rest. No other complication was noted. The outcome was excellent in all patients remaining with no neurological change or showing improvement of aneurysmal compressive symptom.

Conclusions: The authors do not suggest the use of LD for elective aneurysm surgery via pterional or OZ approach as this cohort failed to show any significant usefulness of LD in brain relaxation, use of retractor or dissection capability.

189. Surgical Excision Of Filum Terminale Arteriovenous Fistulae After Lumbar Fusion: Value Of Indocyanine Green And Theory On Origins

Victoria Trinh, BA; Edward A.M. Duckworth, MD, MS (Houston, TX)

Introduction: Objective and importance: Intradural filum terminale arteriovenous fistulas (AVF) are very uncommon. We report 2 cases of this rare entity in which we used Indocyanine green (ICG) videoangiography to identify the fistulous connection of each filum terminale AVF.

Clinical Presentation: Two male patients presented with unresolved lower extremity weakness and paresthesias following lumbar fusion surgery. In each case, angiography showed an AVF between the filum terminale artery (FTA), the distal segment of the Anterior Spinal Artery (ASA), and an accompanying vein of the filum terminale. A magnetic resonance image (MRI) obtained before lumbar fusion was available in one of these cases, and demonstrated evidence of preexisting vascular malformation.

Intervention: Surgical obliteration of each fistulous connection was facilitated by the use of ICG videoangiography. This emerging technology was instrumental in pinpointing fistula anatomy and in choosing the exact segment of the filum for disconnection.

Conclusion: Our findings indicate intradural filum terminale arteriovenous fistulae are likely congenital, and that ICG is an invaluable tool in their successful surgical management. As these cases demonstrate, spine surgeons should remain vigilant in evaluating patients with a clinical picture of myelopathy, even in the presence of obvious lumbar pathology.

190. Terminological Variance For Each Subtype Of Delayed Cerebral Ischemia And Vasospasm After Aneurysmal Subarachnoid Hemorrhage

Gregory Kapinos, MD, MS; Angela M. Hoang, BS; Pina C. Sanelli, MD, MPH (New York, NY)

Introduction: Randomized clinical trials (RCT) use dissimilar criteria to define vasospasm (VSP), evidence of narrowed vessel (NV), deterioration, delayed ischemic neurologic deficits (DIND), delayed infarcts and delayed cerebral ischemia (DCI) after aneurysmal subarachnoid hemorrhage (aSAH).

Methods: We systematically reviewed the 38 RCT listed in the AHA 2009 guidelines for aSAH to extract the defining criteria and semantics used for each subtype of ischemic or vasospastic events.

Results: Deterioration is defined in 16 RCT, 10 use a coma scale, while others prefer neurologic exams, either standardized (NIHSS for 4) or not, and 5 RCT evoke clinical impression. DIND, defined in 21 RCT, always implies neurologic changes with exclusion of non-ischemic causes, but the lists of excluding syndromes differ. DIND is difficult to appreciate in comatose patients (1 RCT). Symptomatic VSP (6 RCT) varies in definition and is misleadingly interchanged with "clinical VSP" (6 RCT): 13 refer to actual DIND with (10) or without excluding other causes of neurologic decline, while 9 RCT mean DIND with or without evidence of NV, and only 3 RCT require a documented NV. Both sonographic (13 RCT) and angiographic VSP (5 RCT) have poor consistency in stratification, poor concordance and poor sensitivity and specificity for DCI. DCI is referred in 3 RCT as "probable" (clinical) or "definite" (clinico-radiologic), but these terms lack descriptiveness. Delayed infarcts have explicit causal allocation in 7 out of 14 RCT.

Conclusions: There is inconsistency in semantics and specific criteria used for each rubric of DCI, and for the disparate amalgamates of each subtypes of DCI.

191. Stent Assisted Embolization Of Wide Necked Rupture Aneurysms

Rafael Rodriguez-Mercado, MD, FACS; Amaury Garcia, MD; Erwin Rayo, MD (San Juan, PR)

Introduction: The use of stent assisted embolization of cerebral aneurysms is well know. There is some controversy with use of intracranial stents in recent rupture aneurysms due to the use of anti platelet therapy and the risk of intracranial hemorrhage.

Methods: A retrospective data of 10 patients with an acute subarachnoid hemorrhage secondary to wide neck aneurysm between 2009-2010. Partial embolization of aneurysm with aneurysm coils was done in the first 24 hours after the diagnosis of cerebral aneurysm was done. Stenting and coiling using the jailing technique in 8 patients was done after 3 to 7 days of the partial embolization. The other 2 patient we deploy first the stent and then we embolized with coils.

Results: From the 10 patients treated no complications was seen in 9. There was 1 complication no related to the procedure but secondary to a hypertensive crisis resulting in a cerebellar bleeding that no require surgery and we keep the anti platelet therapy on.

Conclusions: Stent assisted embolization for wide necked rupture aneurysms is a feasible and save procedure. There some factors to consider as the partial embolization of the aneurysm in the first 24 hours after the diagnosis is made for potential avoidance of re-bleeding, the timing for the antiplatelet therapy and to be sure that after the placement of the stent we obtain a complete embolization of the aneurysm with coils.

192. Endovascular Treatment of Acute Carotid Occlusion

Jonathan A. Grossberg, MD; Mahesh Jayaraman, MD; Curtis Doberstein, MD; Richard Haas, MD (Providence, RI)

Introduction: Acute cervical carotid occlusion is one of the most challenging scenarios encountered in endovascular stroke treatment.

Methods: We analyzed 12 consecutive non-dissection stroke patients with concomitant cervical carotid and intracranial occlusion treated with intraarterial (IA) pharmacologic thrombolysis over five years at two academic hospitals.

Results: Patients included 3 females and 9 males. Average age was 61.8 (range 30-84). All patients had both cervical carotid and intracranial occlusions. The most common sites of intracranial occlusion were the carotid artery (7 patients) and the middle cerebral artery (4 patients). All patients received IA Tissue Plasminogen Activator (TPA) with a mean dose of 14.5mg (range 7-25). Seven patients received carotid stents for cervical occlusion as part of their treatment (6 prior to TPA administration and 1 after TPA), while 5 patients received only IA TPA via collateral circulation. Of the patients receiving stents prior to TPA, 5 of 6 (83.3%) had successful recanalization (Thromoblysis in Cerebral Ischemia 2b or 3 flow). Only 1 of 6 (16.7%) patients who did not receive stents prior to TPA had successful recanalization. The difference in recanalization rates approached statistical significance (p equal to .08). There were 3 total in-hospital mortalities, 2 in the stent group and 1 in the non-stent group. There were 2 clinically significant hemorrhages in the study, both in the stent group.

Conclusions: Revascularization of the cervical carotid occlusion prior to treatment of the intracranial occlusion led to increased rates of recanalization in patients with tandem extracranial and intracranial occlusions.

193. Outcome Comparison Of Clipping Versus Coiling In Small Anterior Communicating Aneurysms

Spiros L. Blackburn; Albert J. Schuette, MD; Mark Bain, MD; Michael Cawley, MD; Daniel Barrow, MD (Atlanta, GA)

Introduction: The coiling of small anterior communicating artery aneurysms has been associated with a higher rate of intra-procedural rupture than aneurysms treated in other locations. In this presentation, we review our outcomes in small clipped and coiled anterior communicating artery aneurysms to determine whether a benefit is seen for either treatment strategy.

Methods: We retrospectively reviewed all aneurysms treated between 1999 and 2010. Patients with anterior communicating artery aneurysms less than 4 mm were included. Data including treatment method and modified Rankin score were collected. Results between the two groups were compared.

Results: A total of 88 small anterior communicating artery aneurysms were treated, 45 via coiling and 43 via clipping. Average age was 51 in the coiled group and 54 in the clipped group. 44 of 45 coiled patients had a SAH with average HH of 2.4, while 32 of 43 patients had SAH with an average HH of 2.4. Modified Rankin score was 2.06 in coiled SAH patients and 2.15 for all coiled aneurysms. In clipped aneurysms, mRS was 2.09 in SAH patients and 1.9 overall.

Conclusions: Outcomes for clipping of small anterior communicating artery aneurysms is equivalent to coiling.

194. Microsurgical Treatment Of Previously Coiled Intracranial Aneurysms: A Review Of The Literature

Bernard R. Bendok, MD, FACS; Omar M. Arnaout, MD; Christopher S. Eddleman, MD, PhD; H. Hunt Batjer, MD, FACS (Chicago, IL)

Objective: As endovascular therapy becomes more frequently utilized to treat intracranial aneurysms the number of lesions that require retreatment will also increase. Currently, retreatment options for previously coiled intracranial aneurysms include repeat endovascular treatment, with or without adjunctive endovascular devices; microsurgical clipping or other microsurgical techniques including revascularization. We aim to assess the technical nuances, durability, safety and outcomes of microsurgical treatment of previously coiled intracranial aneurysms with an emphasis on direct clipping.

Methods: We performed a systematic review of the literature spanning January 1990 to May 2009. A total of 23 papers reporting on microsurgical clipping of previously coiled aneurysms were identified, from which data was collected for analysis.

Results: Of the reviewed aneurysms (N=222), 72% were small (<10mm). Approximately 80% initially presented with hemorrhage. Indications for microsurgical clipping included the presence of a neck remnant (54%) and aneurysm re growth (38%). Coil extraction occurred in only 15% of cases. The median time from initial coiling to clipping was 7.2 months. The overall angiographic cure

rate was 93%, with morbidity and mortality rates of 8.1% and 4.1% respectively.

Conclusions: Microsurgical clipping of previously coiled aneurysms is challenging but can result in high obliteration rates with relatively low morbidity and mortality rates in selected cases. Considerations for microsurgical strategies include the presence of sufficient aneurysmal neck for adequate clip placement and the presence of coil material within and around the parent artery. Revascularization strategies should be considered when parent artery reconstruction is not feasible.

195. Therapeutic Administration Of Alphab-crystallin, an Endogenous Neuroprotectant, In Cerebral Ischemia

Ahmet Arac, MD; Sara E. Brownell, BS; Jonathan B. Rothbard, PhD; Charlene Chen, MD; Rose M. Ko, PhD; Marta P. Pereira, PhD; Gregory W. Albers, MD; Lawrence Steinman, MD; Gary K. Steinberg, MD, PhD (Stanford, CA)

Cryab-KO mice had significantly larger lesions than WT mice at both 2d and 7d and had worse neurologic deficits at both time points. Flow cytometry showed increased neutrophils and macrophages in KO mice brains 2d after stroke. At 7d after stroke, there were more T cells in the brains of KO mice. Furthermore, the plasma level of cryab was significantly increased at 12h after stroke with a gradual decrease over the ensuing 7d in WT mice. This led us to investigate whether restoration of the cryab in the plasma of KO mice would decrease the lesion size. Recombinant cryab administration daily for a week decreased the lesion size in KO group to the level of WT group, suggesting that the increased lesion size in KO mice was due to deficiency of cryab rather than other potential causes. Moreover, upon stimulation, the KO splenocytes from mice 7d after stroke produced more pro-inflammatory and less anti-inflammatory cytokines as compared to splenocytes from both WT and cryab treated KO mice. These results prompted us to try cryab as a therapeutic in WT mice. Starting the treatment 1h before stroke, we were able to decrease the lesion size at 7d, compared to subjects with saline. Furthermore, starting the treatment even 12h after stroke conferred significantly smaller lesion size compared to treatment with saline. In conclusion, our data indicate that cryab is an endogenous neuroprotectant against cerebral ischemia and that it can be administered as an exogenous therapeutic even 12 hours after stroke.

196. Circadian And Climatic Factors In The Onset Of Aneurysmal Subarachnoid Hemorrhage Versus Non-Aneurysmal Perimesencephalic Hemorrhage

Amrendra S. Miranpuri, MD; Erinc Akture, MD; Kutluay Uluc, MD; Ecem Gunes, MD; David B. Niemann, MD; Beverly Aagaard-Kienitz, MD; Anil Arat, MD; Mert Oztas, MD; Alejandra Munoz Del Rio, PhD; Mustafa K. Baskaya, MD (Madison, WI)

Introduction: Previous studies have suggested a possible relationship between circadian and climatic factors and the onset of aneurysmal subarachnoid hemorrhage (aSAH). These factors have not been well studied in non-aneurysmal perimesencephalic hemorrhage (PMH). PMH is believed to be a venous rather than arterial source of hemorrhage. The purpose of this study was to investigate the circadian and climatic factors which may play a role in the onset of aSAH versus PMH.

Methods: We retrospectively reviewed the medical records of 335 aSAH and 38 PMH Midwestern United States patients treated from January 2005-February 2010. Demographic factors (age, gender, family history, smoking), circadian factors (month, day, time) and climatic factors (hourly temperature, barometric pressure from the National Climatic Data Center) were analyzed. Differences in the distribution of continuous variables such as age and temperature were tested with a Kruskal-Wallis test. Categorical variables were tested with Fisher's exact test and within each SAH group with continuity-corrected Pearson Chi-squared test.

Results: A relative peak incidence of aSAH and PMH occurred between 6am- 12pm; however, statistically significance was only reached for aSAH (p=1.70e-11), but not PMH (p=0.274). Comparing the two groups, PMH patients were more likely to be male (p-0.002) and non-smokers (p=0.003). For all other variables tested, there was no difference between groups.

Conclusions: Aneurysmal SAH and PMH patients tend to present between 6am-12pm. However, there was no difference in climatic or circadian factors between aSAH and PMH groups. PMH patients are more likely to be males and non-smokers compared to aSAH in our patient population.

197. Cerebral Oximetry In Patients With Aneurysmal Subarachnoid Hemorrhage: An Observational Study

Inam U. Kureshi, MD; Neil Datta, BS (Hartford, CT)

Introduction: Cerebral vasospasm is a condition that can lead to severe neurological complications in patients who have suffered from aneurysmal subarachnoid hemorrhage (SAH). The usefulness of cerebral oximetry when placed in this patient population has not been previously observed in the presence of cerebral vasospasm. This study was formulated as a retrospective observational study to assess the functionality and utility of intracerebral oxygen monitoring to help detect and possibly treat symptomatic vasospasm.

Methods: In a retrospective cohort of 20 patients treated for high grade aneurysmal SAH at one institution, relationships between the recorded cerebral oximetric data (partial pressure of oxygen, PbO2), and clinical data of vasospasm including the following were observed: intracranial pressure (ICP), cerebral perfusion pressure (CPP), mean arterial pressure (MAP), cerebral temperatures (Temp), and fraction of inspired oxygen (FiO2).

Results: Among the cohort of patients studied, 67% of those who experienced vasospasm (9), survived the disease. While the correlations between oximetry data (PbO2) and the clinical monitoring data for individual patients varied widely, when pooled for all patients, significant (p less than 0.001) Pearson Regression correlations (R) were observed: 0.370 for CPP, 0.113 for MAP, 0.018 for Temp, -0.305 for FiO2 and -0.404 for ICP. We also computed the linear regression coefficients; these R-values, ranging from 0.175 to 0.866, were much higher than the previously mentioned Pearson R values.

Conclusions: Patient survival and the presence or absence of cerebral vasopasm following aneurysmal SAH correlated significantly with cerebral oximetry data. Therefore, cerebral oximetry should be studied further in patients with high grade aneurysmal SAH.

198. Accuracy Of Flat-detector CT-guided Targeting: Extravascular C-arm Applications

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Introduction: Flat-detector CT can be integrated with C-arm fluoroscopy for CT-guided neurosurgical and endovascular procedures. We studied the accuracy and application of this technique (Philips XperGuide) in targeting intra- and extracranial lesions in a cranial model and in vivo.

Methods: Laboratory investigation: An acrylic scale-model skull was filled with foam "parenchyma" into which ten 2.16mm-diameter targets were embedded in one hemisphere. A noncontrast flat-detector CT was performed and registered to the skull's position. The CT was used to plan burr holes for each lesion. Lesions were accessed with biopsy needles under fluoroscopic guidance and CT overlay. Accuracy was measured using flat-detector CT.

Clinical investigation: The XperGuide system was used in three

patients. The first patient required right frontal ventriculostomy after subarachnoid hemorrhage. The second and third patient had vascular lesions in the orbit (lymphangioma, 24x26x21mm) and spine (epidural arteriovenous fistula, 25x5.5x6.5mm), respectively. XperCT-guided procedures were performed under general anesthesia.

Results: All targeted lesions were accessed successfully using the XperGuide system. Flat-detector CT data was incorporated with fluoroscopy in planning and real-time navigation. Targets in the laboratory investigation were accessed to within 1mm (plus or minus 0.7mm). Accuracy did not vary by depth. In the first patient, a ventriculostomy was successfully placed in optimal position in the lateral ventricle. In the second and third patients, lesions were accessed and embolized in the orbit and spine without complication.

Conclusions: Flat-detector CT-guided targeting of intra- and extracranial lesions can be performed easily in real-time with excellent accuracy, expanding the role of the angio suite in neurosurgical disease.

199. Evaluation Of The Laparoscopic Versus Open Techniques For Distal Ventriculoperitoneal Shunt Catheter Placement In Patients With Aneurysmal Subarachnoid Hemorrhage

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Introduction: Laparoscopic ventriculoperitoneal shunt (VPS) surgery is emerging as an attractive alternative to traditional VPS surgery with minilaparotomy. Laparoscopic placement of the distal catheter may simplify and improve the safety of shunt surgery. This study evaluated both techniques in patients with hydrocephalus secondary to aneurysmal subarachnoid hemorrhage.

Methods: Retrospective review of 249 consecutive patients who underwent new ventriculoperitoneal shunt placement for hydrocephalus secondary to aneurysmal subarachnoid hemorrhage from 2004 to 2009. Independent variables in the analysis included age, race and American Society of Anesthesiology (ASA) score. Dependent variables included shunt failure, blood loss and operative time.

Results: Open or laparoscopic VPS distal catheter insertion was performed on 100 and 148 patients, respectively. One patient was converted from laparoscopic to open surgery. There were no significant differences between the groups regarding age, race or ASA score. The incidence of shunt failure was not statistically different between cohorts, occurring in 16% of laparoscopic and 16% of open VPS cases ($p = 0.61$). Laparoscopic VPS patients had shorter operative times (average for laparoscopic 35.8 min, average for open 39.4 min, $p < 0.0003$), as well as less blood loss ($p = 0.009$).

Conclusions: Compared to minilaparotomy, the laparoscopic approach was associated with shorter operative times and less blood loss. Laparoscopic shunt surgery is a viable alternative to traditional shunt surgery.

200. Method Of Validating Middle Cerebral Artery Occlusion Stroke Model With Digital Subtraction Angiography In Rodents

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Introduction: Rodents are one of the most important species utilized in stroke research. The middle cerebral artery occlusion (MCAO) model has been used extensively; however, it has unwanted variability because it relies on indirect measures of vessel occlusion such as transcranial doppler, blind tactile feedback, or accepted suture length and diameter. The merits of digital subtraction angiography (DSA) in the MCAO model have not been studied. We examined the application of DSA in this model in small rats.

Methods: Using a transfemoral approach, we performed DSA on eight Spontaneously Hypertensive rats and eight Sprague Dawley rats weighing 300-500 grams. The left common carotid artery was selectively catheterized and arteriography was done. We then performed a MCAO through a neck incision using a silicon tip intraluminal suture. Further arteriography demonstrated vessel occlusion by the suture. After sixty minutes, the suture was removed and repeat arteriography confirmed reperfusion. Diffusion weighted and T2 MRI sequences delineated the stroke volume.

Results: We were able to perform cerebral angiography in rats with good resolution of the cerebral vessels. We were able to directly verify vessel occlusion and achieve reperfusion consistently. Stroke confirmation was accomplished with MRI.

Conclusions: Cerebral DSA can be performed successfully to validate vessel occlusion in a rat focal ischemia model. Furthermore, the ability to occlude and re-open cerebral vessels with direct angiographic visualization may prove to be extremely valuable when studying selective intra-arterial delivery of agents.

201. Safety And Accuracy Of Bedside External Ventricular Drain Placement By Physician Assistants

Inam U. Kureshi, MD; Zulara N. Wahla, BS; Leon Ho, PA-C (Hartford, CT)

Introduction: Bedside placement of external ventricular drains has been traditionally performed by neurosurgeons and neurosurgical trainees. The safety and accuracy of this procedure has been studied and found to be acceptable. However, to date there has been no study that has been done on this same procedure performed by physician assistant staff.

Methods: Initial computed tomographic studies on 141 consecutive patients who underwent bedside ventriculostomy were reviewed retrospectively at one institution from January 2008 to July 2010 where there are no neurosurgical housestaff. All procedures were performed by neurosurgical physician assistants with an average neurosurgical experience of 8.4 years. Diagnosis, catheter tip location and procedural complications were tabulated. To analyze catheter placement, we used the Kakarla Grading System. Grade 1: optimal placement in the ipsilateral frontal horn or 3rd ventricle; Grade 2, functional placement in the contralateral ventricle or noneloquent cortex; and Grade 3, suboptimal placement in eloquent cortex or nontarget cerebrospinal fluid (CSF) space, with or without functional drainage. Statistical analysis was performed using Fisher's exact test.

Results: Diagnosis included the following: spontaneous subarachnoid hemorrhage (SAH) 50%, trauma 25.7%, intracerebral/intraventricular hemorrhage 16.9% and other, 7.43%. There were 88 (62.4%) Grade 1, 35 (24.8%) Grade 2, and 18 (12.7%) Grade 3 catheter placements. Hemorrhagic complications occurred in 9 (6%). None of the patients were symptomatic since most of these hemorrhages occurred along the catheter tract.

Conclusions: Bedside placement of external ventricular drains by experienced neurosurgical physician assistants can be performed with acceptable safety and accuracy.

202. Digital Subtraction Angiography Measurements Of The Internal Carotid Artery To Gauge Tortuosity

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Introduction: We analyzed the internal carotid artery on digital subtraction angiography to create surrogate measurements of tortuosity. This data may help create realistic, data-driven models for simulation and product design.

Methods: One hundred and two carotid arteries in 101 consecutive patients were evaluated after DSA on a Siemens biplane system. Angiograms were measured for diameter, radii of curvature, the angles subtended by the curves, and artery length between curves. Measurements were taken from the anatomical midpoint of the specified vessel segment and recorded in millimeters.

Results: Internal carotid artery vessel diameters were as follows: middle cervical (4.82), distal cervical (4.24), petrous (4.03), intracavernous (3.65), supraclinoid (3.01), M1 (1.98), A1 (1.96). The radii of curvature in the carotid tree were as follows: cervical (8.0), cervicopetrous (6.0), petro-cavernous (6.0), c4-5 or vertical-horizontal (6.2), carotid genu (5.2). The length of carotid segments were as follows: cervical (25.59), horizontal cervical (13.35), vertical petrous (15.62), horizontal petrous (12.33), vertical intracavernous (12.56), horizontal intracavernous (8.75), carotid genu (8.49), M1 (14.80), A1 (14.17). The angle subtended by curves along the internal carotid artery were as follows: cervical (77), cervical to petrous (100), cervical to intracavernous (107), supraclinoid to ACA (94), supraclinoid to MCA (83), vertical petrous to horizontal petrous (90), horizontal petrous to intracavernous (96), intracavernous to siphon (88), siphon (63).

Conclusion: These measurements can be used to create realistic models and ultimately to judge the feasibility of endovascular interventions. This data will be applied clinically to determine thresholds of vessel tortuosity that will allow endovascular navigation.

203. Experience With Coil Embolization Of Remotely Clipped Aneurysms Presenting With Rupture

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Introduction: Endovascular coil embolization has an established role alongside microsurgical clipping in the treatment of aneurysms. Recent published data in the CARAT study confirmed the durability of microsurgical clipping. We studied previously clipped aneurysms that presented as subarachnoidhemorrhage and were treated by coil embolization.

Methods: A retrospective review was performed of two prospectively maintained databases from two institutions (Cleveland Clinic, Emory University) that spanned twelve years.

Results: Seven patients were identified (five female, mean age 56.9 years) who had previously undergone aneurysm clipping; six were previously ruptured. Aneurysm rupture occurred at 11.5 years (range 4 month to twenty years) following clipping. Aneurysms included AcoA(n=4), PcoA(n=1), ICA terminus(n=1), and anterior choroidal(n=1). Three patients presented in HH grade 1, one in HH2, two in HH3 and one in HH4; two in Fisher(F)1, one F3, and four F4. Four patients underwent unassisted coil embolization while balloon-assistance was employed in three. Angiographic Results: complete occlusion(n=2) and residual neck(n=5). There were no intraprocedural complications. Outcomes: modified Rankin score 0(n=2), 1(n=2), 2(n=1), 5(n=1) and one death. Outcome was associated with clinical grade on presentation: for HH1(mRS 0,0,1), HH2(mRS 1), HH3(mRS 2,5), HH4(mRS 6).

Conclusions: Aneurysm rupture following surgical obliteration is a rare event and may occur remote to the initial treatment. Endovascular embolization with or without balloon assistance can be safely employed in cases of aneurysm recurrence rupture following surgical treatment with satisfactory angiographic treatment. Outcome is associated mainly to clinical grade on presentation.

204. Intracranial Angioplasty And Wingspan Stenting: Snow–plowing The Anterior Cerebral Artery Origin In Four Cases

Max K. Kole, MD; Padamaja Naidu, MD; Horia Marin, MD (Detroit, MI)

Introduction: We report four cases of intracranial angioplasty and stenting across the intracranial carotid bifurcation that resulted in occlusion of the origin of the anterior cerebral artery.

Methods: Four patients with medically refractory symptomatic ICAD suffered occlusion of the origin of the anterior cerebral artery (A1) after undergoing intracranial angioplasty and Wingspan stenting. The preprocedure WASID mean stenosis was 92%. No patient was suspected of having intraluminal clot pretreatment. Two patients had target lesion lengths < 8mm and two > 8mm. Three lesions involved the distal ICA spanning the carotid terminus and proximal M1. One lesion involved the proximal M1. One patient had stenosis involving the A1 origin pretreatment. All patients had patent anterior communicating arteries. All patients were prepared with dual antiplatelet agents and intraprocedural heparinization. All patients underwent balloon inflations (1.5 x 9mm to 2.5 x 9mm) and stent placements (3 x 15mm to 3.5 x 15mm) across the carotid terminus.

Results: One occlusion occurred after predilatation and 3 occlusions occurred after placement of the stent. Three A1 occlusions were partially recanalized with IA Abciximab and post-dilatations of the stent. Attempts to directly angioplasty the A1 crossing through the stent interstices were unsuccessful. The dominant A1 was occluded in 1 patient. This patient had chronic contralateral ICA occlusion and suffered an ACA distribution stroke.

Conclusions: Contrary to the experience with intracranial stenting for aneurysm treatment and extracranial carotid angioplasty and stenting, intracranial angioplasty and Wingspan stenting can lead to occlusion of large side branches such as the anterior cerebral artery.

205. Functional Vascular Neurosurgery Revisited. Wada Testing In The Treatment Of Aneurysms And AVM's

Rashid M. Janjua, MD; Erol Veznedaroglu, MD (Hamilton, NJ)

Introduction: The basic tenet for treatment of vascular pathology is preservation of vascular patency with elimination of the pathological structure, be it aneurysm, arteriovenous malformation (AVM) or other. In most cases, the pathology lends itself to multiple treatment modalities which respective risks and benefits. When the associated risk of eliminating pathology whilst preserving vascular anatomy is deemed high, elimination of the vessel is an option. We present three cases in which Sodium Amytal injection technique (WADA test) was employed as a pre-emptive means to determine eloquence of the supplied nervous tissue, prior to vessel sacrifice.

Methods: Three patients in whom WADA testing was used for vessel sacrificed and related literature reviewed. One patient suffered from intractable chorea secondary to a Grade VI Spetzler-Martin AVM. Using WADA testing of the anterior choroidal territory, the vessel was selectively embolized. Two other patients with fusiform aneurysms underwent selective WADA testing of the affected vessel and underwent vessel sacrifice.

Results: The patient with chorea had postoperative hemiparesis which full resolution of lower extremity function and elimination of the chorea. Both patients with aneurysms and vessel embolizations had elimination of the aneurysms without loss of function.

Conclusions: In patients with untreatable vascular abnormalities and aneurysms that require major vascular reconstruction, WADA testing followed by vessel sacrifice may offer an alternative approach to coil reconstruction, clipping with wrapping or bypass surgery. This may herald a paradigm shift towards a less invasive "functional" approach towards these abnormalities.

206. Outcome Of The Patients With Ruptured Basilar Artery Bifurcation Aneurysm Who Underwent Treatment With Endovascular Approach - A Single Center Experience

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Introduction: Due to the presence of a high morbidity and mortality associated with surgical clipping, most of patients with basilar artery bifurcation (BA) aneurysm are offered endovascular therapy.

Methods: Objective of our study is to report our technical and clinical outcomes of BA ruptured patients who underwent endovascular therapy.

Results: Seventeen patients with a mean age of 51 ± 13 year underwent successful repair of the ruptured BA bifurcation aneu-

rysms. H&H I was present in 29%, H&H II in 23%, H&H III in 12% and H&H IV in 35% of patients. Ten patients required stent-assisted coiling in the acute phase and received oral loading doses of clopidogrel (300 mg) and aspirin (325 mg) at least 2 hours prior to the stent deployment. There was no incidence of intra-operative or post-operative intracranial or systemic hemorrhages or thromboembolic event. Additionally, there was no hemorrhagic complications associated with antithrombotic administration for stent-assisted repair. Immediate complete and near complete obliteration was observed in 76% and subtotal in 23% of There was no mortality and 90 days good outcome (GOS 5 in 13, GOS 4 in 2) in 88% and poor outcome in (GOS 3 in 2) 12% of patient.

Conclusions: Endovascular therapy offers good technical and clinical outcome of ruptured BA aneurysms including those who required stent-assisted repair in acute phase. Poor H&H grade was not associated with poor outcome in our series. Further study is required.

207. Evaluation Of Treatment Outcome In Patients With Intra–parenchymal Hemorrhage From Cerebral Aneurysm Rupture

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Introduction: Presenting neurologic status and expedient aneurysm treatment have been shown to affect long term outcomes in patients presenting with cerebral aneurysm rupture. Large intraparenchymal hemorrhage accompanies subarachnoid hemorrhage in a subset of these patients. For these select patients, immediate surgical treatment may be advantageous over endovascular aneurysm treatment followed by surgery for clot evacuation as it allows for simultaneous evacuation of hemorrhage and treatment of the ruptured aneurysm.

Methods: A retrospective chart review revealed 183 patients with spontaneous subarachnoid hemorrhage presenting to the University of North Carolina between July 2007 and June 2010. Ruptured cerebral aneurysms were identified in 150 patients. Significant intraparenchymal hemorrhage (IPH) upon presentation was noted in 15 patients. 5 patients underwent immediate craniectomy with microsurgical clipping of the ruptured aneurysm and clot evacuation. 7 patients underwent endovascular embolization followed by craniectomy for clot evacuation. 3 patients received no treatment due to poor presenting exams and died.

Results: IPH was associated with pretreatment neurologic deficits, focal neurologic deficits at follow up, worse presenting HH grade, and mortality. A significant difference in mRS outcome was identified between patients with IPH undergoing surgery versus endovascular aneurysm treatment followed by surgery.

Conclusions: Ruptured cerebral aneurysms in patients presenting with large intraparenchymal hemorrhage should be treated expeditiously. In this small study, results reveal improved outcome in patients treated with surgery alone versus endovascular embolization followed by surgery for clot evacuation.

208. Concomitant Surgical–Endovascular Approach To Com–plex Intracranial Dural Arteriovenous Fistulae: One Hand Can't Clap

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Introduction: The endovascular management of intracranial dural arteriovenous fistulae (DAVF) may be challenging when percutaneous transarterial or transvenous access routes are unavailable due to tortuous anatomy, venous thrombosis, or stenoocclusive disease. In such cases, direct surgical exposure of the arterialized dural sinus or a proximal arterial conduit may provide an alternative. We describe surgical techniques that have enabled successful endovascular management of complex DAVFs.

Methods: We reviewed clinical records and imaging studies of all DAVF cases in which surgical exposure of the vascular access site was necessary to facilitate endovascular treatment at 2 neurovascular centers between January 1996 and August 2010.

Results: Three transverse sinus DAVFs trapped by thrombosis of the distal jugular bulb and ipsilateral proximal transverse sinus were accessed through burr holes placed directly over the arterialized sinus. Embolization was performed using a combination of coils and liquid embolic agents. A superior sagittal sinus DAVF was embolized with Onyx through direct puncture of a tortuous stenotic middle meningeal artery through a small craniotomy. One case of transverse sinus DAVF was accessed through surgical exposure of the cervical carotid due to tortuous aortic anatomy. The results of embolization were assessed by angiography in each case. In all cases, the concomitant surgical-endovascular approach permitted safe and effective occlusion of the fistula with excellent immediate angiographic results. There was no procedure-related morbidity or mortality.

Conclusion: A concomitant surgical-endovascular approach enables endovascular treatment of complex DAVFs with minimal procedure-related morbidity and a high technical success rate.

209. Anterior-To-Posterior Circulation Approach For Mechanical Thrombectomy Of An Acutely Occluded Basilar Artery (BA) Using The Penumbra Aspiration System

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Introduction: Prompt access to arterial occlusion is the key to successful endovascular revascularization in acute stroke. We present the first reported case utilizing anterior-to-posterior circulation approach for a successful mechanical thrombectomy and chemical thrombolysis of an acute BA occlusion using the Penumbra Aspiration System.

Case Description: A 39-year-old man with vasculopathy following radiation for lymphoma requiring bilateral internal carotid artery (ICA) stenting, bilateral subclavian artery (SCA) stenting, right vertebral artery (VA) ostial stenting and with left VA origin occlusion presented with sudden dizziness and right hemiparesis. Despite initial improvement from intravenous tPA treatment the patient deteriorated rapidly and became comatose (NIHSS > 25). Catheter angiography revealed BA occlusion and emergent endovascular treatment was undertaken. Right VA guide catheter engagement was unsuccessful due to protrusion of the VA stent into the SCA. Left ICA angiography revealed a patent left posterior communicating (PCOM) artery and left P2 segment. A Penumbra 026 reperfusion catheter and Synchro2-soft microguidewire was used to traverse the left ICA, the left PCOM, and the left P1 segment to the thrombosed BA. Mechanical thrombectomy and chemical thrombolysis were performed. TIMI-3 flow in the BA and TIMI-2 flow in the right posterior cerebral artery were restored 7'17" after symptom onset. The patient followed commands in all extremities 10 hrs after the onset of symptoms. NIHSS on discharge was 2.

Conclusion: In patients with unfavorable VA anatomy, anterior-to-posterior thrombectomy of the BA can be successfully achieved using the 026 Penumbra catheter via an anatomically suitable PCOM.

210. Increased Risk Of Infected Pseudoaneurysms In Immuno–compromised Patients With Angioseal Closure Device Post Cerebral Angiography

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Introduction: Advances in closure devices have revolutionized endovascular access site management. Despite significant benefits they are associated with complications. Access site infection is a potentially morbid complication which can be associated with closure device use. The Angioseal closure device is a highly safe and effective device for which complications have only rarely been reported.

Methods: We report two cases of infected pseudoaneurysms in patients using immunosuppressants after use of the Angioseal closure device despite the use of preprocedural antibiotics and strict sterile techniques.

Results: Case one 22 year-old s/p liver transplant who underwent aneurysm coiling and internal maxillary artery embolization for treatment of epistaxis. The patient returned to the hospital 18 days after discharge with fevers and evidence of groin infection. Cultures revealed growth of Corynebacterium and gram-negative rods. Case two 43 year-old with rheumatoid arthritis who underwent endovascular treatment of arteriovenous fistula and returned 17 days after discharge with evidence of groin infection. Both of our patients required vascular surgery intervention with resection of the infected segment of the femoral artery and homograft reconstruction. We review the literature regarding the risk of infection with the use of closure devices.

Conclusion: Closure devices have been shown to be safe and efficacious in numerous studies. A review of the literature yields little information regarding the incidence of infection with the use of closure devices. It is possible that immune suppressing drugs may increase the risk of infection when using certain closure devices. Further study of this issue is warranted.

211. Large Acute Intracerebral Hemorrhage As The Presenting Feature Of Reversible Cerebral Vasoconstriction Syndrome

Vikas Singh, MD; Huan Wang, MD (Urbana Champaign, IL)

Introduction: Reversible Cerebral Vasoconstriction Syndrome (RCVS) represents a diverse group of disorders characterized by severe headaches associated with reversible and multifocal vasoconstriction of cerebral arteries. Although focal neurological deficits are common, large acute intracerebral hemorrhage (ICH) is a rare and under recognized presenting feature of RCVS. We report two such cases and review the current literature.

Methods: We conducted a retrospective review from 2008 to 2010 and identified two patients with large ICH as the presenting feature of RCVS. Their hospital charts and follow-up records were reviewed and summarized.

Results: Both patients were healthy females (42 year-old and 54 year-old respectively), presenting with large intraparenchymal hemorrhage (9-cm left intraparenchymal hemorrhage with 1-cm midline shift and 4-cm left intraparenchymal hemorrhage with 2-mm midline shift respectively). Neither patient had subarachnoid hemorrhage. One underwent emergent surgical intervention while the other was treated conservatively. Initial cerebral angiograms demonstrated severe multi-focal vasoconstriction, but without any evidence of arteriovenous shunting or aneurysms. In both patients, extensive work-up for vasculitic, immunologic and infectious causes were negative along with essentially normal CSF analysis and leptomeningeal biopsy results. One-week follow-up angiogram documented improvement of vasoconstriction in one patient but worsening finding in another. Three-month follow-up angiograms demonstrated complete resolution in both patients. At three-month follow-up visits, their Modified Rankin Scale was 3 and 0 respectively.

Conclusions: Although acute ICH is a rare presenting feature of RCVS, familiarity of this clinical entity is essential for cerebrovascular neurosurgeons and neurologists.

212. Combined Use Of Fenestrated Aneurysm Clips And Indocyanine Green Videoangiography For Microsurgical Treatment Of Superiorly Projecting Anterior Communicating Artery Aneurysms

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Introduction: The microsurgical treatment of anterior communicating artery (ACoA) aneurysms that project superiorly is technically challenging due to the relationship of the A2 segments and ACoA perforators to these lesions. The goal of this study is to evaluate the efficacy of fenestrated aneurysm clips and intraoperative Indocyanine Green videoangiography (ICG) in their treatment.

Methods: 9 patients harboring superiorly projecting ACoA aneurysms (7 ruptured, 2 non-ruptured) were treated using fenestrated aneurysm clips. ICG was performed immediately after clip application in all cases. Postoperative catheter angiography and intraoperative Doppler ultrasonography was performed in each case and compared with ICG.

Results: Complete aneurysm obliteration and reconstruction of the ACoA complex was achieved in 8 cases. Aneurysm remnant was identified on postoperative angiography in one patient. Persistent aneurysm filling identified on ICG led to additional clip placement in 1 case. Structures incorporated within the clip fenestration(s) were the distal A1 segment, the proximal A2 segment, the A1-A2 junction, the recurrent artery of Heubner and an orbitofrontal branch. The patency of the incorporated vessels, ACoA complex, and perforators was confirmed intraoperatively on ICG and postoperative angiography in all cases. Flow assessment using intraoperative Doppler ultrasonography, however, was limited to large caliber vessels (A1, A2, ACoA). Glasgow outcome scores were 5 (6 patients), 4 (1 patient), 3 (1 patient) and 1 (1 patient).

Conclusion: The use of fenestrated clips and ICG during microsurgical clipping of superiorly projecting ACoA aneurysms allows for excellent reconstruction of the ACoA complex, preservation of parent vessels and perforators, and good clinical outcomes. Postoperative angiography remains indicated.

213. Transtemporal Modification Of The Extreme Lateral Approach

Bernard R. Bendok, MD, FACS; Rudy J. Rahme, MD; H. Hunt Batjer, MD, FACS; Andrew J. Fishman, MD (Chicago, IL)

Objectives: The traditional far lateral surgical approach has been described and advocated for the treatment of neoplastic and vascular lesions of the cervicocranial junction. The standard technique in many cases, has limited degree of surgical freedom, visualization, and may require significant cerebellar retraction. We present a technical modification, which optimizes the exposure by utilizing an intratemporal anatomic dissection directly to the jugular process.

Subjects and Methods: Detailing of modified surgical technique. In addition, we retrospectively reviewed our experience with 8 clinical cases.

Results: Improved angle of view is achieved by following the intratemporal course of the sigmoid sinus to the jugular foramen, thereby removing the jugular process in a safe and complete fashion. Additional pre-sigmoid bone can be removed to the level of the retrofacial region and labyrinthine apparatus, allowing for optimal mobilization and wider exposure. The technique is typically performed in a supracondylar fashion obviating the need for C1 fusion. Because the technique is more anteriorly based than the classically described methods, we have also modified the incision, muscle dissection and reconstruction.

Conclusion: The transtemporal modification of the extreme lateral approach provides a substantial improvement of surgical freedom and view for vascular and neoplastic lesions of the low anterior posterior fossa and cervicocranial junction. The additional time required is minimal in experienced centers. The extended dissection does not result in significant anatomic nor functional deficits. The technique can be performed safely and expanded easily to include laminectomy and vertebral mobilization if required for pathologic extension to the cervical spine.

214. Intraoperative Fluorescent Based Angiography In Carotid Endarterectomy

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Introduction: Carotid Endarterectomy (CEA) is a well established

treatment option for internal carotid artery stenosis. Nevertheless, the presence of remaining plaque and/or dissection flaps after completion of endarterectomy may increase the risk of postoperative stroke or thrombosis. Several modalities have been employed for intraoperative assessment of adequate blood flow at the involved arteries, such as duplex ultrasonography or contrast angiography. We report our preliminary experience with the use of intraoperative fluorescent-based angiography (IFBA) in CEA.

Methods: In three elective cases of CEA, intraoperative fluorescent-based angiography was employed after the closure of the arteriotomy. The images obtained from the microscope were evaluated for presence of flow defects, stenosis or presence of plaque flaps. Intraoperative duplex ultrasonography was used to confirm the presence of adequate flow in the involved arteries. All patients then underwent routine postoperative CTA imaging.

Results: No stenosis or flow defects of the arteries involved were detected. No complications associated with intraoperative fluorescent-based angiography were observed. The IFBA did not significantly prolong the CEA procedure time.

Conclusions: IFBA was feasible in all cases of CEA. It may provide a safe adjunct to the intraoperative evaluation of blood flow of the associated vessels. Further studies may delineate the exact role in CEA.

215. Association Of Intracranial Aneurysm And Loeys-Dietz Syndrome: Case Illustration, Management And Literature Review

Bernard R. Bendok, MD, FACS; Rudy J. Rahme, MD; Joseph G. Adel, MD; John F. Bebawy, MD; Dhanesh K. Gupta, MD; H. Hunt Batjer, MD, FACS (Chicago, IL)

Objective and importance: Loeys-Dietz syndrome (LDS) is a newly described connective tissue disease associated with aortic aneurysms. A strong association between LDS and intracranial aneurysms has not yet been documented in the literature. We present the first detailed report of an intracranial aneurysm finding in a LDS patient.

Clinical Presentation: The patient is a 20 year old female recently diagnosed with LDS and found to harbor 2 incidental intracranial aneurysms on a screening MRA: a 3mm right carotid ophthalmic aneurysm and an 8 mm partially fusiform paraclinoid carotid artery aneurysm.

Intervention: A standard left pterional craniotomy was performed. Intraoperative adenosine was utilized instead of temporary clipping given the fact that her vessels were extremely friable. After reconstruction an intraoperative Indocyanine green angiogram was obtained confirming complete aneurysmal obliteration and internal carotid artery patency.

Conclusion: This is the first detailed report of a clear association between intracranial aneurysms and LDS. An association between LDS and IA, if substantiated in a larger study, has implications for aneurysm screening in this population. Moreover such an association may shed light on mechanisms of aneurysm formation, growth and rupture.

216. Retrieval Of Migrated Coils And Intracranial Stents Using The Merci Retriever

David K. Kung, MD; Kelly B. Mahaney, MD; Wei Liu, MD; James D. Rossen, MD; David M. Hasan, MD (Iowa City, IA)

Introduction: Coil displacement and stent migration are potentially catastrophic complications of endovascular treatment of cerebral aneurysms. We report our use of the Merci Retriever to remove displaced implants.

Case 1: A 53 year-old woman underwent stent-assisted coiling of an incidental 6mm left ophthalmic artery aneurysm. A Neuroform-3 stent was deployed across the aneurysm neck. Placement of the third aneurysm coil was complicated by a prolapsed and stretched coil loop into the internal carotid artery. The coil became detached from the delivery system without activation of the release mechanism. Retrieval using an Amplatz Snare and EV3 Alligator was unsuccessful. A Merci V 2.5 Soft retriever was used to remove the coil in multiple fragments. A small remaining fragment was jailed with another Neuroform 3 stent. The post-operative angiogram showed near-complete occlusion of the aneurysm and preserved flow in the ICA. The post-operative course was uneventful.

Case 2: A 75 year-old woman presented with a ruptured 2.5 mm right posterior communicating artery aneurysm and underwent emergent stent-assisted coiling. An Enterprise stent was deployed. A few loops of the coil herniated into the parent artery during coil embolization. Migration of the stent and herniation of the coil mass out of the aneurysm subsequently occurred. Merci V3 Firm, V2.5 Soft and a V2.0 Firm Retrievers were used sequentially to remove the stent and entire coil mass. Subsequent stent-assisted coiling was successful. Unfortunately the patient suffered respiratory failure and expired one month post-ictus.

Conclusion: The Merci Retrieval System can be used successfully to retrieve malpositioned endovascular implants.

217. Comparison Of Intraoperative Portable CT Scanners In Skull Base And Endoscopic Sinus Surgery: Single Center Case Series

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Objectives: Precise and safe management of complex skull base lesions can be enhanced by intra-operative CT scanning. Surgery in these areas requires real-time feedback of anatomic landmarks. Several portable CT scanners are currently available. We present a comparison of our clinical experience with three portable scanners in skull base and craniofacial surgery.

Design
Clinical Case Series
Participants
Northwestern Memorial Hospital
Main Outcome Measures
Three scanners are studied: one conventional multi-detector CT (MDCT), two digital flat panel conebeam CT (CBCT) devices. Technical considerations, ease of use, image characteristics, and integration with image guidance are presented for each device.

Results: All three scanners provide good quality images. Intraoperative scanning can be used to update the image guidance system in real time. The conventional (MDCT) CT is unique in its ability to resolve soft tissue. The flat panel (CBCT) scanners generally emit lower levels of radiation, and have less metal artifact effect. In this series, intraoperative CT scanning was technically feasible and deemed useful in surgical decision making in 75% of patients.

Conclusion: Intraoperative portable CT scanning has significant utility in complex skull base surgery. This technology informs the surgeon of the precise extent of dissection and updates intraoperative stereotactic navigation.

218. Electron Microscopic Demonstration Of The Interstitial Cajal-Like Cells In The Marginal Zone Of Cerebral Cortex

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Introduction: We sought to compare the ultrastructural features of the Interstitial Cajal-Like Cells (ICLCs) from the marginal areas of cerebral cortex to the deepest arachnoid mater including perivascular spaces.

Methods: We used transmission electron microscopy to identify and describe ectocortical ICLCs in a patient operated on for transitional meningioma.

Results: We observed a few ICLCs distributed within the molecular layer of the cerebral cortex around the tumor which has not invaded the cortex. They were positioned orizontally. Ultrastructurally, ICLCs were characterized by an ovoid nucleus, moderate, long and ramified cellular processes with thinned endings, many mitochondria, intermediate filaments, and multiple attachment sites as intracytoplasmic cavities for connection with other overlapping cells. These ICLCs are only apparently similar to the ectocortical neurons of Cajal and quite different from attenuated fibroblasts of leptomeninges

Conclusions: These ectocortical ICLCs - neither neurons, nor fibroblasts - have showed particular features determined by their microenvironment and spatial relationships with above pial cells. We consider them as the main defenders for brain ("defendocytes") migrated from pia mater, and therefore, the nature of pia mater must be reconsidered. However, a further morphologic comparison of the Cajal-Retzius cells, Cajal cells, cerebral arterial interstitial cells and pial cells in humans must be performed at ultrastructural level.

219. Symptomatic Thoracic Arachnoid Cyst Formation After Posterior Fossa Craniotomy for Aneurysm Clipping

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Introduction: Subarachnoid cysts are usually developmental anomalies and found incidentally due to their typical asymptomatic nature. Acquired cysts following a primary event such as surgery or trauma have an unknown mechanism of growth.

Methods: We present a 52 year-old female who suffered a Hunt/Hess Grade III subarachnoid hemorrhage from a ruptured, dissecting pseudoaneurysm of her left posterior inferior cerebellar artery (PICA). She was treated initially with endovascular coiling of her left vertebral artery to decrease flow to the aneurysm. Following successful thrombosis of the aneurysm the patient recovered and was discharged home. Follow up imaging at three months showed recanalization of the PICA aneurysm, and the patient underwent craniotomy and clipping of the aneurysm. She did well and was discharged home.

Results: Two days later the patient developed ataxia and was admitted to inpatient rehabilitation. Two weeks postoperatively, the patient was found to be completely paraplegic with neurogenic bowel and bladder dysfunction. Magnetic resonance imaging of the spine revealed a previously unknown arachnoid cyst causing severe spinal cord compression and deformation from C7 to T4. Emergent laminectomies and intradural cyst resection was performed. The patient did not improve neurologically post-operatively.

Conclusions: The purpose of this case report is to review the first documented case of symptomatic thoracic arachnoid cyst formation after posterior fossa craniotomy for aneurysm clipping. The cerebrospinal fluid hydrodynamics involved are not completely understood, but in patients status post cranial subarachnoid dissections, spinal pathology should be considered as well when post-operative neurologic changes occur.

220. Comparative Use Of The Turkey And Chicken Wing Brachial Artery Models For Microvascular Anastomosis Training

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Introduction: We describe the turkey wing model for microvascular anastomosis training. In contrast to a live animal model, there is no bleeding, no time pressure, and no need for animal sacrifice, and the neurosurgeon is able to leave and address clinical responsibilities as needed.

Methods: We recorded diameter measurements in each of 5 turkey and 5 chicken brachial arteries at three equidistant points. Usable vessel length was measured from joint-to-joint in each specimen.

Results: The turkey wing brachial artery was consistently larger in diameter (1.47 mm vs. 1.07 mm) ($p<0.01$) and longer (78.1 mm vs. 49.6 mm) ($p<0.01$) than the chicken wing artery and its vessel diameter showed less variability (1.47 ± 0.14 mm in turkeys vs. 1.07 ± 0.25 mm in chickens).

Conclusion: Our institutional preference has shifted to the use of a turkey wing as the initial model for microanastomosis training with nonliving animal models. Increased vessel length allows one vessel to be used for multiple anastomoses. Another concern with the use of chicken wings is the lack of reliability in finding a vessel of a suitable diameter. Half of the measurements in chicken brachial artery were less than 1.05 mm. The tissue durability and handling properties of the turkey wing brachial artery provide additional advantages that make us favor this model over the chicken wing as part of a graduated instruction process.

221. Embolization Of A Pial-dural AVM Via Craniotomy To Access A Large Feeding Artery

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Introduction: Embolization of AVMs can be challenging if feeding artery access is limited by tortuosity or diminutive size. We present a case where a hybrid operating room/endovascular suite was used to perform a craniotomy to gain access to a feeder traversing the inner table of the skull.

Methods: A 42 year female with an AVM previously treated with radiosurgery presented with progressive right-sided weakness. Angiography revealed a 6cm residual left fronto-temporal-parietal mixed pial-dural AVM. We determined that embolization from the left occipital artery would provide a safe, yet effective approach for reduction in the size of the malformation. However, the artery proved unable to catheterize because there were tiny anastomotic arteries that collateralized to form the large feeder. We planned to perform a craniotomy centered over the feeder, then directly catheterize and embolize the AVM via this artery.

Results: The patient was transported to the hybrid OR. The craniotomy was localized utilizing fluoroscopic images. Upon removal of the bone flap, it was apparent that the feeder was a bone emissary and not dural-based. The bone edge bleeding was easily controlled with bone wax. A 4-French sheath was inserted into the bone feeder. Brisk back-bleeding was seen, confirming placement in the feeder. A microcatheter was then advanced into the nidus. Seven mL of liquid embolic agent was injected into the nidus. The catheter and sheath were removed and the bone flap was plated back into place. The patient remained at her neurologic baseline.

Conclusion: Treatment of AVMs is possible using combined endovascular/surgical techniques by cerebrovascular/endovascular neurosurgeons.

222. Double Basilar Fenestration Presenting As Basilar-type Migraine

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Objective and importance: Basilar-type migraine (BTM) is a specific type of migrainous disorder. Its association with basilar artery anomalies has not yet been clearly defined. Double basilar artery fenestration is a rare finding and has never been previously reported in association with BTM. We report the case of a patient who presented to our institution with symptoms typical of BTM and who was found on workup to have a double basilar artery fenestration.

Clinical Presentation: A 50 year old female with a history of migraine headache presented to our institution with a two month history of worsening headaches and episodes of "discombobulation."

Her headaches were dull, throbbing, bifrontal and often associated with photophobia and phonophobia. CT angiogram (CTA) and magnetic resonance angiogram (MRA) of the head revealed two separate short fenestrations of the basilar artery.

Intervention: The patient was started on 325mg of aspirin daily. She was diagnosed with migraine headaches and discharged home on propanolol for migraine prophylaxis after consultation with the neurology service.

Conclusion: We report the first case of a double basilar artery fenestration associated with BTM. The pathophysiology underlying basilar migraine is not yet clearly understood but there is convincing evidence that anatomic abnormalities of the basilar artery may alter the local hemodynamics of the vessel and thus predispose to the development of BTM. Future investigation into these underlying anatomic variations will further elucidate the factors associated with the development of BTM.

223. Stent Assisted Coil Embolization Of A Traumatic Proximal Segment Of An Ophthalmic Artery Pseudoaneurysm Causing Subarachnoid Hemorrhage

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Introduction: Traumatic ophthalmic dissection with pseudoaneurysm formation is a rare event. Coil embolization of a pseudoaneurysm and sacrifice of dissecting ophthalmic artery (OphA) has been reported. We present an unusual case of subarachnoid hemorrhage (SAH) caused by a traumatic pseudoaneurysm of the proximal OphA. This is the first reported case of successful stent reconstruction of a dissected OphA and coil embolization of the pseudoaneurysm with preservation of the OphA.

Case description: A 21 year-old man presented with SAH from an air gun accident. Pellets penetrated from his right cheek into the right orbit. Detailed ophthalmologic examination demonstrated a right direct afferent pupillary defect with preserved blink reflex to visual threat. Computer Tomogram (CT) demonstrated metallic fragment in the right orbital apex. A cerebral angiogram revealed near-occlusion of the right OphA and suboptimal retinal perfusion from right external carotid artery (ECA) collaterals. After ventriculostomy the patient's exam improved. However, his exam worsened on day 7 post-injury. CT perfusion suggested vasospasm and cerebral angiogram revealed a dissecting pseudoaneurysm in the right proximal OphA, which was not seen on the previous angiogram. Severe vasospasm was noted in several vessels requiring balloon angioplasty and nicardipine infusion. In an attempt to preserve vision, a Neuroform Stent was successfully deployed across the dissection into the OphA. The pseudoaneurysm was embolized successfully.

Conclusions: Traumatic dissection of intracranial OphA with SAH and pseudoaneurysm formation is a rare but potentially life-threatening event. To our knowledge this is the first report of successful stent-assisted coil embolization of a pseudoaneurysm of the OphA segment.

224. Propofol Infusion Syndrome (PRIS) During Microsurgical Clipping Of Multiple Cerebral Aneurysms

Aravind Somasundaram; Claude McFarlane, MD; Anand V. Germanwala, MD (Chapel Hill, NC)

Introduction: PRIS refers to a constellation of symptoms, including metabolic acidosis, rhabdomyolysis, cardiac dysfunction, and hyperlipidemia, following the administration of propofol for even a short duration. An unfamiliar entity, it can be fatal if unrecognized. We present a case of a patient developing PRIS after undergoing a unilateral craniotomy for microsurgical clipping of three unruptured aneurysms.

Methods: A 68 year old woman with a prior ischemic stroke underwent an MRI/MRA and had the incidental finding of multiple aneurysms. The patient was taken to the operating room for microsurgical clipping of multiple aneurysms via a right frontosphenotemporal craniotomy with contralateral technique. The patient was placed in burst suppression with propofol during temporary clip placement. Continuous neurophysiological monitoring and an intraoperative post-clipping arteriogram were performed.

Results: Permanent clips were placed on bilateral ophthalmic artery and right middle cerebral artery aneurysms. Intraoperative monitoring remained stable throughout the procedure and an intraoperative arteriogram revealed obliteration of the aneurysms with preservation of the surrounding vasculature. Prior to attempted extubation, the patient had a seizure, which was terminated with propofol and ativan. Postoperatively, the patient remained in a lactic acid coma with decorticate posturing for five days. Multiple other etiologies were explored and ruled out before recognizing PRIS. Termination of propofol resulted in immediate improvement in her acidosis and exam.

Conclusions: An unusual phenomenon, PRIS should be entertained, in the appropriate clinical setting, once common etiologies for lactic acidosis and a poor postoperative exam are exhausted. Early recognition of this entity can result in complete recovery.

225. Simultaneous Posterior Communicating Artery Aneurysm Clipping And Selective Amygdalohippocampectomy: Direct Access Through The Mesial Temporal Lobe To The Basal Cisterns

Adib A. Abla, MD; Kris A. Smith, MD; Peter Nakaji, MD (Phoenix, AZ)

Introduction: We report the case of a patient with intractable epilepsy and an incidental posterior communicating artery aneurysm who was treated simultaneously for both entities. This is the second such case and the first report, to our knowledge, to be done with a selective amygdalohippocampectomy, without removal of temporal lobe neocortex.

Methods/Case Material: A 23-year-old man with intractable epilepsy and a posterior communicating artery aneurysm was counseled regarding the potential to treat both pathologies with one procedure. He elected to undergo a simultaneous approach.

Results: The patient has done well at his 5-month follow-up examination with no residual seizures or neurologic deficits.

Conclusion: Access to aneurysms within the basal cisterns is viable with transchoroidal approaches through the temporal horn of the lateral ventricle. Anterior extension through portions of the amygdala further increases access. In our patient, selective amygdalohippocampectomy and posterior communicating artery aneurysm clipping were performed during the same surgical setting and approach. This directly lateral corridor allowed our young patient with an incidental aneurysm to undergo a less invasive combined operation.

226. The Ultimate Sacrifice. Treatment Of A Recurrent Carotid Pseudoaneurysm.

Rashid M. Janjua, MD; Valentine Nduku, MD; Kenneth Liebman, MD; Erol Veznedaroglu, MD (Hamilton, NJ)

Introduction: Carotid endarterectomy is a widely practiced operation for symptomatic as well as asymptomatic cervical carotid atherosclerotic disease. It is proven to be a safe operation reducing the overall stroke risk for the patient as compared to medical management for a high degree of stenosis. We present a case of a patient treated previously with an endarterectomy and subsequently presenting with a pulsatile mass in the neck eroding through the skin.

Methods: The data in this case report was collected prospectively.

Results: At the initial presentation, an angiogram demonstrated the mass to be a pseudoaneurysm at the site of the endarterectomy. The pseudoaneurysm was stented, subsequently selectively catheterized and successfully obliterated with coils. Patient presented two

weeks later with a carotid blowout with erosion of the pseudoaneurysm through the skin. Angiography demonstrated recanalization of the pseudoaneurysm which was successfully recoiled until a similar event a week later demanded a balloon test occlusion followed by carotid occlusion.

Conclusions: This case demonstrates the recalcitrant nature of a post-endarterectomy carotid pseudoaneurysm finally successfully managed by vessel sacrifice. Successful obliteration may alternatively have been achieved with surgical re-exploration or with endovascular deployment of a coated stent.

227. Inferior Petrosal Sinus Sampling For Cushing Disease

Rafael Rodriguez-Mercado, MD, FACS; Amaury Garcia, MD; Erwin Rayo, MD (San Juan, PR)

Introduction: Cushing's syndrome result from excessive exposure to the hormone cortisol. The disorder is most commonly caused by taking of exogenous steroids over a long period of time. A more rare form of the disorder occurs when the body itself produces an excessive amount of cortisol like in microadenomas of pituitary tumors in 60-80% , adrenal tumors 10-20% and ectopic tumors of the lung or pancreas in 1-10%. Inferior Petrosal Sinus Sampling (IPSS) determine likely side of a microadenoma within the pituitary with 15 %of the time this test falsely lateralizes the tumor.

Methods: Retrospective revision of the results of IPSS done in 4 patients between 2008-2009 with clinical evidence of Cushing Syndrome. Then we proceed with Corticotropin-Relasing Hormone (CRH) stimulation test following the established protocol for the venous sampling. Blood samples once taken was send to a reference laboratory.

Results: From the 4 patients that underwent the procedure no complications was reported. We established the diagnosis of Cushing Disease from pituitary microadenoma secreting ACTH in 3 patients with lateralization. In one patient the blood levels of ACTH was not significant and later on it was found with an ectopic lesion in the pancreas. The 3 patients with microadenomas that underwent surgery got satisfactory results.

Conclusions: Inferior Petrosal Sinus Sampling in patients with Cushing Disease is a excellent tool for the diagnosis of pituitary microadenomas secreting ACTH. This procedure had a low morbidity and mortality but require a well train endovascular and endocrinology team to avoid mistakes in the recollection of blood samples.

228. Hematocrit Dependent Response To Virtual Coil Embolization In A Model Sidewall Aneurysm

Clemens M. Schirmer, MD (Springfield, MA); Adel M. Malek, MD, PhD (Boston, MA)

Introduction: Coiling is believed to protect from aneurysm rupture by inducing thrombosis. We sought to investigate the effect of hematocrit (Hct) and plasma viscosity, a surrogate of thrombosis likelihood, on the hemodynamics of virtual aneurysm coiling.

Methods: An idealized 3-dimensional saccular side-wall aneurysm was modeled using computer-aided design. Computational fluid dynamic analysis was implemented with an adaptation of the Carreau model of non-Newtonian viscosity, reflecting Hct between 20% and 60%. Coil embolization with 3 helical coils was modeled directly for the same hematocrit range.

Results: An idealized 3-dimensional saccular side-wall aneurysm was modeled using computer-aided design. Computational fluid dynamic analysis was implemented with an adaptation of the Carreau model of non-Newtonian viscosity, reflecting Hct between 20% and 60%. Coil embolization with 3 helical coils was modeled directly for the same hematocrit range.

Conclusions: An idealized 3-dimensional saccular side-wall aneurysm was modeled using computer-aided design. Computational fluid dynamic analysis was implemented with an adaptation of the Carreau model of non-Newtonian viscosity, reflecting Hct between 20% and 60%. Coil embolization with 3 helical coils was modeled directly for the same hematocrit range.
