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The Evolution of Endovascular Therapy for Neurosurgical Disease

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The field of endovascular neurosurgery has evolved rapidly and successfully over the past few decades. This dynamic evolution has resulted in numerous new and effective endovascular therapies for the management of intracranial aneurysms; arteriovenous malformations (AVMs); dural arteriovenous fistulae; acute stroke; carotid-cavernous fistulae (CCFs); carotid artery disease; vasospasm; and vascular tumors of the head, neck, and spine. The rapidly advancing technologies as well as our constantly enlarging body of knowledge about the central nervous system are catalyzing this evolution. Although we anticipate the future of endovascular neurosurgery with great enthusiasm, it is important to review its history to gain a sense of direction and discover the renewed pertinence of past ideas.

Cerebral angiography

Cerebral angiography is the foundation of neuroendovascular therapies. Antonio Egas Moniz (Fig. 1), a Portuguese neurologist and the recipient of the Nobel Prize in Physiology and Medicine in 1949, was the first to develop and describe cerebral angiography in 1927 [1]. Moniz exemplified personal traits common to other endovascular pioneers: vision and perseverance despite almost insurmountable obstacles. After successfully obtaining cerebral angiograms in dogs, he transported cadaveric specimens obtained from the pathology department in his limousine to a radiology laboratory in another part of the city to develop the technique further. The first successful cerebral angiogram performed in a living person was obtained in a 48-year-old patient with Parkinson's disease. Moniz ligated the internal carotid artery (ICA) temporarily for 2 minutes and injected a 70% solution of strontium bromide into the ICA at a dose of 13 to 14 mL. The first film showed contrast filling of the middle and posterior cerebral arteries. Unfortunately, the patient died 8 hours later from thrombophlebitis. Thereafter, angiography passed through many phases of development to evolve from a one-time hazardous technique to a simple and safe procedure.

Intracranial aneurysms

Beginnings

Although attempts to induce thrombosis of peripheral aneurysms by introducing foreign bodies or applying local electrical or thermal energy date back to the early 1800s [2], it was not until 1941 that Werner et al [3] reported the first successful electrothermic thrombosis of an intracranial aneurysm (Fig. 2). With a transorbital

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Fig. 1. Antonio Egas Moniz, a Portuguese neurologist who won the Nobel Prize in Physiology and Medicine in 1949, developed and described cerebral angiography in 1927.

approach, "thirty feet of No. 34 gauge coin silver enameled wire was introduced into the aneurysm through a special needle" and "the wire was heated to an average temperature of 80°C for a total of 40 seconds. The aneurysm no longer bled when the needle was cleared at the conclusion of the operation" [3].

1960s and 1970s

In 1964, while attempting to occlude a supraclinoid aneurysm by advancing a silicone balloon, Luessenhop (Fig. 3) and Velasquez made the first endovascular attempt to treat an aneurysm [4]. In 1964 and 1965, Mullan (Fig. 4) et al [5,6] reported their clinical experience with inducing aneurysm thrombosis by applying an electrical current after direct and stereotactic insertion of needles and copper wires transfundally into ruptured and unruptured aneurysms. They acknowledged that controlling the degree of thrombosis was exceedingly difficult. In 1969, Alksne and Fingerhut [7] published their clinical results relating to metallic thrombosis of aneurysms. They embolized aneurysms with iron particles introduced through a needle intravascularly and maintained within the aneurysmal sac by stereotactic application of a magnetic probe against the sac.

After observing how easily helium-filled balloons were maneuvered by simple manipulations of their tether lines, Serbinenko (Fig. 5) developed a balloon-tipped microcatheter with flow-directional capabilities to allow for more effective intracranial catheterization [8]. In the 1970s, he further revolutionized endovascular neurosurgery by developing nondetachable and detachable balloon catheters to allow for direct aneurysmal obliteration or parent artery sacrifice and to make temporary balloon occlusion easy, safe, and

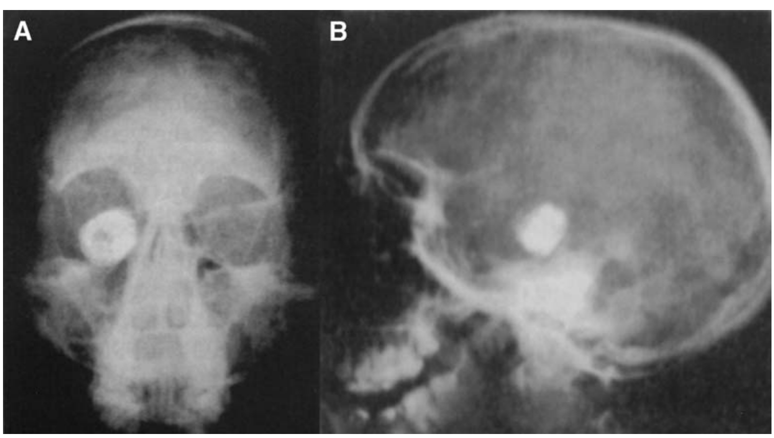

Fig. 2. Anteroposterior (*A*) and lateral (*B*) follow-up cranial radiographs of the patient whose aneurysm was successfully treated with a silver wire inserted through the orbit. (*From* Werner SC, Blakemore AH, King BG. Aneurysm of the internal carotid artery within the skull: wiring and electrothermic coagulation. JAMA 1941;116:578–82; with permission.)

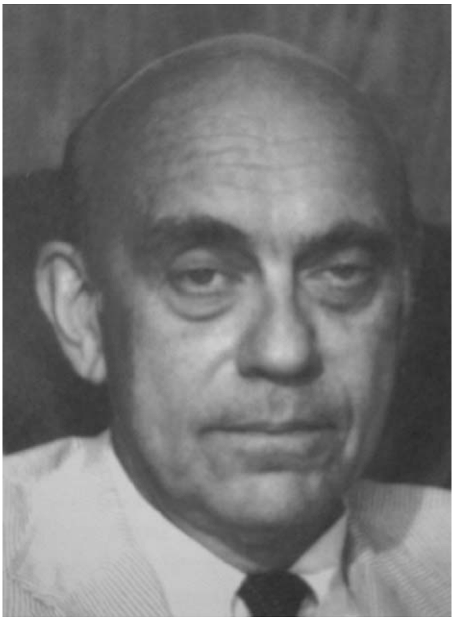

Fig. 3. In 1964, neurosurgeon Alfred J. Luessenhop (along with his colleague A.C. Velasquez) made the first endovascular attempt to treat an intracranial aneurysm. To recognize his invaluable pioneering contributions, a lecture in his name is offered each year at the joint cerebrovascular meeting of the American Association of Neurological Surgeons/Congress of Neurological Surgeons/American Society of Interventional and Therapeutic Neuroradiology.

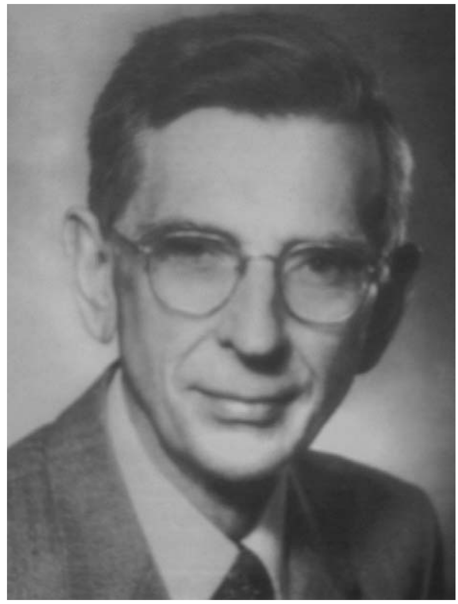

Fig. 4. In 1964, neurosurgeon Sean F. Mullan pioneered the technique of using electrical current to induce aneurysm thrombosis.

reliable. His seminal innovations gave birth to the modern era of endovascular neurosurgery [8].

1970s and 1980s

Balloon occlusion techniques were further developed and refined in the 1970s and 1980s, during which time, a vast amount of clinical experience was accumulated. In 1982, Romodanov and Shcheglov reported 137 intravascular occlusions of saccular aneurysms using detachable balloons [9]. In 1990, Higashida et al [10] reported the use of balloons for endovascular therapy of 87 cavernous carotid artery aneurysms between 1981 and 1989. In 1991, Moret et al [11] reported their results with balloon treatment of 128 aneurysms. Other large reports from these two decades regarding the use of detachable balloons included those by Shcheglov et al (725 cases), Serbinenko et al (267 cases), and George et al (92 cases) [9]. As more experience was acquired, several major disadvantages of this technique became apparent. Catheterization of the aneurysm was difficult, because no guidewire could be used. The preformed shape of the balloon often prevented it from adequately filling a geometrically complex aneurysm without leaving the fundus unprotected or creating a ball-valve system of aneurysmal refilling. Subsequently, the focus of endovascular therapy shifted from balloon occlusion to platinum coil occlusion. Several authors, including Hilal and Solomon, Dowd, Arnaud, and Higashida, reported the occlusion of intracranial aneurysms with “pushable” platinum coils [2]. Coiling for intracranial aneurysms remained a dangerous procedure, however, primarily because of the inability to retrieve the advanced coils as well as the often inadvertent migration of these highly thrombogenic coils into the distal intracranial vasculature.

1990s and 2000s

The invention of detachable coils by the Italian neurosurgeon Guido Guglielmi in the early 1990s ushered in a new era in the endovascular treatment of aneurysms [12]. The design of the Guglielmi detachable coil (GDC) permitted the position and effectiveness of the coil to be examined before the coil was released electrolytically from its tether. In addition, the flexibility and softness of the coil enabled the satisfactory

Fig. 5. Neurosurgeon Fedor A. Serbinenko revolutionized endovascular neurosurgery by inventing and developing the technique of balloon embolization for catheterization and occlusion of major cerebral vessels.

filling of a geometrically complex aneurysm with minimal procedural risk of rupture. On April 12, 1990, the first intracranial aneurysm was treated using this new technology [12]. In 1992, Guglielmi et al [13] published the results of the first multicenter GDC clinical trial. Small-necked and wide-necked lesions showed 81% and 15% immediate complete occlusion, respectively. Procedure-related morbidity and mortality rates were 4.8% and 2.4%, respectively. The GDC system immediately achieved worldwide acceptance and became the focus of most published work on endovascular aneurysm therapy [2].

Despite the newly acquired advantages from the GDC system, larger aneurysms or wide-necked lesions remained difficult to manage. New techniques were clearly required to keep the coils within the aneurysmal sac after deployment. Moret et al [14] pioneered and popularized the balloon-remodeling technique using a balloon as a mechanical barrier to prevent coil herniation into the parent vessel during its delivery. This technique also facilitated a better conformation of the coil mass to the complex geometry of an aneurysm. In 1997, Moret et al [14] published their results with use of the balloon-remodeling technique for the treatment of 56 cases of previously untreatable wide-necked intracranial aneurysms. Their reported morbidity and mortality rates were no higher than rates associated with routine GDC treatment. After some early experimental work done by Wakhloo et al [15] and Geremia et al [16], an alternative approach to advance coils through a stent to treat aneurysms was proposed by several authors [2]. The stent maintained a patent lumen and provided a buttress to prevent coil herniation. Since its introduction, this stent-assistance technique has been further explored and expanded by an increasing number of neuroendovascular surgeons [2].

With the rapidly advancing knowledge of basic science, the new millennium holds exciting promises for the advent of coils coated with various biologic agents, leading to the improved formation of neointima across the aneurysm neck and thus a much reduced risk of coil compaction and aneurysmal recanalization. Additionally, the potential use of liquid embolization agents to treat aneurysms is being evaluated in a clinical setting.

Arteriovenous malformations

Since the successful introduction of cerebral angiography by Egas Moniz in 1927, much progress has been made in the diagnosis and evaluation of AVMs. The modern-day detailed radiographic study of the malformation involves evaluating the hemodynamic and anatomic characteristics of the lesion, including examination of the feeding arteries, the nidus itself, and venous drainage of the lesion. Exponential advances in catheter technology and refinements of embolic agents have greatly facilitated the rapid evolution of AVM embolization.

In 1930, Brooks [17] reported successful closure of a CCF with a muscle embolus introduced surgically into the carotid artery. Three decades later, Luessenhop and Spence [18] expanded this strategy and performed the first embolization procedure on an intracerebral AVM by surgically introducing silastic spheres made of methyl methacrylate into the ICA. Thereafter, in the search for the ideal embolic agent, various materials, including silk sutures, porcelain beads, Gelfoam, steel balls, Teflon-coated spheres, and polyvinyl alcohol, were explored with varying degrees of efficacy [2]. Without the technologies and devices for direct nidus embolization, use of these flow-directed emboli was associated with a high complication rate secondary to inadvertent embolization of a normal cerebral vessel.

In 1976, Kerber [19] developed the first calibrated-leak balloon that allowed the direct embolization of an AVM nidus through the use of a rapidly solidifying polymer. This new system for catheter therapy, in combination with advances in imaging techniques and delivery devices, ushered in the modern era of AVM embolization. Calibrated-leak balloon catheters, however, were associated with a high incidence of arterial perforation. The development of flow-guided and wire-guided microcatheters allowed for superselective catheterization with great improvements in precision and safety. With the introduction of road-mapping techniques, a microcatheter can now be successfully navigated into a small distal vessel while an image generated from a previous contrast injection is superimposed on a negative map of the vascular tree.

Embolization of AVMs has evolved immensely over the last few decades to become a highly valuable adjunct, and even an alternative in some cases, to surgery or stereotactic radiosurgery. Embolization can be used to occlude deep feeding arteries or intranidal arterial aneurysms to reduce venous hypertension and the volume of an AVM before radiosurgery. Endovascular cure of parenchymal AVMs is possible only in some small lesions that possess a limited number of arterial feeders and draining veins and a compact nidus, however. In addition, the morbidity associated with endovascular embolization of parenchymal AVMs is still significant.

Stroke prevention and acute management

As early as 1969, 5 years after introducing percutaneous transluminal angioplasty, Charles Dotter published a new technique to percutaneously place endovascular spiral stents [20]. The revival of interest in the early 1980s contributed to the development of several important stent designs, such as the balloon-expanded stents and Palmaz stents [21]. Since the publication of reports of the successful performance of angioplasty [22] and the placement of stents in the coronary arteries [23], both techniques have become well established, with large, well-organized, multi-institutional trials in the coronary and other peripheral vessels [2]. Concerns about the potentially catastrophic consequences of small distal emboli delayed the development of angioplasty and stenting in diseased carotid and vertebral arteries for stroke prevention [2]. Reports of carotid angioplasty in the 1980s and more recent studies of angioplasty or stenting of extracranial carotid artery disease [2] have suggested that procedural safety and complication rates are comparable with those for carotid endarterectomy (CEA). Although CEA remains the "gold standard" for the treatment of atherosclerotic carotid disease, the rapidly evolving nature of endovascular therapy—with new technologies and devices being developed almost on a monthly basis—begs the question as to whether endoluminal revascularization should be proposed as the true alternative to CEA. Large, prospective, randomized trials are in progress.

The development of new angioplasty balloon catheters and flexible stents has redefined the management strategy for symptomatic intracranial stenosis. A growing number of studies have reported a low complication profile and satisfactory rates of angiographic patency at follow-up [2]. The answer to the question of whether angioplasty or stenting should be the first line of treatment for patients with symptomatic intracranial stenosis requires data obtained from well-designed, prospective, multicenter studies.

The concept of intra-arterial thrombolysis for acute stroke management dates back to 1958, when Sussmann and Fitch reported successful recanalization of an acute ICA occlusion with intra-arterial fibrinolysis using plasmin [24]. After further clinical trials failed to show convincing benefits, this concept of treating acute stroke with pharmacologic revascularization was essentially abandoned [2]. Before 1995, stroke therapy consisted exclusively of supportive management and efforts to prevent recurrence [2]. The development of safer thrombolytic agents and an improved understanding of the pathophysiology of ischemic stroke rekindled the interest in pharmacologic thrombolysis, however. In 1995, the National Institute of Neurological Disorders and Stroke reported that early intravenous thrombolysis using tissue plasminogen activator was more effective than placebo [25]. The concept of intra-arterial pharmacologic thrombolysis was further expanded and solidified in 1999 with the completion of the Prolyse in Acute Cerebral Thromboembolism study [26]. This study clearly showed that intra-arterial injection of the thrombolytic agent into the immediate proximity of or within the thrombus within 6 hours of stroke onset significantly improved patient outcome, despite an increased incidence of early symptomatic intracranial hemorrhage. Intravenous thrombolysis and intra-arterial thrombolysis have received widespread acceptance and truly revolutionized the management of acute stroke.

Summary

The exponential evolution of endovascular neurosurgery over the past few decades has redefined the treatment strategies for cerebrovascular diseases. Entering the new millennium, one must have the mindset to embrace and nurture the progress and technologic advances. Thomas Fogarty eloquently stated: "When envisioning the technologic process, we must think young' and consider the impossible. The mindset is best achieved in an environment where innovators consider the unachievable as being possible" [27]. Indeed, the pioneers of endovascular neurosurgery considered the impossible and tenaciously stood by their dreams. Their revolutionary ideas and inventions truly reflected their courage, faith, and determination. With a better understanding of the molecular basis of diseases and further advancements in gene therapy, the future is ideal and holds exciting promise for endovascular neurosurgery to deliver biologic factors with minimal risk and high precision and to develop effective therapies for the entire spectrum of neurologic diseases.

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