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Epidemiology and pathology of intraventricular tumors

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Intraventricular tumors present a diagnostic challenge to the clinician because of a broad differential diagnosis with significant variability in tumor type between adult and pediatric populations. This expansive differential includes choroid plexus papillomas (CPCs) and choroid plexus carcinomas (CPCs), ependymomas, subependymomas, subependymal giant cell astrocytomas (SEGAs), central neurocytomas, meningiomas, and metastases as well as a number of cysts, inflammatory lesions, and other rare neoplasms. Posterior fossa ependymomas, SEGAs, and choroid plexus tumors are more likely to appear in childhood, whereas subependymomas, central neurocytomas, intraventricular meningiomas, and metastases are more frequent in adults. Each of these tumor types involves the ependymal lining and subependymal plate of the ventricular wall, the septum pellucidum, or the highly vascular choroid plexus. This article reviews the epidemiology, the pathologic characteristics, and the primary diagnostic considerations of each tumor type.

Choroid plexus papilloma and carcinoma

Epidemiology

Choroid plexus tumors are epithelial neoplasms with a prevalence of 0.3 cases per million [1]. In two large series, choroid plexus tumors accounted for 0.4% [2] and 0.6% [3] of all reported intracranial tumors. The tumor predominantly occurs in childhood, although it can be seen at any age. The median age of onset is 3.5 years [4], with 20% of patients presenting in the first year of life and almost 50% in the first decade [5]. The most common locations for choroid plexus tumors are the lateral and fourth ventricles, followed by the third ventricle. Cerebellopontine angle examples are less common and are caused by extension of tumor through the foramen of Luschka [6]. In addition, rare suprasellar cases have been reported [7]. Tumor location is closely correlated with patient age. The most common location in children is the lateral ventricle, whereas the fourth ventricle is the most frequent site in adults. Choroid plexus tumors are divided into the CPP (World Health Organization [WHO] grade I) and the more aggressive CPC (WHO grade III). CPCs make up a small proportion of choroid plexus tumors, primarily present in children less than 3 years of age, and are most commonly found in the lateral ventricles [8]. CPPs and CPCs have been shown to spread through the cerebrospinal fluid, and rare metastatic cases have been documented outside the CNS [4].

Macroscopic and microscopic features

Choroid plexus tumors are often soft to rubbery and may have a gritty texture because of calcification. The tumors are frequently shades of orange-brown. During surgery, an anchoring pedicle can be seen attached to the normal choroid plexus or the ventricular wall. Some papillomas have a cauliflower-like appearance.

CPPs and CPCs exhibit features akin to many papillary neoplasms in other organs. CPPs have well-developed fibrovascular cords within

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papillary structures and do not exhibit architectural or cytologic atypia (Fig. 1A). Epithelial and stromal cells contain many characteristics of the normal choroid plexus, such as calcifications and xanthomatous change [9,10]. In some cases, there is a striking nuclear monomorphism without other aggressive features, such as mitoses or vascular proliferation. Rarely, geographic necrosis without the pseudopalisading that is suggestive of an infarct can be seen in an otherwise typical CPP. Osseous or cartilaginous metaplasia and acinar or tubular differentiation are reported in choroid plexus neoplasms [11–13]. In addition, a number of studies report a pigmented variant that contains neuromelanin and lipofuscin [14]. CPPs with marked oncocytic "transformation" as well as glial differentiation are rare [12]. Transitional zones between the normal and neoplastic choroid plexus can be found in CPPs and CPCs.

Carcinomas of the choroid plexus are tumors that exhibit all the histologic hallmarks of aggressiveness (see Fig. 1B). A typical CPC is a neoplasm with increased architectural complexity demonstrating partially solid and partially nonpapillary growth. Most tumors have marked cytologic atypia, atypical mitotic figures, and frank necrosis. Some high-grade tumors have cytologic and architectural features that resemble anaplastic oligodendrogliomas. Invasion into neuropil is characteristic of CPCs, although some CPPs can occasionally exhibit invasion into surrounding parenchyma. Rare CPCs resemble undifferentiated carcinomas without any distinguishing features [15].

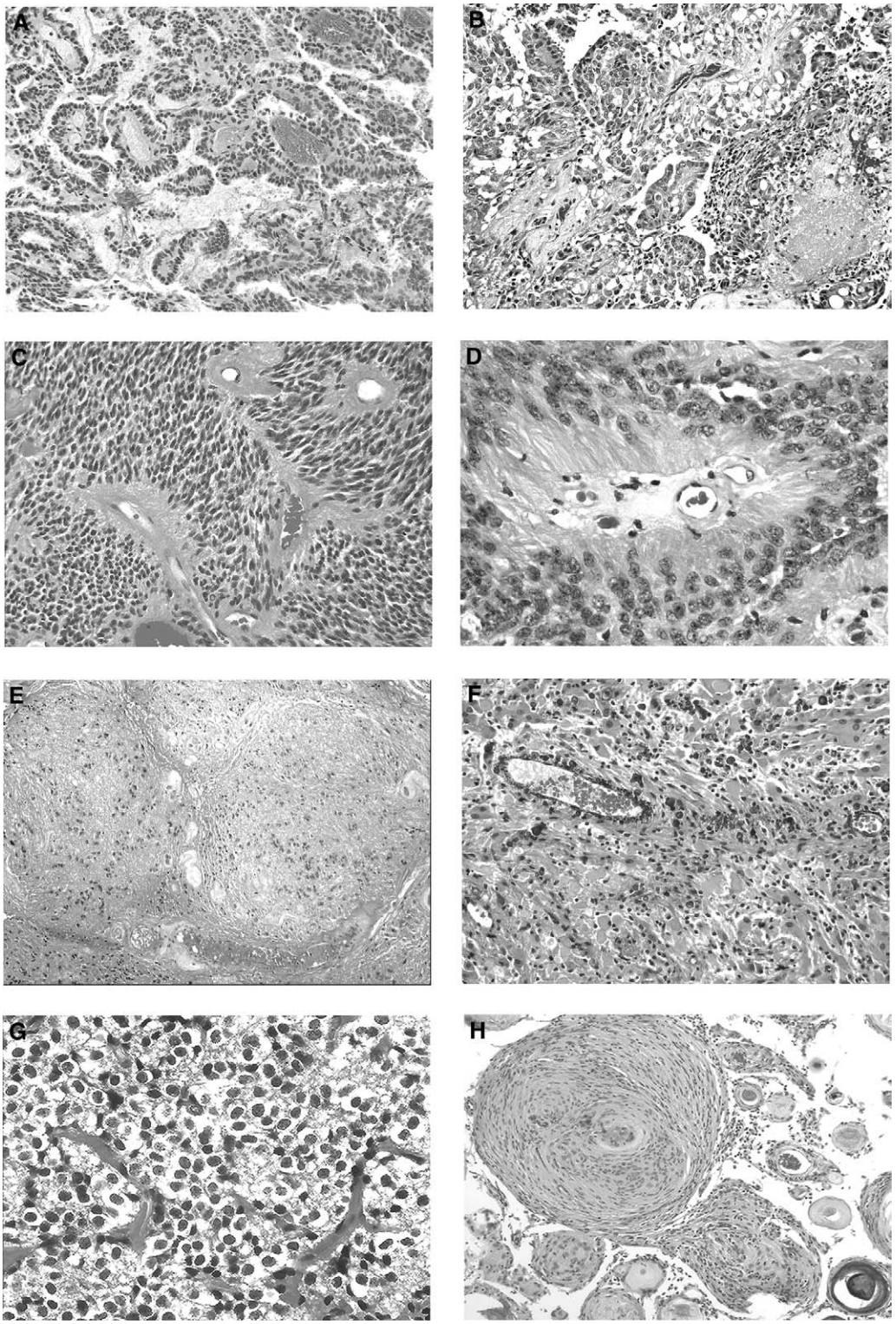
Immunohistochemical features

Cytokeratins and vimentin are expressed by virtually all CPPs and most CPCs. Glial fibrillary acidic protein (GFAP) can be found focally in about 25% to 55% of CPPs and in 20% of CPCs [16]. Most of the GFAP-positive cells are simultaneously positive for cytokeratin [17]. S-100 protein is present in almost all cases of CPP and, less frequently, in CPCs. The staining for S-100 is often stronger and more diffuse than GFAP staining. Synaptophysin has been suggested as a possible marker for choroid plexus epithelium, but staining of tumors with this marker produces variable results. Epithelial membrane antigen (EMA) is positive in tumor cells only focally, if at all. A recent study suggested that immunohistochemical staining for prealbumin and carcinoembryonic acid (CEA) is of significant value for the differentiation of CPPs and CPCs [18]. Staining for insulin-like growth factor-II (IGF-II) is also a potentially useful marker to distinguish normal choroid plexus and CPP from CPC [19]. Additionally, indirect indices of proliferation, such as the Ki-67/MIB-1 antibody, have been used to distinguish CPP from CPC [20,21]. The mean Ki-67/MIB-1 labeling index is often less than 2% in CPPs and greater than 10% in CPCs. Immunohistochemical staining for p53 protein is found more often in carcinomas than in CPPs [22].

Ultrastructural features

Most CPPs exhibit apical microvilli with scattered cilia, junctional complexes, interdigitating lateral cell borders, basement membrane, and fenestrated capillaries. Cilia contain the "9 + 0" microtubule configuration characteristic of neuroepithelial cells. Some tumors have irregularly shaped structures containing lipid droplets, filamentous material, and structures that resemble the "silver bodies" of Biondi seen in normal choroid plexus [23]. CPCs are often more varied in their ultrastructural appearance and can show epithelial features as well as cilia and microvilli, although such findings are focal in many cases. CPCs can also display immature cellular features, such as polyribosomes, glycogen granules, and hypertrophied rough endoplasmic reticulum [24].

Fig. 1. (*a*) Choroid plexus papilloma: low magnification showing well-formed papillae composed of uniform small epithelial type cells. Mitotic figures and necrosis are rare. (*b*) Choroid plexus carcinoma: a tumor with irregular architecture, the presence of marked pleomorphic cells with a less prominent papillary pattern, and frequent mitoses and necrosis. (*c*) Ependymoma: medium magnification showing uniform cells arranged in a perivascular fashion. (*d*) Ependymoma: high magnification of an ependymal pseudorosette, an angiocentric arrangement of cells with fibrillary processes perpendicular to the luminal axis. (*e*) Subependymoma: a paucicellular tumor showing a multinodular compact architecture without mitotic figures. (*f*) Subependymal giant cell astrocytoma: a tumor composed of "gemistocytic" astrocytes, scattered inflammatory cells, and dystrophic calcifications. (*g*) Central neurocytoma: a tumor typically described as "oligodendroglioma-like" with clear cells (fried-egg cells) and a delicate vasculature (chicken-wire vasculature). (*h*) Meningioma: a typical meningioma in the lateral ventricle. The tumor shows multiple whorl formation as well as calcifications known as "psammoma" bodies.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Molecular and genetic features

In CPP, recurrent abnormalities, including partial gains of chromosome 7, have been reported [25]. A comparative genomic hybridization study of a large number of choroid plexus tumors showed that +5q, +6q, +7q, +9q, +15q, +18q, and −21q were significantly more common in CPPs, whereas CPCs were characterized by +1, +4q, +10, +14q, +20q, +21q, −5q, −9p, −11, −15q, and −18q [26].

Choroid plexus neoplasms have been associated with the Li-Fraumeni syndrome as well as the Aicardi syndrome [27–29]. Several reports have identified SV-40 virus genetic material within tumor cells; however, the contribution of this virus to the formation of choroid plexus tumors is unknown [30–32].

Pathologic differential diagnosis

The most frequent challenge during pathologic evaluation is the distinction of CPP from normal choroid plexus. The normal choroid plexus has regular single-layered cells with "hobnail" luminal surfaces, whereas CPP displays a more crowded epithelium with significant nuclear variability. The diagnosis of CPP by the pathologist is unreasonable in the absence of clinical and radiologic findings, especially without a distinct contrast-enhancing intraventricular mass.

The second diagnostic challenge is the exclusion of a rare papillary ependymoma [33]. Papillary ependymomas can form epithelial surfaces but retain a fibrillary background. Ependymomas with focal papillary change can be distinguished by their predominantly glial appearance. In cases where the distinction cannot be made in routine stains, immunohistochemistry and ultrastructural studies are helpful. Large partially intraventricular tumors in young patients with poorly differentiated morphology should also raise the possibility of an atypical teratoid/rhabdoid tumor (AT-RT). Some AT-RTs have been misdiagnosed as CPC in the past. Distinction of AT-RT can be made by using a panel of immunohistochemical markers as well as genetic studies to confirm the presence of characteristic abnormalities.

CPCs are extremely rare in adults, and metastatic carcinoma should be viewed as a more likely cause for an intraventricular papillary carcinoma. Metastases from the pulmonary and genitourinary systems have been shown to mimic CPC [34–36]. Distinction may be difficult because of overlapping histologic, ultrastructural, and immunohistochemical features. Typical CPC immunohistochemistry reveals positivity for cytokeratin cocktail and absent or only faint EMA and CEA immunoreactivity. If positive, synaptophysin can also be used to distinguish CPC. In addition, BerEp4 staining is considered a reliable marker for most metastatic carcinomas, and its presence may exclude a CPC (Marc K. Rosenblum, MD, personal communication, 1999).

Ependymomas

Epidemiology

Ependymomas are neoplasms derived from the ependymal layer lining the ventricular system and can occur intracranially and in the spine. Intracranial ependymomas account for 2% to 8% of all primary CNS neoplasms [37], with more than half presenting in the first two decades of life. In a series of 467 pediatric intracranial neoplasms reviewed by Farwell et al [38], ependymomas made up 9% of all intracranial tumors, making it the third most common pediatric intracranial tumor. Within the pediatric population, ependymomas favor young patients, with more than 50% occurring within the first 3 years of life. No consistent gender predilection has been identified. Intracranial ependymomas can be divided by location into those appearing infratentorially and those appearing supratentorially. Infratentorial ependymomas make up approximately two thirds of all cases [39], comprise most pediatric cases, and most frequently occur in the fourth ventricle [40]. Supratentorial ependymomas occur more frequently in older children and adults. In addition to the lateral ventricles, approximately 50% of supratentorial ependymomas involve the parenchyma [41].

Macroscopic and microscopic features

Ependymomas are often sharply demarcated, fleshy, hemorrhagic, soft, and sometimes rubbery masses. Rare examples are heavily calcified, giving the tumor a gritty texture. Intraventricular examples of ependymomas are often lobulated and display a discrete interface with surrounding brain. Some tumors may exhibit a delicate overlying ependymal layer that gives them a shiny texture.

Ependymomas are glial neoplasms composed of a monomorphous proliferation of neoplastic cells with typical "perivascular pseudorosettes"

(see Fig. 1C, D). Some ependymomas are predominantly glial in appearance and may not have distinct perivascular pseudorosettes, whereas others may be predominantly epithelial. The latter may present as a tumor with oval to round nuclei, discrete cytoplasmic borders, frank papillary structures, and well-formed fibrovascular cores. Other tumors may show "true ependymal rosettes" distinguished by their well-defined lumina and cells forming pseudoglandular structures. Most ependymomas show a substantial number of nuclear grooves that can be identified in intraoperative smears and help with the rapid interpretation of frozen sections [42]. This feature, however, needs to be interpreted in the context of other histologic findings, because many other tumors, such as meningiomas and other gliomas, can exhibit nuclear grooves. The tumor nuclei are uniform, round to oval, and often feature a distinct nucleolus.

Clear cell change in ependymoma is a rare but significant finding [43]. Intraventricular ependymomas may exhibit focal or predominant clear cell change. When clear cell change is predominant, the hematoxylin-eosin appearance of an oligodendroglioma is recapitulated. It is likely that many tumors previously reported as intraventricular oligodendroglioma are examples of clear cell ependymoma [21]. Clear cell ependymomas are usually higher grade and exhibit increased mitotic activity and vascular proliferation. The so-called "tanycytic ependymoma" is remarkably similar to a pilocytic astrocytoma. This highly fibrillary tumor has moderate cell density, spindled cells, and a fascicular architecture. It has also been described as a "piloid tumor with ependymal nuclei" [44]. The tanycytic ependymoma often lacks nuclear pleomorphism or aggressive features, such as mitoses or vascular proliferation. Perivascular pseudorosettes are rudimentary and sometimes absent.

Ependymomas are commonly calcified and rarely exhibit cartilaginous and osseous metaplasia. Rare ependymomas contain cytoplasmic eosinophilic granules, clear vacuoles, lipid, or melanin [45,46].

The current WHO classification defines grade II ependymomas as tumors with mild cellular pleomorphism, pseudorosettes, or true ependymal rosettes. The tumors can have occasional mitotic figures and necrosis without pseudopalisading. Occasional foci of hypercellularity and increased mitoses are allowed. "Anaplastic," "high-grade," or grade III ependymomas have moderate to high cellularity, increased mitotic figures, and vascular proliferation. Necrosis is often present, either in the form of geographic necrosis or, rarely, in the pseudopalisading form. Perivascular pseudorosettes or occasional true ependymal rosettes can be found in most high-grade ependymomas. There is controversy around whether focal "atypia" or "anaplasia" should elevate a lesion to grade III "anaplastic ependymoma." Some require atypia and anaplasia to predominate in the tumor tissue, whereas others report a less favorable prognosis even for tumors with focal anaplastic features.

Immunohistochemical features

Ependymomas are variably positive for GFAP, which highlights the fibrillary processes around vessels. Tumors are diffusely positive for vimentin and stain less avidly with S-100 protein and neurospecific enolase (NSE). Positive staining for epithelial markers, such as EMA and cytokeratins, has been reported in most posterior fossa and spinal cord ependymomas [47]. Rare tumor cells, true rosettes, and occasional papillary structures are EMA-positive.

Studies suggest that high Ki-67/MIB-1 and p53 protein positivity might be reliable indicators of high-grade ependymomas [48]. Even though there seems to be a positive correlation between high-grade features and the Ki-67/MIB-1 index [49], none of the immunohistochemical variables significantly correlate with tumor grade. Conversely, Ki-67/MIB-1 and p53 were reported to correlate with patient survival [50]. Currently, there is no clear evidence for the utility of these markers in determination of tumor grade or behavior.

Ultrastructural features

The acellular zones around pseudorosettes are composed of large numbers of closely packed, filament-rich, cytoplasmic processes. Microlumina are often present, even though they may not be observed by light microscopy [51]. These microlumina contain slender curving microvilli and a variable number of cilia. Bordering cells are connected by unusually long tight junctions. This triad (cilia, intracytoplasmic intermediate filaments, and cell junctions) makes up the typical ultrastructural components. The epithelioid cells found in ependymomas and true rosettes are characterized by intracellular lumina, cilia, and microvilli. Clear cell ependymomas reveal densely packed polyhedral cells with clear cytoplasm and well-developed intercellular junctions. Abundant

hyaloplasmic lipid vacuoles can also contribute to the clear appearance of the tumor cells [46].

Molecular and genetic features

There is a body of evidence suggesting the presence of a tumor suppressor gene on the long arm of chromosome 22 that plays a role in the pathogenesis of ependymomas [52]. In one study, the most frequent copy number abnormality in ependymomas was 22q loss, followed by gain of chromosome 9 and occasional loss of 6q, 3p, 10q, and 15q [25]. A heterozygous mutation in the MEN1 gene has also been reported in ependymomas [53].

Pathologic differential diagnosis

Formulation of the differential diagnosis for ependymoma is dependent on the location of the lesion. In the posterior fossa, medulloblastoma needs to be considered first in the differential diagnosis, although its architecture is more reminiscent of a small blue round cell tumor than that of a glioma. Pilocytic astrocytoma of the cerebellum or brain stem is a second possibility but can be easily excluded when classic features of pilocytic astrocytomas, such as Rosenthal fibers, eosinophilic granular bodies, and a fairly paucicellular appearance, are present. Infiltrating astrocytomas or the so-called "brain stem gliomas" may have an exophytic quality and may resemble ependymoma. They are easily distinguished by their invasive quality, lack of epithelial features or pseudorosettes, and marked nuclear pleomorphism.

Supratentorial intraventricular ependymomas need to be distinguished from subependymomas. Such distinction is often subjective and may not always translate into a significant change in clinical outcome. Nevertheless, based on the overall clinical behavior of ependymomas and the likelihood of supratentorial examples being higher grade, one is compelled to make the distinction. The distinction is usually not difficult, and the differential diagnosis is confounded by limited tissue sample size. A second yet more important differential diagnosis is oligodendroglioma, which can easily be confused with clear cell ependymoma. Clear cell ependymomas are noninfiltrating, solid, and distinct from the surrounding brain. Purely intraventricular neoplasms are not likely to be oligodendrogliomas, but when a question exists, immunohistochemistry and electron microscopy readily settle the issue. Another diagnostic consideration is the central neurocytoma. The central neurocytoma is a highly cellular neoplasm that may show perivascular pseudorosettes. The cells appear more neurocytic, and the fibrillar areas resemble neuropil. The tumor strongly reacts with synaptophysin and only weakly (if at all) with GFAP. Electron microscopy can distinguish the two entities. Papillary ependymomas may resemble CPP. The overall immunohistochemical profile and ultrastructural features can be used to separate the two entities.

Subependymoma

Epidemiology

Subependymomas are slow-growing, benign intraventricular lesions first identified as a separate entity in 1945 by Scheinker [54]. They originate in the subependymal glial matrix and typically project into the ventricular lumen. Intracranial subependymomas frequently remain asymptomatic and are documented on autopsy or as an incidental finding on imaging. A prevalence of 0.4% has been reported in a series of 1000 necropsies of asymptomatic patients reviewed by Matsumura and colleagues [55]. Subependymomas have been reported over a wide age range, but generally occur in middle-aged to older adults. The fourth ventricle, followed by the lateral ventricles, is the most common site of presentation. Less common locations include the third ventricle, the septum pellucidum, and the cerebral aqueduct.

Macroscopic and microscopic features

Subependymomas are solid nodular tumors firmly attached to the ventricular surface. Tumors are typically soft but can be rubbery and, rarely, cystic and occasionally have a gritty texture.

Subependymomas are typically paucicellular, fibrillar, and markedly nodular neoplasms (see Fig. 1E). Tumor nuclei cluster within the nodular regions. Supratentorial tumors, especially those near the foramen of Monro, are predominantly microcystic and focally myxoid. The cells are often spindled with oval nuclei and fibrillary processes. The tumor exhibits an extensive fibrillary background on intraoperative smear preparations. Nuclear pleomorphism is rare, and mitoses are typically absent. Tumor vessels show focal hyalinization with occasional hemosiderin deposition. There is some evidence that the

histologic features in larger and symptomatic subependymomas may be different. Larger symptomatic tumors more frequently demonstrate cyst formation, microcalcification, and vessel degeneration accompanied by hemorrhage [56]. Subependymomas in the posterior fossa are usually smaller without significant microcystic change. The tumors are prominently nodular and show nuclear clustering and calcifications. Mitoses are rare, and vascular proliferation and necrosis are absent.

Immunohistochemical features

Subependymomas are strongly GFAP-positive in accord with their high content of intermediate glial filaments. Vimentin staining is often strong, and S-100 protein stains the cytoplasm and the nuclei. Compared with other ependymal tumors, subependymomas have the lowest rate of cell proliferation, as evidenced by a Ki-67/MIB-1 index of less than 1% [57]. In contrast to ependymomas, staining with epithelial markers, such as EMA, is usually not observed.

Ultrastructural features

Subependymomas display an abundance of closely packed cell processes filled with intermediate filaments. This meshwork of processes widely separates small clusters of tumor cells. Larger cells lacking specialized features and resembling ependymal precursor cells are often found. Other cells with transitional forms between these two types can be identified [58]. Pockets of microvilli are present, but they differ from ependymal type rosettes because of the lack of tight junctions.

Molecular and genetic features

There is limited information on the cytogenetics and molecular genetics of subependymomas. A few case reports have demonstrated a normal karyotype in subependymomas investigated with conventional cytogenetic techniques [59].

Pathologic differential diagnosis

The main component of the differential diagnosis for intraventricular subependymoma is the classic ependymoma. It may not be possible to distinguish all cases, especially if the amount of tissue available for pathologic analysis is limited. Both neoplasms appear remarkably similar, and foci identical to subependymoma are commonly seen in ventricular ependymomas. In general, ependymomas can be distinguished by occurrence primarily in children, hypercellularity, perivascular pseudorosettes, and true ependymal rosettes. Most supratentorial ependymomas have a solid cystic appearance and are symptomatic. Subependymomas may also be confused with the tanycytic variant of ependymomas. Often, tanycytic ependymomas are more cellular and resemble pilocytic astrocytomas. Ultrastructural examination of tanycytic ependymoma reveals characteristic ependymal features, including intracytoplasmic intermediate filaments, prominent intercellular junctions, numerous slender surface microvilli, and microvilli-lined lumina.

Subependymal giant cell astrocytoma

Epidemiology

SEGAs are intimately associated with the tuberous sclerosis complex, an autosomal dominant dysgenetic syndrome that is associated with the classic triad of seizures, mental retardation, and papular facial lesions. In the CNS, the complex is characterized by cortical tubers, subependymal nodules, and SEGAs. The incidence of tuberous sclerosis is approximately 1:10,000 [60] in the general population. Approximately 6% [61] of these patients develop SEGAs. Almost all SEGAs arise near the foramen of Monro and typically present with hydrocephalus or increased seizure frequency, most commonly within the first two decades of life [61].

Macroscopic and microscopic features

SEGAs are well-defined typically pedunculated intraventricular masses that can be soft to rubbery and often have a broad base on the ventricular surface. The tumor can be easily removed from its base. Tumors may be friable, pink as a result of vascularization, and occasionally gritty from calcification.

SEGAs are characteristically solid and have a typical swirling architecture. They exhibit compact growth with spindled and "gemistocytic" cells and are sharply demarcated from the adjacent normal parenchyma (see Fig. 1F). Spindled cells are responsible for the swirling appearance of the tumor on low magnification. The gemistocyte-like cells have round vesicular nuclei with distinct nucleoli and an eosinophilic cytoplasm. In addition, they display thick hairlike processes and have a tendency to form cohesive

clusters and occasional pseudorosettes [62]. The tumor maintains a compact and uniform appearance despite varying tumor cell types. SEGAs often contain inflammatory cells, including occasional mast cells. Even though rare mitotic figures are occasionally seen, brisk mitotic activity, necrosis, or vascular proliferation is typically absent. Some tumors undergo focal infarction, which can appear ominous and be confused with the necrosis characteristic of a high-grade astrocytic neoplasm. Calcification is sometimes present.

Immunohistochemical features

The gemistocytic and spindle cells are often strongly positive for GFAP; however, the absolute number of positive cells in each tumor is highly variable. SEGAs also show strong positivity for S-100 protein. Neurofilament epitopes, class III β-tubulin, and calbindin 28-kDa are expressed in some cases [63]. Cytoplasmic staining for somatostatin, met-enkephalin, 5-hydroxytryptamine, β-endorphin, and neuropeptide Y has also been noted in more than half of cases of SEGA [63,64]. The divergent glial and neuronal staining has been shown to colocalize within the same cell. SEGAs are negative for HMB-45 antibody, and the Ki-67/MIB-1 labeling index is usually less than 2% [65].

Ultrastructural features

SEGAs contain numerous intermediate filaments, frequent lysosomes, and occasional rectangular or rhomboid membrane-bound crystalloids that exhibit lamellar periodicity and structural transition to lysosomes. Microtubules and stacks of rough endoplasmic reticulum are common, but true neuronal differentiation, such as neurosecretory granules or synaptic formations, is often absent [63]. Rare tumor cells have features suggestive of neuronal differentiation, including stacks of rough endoplasmic reticulum, occasional microtubules, and a few poorly defined dense core granules. Gemistocytic cells are characterized by abundant intermediate filaments within the cell body and the processes. Lysosomes are common and, rarely, may contain distinctive membrane-bound crystalloids.

Molecular and genetic features

Cytogenetic analysis of SEGAs within the tuberous sclerosis complex (TSC) reveals clonal chromosomal changes, resulting in the partial loss of chromosome 22q in some tumors [66]. TSC-associated tumors also demonstrate loss of heterozygosity in chromosomes 9 and 16, which are known to harbor TSC genes [67]. One of two suspected genes, TSC2, was found in chromosome 16 by positional cloning. The gene product from TSC2 has been named tuberin. TSC1 was discovered earlier in chromosome 9 but has not yet been characterized. Genetic analysis on TSC families reveals mutations in chromosome 9q34 (TSC1) and chromosome 16p13 (TSC2) as the only common genetic anomalies [68].

The Eker rat, a naturally occurring animal model of TSC, provides a powerful tool for investigations of TSC. In this model, a conserved linkage group on rat 10q corresponds to human 16p13.3 (TSC2 gene) [69]. Currently, it is believed that the products of TSC1 and TSC2 genes interact with each other in the cell.

Pathologic differential diagnosis

SEGAs are fairly distinct intraventricular neoplasms that may be confused with gemistocytic astrocytoma or high-grade glioma if the typical pathologic and radiologic features are overlooked. Small biopsies can also potentially be interpreted as tanycytic ependymoma or subependymoma, but this is less likely, because SEGAs are invariably more cellular, less fibrillary, and far more "gemistocytic."

Central neurocytoma

Epidemiology

The term *central neurocytoma* was first used by Hassoun et al [70] in 1982 to describe differentiated intraventricular neuronal lesions observed in 2 cases. Central neurocytomas are rare neoplasms, with 127 reported cases through 1993 [71]. Reported rates in series of pathologically confirmed primary CNS neoplasms range from 0.1% to 0.5% [72–74]. Central neurocytomas are primarily tumors of young adults, with 45% occurring in the third decade of life and almost 75% between the ages of 20 and 40 years [71]. Gender distribution is equal. Central neurocytomas arise predominantly from the septum pellucidum or, less frequently, from the lateral ventricular wall. The anterior lateral ventricle is the most frequent site (77%), followed by lateral and third ventricle involvement (21%) [71]. Bilateral lateral ventricular involvement is uncommon.

Rare cases have been reported in the third and fourth ventricles.

Macroscopic and microscopic features

The tumor forms a soft to gritty, tan, discrete mass that may be solid or partly cystic.

Central neurocytomas are histologically and cytologically uniform neoplasms. The cells are strikingly monomorphous with finely distributed chromatin and a fine fibrillary matrix. The tumor is one of several neuroepithelial neoplasms with "salt and pepper" chromatin. Central neurocytoma joins the list of oligodendroglioma-like tumors because of a striking preponderance of cells with perinuclear halos that resemble classic oligodendroglioma (see Fig. 1G). In some cases, there are perivascular fibrillary zones reminiscent of ependymal pseudorosettes. In addition, some examples resemble nodular medulloblastomas by exhibiting neurocytic differentiation with cell streaming and nodular growth.

Intraoperative frozen sections can sometimes obscure the histologic and cytologic uniformity typical of central neurocytomas. The processing of frozen tissue also adds a degree of nuclear pleomorphism that can raise the possibility of a "small blue round cell tumor." This is further confounded in permanent sections of frozen tissue because of the obscured neuronal/neurocytic background. Most central neurocytomas are grade II lesions with minimal nuclear pleomorphism and rare mitotic figures. Tumors with "atypical" features and transitional characteristics between neurocytoma and neuroblastoma have been reported [75].

Central neurocytomas may show ganglionic cell differentiation and have a preponderance of neuropil with variable numbers of ganglion-like cells. Such cases have been designated as "ganglioneurocytoma" or "differentiated neurocytoma." An intraventricular lesion that combines the features of a neurocytoma with ganglion cells and a malignant small cell component has been reported but is extremely rare. It has also been suggested that some central neurocytomas can express photoreceptor differentiation, potentially relating them to pineocytomas [76]. Rare central neurocytomas exhibit lipofuscin or neuromelanin pigment [77].

Immunohistochemical features

Central neurocytomas consistently exhibit immunoreactivity for NSE and synaptophysin, indicating neuronal differentiation [78]. Synaptophysin antibody stains the fibrillar zones and, to a lesser extent, the perinuclear cytoplasm of tumor cells. Anti-Hu autoantibodies stain neurocyte nuclei. Tumor cells are also positive for Leu-7 and S-100 protein, whereas staining for GFAP is predominantly negative and vimentin is confined to the nonneoplastic mesenchymal elements of blood vessels [79]. Staining for myelin basic protein, chromogranin, and neurofilament is often negative. Some studies have shown a small subpopulation of GFAP-positive neoplastic cells, and glial differentiation has been suggested in tissue culture. This mixed phenotype of glial and neuronal marker positivity in central neurocytoma can be interpreted as a glioneuronal neoplasm, with an overwhelmingly neurocytic component. In rare examples, a tumor may have an increased Ki-67/MIB-1 index. Such neoplasms are described as "atypical neurocytomas" and have a significantly elevated incidence of local recurrence [80]. Even though no clear cutoff point exists between classic and atypical neurocytomas, most authors suggest that tumors with an MIB-1 index of greater than 2% be placed in the atypical category. Nevertheless, some studies show no difference in MIB-1 labeling between tumors with "atypical" features and typical central neurocytomas [81]. Currently MIB-1 labeling is not used to modify grading of central neurocytomas.

Ultrastructural features

Central neurocytoma is readily recognizable as neuronal, with microtubules, terminations, clear vesicles, and dense core granules [79,82,83]. Some examples may display round cells with abundant cell processes containing microtubules, cellular junctions, and lysosome-like structures. Others contain numerous synaptic vesicles, neuritic processes, and neurosecretory granules. In addition, rare tumors contain ganglionic cells with well-developed processes.

Molecular and genetic features

Reported recurrent genetic changes in central neurocytomas include alterations on chromosomes 2p, 10q, and 18q. The candidate genes in these loci are currently unknown [84]. Other studies have suggested gain of chromosome 7 as a nonrandom genetic alteration in central neurocytomas [85]. Recent studies have demonstrated that central neurocytomas are genetically distinct from oligodendrogliomas and that chromosomes 1p and 19q probably do not play an important

role in their pathogenesis. In addition, N-myc and epidermal growth factor receptor amplifications are rare or absent in these tumors [86].

Pathologic differential diagnosis

The critical differentiation for central neurocytoma is from oligodendroglioma. Some cases of central neurocytoma perfectly recapitulate oligodendroglioma in routine microscopic examination. In such cases, it is important to use a panel of immunohistochemical stains and to perform an ultrastructural examination to establish the correct diagnosis. Furthermore, radiologic information should be critically interpreted and the diagnosis of oligodendroglioma challenged in purely intraventricular tumors. A second entity in the differential diagnosis is the clear cell ependymoma, which also exhibits a remarkable resemblance to oligodendroglioma. The presence of ependymal features as well as immunohistochemical analysis should distinguish a clear cell ependymoma from central neurocytoma. Small biopsies from a dysembryoplastic neuroepithelial tumor may also mimic central neurocytoma, but exclusive intraventricular location, the absence of "floating" neurons, and the immunohistochemical profile should distinguish between the two. Lastly, the presence of an intraventricular clear cell neoplasm in older patients should raise the possibility of a metastatic lesion, especially a renal cell carcinoma. Often, the highly anaplastic histologic features are sufficient to distinguish a renal carcinoma metastasis from a classic central neurocytoma. Additional immunohistochemical studies can be used to provide further support.

Other tumors and tumor-like lesions within the ventricular system

Other purely intraventricular tumors and tumor-like lesions are rare. One example includes the intraventricular meningioma [87–89]. The intraventricular location is uncommon, with an approximate incidence of 0.5% to 4.5% among all intracranial meningiomas [89]. Intraventricular meningiomas are more common in adults because of the higher overall frequency of meningiomas but make up a larger percentage of meningiomas in the pediatric population [90–92]. Meningiomas can arise anywhere in the ventricular system and exhibit the histologic features common to all meningiomas (see Fig. 1H). Rare cases of intraventricular clear cell meningioma [93] and malignant meningioma [94] have been reported.

Intraventricular metastases from epithelial malignancies are extremely rare but can mimic a choroid plexus tumor clinically and pathologically. Intraventricular metastases originate from a number of cancers, including renal cell carcinoma [35,95,96], pulmonary adenocarcinoma [34], gastric carcinoma [97], adrenocortical carcinoma [98], and bladder carcinoma [36]. In such cases, immunohistochemical analysis, including a cytokeratin panel, can help to identify the nature of the neoplasm and differentiate such tumors from CPCs [99].

Rare cases of perineurioma from the choroid plexus of the third ventricle, "malignant schwannoma," solitary fibrous tumors, and hemangiopericytoma have been reported as purely intraventricular tumors [100–102].

A diverse list of cystic tumor-like lesions can exist within the ventricular system and can be confused with a neoplasm [103]. Colloid cysts of the third ventricle [104], ependymal or glioependymal cysts [105], choroid plexus cysts [106], arachnoid cysts [107], and cavernous angioma [108] have been reported as intraventricular masses. Choroid plexus cysts are more common in fetuses with chromosomal aneuploidies, particularly trisomy 18.

Inflammatory or infectious processes can also present as purely intraventricular masses that resemble tumors. Such a presentation is much less common than the usual parenchymal or leptomeningeal forms. Reports of infectious or inflammatory processes that present as masses within the ventricular system include cysticercosis [109], cryptococci [110], and nocardiosis [111] among others.

Summary

Tumors that primarily or exclusively involve the ventricular system constitute a rare and heterogeneous group. Certain histologic tumor types predominantly occur in children, whereas others are more common in adults. Tumor location provides additional clues to correct diagnosis. When used in conjunction with clinical and radiologic data, histopathologic features can distinguish among this wide range of possibilities to provide the correct diagnosis for optimal patient management.

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References

[1] Janisch W, Staneczek W. Primary tumors of the choroid plexus. Frequency, localization and age [in German]. Zentralbl Allg Pathol 1989;135(3): 235–40.
[2] Schiffer D. Brain tumors. Pathology and biological correlates. Berlin: Springer Verlag; 1993. p. 217–21.
[3] Zulch K. Brain tumors. Their biology and pathology. 3rd edition. Berlin: Springer Verlag; 1986.
[4] Wolff JE, et al. Choroid plexus tumours. Br J Cancer 2002;87(10):1086–91.
[5] Matson DD, Crofton FDL. Papilloma of the choroid plexus in childhood. J Neurosurg 1960; 17:1002–27.
[6] Burger PC, Scheithauer BW. Tumors of the central nervous system. Washington, DC: Armed Forces Institute of Pathology; 1994.
[7] Kimura M, et al. Primary choroid plexus papilloma located in the suprasellar region: case report. Neurosurgery 1992;31(3):563–6.
[8] Pierga JY, et al. Carcinoma of the choroid plexus: a pediatric experience. Med Pediatr Oncol 1993; 21(7):480–7.
[9] Kepes JJ. "Xanthomatous" changes in a papilloma of the choroid plexus. Acta Neuropathol (Berl) 1970;16(4):367–9.
[10] Nakashima N, et al. Choroid plexus papilloma. Light and electron microscopic study. Virchows Arch A Pathol Anat Histopathol 1983;400(2): 201–11.
[11] Cardozo J, et al. Choroid plexus papilloma containing bone. Acta Neuropathol (Berl) 1985; 68(1):83–5.
[12] Bonnin JM, Colon LE, Morawetz RB. Focal glial differentiation and oncocytic transformation in choroid plexus papilloma. Acta Neuropathol (Berl) 1987;72(3):277–80.
[13] Stefanko SZ, Vuzevski VD. Oncocytic variant of choroid plexus papilloma. Acta Neuropathol (Berl) 1985;66(2):160–2.
[14] Reimund EL, Sitton JE, Harkin JC. Pigmented choroid plexus papilloma. Arch Pathol Lab Med 1990;114(8):902–5.
[15] Paulus W, Janisch W. Clinicopathologic correlations in epithelial choroid plexus neoplasms: a study of 52 cases. Acta Neuropathol (Berl) 1990; 80(6):635–41.
[16] Rickert CH, Paulus W. Tumors of the choroid plexus. Microsc Res Tech 2001;52(1):104–11.
[17] Kouno M, et al. An immunohistochemical study of cytokeratin and glial fibrillary acidic protein in choroid plexus papilloma. Acta Neuropathol (Berl) 1988;75(3):317–20.
[18] Kato T, et al. Clinicopathological study of choroid plexus tumors: immunohistochemical features and evaluation of proliferative potential by PCNA and Ki-67 immunostaining. Noshuyo Byori 1996;13(2): 99–105.
[19] Kubo S, et al. Immunocytochemical detection of insulin-like growth factor II (IGF-II) in choroid plexus papilloma: a possible marker for differential diagnosis. Clin Neuropathol 1999;18(2):74–9.
[20] Coons S, et al. Choroid plexus carcinoma in siblings: a study by light and electron microscopy with Ki-67 immunocytochemistry. J Neuropathol Exp Neurol 1989;48(4):483–93.
[21] Carlotti CG Jr, et al. Evaluation of proliferative index and cell cycle protein expression in choroid plexus tumors in children. Acta Neuropathol (Berl) 2002;103(1):1–10.
[22] Jay V, et al. P53 expression in choroid plexus neoplasms: an immunohistochemical study. Arch Pathol Lab Med 1996;120(11):1061–5.
[23] Navas JJ, Battifora H. Choroid plexus papilloma: light and electron microscopic study of three cases. Acta Neuropathol (Berl) 1978;44(3):235–9.
[24] Anguilar D, et al. The fine structure of choroid plexus carcinoma. Histopathology 1983;7(6): 939–46.
[25] Grill J, et al. Comparative genomic hybridization detects specific cytogenetic abnormalities in pediatric ependymomas and choroid plexus papillomas. Cancer Genet Cytogenet 2002;136(2):121–5.
[26] Rickert CH, Wiestler OD, Paulus W. Chromosomal imbalances in choroid plexus tumors. Am J Pathol 2002;160(3):1105–13.
[27] Yuasa H, Tokito S, Tokunaga M. Primary carcinoma of the choroid plexus in Li-Fraumeni syndrome: case report. Neurosurgery 1993;32(1): 131–4.
[28] Uchiyama CM, et al. Choroid plexus papilloma and cysts in the Aicardi syndrome: case reports. Pediatr Neurosurg 1997;27(2):100–4.
[29] Vital A, et al. Astrocytomas and choroid plexus tumors in two families with identical p53 germline mutations. J Neuropathol Exp Neurol 1998; 57(11):1061–9.
[30] Palmiter RD, et al. SV40 enhancer and large-T antigen are instrumental in development of choroid plexus tumours in transgenic mice. Nature 1985;316(6027):457–60.
[31] Van Dyke TA, et al. Relationship between simian virus 40 large tumor antigen expression and tumor formation in transgenic mice. J Virol 1987; 61(6):2029–32.
[32] Chen J, et al. T-antigen mutant activities in vivo: roles of p53 and pRB binding in tumorigenesis of the choroid plexus. Oncogene 1992;7(6):1167–75.
[33] Park SH, Park HR, Chi JG. Papillary ependymoma: its differential diagnosis from choroid

plexus papilloma. J Korean Med Sci 1996;11(5): 415–21.
[34] Tanimoto M, et al. Choroid plexus metastasis of lung carcinoma—case report. Neurol Med Chir (Tokyo) 1991;31(3):152–5.
[35] Mizuno M, et al. Renal cell carcinoma metastasizing to choroid plexus of lateral ventricle; a case report [in Japanese]. No Shinkei Geka 1992; 20(4):469–74.
[36] Qasho R, et al. Choroid plexus metastasis from carcinoma of the bladder: case report and review of the literature. J Neurooncol 1999;45(3):237–40.
[37] Duncan JAI, Hoffman HJ. Intracranial ependymomas. In: Kaye AH, editor. Brain tumors. Edinburgh: Churchill Livingstone; 1995. p. 493–504.
[38] Farwell JR, Dohrmann GJ, Flannery JT. Central nervous system tumors in children. Cancer 1977; 40(6):3123–32.
[39] Mork SJ, Loken AC. Ependymoma: a follow-up study of 101 cases. Cancer 1977;40(2):907–15.
[40] Schiffer D, et al. Histologic prognostic factors in ependymoma. Childs Nerv Syst 1991;7(4):177–82.
[41] Schwartz TH, et al. Supratentorial ependymomas in adult patients. Neurosurgery 1999;44(4):721–31.
[42] Kumar PV. Nuclear grooves in ependymoma. Cytologic study of 21 cases. Acta Cytol 1997; 41(6):1726–31.
[43] Kawano N, Yada K, Yagishita S. Clear cell ependymoma. A histological variant with diagnostic implications. Virchows Arch A Pathol Anat Histopathol 1989;415(5):467–72.
[44] Langford LA, Barre GM. Tanycytic ependymoma. Ultrastruct Pathol 1997;21(2):135–42.
[45] Rosenblum MK, et al. Melanotic ependymoma and subependymoma. Am J Surg Pathol 1990; 14(8):729–36.
[46] Severi B, et al. Ependymoma of the foramen of Monro: ultrastructural characterization. Ultrastruct Pathol 1989;13(1):35–42.
[47] Takeuchi H, et al. Epithelial differentiation and proliferative potential in spinal ependymomas. J Neurooncol 2002;58(1):13–9.
[48] Rushing EJ, et al. Correlation of bcl-2, p53, and MIB-1 expression with ependymoma grade and subtype. Mod Pathol 1998;11(5):464–70.
[49] Ritter AM, et al. Ependymomas: MIB-1 proliferation index and survival. J Neurooncol 1998; 40(1):51–7.
[50] Verstegen MJ, et al. Proliferation- and apoptosis-related proteins in intracranial ependymomas: an immunohistochemical analysis. J Neurooncol 2002;56(1):21–8.
[51] Sara A, Bruner JM, Mackay B. Ultrastructure of ependymoma. Ultrastruct Pathol 1994;18(1– 2): 33–42.
[52] Park JP, et al. Constitutional de novo t(1;22)(p22;q11.2) and ependymoma. Cancer Genet Cytogenet 1996;86(2):150–2.
[53] Urioste M, et al. Complex cytogenetic abnormalities including telomeric associations and MEN1 mutation in a pediatric ependymoma. Cancer Genet Cytogenet 2002;138(2):107–10.
[54] Scheinker I. Subependymoma: a newly recognized tumor of subependymal derivation. J Neurosurg 1945;2:232–40.
[55] Matsumura A, et al. Intracerebral subependymomas. Clinical and neuropathological analyses with special reference to the possible existence of a less benign variant. Acta Neurochir (Wien) 1989;96 (1– 2):15–25.
[56] Scheithauer BW. Symptomatic subependymoma. Report of 21 cases with review of the literature. J Neurosurg 1978;49(5):689–96.
[57] Prayson RA, Suh JH. Subependymomas: clinicopathologic study of 14 tumors, including comparative MIB-1 immunohistochemical analysis with other ependymal neoplasms. Arch Pathol Lab Med 1999;123(4):306–9.
[58] Moss TH. Observations on the nature of subependymoma: an electron microscopic study. Neuropathol Appl Neurobiol 1984;10(1):63–75.
[59] Dal Cin P, et al. Cytogenetic investigation in subependymoma. Cancer Genet Cytogenet 1999; 108(1):84.
[60] Wiederholt WC, Gomez MR, Kurland LT. Incidence and prevalence of tuberous sclerosis in Rochester, Minnesota, 1950 through 1982. Neurology 1985;35(4):600–3.
[61] Shepherd CW, et al. Subependymal giant cell astrocytoma: a clinical, pathological, and flow cytometric study. Neurosurgery 1991;28(6):864–8.
[62] Altermatt HJ, Scheithauer BW. Cytomorphology of subependymal giant cell astrocytoma. Acta Cytol 1992;36(2):171–5.
[63] Hirose T, et al. Tuber and subependymal giant cell astrocytoma associated with tuberous sclerosis: an immunohistochemical, ultrastructural, and immunoelectron and microscopic study. Acta Neuropathol (Berl) 1995;90(4):387–99.
[64] Lopes MB, et al. Immunohistochemical characterization of subependymal giant cell astrocytomas. Acta Neuropathol (Berl) 1996;91(4):368–75.
[65] Gyure KA, Prayson RA. Subependymal giant cell astrocytoma: a clinicopathologic study with HMB45 and MIB-1 immunohistochemical analysis. Mod Pathol 1997;10(4):313–7.
[66] Debiec-Rychter M, et al. Cytogenetic changes in two cases of subependymal giant-cell astrocytoma. Cancer Genet Cytogenet 1999;109(1): 29–33.
[67] Sampson JR, Harris PC. The molecular genetics of tuberous sclerosis. Hum Mol Genet 1994;3: 1477–80.
[68] Janssen B, et al. Refined localization of TSC1 by combined analysis of 9q34 and 16p13 data in 14 tuberous sclerosis families. Hum Genet 1994; 94(4):437–40.

[69] Hino O, et al. The predisposing gene of the Eker rat inherited cancer syndrome is tightly linked to the tuberous sclerosis (TSC2) gene. Biochem Biophys Res Commun 1994;203(2):1302–8.
[70] Hassoun J, et al. Central neurocytoma. An electron-microscopic study of two cases. Acta Neuropathol (Berl) 1982;56(2):151–6.
[71] Hassoun J, et al. Central neurocytoma: a synopsis of clinical and histological features. Brain Pathol 1993;3(3):297–306.
[72] Maiuri F, et al. Central neurocytoma: clinicopathological study of 5 cases and review of the literature. Clin Neurol Neurosurg 1995;97(3):219–28.
[73] Kim DG, et al. Intraventricular neurocytoma: clinicopathological analysis of seven cases. J Neurosurg 1992;76(5):759–65.
[74] Yasargil MG, et al. Central neurocytoma: histopathological variants and therapeutic approaches. J Neurosurg 1992;76(1):32–7.
[75] Favereaux A, et al. Histopathological variants of central neurocytoma: report of 10 cases. Ann Pathol 2000;20(6):558–63.
[76] Mena H, et al. Central neurocytomas express photoreceptor differentiation. Cancer 2001;91(1): 136–43.
[77] Ng TH, et al. Pigmented central neurocytoma: case report and literature review. Am J Surg Pathol 1999;23(9):1136–40.
[78] von Deimling A, et al. Patterns of differentiation in central neurocytoma. An immunohistochemical study of eleven biopsies. Acta Neuropathol (Berl) 1990;79(5):473–9.
[79] Kubota T, et al. Central neurocytoma: immunohistochemical and ultrastructural study. Acta Neuropathol (Berl) 1991;81(4):418–27.
[80] Mackenzie IR. Central neurocytoma: histologic atypia, proliferation potential, and clinical outcome. Cancer 1999;85(7):1606–10.
[81] Sharma MC, et al. A study of proliferative markers in central neurocytoma. Pathology 1998;30(4):355–9.
[82] Robbins P, et al. Central neurocytoma. A clinicopathological, immunohistochemical and ultrastructural study of 7 cases. Pathol Res Pract 1995;191(2):100–11.
[83] Tsuchida T, et al. Neuronal and glial characteristics of central neurocytoma: electron microscopical analysis of two cases. Acta Neuropathol (Berl) 1996;91(6):573–7.
[84] Yin XL, et al. Detection of chromosomal imbalances in central neurocytomas by using comparative genomic hybridization. J Neurosurg 2000;93(1): 77–81.
[85] Taruscio D, et al. Nonrandom gain of chromosome 7 in central neurocytoma: a chromosomal analysis and fluorescence in situ hybridization study. Virchows Arch 1997;430(1):47–51.
[86] Tong CY, et al. Central neurocytomas are genetically distinct from oligodendrogliomas and neuroblastomas. Histopathology 2000;37(2):160–5.
[87] Hoffman JC, Jr, Bufkin WJ, Richardson HD. Primary intraventricular meningiomas of the fourth ventricle. Am J Roentgenol Radium Ther Nucl Med 1972;115(1):100–4.
[88] Criscuolo GR, Symon L. Intraventricular meningioma. A review of 10 cases of the National Hospital, Queen Square (1974–1985) with reference to the literature. Acta Neurochir (Wien) 1986;83(3–4):83–91.
[89] Imielinski BL, Kloc W. Meningiomas of the lateral ventricles of the brain. Zentralbl Neurochir 1997; 58(4):177–82.
[90] Vassilouthis J, Ambrose JA. Intraventricular meningioma in a child. Surg Neurol 1978;10(2):105–7.
[91] Diaz P, et al. Multiple meningiomas of the fourth ventricle in infancy: case report. Neurosurgery 1990;26(6):1057–60.
[92] Sgouros S, Walsh AR, Barber P. Intraventricular malignant meningioma in a 6-year-old child. Surg Neurol 1994;42(1):41–5.
[93] Kakita A, et al. Clear cell variants of intracranial tumors: meningioma and ependymoma. Noshuyo Byori 1995;12(2):111–6.
[94] Kamiya K, Inagawa T, Nagasako R. Malignant intraventricular meningioma with spinal metastasis through the cerebrospinal fluid. Surg Neurol 1989;32(3):213–8.
[95] Killebrew K, et al. Metastatic renal cell carcinoma mimicking a meningioma. Neurosurgery 1983; 13(4):430–4.
[96] Raila FA, Bottoms WT Jr, Fratkin JD. Solitary choroid plexus metastasis from a renal cell carcinoma. South Med J 1998;91(12):1159–62.
[97] Nakabayashi H, et al. Choroid plexus metastasis from gastric cancer—case report. Neurol Med Chir (Tokyo) 1994;34(3):183–6.
[98] Piniella AM, Siatkowski RM. Adrenal cortical carcinoma metastatic to the brain in a child. J Neuroophthalmol 2000;20(1):35–7.
[99] Gyure KA, Morrison AL. Cytokeratin 7 and 20 expression in choroid plexus tumors: utility in differentiating these neoplasms from metastatic carcinomas. Mod Pathol 2000;13(6):638–43.
[100] Giannini C, et al. Intraventricular perineurioma: case report. Neurosurgery 1998;43(6):1478–82.
[101] Jung JM, et al. Malignant intraventricular schwannoma. Case report. J Neurosurg 1995;82(1):121–4.
[102] Abrahams JM, et al. Hemangiopericytoma of the third ventricle. Case report. J Neurosurg 1999; 90(2):359–62.
[103] Hirano A, Hirano M. Benign cystic lesions in the central nervous system. Light and electron microscopic observations of cyst walls. Childs Nerv Syst 1988;4(6):325–33.
[104] Jeffree RL, Besser M. Colloid cyst of the third ventricle: a clinical review of 39 cases. J Clin Neurosci 2001;8(4):328–31.
[105] Tillich M, et al. Symptomatic neuroepithelial (ependymal) cyst of the fourth ventricle: MR appearance. AJR Am J Roentgenol 1999;172(2):553–4.

[106] Gratton RJ, Hogge WA, Aston CE. Choroid plexus cysts and trisomy 18: risk modification based on maternal age and multiple-marker screening. Am J Obstet Gynecol 1996;175(6):1493–7.
[107] Lee KS, Bae HG, Yun IG. Intraventricular arachnoid cyst. J Neurosurg 1989;70(1):154–5.
[108] Suess O, Hammersen S, Brock M. Intraventricular cavernoma: unusual occurrence in the region of the foramen of Monro. Br J Neurosurg 2002;16(1):78–9.
[109] Madrazo I, et al. Intraventricular cysticercosis. Neurosurgery 1983;12(2):148–52.
[110] Vender JR, et al. Intraventricular cryptococcal cysts. AJNR Am J Neuroradiol 1996;17(1):110–3.
[111] Mogilner A, et al. Nocardia abscess of the choroid plexus: clinical and pathological case report. Neurosurgery 1998;43(4):949–52.