Intraventricular brain tumors in children

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INTRODUCTION

Intraventricular neoplasms demonstrate a diagnostic and therapeutic challenge. They appear with various types in relation to histology, age of occurrence, site of tumor growth and malignancy potential. They originate from cells forming the ependymal lining or the subependymal plate of the ventricular wall, the choroid plexus and the glial lined structures like septum pellucidum. Sometimes, vestigial structures e.g. colloid cysts contained within the ventricular system behave like neoplasms in means of clinical signs and symptoms.

Although, intraventricular neoplasms show a relative small incidence in the group of CNS neoplasms, their heterogeneous presentation of types and malignant potential requires deep understanding of their origin and their disease-course behavior in order to be able to construct an effective treatment plan.

EMBRYOLOGY OF THE VENTRICLES

The embryological pathway that leads to the development of the ventricles starts from the neural groove. In the 22nd day of development, the neural groove closes and forms the neural tube, which is an open tube with two neuropores, filled with amnion. The neuropores are located at the rostral and caudal end of the neural tube. The hollow neural tube is the origin of the ventricular system since the development initiates from its single cavity. The neural tube fuses and the neuropores close (rostral neuropore closes in 24 days while the caudal one closes in 26 days) so the ventricular system in development is separated from amnion. The ventricular space will be generated in Week 4 by the neural tube. Choroid plexus development starts from the floor of the lateral ventricle and the roof of third and fourth ventricle. It is a modified vascular epithelium that differentiates in order to produce cerebrospinal fluid (22, 171, 173).

INCIDENCE

Central nervous system neoplasms present into the ventricular system or they are located in close anatomical relation in a percentage about 10% (174, 233). The literature concerning intraventricular neoplasms deals often with their supratentorial presentation (lateral ventricular neoplasms), while infratentorial presentation is usually referenced under the group of posterior fossa tumors in children.

According to Pendl et al (181) and Koos et al (118) supratentorial and infratentorial intraventricular tumors demonstrate an overall incidence of 7% in adults and 41% in children. So there is a clear predominance of intraventricular tumors in children.

Half of all adult intraventricular tumors occur in the lateral ventricle while this is true for one quarter of pediatric tumors (118, 181).

In Vienna tumor series, infratentorial intraventricular brain tumors are found in 55% of pediatric cases (118) so this tumor location predominates in the pediatric group. Lateral ventricle tumors account for less than 1% of intracranial neoplasms according to Zuccaro et al (265). Other series concerning lateral ventricle tumors present a percentage of 0.8-1.6% in adults and children (41, 71, 122, 181). There are differences in the literature concerning the predominance of lateral ventricular tumors. Lapras et al (122) and Zuccaro et al (265), show that the incidence of lateral ventricle tumors in pediatric population is higher than adult population and it is presented as 5% in Zuccaro's series or 9.1% in Lapras's series.

DEFINITION

Various definitions concerning intraventricular tumors are present in the literature. A lot of published papers and textbooks utilize the term "intraventricular tumors" only for describing supratentorial intraventricular tumors and sometimes only the subgroup of lateral intraventricular tumors is used. Infratentorial intraventricular lesions are not usually studied as an individual subgroup but are referenced in the parent group of posterior fossa tumors. Apart from supratentorial and infratentorial nomenclature variability of intraventricular brain tumors, the issue of primary and secondary types is addressed. According to D'Angello et al (37), Pendl et al (181), Yasargil et al (261) and Zulch et al (266), neoplasms that originate in the ventricular wall and its lining are considered primary ventricular tumors with or without transependymal development. "Secondary or paraventricular tumors" is a definition used when these neoplasms originate from adjacent brain substance and demonstrate more than two-thirds exophytic growth within the ventricle. These tumors are called "secondary ventricular tumors with transependymal development" (37, 181, 266). We believe that the term "intraventricular tumors" should follow the supratentorial-infratentorial scheme and should not be limited to the representation of lateral ventricular tumors solely.

CLINICAL PRESENTATION

Cushing and Eisenhardt (35) described the clinical features-axons met in lateral ventricular tumors in adults:

1. Pressure symptoms with ipsilateral headache
2. Contralateral macula splitting homonymous hemianopsia
3. Contralateral sensorimotor paresis affecting mainly trigeminal distribution
4. Cerebellar involvement in more than half of patients
5. Paralexia in left-side tumors (when left is the dominant hemisphere)

The clinical presentation of intraventricular tumors varies among different age groups. The cornerstone of clinical presentation depicts by the evolution of CSF obstruction and subsequent hydrocephalus due to ventricular involvement. The clinical history varies and is about twice as long in tumors confined to the ventricular lumen as in paraventricular growths (118). Children tend to express the symptoms of a disease in accordance to their behavioral evolution, which is consistent with their age (147, 233). Thus, small children especially with lack of speech present raised intracranial pressure signs and symptoms in the form of macrocrania, irritability, anhedonia, loss of appetite with subsequent reduced growth curves. Older children usually demonstrate recurrent, intense morning headaches and frequent episodes of vomiting. Delfini et al (41) report that "two age related clinical patterns emerge: one dominated by hydrocephalus in neonates and a pattern of intracranial hypertension associated with focal signs of various types in children and adults". Papilledema is a common sign since it is a consequence of raised intracranial pressure. The alteration of consciousness level is in accordance to the signs of raised intraventricular pressure so the acute presentation of an intraventricular tumor with the clinical picture of a comatose child is not uncommon. Less frequently hemiparesis or seizures may be parts of the clinical picture. Seizures tend to accommodate intraventricular brain tumors in children that are associated with tuberous sclerosis and subependymal giant cell astrocytomas. Visual disturbances can also be clinical signs of intraventricular tumors and may be attributed to raised intracranial pressure or mass effect phenomena in cases of third ventricle tumors in proximity to the optic-hypothalamic region or the trigone. Psycho-organic manifestations can be pronounced in children with ages consistent with the expression of higher cognitive skills (130, 233).

Fourth ventricle tumors give rise to hydrocephalus and altered consciousness more frequently. Also cranial nerve palsies can be observed usually by nuclear damage in the floor of the 4th ventricle or direct lower nerve lesions. Cerebellar dysfunction represented by truncal ataxia and dysmetrias can be observed in accordance to the infratentorial intraventricular location of the tumor or parechymal invasion (33, 226).

DIFFERENTIAL DIAGNOSIS

These tumors demonstrate a great heterogeneity concerning their tumor types, their location, their clinical presentation and their malignant potential. The majority of tumors (85%) that arise within the lateral ventricles are benign or low grade (184), while malignancy, is more common in pediatric infratentorial brain tumors since medulloblastomas and ependymomas, predominate. The differential diagnosis of these lesions becomes a challenging task for the neurosurgeon. Published series and reviews (103, 147, 233) show that two important factors are the key concepts in unveiling the secrets of diagnosis. These are the child's age and the location of the tumor.

Age is a key factor in interpreting the probability of recognizing the type of a tumor. Age also forms the clinical picture of intraventricular brain tumors. The cognitive milestones in a child's life, such as the ability of spoken language, or the behavioral milestones like pain localization and expression, alter the clinical picture. The entrance to an elementary school, usually at the age of six, is also a cognitive milestone that significantly influences child's expression ability and reasoning and thus influences clinical picture.

TUMOR TYPES

SUPRATENTORIAL INTRAVENTRICULAR BRAIN TUMORS

Choroid plexus tumors

Choroid plexus tumors arise from the cells of the choroid plexus, with an embryological origin from the ependymal lining of the neural tube (209). Ependymal, neural tube lining is present in all four ventricles but the distribution of the choroid plexus varies. The choroid plexus is denser in the trigone of the lateral ventricle and in the fourth ventricle than the other ventricular locations, while is absent across the route of the aqueduct of Sylvius.

Epidemiology

Choroid plexus papillomas (CPPs) and choroid plexus carcinomas (CPCs) show a prevalence of 0.3 cases per 1,000,000 (102) while they demonstrate a frequency of 0.5% to 0.6% of all adult and childhood brain tumors (80). Pediatric population shows a higher percentage (1.8-2.9%) of choroid plexus tumors (7, 50, 211). Choroid plexus tumors are diagnosed as choroid plexus papillomas in 80% and choroid plexus carcinomas in 20% (1). In adult and pediatric series, the lateral ventricle is the most common location site (50%). The infratentorial presentation at the fourth ventricle follows with a percentage of 40% and the third ventricle gives rise to 5% of these tumors (1). Literature indicates that the remaining 5% of tumors shows multiple seeding locations or extraventricular appearance in sites including the cerebellopontine angle, the suprasellar region, the frontal lobe, the posterior commissure, the pineal gland and the cerebellum (116). Supratentorial presentation of these tumors occurs mainly in infants (256). The frequency of choroid plexus tumors in the first year of life is 14% according to Galassi et al (65) or 12.8% according to Haddad et al (83). Laurence et al (123) reported that 75% of them occur in the first decade. The most common location of a choroid plexus tumor is supratentorially for children and infratentorially for adults. The seeding location of choroid plexus tumors is mainly the trigone of the lateral ventricle (50, 184, 233).

Pathology

Choroid plexus tumors are neoplasms derived from epithelium. Macroscopically they appear as cauliflower patterned tumors with shaded, orange and brown areas. They characteristically consist of a tube like seeding structure that is close related to the feeding vessels. This structure attaches to the normal choroid plexus or to the ventricular wall surface (247).

Choroid plexus papillomas show a papillary structure with cords of fibrous tissue and vessels (247). There is a close relation to the appearance of normal choroid plexus and calcification foci can be observed. Attributes of malignancy, like cellular atypia or disorientated tissue architecture are not present and CPPs are classified by WHO as Grade I tumors (1, 133). Variants of the basic type can be observed. Choroid plexus tumors may demonstrate foci of osseous or cartilaginous metaplasia or pigmentation variations concerning neuromelanin and lipofuscin (247). There is a subset of atypical CPPs observed by Levy et al (127), which demonstrates parenchymal invasion and loss of villous architecture at the invasion site with benign characteristics. The atypical CPP was been diagnosed as CPC in the past but its survival follow-up profile shows the possibility of cure, after gross resection without adjuvant supportive treatment (233). Recently, the latest WHO classification scheme (133), recognized atypical CPP under a new additional entity named

"atypical choroid plexus papilloma" and assigned it with WHO grade II. It is primarily distinguished from CPP by increased mitotic activity (134).

Carcinomas of the choroid plexus demonstrate malignant characteristics and are far more common in children than in adults (116). There are frequent mitoses, cell atypias and diminished papillary pattern. Parenchymal invasion is typical with perilesional edema, disturbed tissue architecture and areas of necrosis, features that lead to WHO Grade III category (1, 133). Carcinomas of the choroid plexus may resemble metastatic tumors to the choroid plexus like adenocarcinomas originating from pulmonary and genitourinary systems. Malignant potency is also demonstrated by the ability of CPCs to disseminate through CSF in other CNS regions. Although there is documented dissemination capability, the incidence of metastatic spread of CPCs outside CNS is low (146).

The differential diagnosis concerning pathology is challenging since some benign or malignant tumor types or normal variation show an overlapping picture. It is difficult to identify the subtle changes that CPP bears and thus it differs from normal choroid plexus. According to Gupta (80), villous hypertrophy is a poorly defined entity. In most cases is a normal variation of the choroid plexus histology associated with the clinical picture of hydrocephalus from birth. Atypical rhabdoid cells have been discovered in some CPCs, which perplex the picture with the typical presentation of these cells in atypical teratoid rhabdoid tumors (259). The rare type of papillary ependymoma is also a differential challenge that should be considered (177). Metastases from pulmonary and genitourinary systems occur frequently in choroid plexus and a malignant type of adenocarcinoma addresses a differential diagnosis issue related to choroid plexus tumors. In children retinoblastoma, neuroblastoma and Wilms' tumor are the most common tumors found to metastasize at the choroid plexus (191).

Li-Fraumeni syndrome, an autosomal dominant hereditary disorder with p53 tumor suppressor gene mutations, is related to choroid plexus tumors (263). Aicardi syndrome (absence of corpus callosum, infantile spasms, and brain congenital malformations and tumors) is also related to choroid plexus tumors (241). A possible association with choroid plexus tumors and Simian Virus 40 (SV40) is observed in the literature since DNA sequences of the virus have been identified in the tumor's genome (15, 66, 124).

Clinical Presentation

The most common clinical picture met is the characteristic asymmetrical hydrocephalus and raised intracranial pressure as stated at the description of the general clinical picture before (50). There are a lot of theories related to the clinical picture evolution concerning the choroid plexus tumors. The first and most widespread theory in the literature is the overproduction of CSF from the tumor (49). Various articles indicate that the removal of the tumor may reverse the hydrocephalus present and this is true for some cases (78).

Research papers also note that the CSF fluid aspirated in various cases of CPPs and CPCs may be xanthochromic, which indicates silent intratumoral hemorrhage (180). This subclinical hemorrhage could be responsible for altering the protein composition of CSF and thus blocking the arachnoid granulations leading to communicating hydrocephalus. Finally the last theory applies to oversized choroid plexus tumors, which may obstruct directly the foramen of Monro (29).

Neuroimaging

Neuroimaging studies are characteristic of CPPs and CPCs. Choroid plexus papillomas demonstrate a discrete barrier from healthy brain, while calcification is present in 14% of the CT studies. They are generally isoattenuated to hyperattenuated intraventricular masses, which are intensely enhanced in post-contrast CT scan. Studies with MRI usually show isointense to hypointense intraventricular masses comparing to the adjacent brain parenchyma that also become intense with the utilization of a paramagnetic contrast enhancement agent. The tumor is quite vascular so flow voids can be seen in MRI (116). Blood supply can be demonstrated in angiographies as enlarged choroidal arteries provide the feeding source to the tumor. CPCs usually present vague boundaries and are heterogeneous. There is healthy brain infiltration and necrosis with perilesional edema depicting a malignant potential. Leptomeningeal dissemination demonstrated with MRI studies is present in 45% of patients at diagnosis (154). Magnetic resonance spectroscopy seems to play a significant role in the differential diagnosis of choroid plexus tumors. Myo-inositol spectrum seems to be elevated in choroid plexus papillomas distinguishing them from CPCs and other tumors. Choline spectrum level seems to be elevated in CPCs comparing to CPPs (121). Digital subtraction angiography demonstrates enlarged normal choroidal arteries that feed the tumor (116).

Hydrocephalus is present in almost all cases and is a characteristic feature of these tumors (116). In a series presented by Humphreys et al (95), the percentage of hydrocephalus was 78% while Ellenbogen et al found that the accompanying hydrocephalus observed in 95% of the cases (50).

Surgical treatment

Literature shows that the principle governing the treatment of choroid plexus papillomas is the gross total resection (14, 50, 149, 180, 256). Hydrocephalus is an accompanying situation that has to be treated and surgical planning involves the identification of vascular supply to the tumor and the estimation of tumor volume (80). The surgical plan should be fit to the principle of safely approaching and protecting noble anatomic and physiologic regions that deal with speech, motor, sensory systems and vision.

The key concept in surgery lies mainly in approaching the feeding vessel and thus interrupting the blood supply to the highly vascular tumor (80, 184). We should always bear in mind that the patient is a child with a small blood volume comparing to the adult and the possibility of generous blood loss when dealing with vascular tumors is quite raised and may lead to perioperative morbidity. Another helpful approach is the preoperative selective embolization of the feeding vessel that ensures a clean operative field and tumor volume reduction (47, 175). In a study published by St Clair et al (231), preoperative chemotherapy reduces the high degree of CPC vascularity which may facilitate complete tumor resection Lateral ventricular tumors are approached utilizing various transcallosal or transcortical approaches while third ventricular tumors are approached via a midline transcallosal group. Infratentorial choroid plexus tumors are usually approached via posterior fossa midline craniotomy.

Hydrocephalus deserves special considerations when dealing with choroid plexus tumors. It is the first line step that demands a decision. Age plays a critical role since infants < 10 months maximum can compensate through the open sutures. The decision of using a ventriculoperitoneal shunt or a temporal external ventricular drainage device can be affected by two parameters (80). The first parameter according to the literature (78), indicates that in a group of cases there is postoperative hydrocephalus resolution so the VP shunt might be futile. The second parameter underlines, that the perioperative management of tumor environment and the presence of hemorrhage might lead to blood clot accumulation and raised protein CSF content. These two factors might lead to VP shunt obstruction and malfunction. It seems that the profile of surgeon and the method he chooses relies mainly in his beliefs. Hydrocephalus is more prominent, when the fourth ventricle is involved and addresses an urgent issue in treatment, since CSF drainage ensures preoperative and perioperative stability in means of avoiding imminent herniation (80).

Outcome

Outcome is favorable for CPPs but CPCs show a poor prognosis. Literature indicates, that the 5-year prognosis for CPPs approaches 80-90% after gross total resection (14, 50, 149, 180, 256). Wolff et al (256) observed that the survival rates for papillomas concerning 1, 5 and 10-year survival were respectively 90%, 81%, 77% while the relevant survival for CPCs was 71%, 41% and 35% respectively. There is no need for an adjuvant treatment modality concerning CPPs (233).

On the other side, the situation met with CPCs is difficult due to their invasion and malignant profile. The 5-year survival rates observed in the literature show a variation between 26%-50 (14, 50, 149, 180, 256). Gross total resection can be achieved in less than 50% of cases (80) but improves the survival significantly(50, 180). Fitzpatrick et al (61) report that the survival after gross total resection combined with adjuvant radiation therapy or

chemotherapy ranges from 67%-91%. Chemotherapy utilizes protocols based on platin, vincristine, etoposide, cyclophosphamide (80). A meta-analysis was published in 2007 by Wrede et al (258) concerning CPCs in adults and children. This meta-analysis showed that patients with less than completely resected CPC should receive chemotherapy. Radiation therapy has to be utilized wisely in relation to the child's age. Radiation protocols can be used when a child is older than 3 years otherwise late neurological sequelae may be observed (80, 180, 257, 258). The disease relapse is a negative prognostic factor that influences survival.

Subependymal giant cell astrocytomas (SGCAs)

Subependymal giant cell astrocytomas, tubers and subependymal nodules are brain lesions that are associated with tuberous sclerosis. They are considered to derive from embryological precursor cells in the periventricular zone. Their mission is to become neurons or glial cells. When migrational or organizational abnormalities concerning the development of neurons or glia evolve, they give rise to the clinical manifestations of tuberous sclerosis (34). The pathogenesis of SGCAs involves theories about their evolution from subependymal nodules (140).

Epidemiology

It is generally an uncommon, benign pediatric tumor (1.4% in 733 pediatric neoplasms) as stated by Sinson et al (229). Most cases occur in the first two decades (223, 229, 253). There is a strong association with tuberous sclerosis since 6-16% of these patients develop a SGCA (253). Subependymal giant cell astrocytoma was also the most frequent type (n=14) in a series of 54 lateral ventricle tumors in children by Zuccaro et al (265). Subependymal giant cell astrocytomas are usually located adjacent to the foramen of Monro (116, 233) and probably arise from subependymal nodules in the ventricular wall of patients with tuberous sclerosis, which demonstrates an autosomal dominant pattern of inheritance (229).

Pathology

Subependymal giant cell astrocytomas have a distinct cytoarchitecture. They are mainly intraventricular solid masses. A peduncle is usually present with a broad base. The tumor possesses a rubbery texture and is usually pink colored due to neoangiogenesis. Friable areas can be identified while calcified foci can also be observed (247).

The cell types that form the tumor are spindled and gemistocyte-like. This microstructure renders the tumor with a swirl-like texture. Gemistocyte-like cells possess hairy processes that aid in forming clusters and pseudorosettes. There is low mitotic activity, no vascular proliferation or necrosis (247). The benign characteristics observed in SGCA led to its classification as a WHO Grade I tumor (133). The differential diagnosis concerning pathology may include a gemistocytic astrocytoma, a high-grade astrocytomas, a tanycytic ependymoma or a subependymoma (247).

Clinical presentation

The clinical picture observed is mainly affected by the underlying disease of tuberous sclerosis. Neurocutaneous stigmata can be present, mental retardation is obvious, while hard to control seizures emerge (Vogt triad). Intracranial hypertension is almost always present when the lesion demonstrates close relation to the foramen of Monro (224).

Neuroimaging

Subependymal giant cell astrocytomas appear as isoattenuated to hypoattenuated intraventricular masses near foramen of Monro (229) on CT images. Calcification areas are commonly identified since biopsy specimens can show calcified foci (229). Hyperattenuation areas may represent an evidence of rare intratumoral hemmorhage (105). According to Cuccia et al (34) the best indicators of an SGCA as demonstrated in neuroimaging studies are:

1. Tumor size >12mm
2. Gradually increasing size
3. Associated hydrocephalus

A subependymal nodule is a distinct lesion from SGCA. Subependymal giant cell astrocytoma shows post-contrast CT enhancement near the foramen of Monro while there is no enhancement for a subependymal nodule (11, 151).

Magnetic resonance imaging concerning SGCAs may be confusing since altered patterns are present between older children and neonates. In older children, SGCAs show lower signal comparing to white matter in T1W and heterogeneous signal in T2W (229). Neonates with SGCAs show high signal in T1W and low signal in T2W, which is the opposite observed usually. An possible explanation for these observations can be constructed utilizing the comments of Oikawa et al (172) about the abundance of water in neonatal brain, the low cell count of SGCA and the presence of calcification.

Special condiderations

Neurocutaneous disorders like tuberous sclerosis and neurofibromatosis are related to brain tumors (108, 163, 223, 224, 229, 233, 253, 265). Zuccaro et al (265) report that 31.5% of their intraventricular SGCAs were related to tuberous sclerosis. Nabbout et al (163) and Shepherd et al (224) showed in their series, that SGCAs are discovered in 10-15% of patients with tuberous sclerosis. Children with subependymal nodules will develop a SGCA in a percentage of 2-14% according to Shepherd et al (224). Intraventricular tumors with concomitant neurofibromatosis can be found usually associated with type II and intraventricular meningioma or astrocytoma formation as demonstrated in the series of Bhatoe et al (17), Kendall et al (108) and Zuccaro et al (265). Neurofibromatosis type I is associated with optic nerve gliomas (128) and dysplastic thickening of the septum (233).

Treatment and outcome

Subependymal giant cell astrocytomas are benign WHO Grade I tumors (133). The complete resection of the tumor and its benign behavior can lead to favorable outcome (202). According to Cuccia et al (34), surgical criteria must be implemented in the surgical treatment of a SGCA. These are:

1. The presence of hydrocephalus
2. Interval increase in tumor size
3. New focal neurological deficit attributable to tumor, and/or
4. Symptoms of increased intracerebral pressure

The presence of preoperative hydrocephalus according to Cuccia et al (34) seems to resolve with tumor excision so the authors do not encourage the placement of a preoperative or postoperative shunt when increased intracranial pressure is absent.

There is excellent long-term survival (39, 46, 202). The possibility of acute and emergent rise in intraventricular tumor due to tumors proximity to the foramen of Monro can lead to increased mortality (34, 164). The resection of the tumor may not diminish the course of seizures in some cases and mental retardation is not affected (34).

Literature indicates that patients with a diagnosis of tuberous sclerosis should have an MRI scan at the age of 2 years and after should be followed annually with scanning for tumor size increment (164). Subtotal resection of the tumor should also have a frequent MRI follow-up and relatives of first degree should also undergo neuroimaging (116, 233).

Figures **1a**, **1b**, **1c**, and **1d** demonstrate a pediatric case of a 3rd ventricular subependymal giant cell astrocytoma near foramen of Monro.

Astrocytoma

The seeding location of intraventricular astrocytomas is usually an extraventricular structure next to the ventricle such as thalamus or the opticothalamic region. Supratentorial intraventricular astrocytomas usually arise from thalamus and opticothalamic region and show infiltrative properties and thus malignant potential (147, 176). When the evolution of tumor is more than two thirds in a ventricle we consider them secondary ventricular tumors with transependymal development.

Epidemiology

Astrocytomas are found in 35% of all brain tumors in children (233). Zuccaro et al (265) in their series of lateral ventricular tumors in children found 6 intraventricular astrocytomas (SGCAs not included) in 54 cases (11%) and agree with Silver et al(228) who found 2 in 18 cases (11%) of adult-pediatric lateral ventricular tumors. Jelinek et al (103) found 2 (4.2%) intraventricular pilocytic astrocytomas in a series of lateral ventricular tumors in 47 adult and pediatric patients. The most common intraventricular astrocytomas types in children are fibrillary astrocytomas, juvenile pilocytic astrocytomas (JPAs) and subependymal giant cell astrocytomas (SGCAs) mentioned earlier (233). Juvenile pilocytic astrocytomas in children with intracranial neoplasms are supratentorial in a percentage of 11% and are usually found in the hypothalamic-optic region (75% of JPAs of the optic pathway in children younger than 12 years old). They intraventricular JPAs may involve the anterior body of the lateral ventricle and the anterior part of the third ventricle. The location of trigone is a rare site for JPA presence (233). Fibrillary astrocytomas that involve the ventricles may belong to tumors at the third ventricle (170, 244), thalamic tumors, hypothalamic tumors (42), optic pathway tumors extending to the third ventricle or exophytic brainstem gliomas involving the 4th ventricle (59).

Pathology

Juvenile Pilocytic astrocytomas

Juvenile pilocytic astrocytomas are a variant of pilocytic astrocytomas observed most in children and young adults. Macroscopically an infratentorial JPA is a cystic lesion with a mural nodule that is usually well defined from the adjacent parenchyma. This setting cannot be applied to the JPAs involving the hypothalamus and the optic chiasm, which are solid masses without a cystic association (233). This type of tumor is believed to arise from reactive astrocytes (20, 21). It shows a biphasic type of morphology with a loose glial component and compact piloid type areas. Eosinophilic granular bodies, named "protein

droplets" and Rosenthal fibers can be seen. Juvenile pilocytic astrocytomas belong to the WHO Grade I group (133). A special astrocytoma subtype called "pilomyxoid astrocytoma" shows affinity for the hypothalamic/chiasmatic region, appears to have less favorable prognosis and recurrences are possible. The last 2007 WHO classification graded this tumor type as grade II (134). In general, these tumors show benign behavior when located infratentorial and malignant behavior in a supratentorial setting. Infratentorial location is mainly associated with pilocytic cerebellar astrocytomas that encroach the 4th ventricle when they demonstrate intraventricular location (233).

Fibrillary astrocytomas

Fibrillary astrocytomas are the most frequent histological variant of the diffuse, low-grade astrocytomas. There is a close resemblance of these cells with cells from the cerebral white matter. Fibrillary pattern is a distinct characteristic. The cells are small, oval and well differentiated. There is a marked increased cellularity and GFAP (glial fibrillary acidic protein) expression can aid significantly in histological differentiation. This tumor type belongs to WHO Grade II (133).

Clinical presentation

The intraventricular presentation of astrocytomas is consisted with signs and symptoms of hydrocephalus and raised intracranial pressure to smaller extent since a lot of cases are exophytic. Special clinical characteristics emerge through the observations of these tumors. Visual disturbances and endocrinological dysfunction tend to occur late in the disease process although a lot of these tumors involve the third ventricle (233). A characteristic syndrome called "diencephalic syndrome" can be observed when mass effect concerning the hypothalamus is present in infants. This syndrome is a rare and potentially lethal syndrome in infants and young children. Emaciation, normal linear growth, normal or precocious intellectual development, hyperkinesis and irritability are the manifestations of the syndrome, associated with brain tumors (62). When the tumors are exophytic brainstem tumors involving the 4th ventricle, hydrocephalus with abducens palsy or torticollitis can be observed (59, 115).

Special considerations

Optic pathway gliomas in children are associated with Neurofibromatosis type 1 (NF1) (128). Pilocytic astrocytomas are the most common tumors in patients with NF1 with a percentage of 15%-21%. There is a typical involvement of optic nerve or optic chiasm (115). We should consider that 75% of optic pathway pilocytic astrocytomas are observed in children younger than 12 years old.

Neuroimaging

Juvenile pilocytic astrocytomas

The CT scans of JPA lesions are iso- to hypodense to the nearby tissues. The MRI characteristics of these tumors are low signal in T1W MRI scans or normal signal comparing to adjacent parenchyma, with high signal T2W especially when peritumoral edema is present (147, 233). Infratentorial JPAs usually show the cyst and mural nodule pattern while JPAs of the optohypothalamic region appear more solid. Magnetic resonance spectroscopy may aid the diagnosis since ratios of choline to N-acetylasparate or choline to creatine and lactate to creatinine have been observed (115).

Fibrillary astrocytomas

When fibrillary astrocytomas show their diffuse-infiltrative pattern they appear hypodense in CT scans. Some cases show calcification in a percentage of 20% in CT scans. Magnetic resonance images show low signal in T1W and high signal in T2W. The application of a paramagnetic substance may produce a mild enhancement (233).

Treatment and outcome

The surgical treatment of intraventricular JPAs and fibrillary astrocytomas involves meticulously planning, based on the site of lesion, the imaging studies, the histology of the tumor, the age of the patient and the clinical picture. Surgery has been assigned the 1st role for juvenile pilocytic astrocytomas, which demonstrate a benign behavior especially when they are associated with NF1. Gross total resection (GTR) is the goal for JPAs that can be easily approached while pediatric midline low-grade astrocytomas are usually subtotally resected. Fisher et al (60) report that the 5 years overall survival for all children in their series undergoing GTR was 100% with progression free survival near 90%. The coexistence of JPA and NF1 in a child with optic pathway glioma is related with favorable prognosis (128), while a spontaneous regression of a JPA has been observed (216). Due to favorable results concerning gross total resection and JPAs in children, a lot of authors do not implement adjuvant therapies (233).

Subtotal resection of JPAs and diffuse astrocytomas require different treatment strategies since the survival rates and the ability to approach and excise the lesions

adequately, influence our choices. Sutton et al (234) report that 10-year survival for low-grade astrocytomas is 75% for subtotal resection or biopsy strategies (63). Tumors at the midline and especially at the hypothalamic-optic region in children are associated with high perioperative morbidity. In this specific group the utilization of adjuvant therapies (chemotherapy, radiotherapy) with subtotal resection may show some benefit (Sutton et al). Immediate postoperative irradiation does not show an advantage in children with residual pilocytic astrocytomas (60) so adjuvant therapies may be used when the disease shows progression (233). Gnekow et al (70) showed that chemotherapy might be beneficiary for delaying the progress of optic region gliomas in children not adequate for radiation protocols due to their age. Mamelak et al (139) recommend the utilization of focal radiotherapy in children older than 5 years with subtotally resected low-grade gliomas. In cases of dissemination, chemotherapy and radiotherapy should be used. Literature indicates that JPAs can undergo malignant transformation or disseminate (233) but recent meta-analysis by Parsa et al (178) indicates that spontaneous malignant transformation does not occur. If malignant transformation is found it is owed to radiation exposure.

Subependymoma

Subependymomas have been speculated to originate from an ependymal-glial precursor cell, which shows the ability to differentiate to an ependymal cell or an astrocyte and this theory predominates in the literature (143, 144, 254). Another theory states that subependymomas may be hamartomatous lesions that represent a response to chronic ependymitis (19, 162).

Epidemiology

The incidence of subependymomas is estimated as 0.2% - 0.7% of intracranial tumors. Matsumura et al (144) in an autopsy series of 1000 cases found that subependymoma accounted for 0.4% of the total. When the same authors analyzed 1000 surgical specimens, they found a percentage of 0.7%, which have been given the diagnosis of a subependymoma. This tumor type occurs most commonly in middle aged and elders (169) while few cases reported in children exist (25, 30, 131, 213). When this tumor type occurs in children, it usually occurs in adolescence or after 10 years. The most frequent location is the fourth ventricle accounting for 50-60% (190) while location at the lateral ventricles follows with (30%-40%).

Pathology

According to WHO latest classification scheme, subependymoma is assigned to WHO grade I since it shows benign features. Macroscopically, a subependymoma is usually a gray to white avascular lesion, attached to the ventricle wall by a pedicle. Microscopy reveals nuclei that resemble subependymal glia and multiple small cysts among a dense fibrillary matrix. Literature reports in a percentage of 10% a mixed type with the addition of ependymoma can be seen (116, 132, 133, 213).

Clinical presentation

The clinical presentation of subependymoma follows the general rules of intraventricular tumors with increased intracranial pressure and hydrocephalus signs and symptoms. Cranial nerve palsies with cerebellar signs can be observed when the tumor is located in the 4th ventricle (116, 190, 204).

Neuroimaging

Subependymoma is usually an intraventricular lobulated lesion with a narrow peduncle. The benign behavior of the tumor can be identified by the well-defined, tumor-parenchyma borders, which show no adjacent infiltration. Typically, the CT scan shows a isointense or a slightly hypointense lesion comparing to the parenchyma. Hydrocephalus (85%), calcification (about 32%) and cystic degeneration (18%) are common.

Magnetic resonance imaging renders subependymomas with low signal in T1W and high signal in T2W profiles. There are parts that show altered imaging appearance prior or after the utilization of paramagnetic contrast agents. The major differential diagnosis pitfalls can be observed when trying to differentiate subependymomas from ependymomas. We should always think that subependymomas are usually confined to the ventricle while ependymomas may show extraventricular extension (116).

Treatment and outcome

Subependymomas are WHO grade I tumors so a benign behavior is expected. Gross total resection and restoration of CSF flow are the gold standards that lead to excellent results. Even if partial resection is achieved the progression of the tumor is slow. The size and the location of the tumor should be considered when arranging the surgical plan. The role of radiotherapy remains unclear cause few cases have been observed while the opportunity for application in partial resection or recurrent cases must be considered (190).

Central neurocytoma

Central neurocytoma is a tumor that it derives from bipotential, progenitor cells originating from subependymal plate. Current literature suggests that these cells are capable of undergoing differentiation to neurons or glia (98, 116, 240, 243, 246). Hassoun et al (86) described the first cases of central neurocytomas in 1982. Central neurocytomas typically arise at the inferior septum pellucidum, near the foramen of Monro (233) or at the anterior lateral ventricle (87).

Epidemiology

Central neurocytomas account for 0.25-0.5% of all intracranial tumors (87). The age range between 20-40 years accounts for 75% of reported cases. The mean age at diagnosis is 29 years old (57). Rades et al (189) report that a review in the literature till 2004 revealed about 60 cases reported for patients under 19 years old, so this type of type of tumor is not common in pediatric population and should be considered a rarity. Rades at al report that children accounted for 17% in a meta-analysis of 438 patients with central neurocytomas (188). According to Waldron et al (247) and Hassoun et al (87) the most frequent site of seeding is the anterior lateral ventricle (77%) and the lateral and third ventricle appearance (21%) while few cases were reported in the fourth ventricle.

Pathology

The present (as of 2008) classification scheme, used by WHO, utilizes Grade II for Central Neurocytoma (133). The tumor is a discrete, solid mass with cystic regions and monomorphous cells. There is close resemblance to oligodendroglioma. The cells are round and the nuclei are usually oval so the classic "fried egg" appearance emerges. There are common calcification foci. There is immunoreactivity to synaptophysin and neuron-specific enolase, which are markers of the neuronal differentiation of the tumor.

Extraventricular neurocytomas are a variant categorized by WHO under Grade II and are found outside ventricular system as their name states. Favereaux et al (55) report few cases of a variant called "atypical" central neurocytoma that shows intermediate features between neurocytoma and neuroblastoma. Atypical neurocytomas show a MIB-1 labeling index > 3% and atypical histology and account for 20% of the total cases or 15% in children series (8, 187).

Clinical presentation

Central neurocytomas are intraventricular tumors so the main clinical picture is formed through the evolution of increased intracranial pressure. Headaches, visual disturbances, nausea and vomiting are common symptoms. Papilledema, ataxia, hemiparesis and alteration in the level of consciousness can be observed. Rarely, a patient with neurocytoma presents with a disastrous clinical picture in the form of intraventricular hemorrhage (125), intraparenchymal hemorrhage (235) or sudden death due to unopposed raise in the intraventricular pressure and subsequent brain herniation (116, 125).

Neuroimaging

The presentation and differential diagnosis of central neurocytomas (CMs) in neuroimaging modalities is challenging. In CT images central neurocytomas appear hyperattenuated comparing to the brain parenchyma, usually near the foramen of Monro. Post-contrast enhancement in CT images is of medium intensity while calcifications are present in about 50%.

Magnetic resonance images demonstrate high signal in T1W and T2W comparing to the adjacent white matter. The application of a paramagnetic substance leads to medium tumoral enhancement in MRI. The cystic parts of the tumor with the presence of adjacent flow voids render a heterogeneous picture.

Magnetic resonance spectroscopy of central neurocytomas shows high choline-to-creatinine and choline-to-N-acetylaspartate ratios (116).

Treatment and outcome

Central neurocytomas demonstrate favorable outcomes since they are considered benign tumors. Gross total resection is the gold rule. Rades et al (188) published the biggest, recent meta-analysis of 438 patients with a subgroup of 73 children (≤18 years) and showed that the 10-years overall survival in children was 100%, after complete total resection, complete total resection implementing radiation therapy and incomplete resection implementing radiation. The overall survival in ten years for incomplete resection alone was 82% in children. Radiation therapy after incomplete resection in children improves significantly local control but not overall survival. The dose that seems effective in children is 50Gy. Caution should be taken and more conservative treatment should be followed concerning the application of radiation therapy in children who have not achieved full height or are at high risk for developing cognitive dysfunctions (188, 189).

Meningioma

Intraventricular meningiomas arise from arachnoid cap cells contained within the choroid plexus (17), the tela choroidea, or the velum interpositum (221, 232). Meningiomas of the fourth ventricle arise from the choroid or the inferior tela choroidea (79). Left side localization predilection is observed (148).

Epidemiology

Pediatric meningiomas are quite rare tumors, accounting for less than 5% of pediatric brain tumors. In the group of meningiomas they account for 2% (12, 35, 56, 196). Intraventricular meningiomas are quite rare tumors accounting from 0.5% to 5% of all meningiomas (17, 116, 232). Pediatric patients show a higher incidence of intraventricular meningiomas from 5%-44% (5, 68, 74, 89, 129, 130, 205). In adult series, females predominate but this is not observed in pediatric series (56, 68, 138). Rare seeding sites are the 3rd or the 4th ventricle, while the atrium (trigone) of the lateral ventricle is the most common location (40, 89).

Pathology

Intraventricular meningiomas are generally benign tumors in adults, consisting mainly of fibroblastic, meningotheliomatous and psammomatous types, which belong to Grade I WHO classification (79, 133). The behavior of intraventricular meningiomas in pediatric population seems to be altered. Malignant behavior is observed more frequently (5, 40, 74, 129, 130). Pediatric intraventricular location may render sarcomatous changes (221). There is also an association with Neurofibromatosis type 2 (17) and radiation exposure (74).

Clinical presentation

Clinical characteristics appear through the expression of intracranial hypertension signs and symptoms. Intraventricular meningiomas appear frequently at the trigone. The trigone is in close relation to the hippocampus, part of the visual pathway and speech centers in the dominant hemisphere so site specific symptoms like temporal lobe seizures, psycho-organic syndromes, visual symptoms and speech dysfunctions may be observed more frequently. Headache is one of the most common symptoms presented in series (12, 17, 74, 113, 148).

Neuroimaging

Computerized tomography imaging demonstrates hyperattenuation, or calcification (50% of cases), with post contrast enhancement and well-circumscribed borders. Periventricular edema from CSF transependymal flow can be observed. The T1W MR images may be hypo- or isointense and show post-gadolinium enhancement. Occasionally cystic areas may be noted (116). Magnetic resonance spectroscopy can aid in diagnosis since high alanine to creatinine ratio can be a specific finding in meningiomas (137). Digital subtraction angiography can aid in recognizing the feeding vessel and provide an option of preoperative embolism when this is feasible (116).

Special considerations

The risk for the presence of a meningioma in a child is increased fourfold when there is a documented radiation exposure (157). So a child's history presenting with a meningioma should always include a research about previous radiation exposure (3). Neurofibromatosis type 2 (NF-2) is a medical condition that is associated with a variety of tumors and meningioma is a common type observed (53, 183). The prevalence of NF-2 in pediatric meningiomas patients is 25-40% (74).

Treatment

Gross total resection is the goal for intraventricular meningiomas since most of these tumors occur at the atrium of the lateral ventricle and can be accessed via microsurgical approaches. The identification of blood supply and the strategy of occluding the feeding vessels aid the total process of resection. Special considerations have to be taken because the optic radiation runs lateral and inferior to the atrium. When the tumor involves the dominant lobe, the preoperative check should include neuropsychological tests in order to assess a cognitive dysfunction postoperatively (17, 148).

Outcome

There is no detailed and specific research published concerning the outcome of pediatric intraventricular meningiomas. Research about pediatric meningiomas in general, indicates that subtotal excision, malignancy and neurological deficits are associated with poor outcome (5, 74, 130, 138).

Greene et al (74) identify a distinct behavior in radiation-induced meningiomas and NF-2 associated meningiomas comparing to spontaneous arising meningiomas. A less aggressive tendency is noted in radiation-induced and NF-2 associated meningiomas.

Craniopharyngioma

The origin of primary or "strict" intraventricular craniopharyngiomas was a hit to the theory of origin from remnants of Rathke pouch in the beginning. Later, a novel embryological theory for this subgroup was raised. According to Ciric (27), embryological events at the sellar-suprasellar region determine the location of the tumor. The development of the pial membrane from mesoderm normally excludes Rathke's pouch cells from subpial space in this region so if a craniopharyngioma develops it appears extraventricularly. In case the development of pial membrane is delayed then Rathke's pouch cells become implanted within the neuroectoderm of cerebral vesicle and thus they are located intraventricularly (13).

Epidemiology

Craniopharyngioma (CPG) is a common pediatric tumor observed in 1-2% of all intracranial neoplasms and in 50% of all suprasellar masses in children. The peak incidence is demonstrated between 5 and 10 years of age but a biphasic distribution is noted. The observed age-range in adults is from 50 to 60 years (90, 91). According to Suh et al (233) and Pascual et al (179), intraventricular CPGs account for approximately 5%-10% of all CPGs. Intraventricular craniopharyngiomas are considered "primary", when they are solely located in the third ventricle and the criteria set by Migliori et al (156) (intact 3rd ventricle floor, patent suprasellar cistern, normal pituitary stalk, absence of sellar abnormality) are met or "secondary", when they originate extraventricularly and invade the third ventricle. Pascual et al (179) proposed the definitions "strict" and "non-strict" respectively. A meta-analysis published in 2004 (179), reported 105 of "strict" or "non-strict" intraventricular craniopharyngiomas in adult and children. Fifteen pediatric cases, demonstrating a male predominance, were found (14.8% of the total), while 8 cases of them belonged to the strict intraventricular, pediatric craniopharyngioma group, demonstrating the rarity of this entity as also noted by Maira et al (135), in 2000 who report 30 purely intraventricular pediatric cases. So the data published by Pascual et al indicate that about 53% of pediatric intraventricular craniopharyngiomas (CPGs) are strictly defined as pure, primary intraventricular in location.

Pathology

Two types predominate. These are the classic adamantinomatous and the papillary type. Suh et al (233) report that the papillary type predominates in 3rd ventricular CPGs and accounts for 10% of total CPGs.

Papillary CPGs are usually solid, non-cystic, non-calcified neoplasms. They frequent in the adult group. Adamantinomatous CPGs are usually cystic, calcified and tend to recur. They usually appear in the suprasellar region and they are frequently met in the pediatric group.

Both tumor types show benign characteristics so WHO used Grade I for craniopharyngioma (133).

Clinical presentation

Their clinical presentation involves raised intracranial pressure, bifrontal headaches and visual disturbances (13). Headache is the most frequent symptom met. It is followed by visual disturbances and endocrine dysfunctions in supracellar CPGs in general but literature indicates that symptoms like mental and gait disturbances, memory dysfunction and somnolence show a rising frequency in the group of intraventricular CPGs (179).

Neuroimaging

The computerized tomography of a craniopharyngioma shows contrast heterogeneity and calcification especially if the tumor is of adamantinomatous type.

Neuroimaging usually reveals a cystic, calcified component with signal heterogeneity in MRI and strong post-gadolinium enhancement (13). The floor of the third ventricle should be intact if we want to be sure about the primary or else described "strict" intraventricular CPG according to Migliori et al (156) and Pascual et al (179). Great heterogeneity is demonstrated in both CT and MRI scans due to the various contrast intensity of tissues viewed (13).

Treatment and outcome

Few cases of pediatric intraventricular CPGs exist and CPGs are benign tumors thus gross total resection is the gold standard but caution should be taken since special considerations exist. Intraventricular CPGs are in close contact to noble tissues like hypothalamus, optic tract, fornices, nuclei of the diencephalos, so critical damage is possible while chasing the complete resection. We should also consider the relation of these tumors with a dense vascular brain territory crowded with vital vessels. Tumoral adhesions to noble tissues are frequently encountered and may lead to an increment in perioperative and postoperative morbidity with unfavorable results for a benign tumor. Non-strict intraventricular CPGs show a worse prognosis comparing to "strict" ones. Cautious surgical planning is needed and the decision of subtotal or partial removal should be considered in

cases that danger might lead to death. The role of stereotactic cyst aspiration and stereotactic radiotherapy is promising (17, 135, 179, 233).

Teratoma

Teratoma belongs to the group of germ cell tumors. This tumor type originates from three, fully differentiated germinal layers (ectoderm, mesoderm, endoderm) when it is identified as a "mature teratoma". Immature teratoma is a subtype that originates from more primitive elements of all or any of the three germinal layers (220). Teratocarcinoma, the last subtype, appears as a structure of cellular and tissue elements that show a more aggressive, malignant behavior comparing to the other subtypes (31, 220, 233).

Epidemiology

The incidence of intracranial teratomas is reported between 0.4 to 0.5% of all primary brain tumors (212, 222) in series including all age groups while few data exist for pediatric intracranial teratomas. According to Hunt et al (96), teratoma is the most common hemispheric tumor diagnosed in infants or neonates and the most common intracranial neoplasm diagnosed in stillborn neonates and babies. Fifty percent of teratomas are located in the midline and to the posterior region of the third ventricle (233). The pure intraventricular location of teratomas is a quite rare entity with few cases reported in adults and pediatric case reports. When a pure intraventricular location is observed, it is usually at the 3rd ventricle or the lateral ventricles (28, 29, 42, 52, 58, 71, 97, 103, 111, 122, 141, 158, 160, 168, 170, 181, 184, 192, 220, 239, 260, 265).

Pathology

Mature teratoma consists of fully differentiated cells and tissues from all three germinal layers. Endodermal, mesodermal, ectodermal elements belong to the structure of the tumor. Skin, skin adnexae or neural tissues may constitute parts of the observed ectoderm. There are reports of the observation of a mature brain structure. Cartilage, bone, fat, fibrous tissue and smooth muscle may represent the evolution of the mesoderm while epithelia of lung or gastrointestinal tract represent the endodermal part of the tumor.

Immature teratomas may originate from all three layers or some of them. Their histological appearance features primitive cells that are steps behind the complete differentiation. The lesser degree of differentiation equips this tumor subtype with a

malignant potential. Teratocarcinoma is the most aggressive tumor subtype among the total three subtypes of teratoma. It demonstrates malignancy, invasion patterns and results in unfavorable prognosis (31, 145, 220).

Clinical presentation

The clinical presentation of intraventricular teratomas is associated with increased intracranial pressure. Endocrinological dysfunction, like precocious puberty or diabetes insipidus may be observed, especially when the tumor is located in the third ventricle and thus exerts mass phenomena to the hypothalamo-hypophysial axis. Elevated levels of AFP may indicate malignancy (31, 90, 91, 220).

Neuroimaging

Mature teratomas may show calcification foci to the development of teeth elements or tissues with high calcium concentration so the CT imaging may identify these areas. Immature teratomas usually do not show calcification areas.

The magnetic resonance appearance shows great heterogeneity since a lot of tissues are involved in the structure of the tumor, with varying spin echo properties and thus varying signal distribution and intensity. Fat tissue component may be identified easily in T1W images (31).

Treatment and outcome

Mature teratomas demonstrate a distinct, circumscribed structure with benign features. The surgical resection of these tumors is aided by the existence of a surgical plane so a gross total resection can be achieved. Some immature teratomas can also be resected using an appropriate surgical plane. According to Weiner et al (249, 250), radiation therapy does not offer an advantage when it is applied to unresected tumors. Gross total resection of benign teratomas assures that postsurgical radiation therapy is not needed for these tumors (93). Matsutani et al (145), in a series of 147 adult and pediatric patients with intracranial germ cell tumors, found that the 10-year survival rate for 16 patients with mature teratoma who had been subjected to total or subtotal resection was 92.6%. In the same series, the overall 10-year, survival rate of 11 patients with malignant teratoma was 70.7% and the authors indicate that the extensive removal of the tumor and the application of postoperative radiation therapy and chemotherapy are effective for this subtype. The potential of immature teratomas to disseminate should always be considered and included in follow-up planning (31, 104, 145, 220).

Germinoma

The origin of extragonadal germ cell tumors is connected to primordial germ cells. When these cells migrate to the gonads can be misplaced. When these cells are misplaced they do not undergo the programmed cell death (apoptosis) and thus they seed ectopic germ cell tumor lines. Germinomas are a subset of germ cell tumors (4, 23, 218).

Epidemiology

North America and Europe report, that germ cell tumors of the CNS account for 0.1-2.4% of all childhood brain tumors. Japan and Far East report higher rates, since the reported rate is 2.1-9.4% according to the literature, which is much higher that the other world locations (93, 107). A recent multicentral retrospective research in Canada reports that the annual incidence of intracranial germinoma is 0.71±0.44 per 1,000,000 children under 18 years of age (107). Strong male predominance is noted and age groups around 10 and 30 years sum up the most cases of pineal region germinomas (233). The percentage of pediatric germinoma cases comparing to the total of germ cell tumors in childhood is 66-69% according to Hoffman et al (93) and Keene et al (107) and it is close to the percentage of 65% observed in all age groups as stated by Jennings et al (104). The most common location is the pineal region while suprasellar germinomas can be observed in the anterior part of the third ventricle when extension from the infundibular stalk has taken place (233, 251). Pure, primary intraventricular germinomas are rare since most of the cases are the result of extraventricular seeding and secondary ventricular invasion (10, 26, 36, 64, 99, 100, 104, 142, 200, 217, 236, 251, 262).

Pathology

Intracranial germinoma shows a solid, well-circumscribed appearance. Large cells can be observed with clear cytoplasm and round shape. There are calcification foci but this is not a property that aids the diagnosis when this tumor is located in the pineal region since it cannot be distinguished from normal pineal calcification. Occasionally, cysts can be found. There are few fibrous septa (242).

Clinical presentation

The clinical presentation of the tumor is a result of hydrocephalus. Papilledema can be observed, as well as nausea and vomiting. Visual loss due to papilledema or direct optic

pathway involvement can be a sign. Neuroendocrinological signs and symptoms like precocious puberty, diabetes insipidus or decreased libido are more frequently observed in these tumors since there is a hypothalo-hypophysial dysfunction (93, 145, 233).

Neuroimaging

Hyperdensity is a characteristic CT appearance for a germinoma. Magnetic resonance imaging demonstrates an isointense mass comparing to the adjacent parenchyma but T1W and T2W sequences cannot provide more differential information since the appearance is about the same in both of them. The utilization of paramagnetic substances provides a homogenous enhancement (233).

Treatment and outcome

The treatment planning concerning intracranial germinoma should be carefully tailored to each case since the histology of the tumor and the patterns identified can influence survival and treatment outcome. The first step involves the recognition of a pure intracranial germinoma from other germ cell tumors or a mixed type of tumor (e.g. choriocarcinoma, embryonal carcinoma). This decisive step is required since the response to radiation therapy or chemotherapy is unfavorable when other tumor subtypes coexist (145). Tumor markers in serum and CSF may aid the treatment planning and diagnosis. Placental alkaline phosphatase is increased in intracranial germinomas. Occasionally some variants of germinoma may demonstrate increased levels of HCGβ or human placental galactogen but this is not the rule (233).

Intracranial germinomas are radiosensitive and respond to chemotherapy so the treatment protocols used in the literature try to achieve the best survival, complication free and low recurrence rates by adjusting the radiation site, dose, or combining chemotherapy agents. Radiation therapy is assigned a pivotal role. Germinomas potentially disseminate through CSF to craniospinal axis so the craniospinal radiation protocol is one of the most common treatment modality met in the literature. The overall survival at 10 years is 90% (199). When microscopic or macroscopic CSF dissemination is present at diagnosis, the patient should receive craniospinal irradiation accompanied by radiation boost of at the tumoral bed and its metastatic sites. The overall, 5-year, survival with these practice approaches 97% (84).

Recently the literature tries to find alternative pathways in order to reduce the toxic radiation dose effects and implement local boost for local germinoma in radiation only protocols (199, 225). This treatment effort is of particular importance when the patients are children < 3 years old, an age group that radiation therapy may lead to cognitive

developmental problems as this complication was recognized in protocols for treatment of posterior fossa tumors (186, 230).

Cystic lesions

Colloid cysts

Midline cystic lesions in children may occur as autonomous entities or be a part of brain developmental anomalies (182). Colloid cysts of the third ventricle attribute to the 0.5-1% of all intracranial mass lesions. They appear rarely in pediatric population since 1-2% of them occur in patients younger than 10 years (227, 233). They arise from the anterior third of the third ventricle and two thirds of them show a hyperdense CT pattern due to their gelatinous fluid content (108, 182) while the MRI appearance may vary and it is associated with the content of the cyst. In a series of 262 tumors located in the third ventricle in adults and children reported by Lejeune et al (126), colloid cysts found in 55% of cases. Typically their clinical picture is formed with headaches and the "bobble-head doll syndrome", which is attributed to acute ventricular obstruction due to head position changes.

Treatment should aim at the microsurgical resection of the cyst since cyst aspiration lead to reaccumulation and recurrence. The approaches used are the transcallosal or the transcortical approach to the third ventricle. Neuroendoscopy may aid resection (43, 94).

Arachnoid cysts

Arachnoid cysts occur most often in the middle fossa (92). In rare cases they occur at intraventricular location. Most often this site is the lateral ventricle while cases in the third ventricle, or in the fourth ventricle are considered quite rare (45, 119, 182). A theory concerning the origin of intraventricular arachnoid cysts speculates that they rise from the invagination of the arachnoid through the choroidal fissure into the choroid plexus (165). Arachnoid cysts contain CSF-like fluid that resembles CSF appearance in neuroimaging modalities. They present with headaches, hydrocephalus, seizures or organic psychosomatic syndrome.

The treatment of intraventricular arachnoid cysts involves the fenestration of symptomatic cysts. Endoscopy, that aids in fenestration process or microsurgery via common approaches is utilized when total control of the processes is required (182).

Figures **2a**, **2b** and **2c** demonstrate a pediatric case of a lateral ventricular cyst with imaging characteristics of an arachnoid cyst. Neuroendoscopy defined the diagnosis of a post inflammatory cyst formation (Figure 2).

Choroid plexus cysts

Cysts of the choroids plexus are identified early in infancy. Their origin is neuroepithelial. The common seeding location of choroid plexus cysts lies in the lateral ventricle and they usually resolve while the child proceeds to adulthood. The clinical picture is formed by intermittent CSF obstruction at the foramen of Monro, that gives rise to spikes of intracranial hypertension (182). Neuroimaging shows CSF like properties of the cysts.

The treatment of choroid plexus cysts is the "watchful waiting" approach since a lot of them resolve as age progresses. Only symptomatic cysts require further microsurgical or neuroendoscopy approaches (182).

INFRATENTORIAL INTRAVENTRICULAR BRAIN TUMORS

Medulloblastoma

A lot of theories try to approach the origin of medulloblastoma. Bailey and Cushing (9) proposed that medulloblastoma rises from the "medulloblast". The "medulloblast" is an embryonal, undifferentiated cell at the external granular layer of the cerebellum with the potency to "create" other structular cells of the tumor. Another origin theory speculates that the external granular layer is the site of origin. This layer is formed from cells originating from the roof of the 4th ventricle and posterior medullary velum that migrate (109, 193). A third theory proposes that medulloblastomas are primitive neuroectodermal tumors of the posterior fossa (PNETs) (201). Finally the last theory sets aside the clonal origin of medulloblastoma and proposes that multiple cells are the origin of the tumor (69).

Epidemiology

The incidence of medulloblastoma ranges form 1 per 178,000 to 1 per 201,000 in the age group of 0-19 years (54). Medulloblastoma in general, is the most common malignant pediatric CNS tumor. Thirty eight percent of all pediatric posterior fossa tumors are attributed

to medulloblastomas (6, 54, 193). The age group 0-19 year accounts for the 77.4% of the total cases as showed in a wide adult-pediatric medulloblastoma clinical series by Roberts et al. The mean age of diagnosis in the pediatric group of the study was 7.4 years and a bimodal distribution with peaks at 3 and 7 years was observed. The seeding site of medulloblastoma is the cerebellar vermis in a percentage of 75%, while only 3% of the total medulloblastomas present with a solely 4th ventricular location (193).

Pathology

Medulloblastoma is a highly malignant central nervous system tumor that belongs to WHO Grade IV (133). The appearance of the tumor may vary among different subtypes-variants. According to the latest WHO classification the types-variants observed are: *classic*, *desmoplastic*, *large cell*, *anaplastic*, *medulloblastoma with extensive nodularity* (formely known as "extensively nodular with advanced neuronal differentiation" or "cerebellar neuroblastoma"), *medulloblastoma with myogenic differentiation* (formely known as "medullomyoblastoma") and *medulloblastoma with melanotic differentiation* (formely known as "melanotic medulloblastoma") (114, 133).

> Classic medulloblastoma. Shows areas of necrosis and increased mitosis of cells that grow in "sheet" pattern. Oval nuclei can be seen and neuroblastic or Homer-Wright rosettes are usual (69).

> Desmoplastic medulloblastoma. There are characteristic islands of cells surrounded by collagen fibers. Reticulin stains the fibers but the cell islands do not stain (69).

> Large cell medulloblastoma. This subtype is associated with the poorest prognosis and it is quite rare. We can observe large, round prominent nuclei surrounded by an abundant cytoplasm (114).

> Anaplastic Medulloblastoma. In the recent update of WHO the anaplastic medulloblastoma variant has been recognized. It shows pathology overlap with large cell medulloblastoma. High mitotic activity, nuclear molding, cell-cell wraping and atypic forms are the basic characteristics (134).

> Medulloblastoma with extensive nodularity. It is also formely known as "extensively nodular with advanced neuronal differentiation" or "cerebellar neuroblastoma". The latest WHO classification identifies this variant that resembles desmoplastic/nodular medulloblastoma. It occurs in infants and shows a lobular architecture. It shows more favorable outcome than classic medulloblastoma (134).

> Medulloblastoma with myogenic differentiation. It was known as "medullomyoblastoma" in previous classification schemes. Since this variant is not any more considered a distinct medulloblastoma entity, it is used as a descriptive term for other variants containing rhabdomyoblastic elements with immunoreactivity to desmin, myoglobin, fast myosin but not solely to smooth muscle α-actin (134).

> Medulloblastoma with melanotic differentiation. The previous classification scheme addressed this variant as "melanotic medulloblastoma". It is also a descriptive term for other variants and not a distinct entity. Strong expression of S-100 protein is observed and melanotic tumor cell may be undifferentiated or epithelial (134).

The various subtypes and variants describe the pathology heterogeneity of the malignant medulloblastoma. The treatment modalities utilized need a tumor-staging scheme in order to be applied adequately. Chang et al (24) developed the "Classification for cerebellar Medulloblastoma" in 1969, which is used today (see Table 1).

Clinical presentation

Their clinical picture consists of two axons. The first is the axis of raised intracranial pressure with a prominent hydrocephalus and abducens nerve or lower nerve palsies. The second axis involves the vermis and cerebellar hemisphere participation in the form of the characteristic truncal ataxia (vermis) or dysmetrias (cerebellar hemisphere). Headaches and intractable vomiting are the main symptoms and are interpreted as raised intracranial pressure and area postrema involvement (193). A clinical picture of acute level of consciousness deterioration is usually accompanied with extensive tumoral hemorrhage and death. The ability of dissemination of the tumor via CSF flow can result in spinal cord compression in case that the seeded tumor cells develop within the spinal canal (114).

Neuroimaging

The classic computed tomography appearance is a hyperattenuated well-circumscribed mass with surrounding vasogenic edema and posterior fossa compression with hydrocephalus (114). This mass is usually located at the vermis. Cyst formation (in 59%) or calcifications (in 22%) can be observed (167). Post-contrast enhancement is usually homogenous in CT imaging. Vasogenic edema is usually present.

Magnetic resonance images demonstrate iso- or hypointense signals comparing to white matter in T1W images. Magnetic resonance images using T2 repetition time demonstrate a signal heterogeneity or hyperintensity. Gadolinium enhances MR images of medulloblastomas but the pattern of enhancement does not follow the homogeneity of post-contrast CT images.

Magnetic resonance spectroscopy show high N-acetyl aspartate, high choline and high creatinine with occasionally lactic acid and lipid rising. This type of spectrogram can be identified in neuroectodermal tumors and does not differentiate medulloblastoma in this group (114).

Special considerations

Medulloblastoma is a highly malignant tumor. The malignant potential is expressed through its pathology profile as well as its CSF dissemination properties. Unfortunately the percentage of leptomeningeal seeding at the time of diagnosis according to David et al (38) rises to 33% in children. This feature should lead us to MRI scanning of the craniosacral axon in order to reveal occult malignant seeding sites. The dissemination property is attributed to the malignant potential of the tumor but in a percentage up to 20% is associated with CSF diversion procedures since hydrocephalus is a common clinical feature (193). Leptomeningeal seeding is associated with poorer prognosis according to Meyers et al (155), while a recent publication from a single institution, by Kombogiorgas et al did not find survival influences (117). Apart from the neuroimaging proof of leptomeningeal dissemination, CSF samples should be collected 2 weeks postoperatively in order to be scanned for tumor cells (33).

Medulloblastoma can also give rise to extraneural spread. It is a quite rare complication, which is associated with young age and leptomeningeal dissemination (197).

Treatment and Outcome

Maximum surgical resection is the goal set in the treatment of medulloblastoma. The approach usually used is the midline suboccipital approach when the tumor is located mainly in the fourth ventricle or lateral approaches in cases with a lateral tumor growth. Adjuvant therapies in the form of chemotherapy or radiation therapy are utilized in various protocols in order to achieve the best survival rates, low recurrence rates and adequate neurological function outcome. The proximity of the seeding location of the tumor to CSF pathways may lead to hydrocephalus so adequate reestablishment of the normal CSF flow is imperative. About 30% of patients will undergo a shunt operation due to CSF pathway scarring (33).

Children with a 4th ventricle medulloblastoma that is confined to the ventricle or it is a result of ventricular invasion or children less that 2 years old, are considered high risk patients (193). Intraventricular medulloblastoma requires special attention since hydrocephalus is almost a definite fact, neurological deterioration and possible death from herniation are more possible scenarios and seeding of the tumor via CSF flow and pathways is almost certain (114, 193, 210).

Post-surgical posterior fossa mutism syndrome is a post-operative complication that occurs frequently in children operated for medulloblastoma. Up to 50% of patients may have long-term speech and language apraxia. It is associated with preoperative brainstem invasion of the tumor and surgical damage to the vermis as a provocative factor (194).

The key concept in treatment of children medulloblastoma is the age group and the existence of disseminated disease according to Crawford et al (33). After the initial surgical

resection of the tumor there are guidelines of treatment concerning the utilization and the timing of application chemotherapy or radiotherapy. Children who receive adjuvant therapy showed an approximately four times higher instantaneous rate of remaining alive than those who did not in a series of children with medulloblastoma in Greece (161).

Children less than 3 years. This is a special group of patients that shows the worst prognosis and is sensitive to cognitive complications due to radiation brain-spinal therapy so the latter treatment modality is usually not used in this group or delayed (33, 210, 248).

Disseminated disease. In case of disseminated disease the child after the surgical resection should follow chemotherapy with or without methotrexate. The next step is local or craniospinal radiotherapy and targeted therapy in agreement with the tumor's biological regime. The 5-year, event-free, survival in this group is < 20% (33).

Non disseminated disease. The children of this group should follow chemotherapy and there is a strong debate concerning the timing. Should chemotherapy used after radiation? The answer remains unclear. The radiotherapy utilization in means of craniospinal or local exposure is a practice not yet determined through the literature. The desmoplastic variant is a predictor of better survival. The 5-year, event-free, survival in this group with desmoplastic variant approaches 60% while 20-40% 5-year, event-free, survival is observed in other tumor subtypes (33). Dhall et al (44) report that all patients in this group show a 52% 5-year, event-free, survival with 70% overall survival. When gross total resection is examined the 5-year, event-free, survival is about 64% and overall survival 79%. In this series, when residual tumor group is studied, it shows 29% 5-year, event-free, and 57% overall survival.

Children older than 3 years. This group shows the best survival rates. The presence of dissemination plays an important role in this age group too.

Disseminated disease. Radiation therapy is utilized with 36-39.6 Gy craniospinal and 55.8 Gy local tumor boost. There is a concern about the timing of chemotherapy. Should it be used before, during or after radiotherapy ? The answer raises great controversies. Of course the treatment options should be tailored to tumor's biological profile. This group shows 50-60% event-free survival (33).

Non-disseminated disease. Radiation protocols are usually less intensive in this group. Craniospinal irradiation is achieved with 23.4 Gy with 55.8 Gy local tumor boost. Chemotherapy follows radiation therapy. The event free survival approaches 80%(33).

Future considerations

There are evolving treatment strategies and options that draw the vivid future of medulloblastoma treatment. A lot of treatment promising new protocols try to utilize intensive chemotherapy only, while neglecting radiation therapy due to age limitations (33). Rutkowski et al (207) report a series with post-operative chemotherapy and intraventricular

methotrexate only with a 5-year, event-free survival 82% and 93% overall survival for gross total resection, 50% and 56% for residual tumor and 33% and 38% for macroscopic metastases respectively. These results are much higher that the mean found at the literature but are accompanied with high rates of cognitive dysfunction due to leukoencephalopathy (206).

A lot of effort is directed to molecular biology risk and survival stratification with TrkC presence favoring prognosis and c-Myc presence leading to unfavorable outcome (33, 208).

Future treatment strategies try to take advantage of the evidence governing the tumorigenesis and tumor progression of medulloblastoma, involving the "hedgehog pathway" (16), TrkC receptors, Wnt receptors, retinoids, Notch/CXCR4 pathways and inhibitors of apoptosis (33).

Ependymoma

Intracranial ependymoma is thought to arise from embryonic rests of ependymal tissue trapped within the developing cerebral hemispheres. When the tumor originates from the 4th ventricle it is usually seeded from its floor or roof. The foramen of Luschka aids the extension of the tumor to the cerebellopontine angle or to the foramen magnum (255).

Epidemiology

Intracranial ependymomas account for a percentage of 2-9% of pediatric brain tumors (73, 81) and almost one-third of all brain tumors in patients younger than 3 years (255). They rank in the third place of pediatric primary brain tumors behind pilocytic astrocytomas and medulloblastomas (166). Ependymomas can be found in a percentage of 33% of all brain tumors in patients younger than 3 years (116, 255).

The fourth ventricle predominates in location since 58-66% of ependymomas are seeded at this site. This is the typical location for most pediatric cases (159, 214, 215). The supratentorial location of ependymomas is associated with older children and adults while half of them involve the parenchyma (219, 247).

Pathology

Intracranial ependymomas are classified as WHO grade II tumors, while a more aggressive tumor type named "anaplastic ependymoma" is classified as WHO grade III (133).

Ependymomas are divided in 4 subtypes. These are the cellular, the papillary, the clear cell and the tanycytic ependymoma types (133). Ependymomas are rubbery, soft masses that may include calcification areas. Lobes are observed when these lesions appear in the ventricle. Perivascular pseudorosettes are characteristic features of the tumor especially when the glial form predominates. True ependymal rosettes and occasional necrosis areas can be identified. Nuclear grooves can also be observed. Nuclei are round or oval shaped with a distinct nucleolus. Clear cell ependymomas are rare but they show increased mitotic activity and thus higher grade of malignancy. Tanycytic ependymomas resemble pilocytic astrocytomas and they demonstrate highly fibrillary characteristics. Malignant potential is low since this tumor type does not show increased mitosis. Ependymomas can be calcified or exhibit osseous or cartilaginous metaplasia (247).

Anaplastic ependymoma (WHO Grade III) exhibits malignancy though its high cellular appearance, its increased mitosis and its augmented vascular proliferation. Necrosis areas are common and prognosis unfavorable. This tumors type is more frequent in children (116).

The pathology differential diagnosis of ependymomas includes medulloblastoma in the posterior fossa, pilocytic astrocytomas of the cerebellum or brainstem, subependymoma in supratentorial location, oligodendroglioma or central neurocytoma (247).

Clinical presentation

The signs and symptoms are related to increased intracranial pressure and cerebellar involvement since this tumor is usually located in the 4th ventricle. Nausea, vomiting, headache are common. Ataxia, deterioration of the level of consciousness and dysmetrias with lower cranial nerve palsies can be observed with 4th ventricle involvement. In children with age below 2 years, common signs and symptom are vomiting, lethargy, irritability and failure to thrive as demonstrated in growth curves (110, 116, 255).

Neuroimaging

The CT appearance of intracranial ependymomas is an isoattenuated lesion with foci of calcification (40-80%). The tumor is heterogenous so its soft component is usually hypoattenuated or isoattenuated comparing to the adjacent brain parenchyma. Cysts and hemorrhage are quite common. When a contrast agent is used the heterogeneity of tumor is reflected in the variety of contrast enhancement. Supratentorial ependymomas are usually primary extraventricular and cystic.

Magnetic resonance appearance is usually heterogeneous. Isointense appearance is prominent in T1W images while T2W images demonstrate hyperintense areas comparing to the grey matter. The utilization of a paramagnetic contrast agent reveals a varying contrast

distribution (116). A characteristic finding of a 4th ventricular ependymoma, that is occasionally seen, is the caudal extension of the tumor through the foramen of Magendie in the cervical subarachnoid space or its extension to the cerebellopontine cistern via Luschka foramen (110). Neuraxis dissemination can be present at the time of diagnosis although it is observed in a small percentage (about 5%) comparing to medulloblastomas (153).

Treatment and Outcome

Gross total resection is the first step that has to be accomplished when treating pediatric intracranial ependymomas. Literature shows (106, 198), that gross total resection influences overall survival and progression free survival in children with intracranial ependymomas since it provides us with more favorable outcome than partial resection of the tumor (51, 166, 195, 203). Interestingly the success rate for a gross total resection ranges from 53%-72% concerning supratentorial ependymomas and 27%-55% for infratentorial ependymomas (110).

The standard approaches for supratentorial and infratentorial ependymomas are used with low operative mortality but result in high morbidity for infratentorial 4th ventricle ependymomas. The close relation of these lesions to cranial nerve nuclei at the 4th ventricle may give rise to dysfunction that affects swallowing and vocal cord paralysis (153).

Hydrocephalus is an entity that accompanies ependymomas especially when they are located in the 4th ventricle. The resection of the tumor can usually restore the flow of the CSF (51). About 80% of patients will be shunt-free after a surgical resection of an ependymoma (238). Preoperative shunting is not indicated (except from imminent herniation) cause it may lead to opposite results like an upward brain herniation (51).

Tumor type is associated with overall survival, progression-free survival (106, 153) and recurrence when the molecular biology profile of the tumor is considered (203). Recurrence is associated strongly with the age of the patient, the location of the tumor and the extent of resection (245).

Children > 3 years. Radiation therapy (RT) has been implemented with success in the treatment protocol of pediatric intracranial ependymomas after surgery (153). There is evidence of response to radiation therapy doses of 45Gy to 50Gy (72, 203). The combination of maximal feasible extent of tumor resection with postsurgical radiotherapy has led to 5-year, progression-free survivals of 50-60% for adults and children > 3years(153). Chemotherapy protocols fail to prove their significance concerning the improvement of survival (18, 75) but promising protocols emerge (264) while the role in the treatment of children < 3 years for delaying the exposure of this group to radiation therapy has to be possibly reconsidered (76, 252). Recent advances in neuroimaging, radiation therapy protocols and operative techniques implementing extensive tumor resection have led to the

improvement of outcome as this is demonstrated in latest trials CCSG-9945 (67) and St. Jude RT-1 trial (120), so the 3-year, progression-free survival rates approximates 75% (153).

Children < 3 years. This pediatric group encounters special difficulties in the utilization of treatment algorithms since radiation therapy has been associated with cognitive dysfunction in children with a developing brain (77). The survival rates reported in the literature are much worse for this group. Healy et (88) reported that the survival rates at 12 years for children younger than 24 months at diagnosis was 0% compared to 68% for younger children, while Pollack et al (185) observed a 22%, 5-year, overall survival for children < 3 years comparing to 75% for older children (110). A trial conducted in St. Jude by Korshunov et al (120) showed promising results when combining surgical resection and radiation therapy in this group and opened a new road to the implementation of radiation therapy. Improved rates of disease control as well as excellent functional outcomes were observed in 48 children. This trial was the trigger for an ongoing trial from Children's Oncology Group (152) with an estimated completion in October 2008, concerning treatment options in childhood ependymoma. Chemotherapy may have a role in delaying the application of radiation therapy at the developing brain as shown on French and Australian working groups (76, 252).

OTHER TUMOR TYPES

Literature concerning pediatric and adult intraventricular tumors includes some tumor types, that are rarely observed such as PNET (233), DNET (85), ganglioglioma (101), ganglioneurocytoma, epidermoid (150) and dermoid tumors (136), oligodendroglioma (48), sarcoma(228), glioblastoma (112), rhabdoid tumor (2). Vascular malformations like AVMs are also reported showing an uncommon intraventricular location (160). Central nervous system parasitoses, like neurocysticercosis (32, 237) and hydatid cysts(82) can also be found in the ventricles mimicking tumor seeds. Metastases also can be observed in the ventricles extremely rarely in children (103, 116, 160, 191).

CONCLUSION

Intraventricular brain tumors in children are a distinct group of tumors, which demonstrates specific characteristics concerning their challenging differential diagnosis. The neurosurgeon should undertake two major steps in aiding this difficult step. The first step is the definition of the age group. The second step should implement information obtained from neuroimaging studies that limit the possible diagnoses in a primary location manner like supratentorial or infratentorial tumors, tumors of the body, tumors of the third ventricle or tumors at the trigone of lateral ventricles. The distribution of frequency of pediatric intraventricular tumors as represented through the current literature reviewed is illustrated in Figure 3.

The clinical picture does not significantly contribute to the differential diagnosis since symptoms of raised intracranial pressure and hydrocephalus are common in most of these tumors while non specific signs and symptoms e.g. nausea and vomiting can often mislead when attributed to other more common diseases like gastroenteritis.

We should always consider the possibility of a malignant tumor when we find a 4th ventricular mass in a child. This is the most common location for malignant medulloblastoma and ependymoma in children. Common tumors with supratentorial location are choroid plexus tumors and subependymal giant cell astrocytomas (SEGA). The aid in the differential diagnosis concerning these tumor types should be their seeding location and associated syndromes. We should meticulously search for neurocutaneous stigmata, mental retardation and seizure episodes when we think of SEGAs and vice versa. Their common calcified appearence near the foramen of Monro should lead us to correct diagnosis when compared to the trigonal predilection found in choroids plexus tumors.

TABLES

TABLE 1
Classification for Cerebellar Medulloblastoma according to Chang et al (24)

Stage	Feature
T1	< 3cm diameter; limited to vermis, roof of 4th ventricle, or hemisphere
T2	> 3cm diameter; invades one adjacent structure or partially fills 4th ventricle
T3a	Invades two adjacent structures or completely fills 4th ventricle with extension into cerebral aqueduct, foramen of Luschka or Magendie
T3b	Arises from floor of 4th ventricle or brainstem; 4th ventricle completely filled
T4	Spreads to involve cerebral aqueduct, third ventricle, midbrain, or upper cervical cord
Metastasis stage	
M0	No evidence of metastasis
M1	Tumor cells in CSF
M2	Gross nodular seeding of brain CSF spaces
M3	Gross nodular seeding of spinal CSF space
M4	Extraneural spread

FIGURES

Figure 1
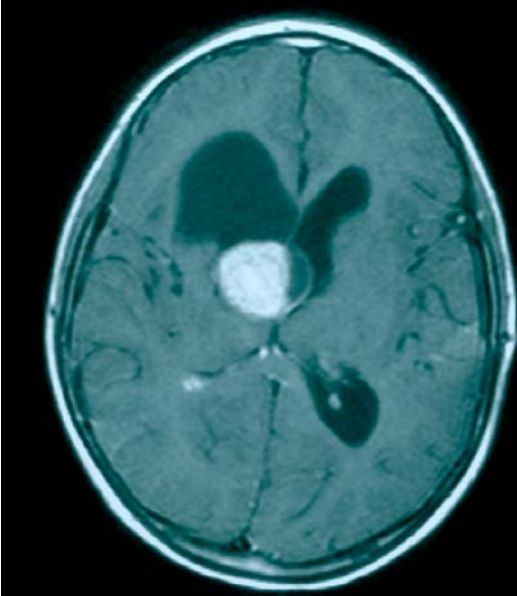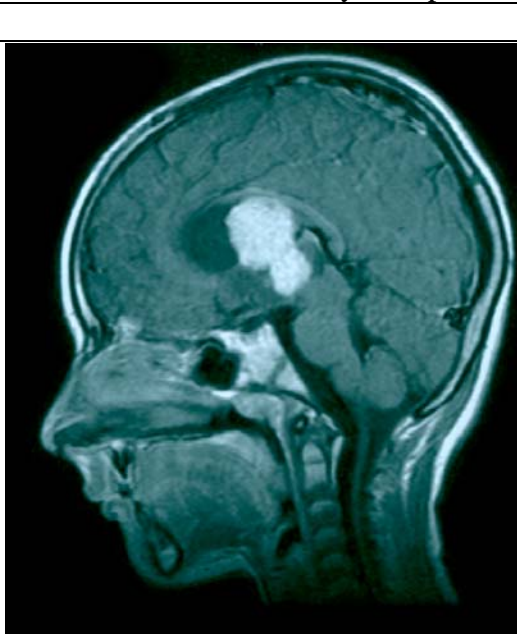

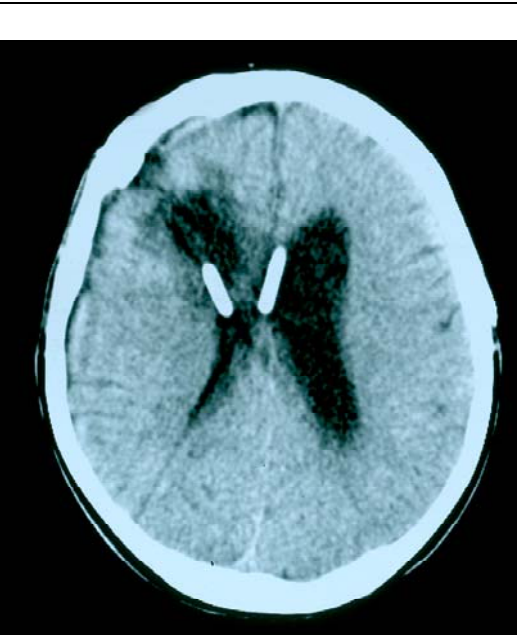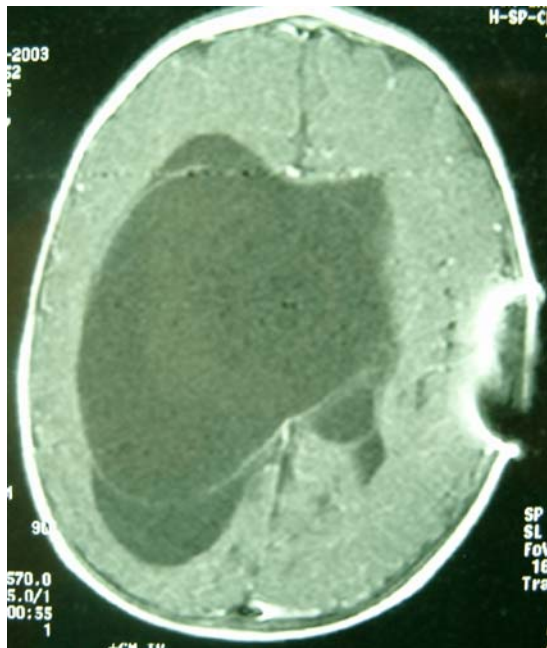|	
FIGURE 1a *MRI T1W Transverse plane* A 5-year old child with a subependymal giant cell astrocytoma near the foramen of Monro and obstructive hydrocephalus.	**FIGURE 1b** *MRI T1W Coronal plane*
FIGURE 1c *MRI T1W Sagittal plane*	**FIGURE 1d** *CT scan Coronal plane* Follow-up imaging with complete resection of the tumor and bilateral ventriculoperitoneal shunt

Figure 2

FIGURE 2a
MRI T1W Transverse plane
A giant cyst of the lateral ventricle
presented in a 9-month infant, initially
considered an arachnoid cyst.
Neuroendoscopically proved to be a post
infectious cyst.
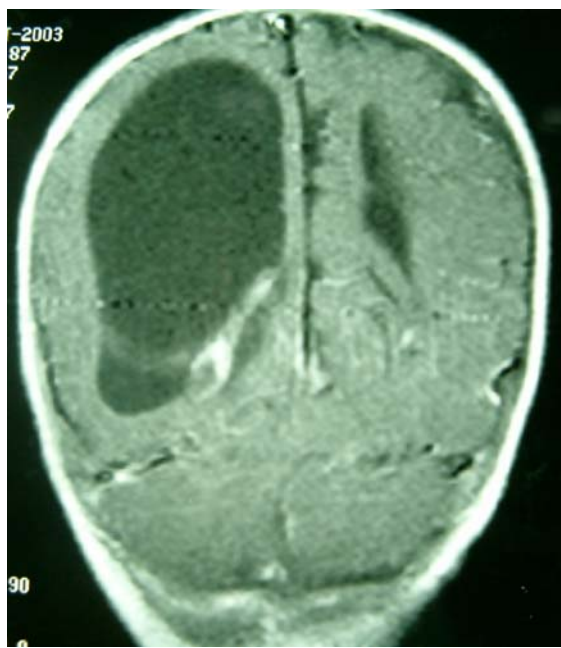
FIGURE 2b
MRI T1W Coronal plane

FIGURE 2c
MRI T1W Sagittal plane

Figure 3

Filippidis AS, Tsonidis CA: Intraventricular brain tumors in children, in Narenthiran G (ed): *Textbook of Paediatric Neurosurgery*. Sutton, UK, G Narenthiran, 2008.© Annals of Neurosurgery

*SGCAs = Subependymal Giant Cell Astrocytomas

modified Gray's Anatomy ventricular pictures from the 20th U.S. edition of Gray's Anatomy of the Human Body, originally published in 1918 and therefore lapsed into the public domain
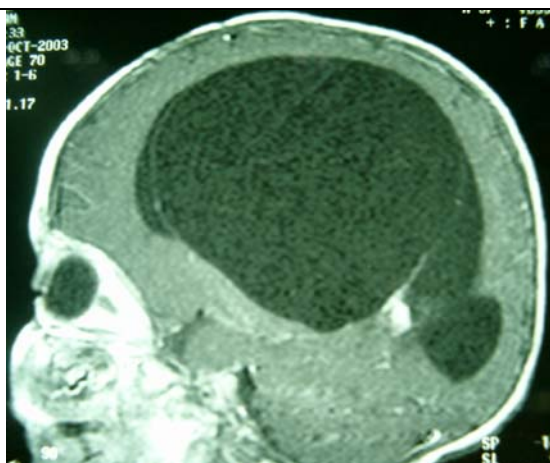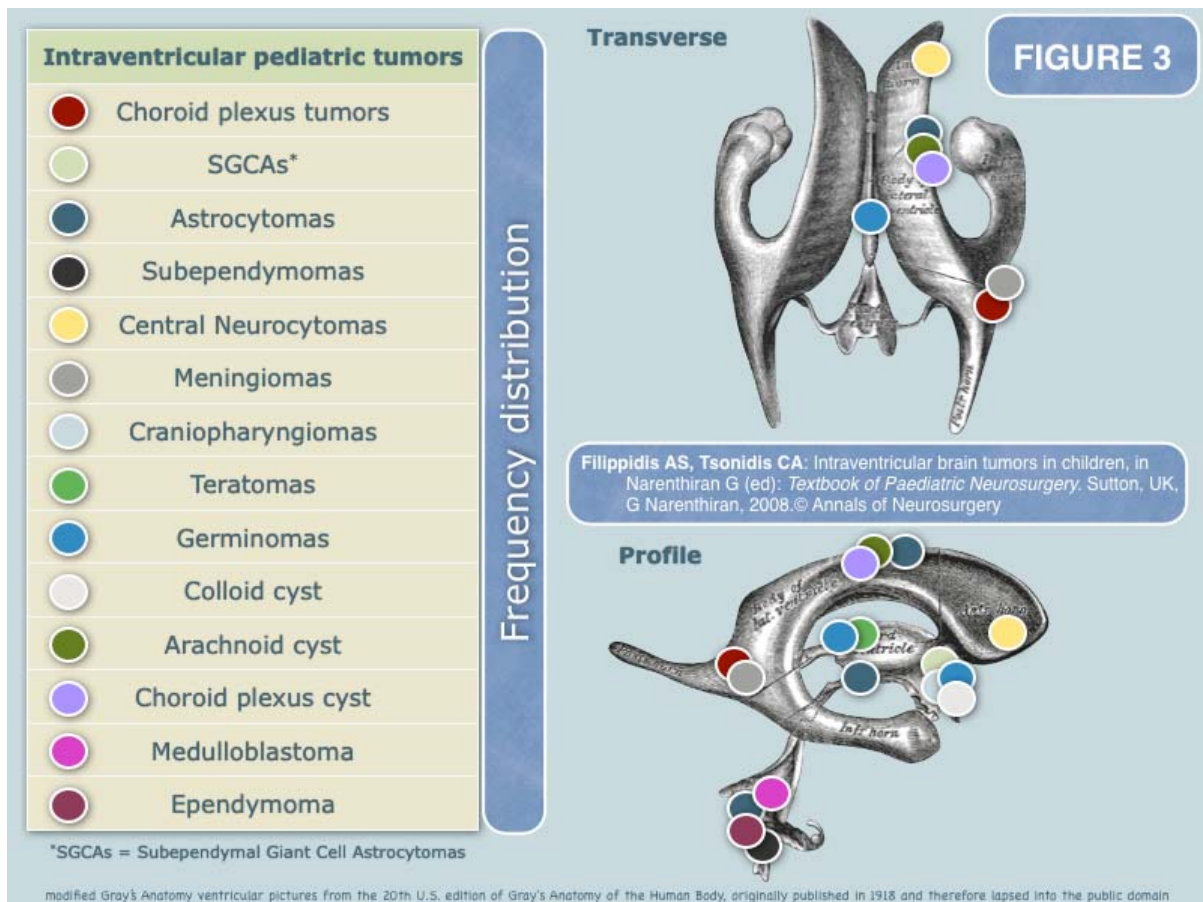
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