Posterior fossa brain tumors in children

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Abstract

Posterior fossa is the most common site for brain tumors in the first decade of life. Tumors occurring in this area are usually of either neuronal or glial origin. The common tumors include pilocytic astrocytoma, medulloblastoma, ependymoma, brainstem glioma and rarely atypical rhabdoid teratoid tumors. These account for approximately 50 to 55% of all tumors found in childhood. Less frequently, hemangioblastomas, dermoids, or arachnoid cysts are also encountered. In the Indian subcontinent, tuberculoma is an important entity and must be considered in the differential diagnosis of posterior fosss masses in children.[1]

Key words: children, infratentorial, posterior fossa, surgery, tumor.

Introduction

Posterior fossa is a limited spatial cavity bounded by the petrous bones superolaterally and the foramen magnum inferiorly which contains brainstem,cerebellum,vertebrobasilar circulation and 5th to 12th cranial nerves. The posterior fossa contents are concerned mainly with the maintenance of consciousness, respiration, pulse, blood pressure, facial expression and sensations, hearing and swallowing mechanisms. The common tumors arising in posterior fossa usually involve these vital structures or compress them compromising the above mentioned functions leading to severe disability, morbidity and fatality. Since posterior fossa is a limited space, the tumors presenting in this region cause early symptoms and require prompt treatment to avoid potential morbidity and mortality. Early detection and diagnosis of these tumors and prompt neurosurgical consultation is crucial in the optimum management of pediatric infratentorial brain tumors.

Medulloblastoma

Medulloblastoma is the most common brain tumor in children. It accounts for 90% of embryonic tumors[2].Of all childhood brain tumors, the most dramatic change in survival have occurred with medulloblastomas. The increase in survival occurred as a result of more aggressive neurosurgery and the administration of high dose radiation to the tumor bed coupled with craniospinal irradiation[3].

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Epidemiology

Medulloblastoma is 1.75-times more common in white people than black people, it occurs predominantly in males (male-female ratio is 1.4:1.0) and at a median age of 5 to 7 years[2]. In 1-2% of patients, medulloblatoma is associated with Gorlin's syndrome-a nevoid basal carcinoma syndrome that is diagnosed by characteristic dermatological and skeletal features. Medulloblastoma also occurs in up to 40% of patients with familial adenomatosis polyposis due to gene mutations on chromosome 5q21 (Turcot's syndrome) [4, 5]. Disseminated disease along the craniospinal axis is found in 11-43% of patients and is one of the most important predictors of outcome.

Molecular biology of medulloblastoma

Medulloblastoma is postulated to arise from the two germinomal zones of the cerebellum; the ventricular zone, which contains multipotential stem progenitors, for classic and midline tumors, and the external granular layer for the less common, laterally placed and often desmoplastic tumors that possibly arise from more restricted neuronal progenitor cells. Although pathologists have more than 50 years

of experience with this tumor, there is no consensus as to the origin of medulloblastoma[6]. The tumor was termed medulloblastoma by Bailey because he believed that the neoplasm consisted of embryonic stem cells with pleuripotent nature[7]. However, the medulloblast, as a normally occurring cell capable of differentiating along multiple cell lines, has never been satisfactorily identified. As such, present day pathologists believe that the medulloblastoma is a primitive neuroectodermal tumor with nonspecific differentiation. Detailed histologic analysis reveals that these tumors may differentiate along ependymal, astroglial, or neuroblastic cell lines. These observations support the concept that the medulloblastoma may represent a tumor of stem cell origin[4, 6].

Pathology

Medulloblastoma is currently divided into WHO-defined subsets-which include classic medulloblastoma and the large cell anaplastic, desmoplastic, medullomyoblastoma, and melanotic variants- on the basis of light microscopy and immunohistochemical findings. For clinical purpose patients are mostly separated into classic, desmoplastic, anaplastic or large-cell, and nodular variants[4]. Sheet like areas of small, round, blue cells with scant cytoplasm and dense hyperchromatic nuclei are the hallmark features of classic, undifferentiated medulloblastoma. Homer-Wright rosette patterns, consisting of a circular nuclear array with tangled cytoplasm, are seen in less than half of medulloblastomas. Mitosis is seen in up to 80% of tumors, as assessed by positive staining with Ki-67/MIBI antibody[8, 9]. Medulloblastomas are frequently positive for vimentin and synaptophysin staining[10, 11]. The desmoplastic medulloblastoma variant is composed of highly proliferative, densely packed, reticulin-rich, mitotically active areas that surround reticulin-free nodules. Desmoplastic variants are seen in up to 50% of adult cases of medulloblastomas compared with 15% in children[12].

The large cell anaplastic variant is the most malignant and accounts for 4% of cases. Histological examinations shows lobular sheets of large round cells with abundant cytoplasm, prominent nucleoli, and pleomorphic nuclei. Large areas of necrosis with high mitotic and apoptotic rates are also seen. Large cell medulloblastoma can arise from an anaplastic background of markedly atypical neoplastic tissue and is thought to be closely related to the anaplastic variant[13, 14].

The other two variants of medulloblastoma are extremely rare: melanotic medulloblastoma consists of accumulated melanotic tumor cells, whereas medullomyoblastoma contains areas of focal myogenic differentiation[15, 16].

Medulloblastomas occurring in the midline tend to be soft, fleshy and well demarcated; haemorrhage, cyst formation, and calcification are uncommon.[8,9]. Little consensus exists over the prognostic impact of pathologic variables like mitotic index and nuclear features. Current staging regimens are based solely on clinical criteria. Some work suggested that c-myc amplification may be associated with aggressive behavior and that the presence of this oncogene in medulloblastomas, as with N-myc amplification in neuroblastomas, has an adverse impact on prognosis[17, 18]. As with other primitive tumors, medulloblastomas tend to seed the subarachnoid space, both locally and distally. Approximately 70-80% recur initially in the posterior fossa. Recurrence in the area of the cribriform plate has been related to the failure to adequately irradiate this region. Extraneural metastasis is well documented and in some series approaches 5-30%. The primary sites of extraneural metastasis are bone and bone marrow[19, 20].

Clinical presentation

Patients with medulloblastoma frequently present with obstructive hydrocephalus, an increase in head circumference in children whose fontanelles are still open, and early morning headache with vomiting (60%), ataxia (40%), and nausea (39%) are the predominant symptoms. Involvement of lateral cerebellum is rare in children compared with adults (10 vs. 50%) and can lead to more obvious appendicular ataxia and dysmetria[21, 22]. Interestingly, there is an inverse relation between the duration of symptoms and stage of medulloblastoma[23]. Head tilt may occur secondary to ophthalmoparesis or incipient cerebellar herniation. This finding may

accompany or precede other signs and may be associated with neck stiffness. Nystagmus is absent or mild in nature[24].

Diagnosis

CT is usually the first line neuroimging modality for patients with posterior fossa tumors because of its availability in an emergency setting. Atypical (only 30-55% of patients) feature of medulloblastoma seen with CT is a midline, homogenous, contrast enhancing cerebellar vermian mass. Atypical CT features include cystic changes, hypodense non-enhancing lesions, and calcifications[25, 26].

MRI features include a heterogeneous hypo intense mass on T1-weighted imaging. On T2 weighted sequences, medulloblastomas are intermediate between grey and white matter, which is a feature that distinguishes medulloblastomas from other CNS tumors that show T2-weighted hyperntensity compared with grey matter. Contrast enhancement of medulloblastomas is heterogeneous; however atypical features of homogenous or patchy enhancement can occur (Fig.1). Drop metastases, occur in up to 40% of patients, most commonly seen in lumbosacral and thoracic areas and are best seen on post contrast T1-weighted images. Drop metastases have a "zuckerguss" (icing sugar) appearance. Therefore it is imperative to have MRI of the spine before and after treatment for comparison[27].

Other imaging modalities such as magnetic resonance spectroscopy (MRS), PET, and single photon emission computed tomography (SPECT) are used as clinical aid to distinguish tumor recurrence from post radiotherapy necrosis and gliosis[28].Occasionally, decreased taurine, which is usually raised in astrocytomas, is a feature of medulloblastoma seen on MRS[29].

Newer imaging modalities, such as diffusion tensor imaging, have been studied for preoperative and postoperative assessment of corticospinal tract invasion in tumors invading brain stem[30].

Management

Staging and risk stratification

The Chang staging system has been modified to incorporate information from neuroimaging to identify risk categories on the basis of age, the degree of resection, and disease dissemination. Analysis of the CSF and contrast enhanced MRI of the brain and entire spine is included. CSF should be obtained from the lumbar region 2 weeks postoperatively to avoid the false-positive cytology from initial resection. Upto 10% of adults and 30% of children have evidence of disseminated disease at presentation. M0 staging is assigned if there is no evidence of disseminated disease whereas M1 denotes malignant cells in the CSF. Patients with tumors seen on MRI have M2-M3 classification. M4 staging is assigned if there is extra neural spread usually seen in infants and less than 1% of all patients with medulloblastoma[31, 32, 33, 34]. Patients older than 3 years of age who have no evidence of tumor after surgery and no evidence of metastasis throughout the subarachnoid space have good results [31, 32, 33, 34].

Surgery

Cushing[7] proposed radical excision of medulloblastoma in 1930. Aggressive surgery without compromising function provides pathologic diagnosis and reestablishes CSF pathway. A CSF diversion procedure should be avoided to prevent a possible portal for extra neural metastasis[35].In children of age less than 3 year gross total resection strongly correlated with improved survival[36]. Recent studies have postulated a safe radical removal of the tumor without endangering life or causing significant morbidity. The mortality rate from surgical treatment ranges from 1% to 5%.

A sample of CSF to stage the medulloblastoma can usually be obtained safely from the lumbar region 2 weeks after surgery[37]. Surgical morbidities can be infectious (aseptic or septic meningitis) or non-infectious (CSF leak or pseudomeningocele). In 8-38% of patients with midline cerebellar tumors is posterior fossa

mutism syndrome, which typically occurs in younger patients with high risk disease. Mutism develops over 48-72 hours after resection of the tumor and can persist from weeks to months, with associated findings of dysmetria, hypotonia, dysphagia, hemiparesis, and increased mood lability. Upto 50% of patients have long term speech and language apraxia. Preoperative brainstem invasion was the only feature that was associated with a risk of posterior fossa mutism syndrome. The proposed neurophysiologic mechanism is the disruption of the dentatorubrothalamic pathways to the supplementary motor cortex, secondary to surgically induced vermian damage, leading to global akinesia and speech apraxia[38, 39].

Radiation therapy

Current recommended doses are 5000 to 6000 Gy to the posterior fossa and 3500Gy to the craniospinal axis. In cases of recurrence of medulloblastoma repeat surgery improves the prognosis[40]. Radiation therapy in young children causes severe neurological morbidity; hence radiation therapy is delayed or not given to children younger than 3 years[36]. The aim of craniospinal irradiation is to obliterate potential microscopic disease that is not detected in the CSF or with MRI. The 5-year event-free survival rate is 60%. The deleterious side effects of radiation therapy, including neurocognitive decline and endocrinopathies, have led to reduction in dose of radiation therapy given to patients with average-risk medulloblastoma. For patients with high-risk, disseminated disease there is no evidence that the dose or volume of radiotherapy can be reduced[3].Adjuvant chemotherapy with reduced dose radiation therapy is now the mainstay of conventional treatment for patients with average-risk medulloblastoma[41, 42, 43]. More sophisticated radiation therapy modalities aim to target the tumor specifically but spare the crucial CNS structures that are frequently damaged, such as the cochlea, temporal lobe, and pituitary-hypothalamus axis[41].

Conformal radiation and intensity-modulated radiation therapy have improved the specificity of irradiating tumors, with 1-2 cm margins compared with irradiating the entire posterior fossa. With modern conformal techniques, disease control rates are similar to those seen when whole posterior fossa boost were used[44, 45, 46, 47]. Hyperfractionated radiotherapy increases the chance of irradiating actively dividing cells without killing normal cells, such as glial cells, microglia, neurons, or astrocytes, which have improved DNA repair mechanisms when they receive sublethal doses of radiation. A study of treatment of children with average-risk medulloblastoma with hyperfractionated radiation to the craniospinal axis followed by a tumor bed boost of conformal therapy showed promising results (83% of patients were progression free) [44, 45]. Proton beam irradiation is an alternative to conventional high energy X-rays (photons) that is currently being studied for pediatric brain tumors. Theoretically, it has better physical qualities and might reduce the incidence of late effects of conventional radiation toxicity[47].

Chemotherapy

Chemotherapy is the standard of care for children in all risk groups[3]. Chemotherapy alone can be curative in patients with non-metastatic medulloblastoma after gross total resection. Cisplatin, vincristine, lomustine, cyclophosphamide, CCNU, and oral etoposide are used most commonly alone or in combination[48, 49, 50]. In patients with high risk medulloblastoma who are treated with surgery and radiation therapy, progression-free survival rates of 24- 40% have been reported. The progression-free survival following addition of chemotherapy is about 50%. Rutkowski et al reported that chemotherapy (cyclophosphamide, vincristine, methotrexate, carboplatine and etoposide) and intra-ventricular methotraxate alone is a promising treatment for medulloblastoma in young children without metastases [50].

A recent study of radiotherapy plus high dose, chemotherapy supported by stem cell rescue reported excellent outcomes in patients with average-risk medulloblastoma and encouraging survival rates in patients with high-risk medulloblastoma compared with radiation therapy alone[51].Multidrug chemotherapy has been the most common approach to children with recurrent medulloblastomas[52]. International society of pediatric oncology and

children's cancer study group studies demonstrated that children with adverse risk factors could be benefited from the addition of chemotherapy[53]. No study has shown that in good risk patients (i.e. more than 3 years of age with gross totally resected tumors and no metastasis) adjuvant chemotherapy plus standard radiation offer a survival advantage over radiation alone[3, 54, 55, 56]. Nearly 75% of the relapses occur within 2 years. Imaging of brain and spine is recommended every 3 months for the first two years. In older children who have received craniospinal radiation as a part of their initial therapy, focal radiation with conformal techniques or proton beam might be an option for solitary recurrences and should be considered on a case-to-case basis[52,57]. Pretherapy neurological state of the children, surgical complications, and the deleterious effect of the local boost dose of radiotherapy on the cerebellum are other factors which affect the intellectual outcome[58, 59, 60, 61]. Chemotherapy alone should be used in children aged less than 3 years as the initial treatment[3]. Neoadjuvant chemotherapy has not reduced the incidence of postoperative complications[62]. Adjuvant, high dose chemotherapy with peripheral stem cell rescue has not been shown to be more effective than standard chemotherapy for newly diagnosed patients. This form of therapy is highly recommended in patients with relapsed disease, it seems to be primarily effective in either patients who have been treated initially with chemotherapy alone, where high dose chemotherapy can be coupled with radiation therapy, or in patients with isolated relapse at the primary site who are amenable to gross total resections of recurrent tumor[3,63,64]. An exciting progress has been in understanding and classifying the molecular biology of medulloblastoma. The mechanisms of signal transduction in neuro-oncogenesis are elucidated; more specifically targeted therapies can be developed. A greater understanding of the genetics of medulloblastomas will enable more sophisticated stratification[3, 63, 64].

Cerebellar astrocytomas

Epidemiology

These represent 12% of brain tumors in children younger than 15 years[2, 21]. These tumors are the second most common cerebellar tumors, consisting approximately 1/3rd of the posterior fossa tumors. Peak incidence is in the later half of the first decade with a second peak in the first half of second decade. There is no gender preference[65].

Pathology

Astrocytomas may occur anywhere in the cerebellum and may involve the hemispheres, the vermis or both regions simultaneously. Approximately 80% of astrocytomas are cystic[66]. Some have suggested that tumors located in the hemisphere are typically cystic whereas solid tumors are more commonly located in the vermis[67]. The tumors are generally well circumscribed and non invasive. These tumors either consist of a large cyst with a solid mural nodule or may be solid with smaller cyst throughout the tumor substance. The wall of the cyst may contain reactive non neoplastic tissue or occasionally neoplastic tissue. Approximately 20 % of the cerebellar astrocytomas are solid and similar to those in the supratentorial compartment[68].

The histopathology of these tumors consists of compact, strongly fibrillated cells alternating with loose areas composed of micro cysts. Compact areas contain an abundance of Rosenthal fibers. Calcification may be found in 25% of patients. Invasion of the tumor by leptomeninges is common and endothelial hyperplasia may be seen. When mitosis is present aggressive tumor behaviour should be suspected[8, 9].

Gjerris and Klinken[69] divided astrocytomas into two types-classic juvenile pilocytic astrocytoma (70%) and diffuse astrocytoma (30%). The diffuse form was found primarily in the older age group i.e. 10 to 14 years of age whereas the juvenile form was found in children younger than 10 years. The 25 year survival rates were 94% for juvenile and only 38% for diffuse types. It is the most common astrocytoma in children comprising 20% of all brain tumors. Based on clinicopathologic features using WHO classification system, JPA is classified as a Grade I tumor. Although JPA can occur anywhere in the CNS the classic site of presentation is the cerebellum. The classical but not exclusive neuroradiological findings of JPA are the

presence of a contrast enhancing mural nodule within the wall of a cystic mass. The microscopic findings exhibit a biphasic appearance of bundles of compact fibrillary tissue interspersed with loose micro cystic spongy areas. The presence of Rosenthal fibers, condensed masses of glial filaments occurring in the compact areas helps to establish the diagnosis. JPA has a low metastatic potential and is rarely invasive. A small proportion of these tumors can spread and develop leptomeningeal spread[8, 9].

Diffuse astrocytomas behave more like fibrillary astrocytomas of the brainstem or cerebral hemispheres and are associated with recurrence therefore diffuse astrocytomas may require adjuvant therapy[8, 9].

Gilles et al [70] defined two groups of tumor to prognosticate the microscopic features-gliomaA & B. Glioma A is defined as having microcyst, Rosenthal fibers, leptomeningeal deposits and foci of oligodendroglia.Group A has better prognosis(10 year survival rate of 94%). In contrast glioma B group has worst prognosis (10 year survival rate of 29%).

Glioblastoma multiforme (GBM) of the cerebellum is rare in children. Prognosis is invariably poor. This tumor should be considered as a distinct pathologic entity from benign cerebellar astrocytoma[9].

Clinical features

These tumors typically manifest with signs of raised intracranial pressure. The children with tumors located primarily in the vermis will have truncal ataxia, whereas those with hemispheric tumors will have ipsilateral appendicular ataxia.

Diagnosis

In the case of cystic cerebellar astrocytomas, CT and MRI scan show cystic mass with an enhancing mural nodule (Fig.2). At times the walls of the cyst may show enhancement after intravenous contrast suggesting neoplastic lining of the cell wall[71]. Diffuse astrocytomas have slightly decreased density and uniform enhancement. In diffuse tumors MRI is more valuable to identify recurrence and invasion of the brainstem[71].

Management

Harvey Cushing first emphasized the removal of the mural nodule to prevent recurrence[72]. Today the goal of surgery is complete resection of the tumor. Radical resection provides 100% cure rate without no necessity of adjuvant therapy[71]. Local recurrence is common after partial removal of the tumor. Repeat surgical resection after recurrence may also provide cure.

There has been little experience regarding chemotherapy in cerebellar astrocytomas. Overall cerebellar astrocytomas have the best prognosis amongst all pediatric brain tumors. Complete removal of the tumor is the goal. In patients with partial resection of diffuse cerebellar astrocytomas adjuvant radiotherapy may provide prolonged relapse free survival[73].

Ependymomas

Epidemiology

Ependymomas constitute approximately 8% of brain tumor in children younger than 15 years of age. 60% of children with ependymomas are younger than 5 years of age, with only 4% older than 15 years of age at diagnosis[74]. Ependymomas represent the second most common malignant brain tumor in children aged lesser than 3 years of age. Approximately 70% of ependymomas of childhood occur in the posterior fossa.The incidence of leptomeningeal spread is 5 to 10 %[75].

Pathology

Ependymal tumors are derived from the ependymal lining of the ventricular system. Ependymomas may arise anywhere in the ventricular system. In general 2/3rd is supratentorial and 1/3rd are infratentorial. Infratentorial ependymomas arise from the roof, floor or lateral recesses of the fourth ventricle. The tumor can occlude the ventricle; extend cephalic to the aqueduct, caudal through the foramen Magendie into the upper cervical spinal cord or laterally into the cerebellopontine angle. Supratentorial ependymomas may be found anywhere within the lateral or third ventricles or within the cerebral hemispheres. Ependymomas may be purely intraventricular,

entirely extra ventricular or mixed in supratentorial compartment[75].

Histological characteristics of these tumors include perivascular pseudorossettes, ependymal rosettes, monomorphic nuclear morphology and occasional non palisading foci of necrosis. Ependymomas are well defined, homogenous, partially encapsulated tumors. These may be extensively cystic. Low grade ependymomas are cellular with a regular histological pattern. Ependymal rosettes are diagnostic which consist of tumor cells lining a small central tumor. Pseudorossettes are observed even more commonly. Areas resembling oligodendroglioma and astrocytomas are frequently present[8, 9]. The presence of mitotic figures, vascular proliferation, hypercellularity and necrosis has been associated with aggressive lesions. However it is extremely difficult to determine the degree of malignant nature of astrocytomas on histological features[76, 77].

Anaplastic ependymoma (WHO grade III) is less common in childhood and is characterized by a high mitotic index, micro vascular proliferation and pseudopalisading necrosis[77, 78].

Clinical features

The signs and symptoms vary with the tumor location. Children present with early vomiting when the tumor arises from the floor of the fourth ventricle. Other features are nystagmus, meningismus, papilledema and dysmetria[75].

Diagnosis

CT demonstrates calcification that may not be readily apparent on MRI; the latter modality defines the extension of the tumor through the foramina (Fig.3). Ependymomas may seed the CSF access but not as common as with medulloblastomas[79].

Management

Surgery is the primary treatment modality with extent of surgical resection a major prognostic factor along with age and tumor location. Younger children have worse outcomes. Several trials have shown no benefit to the use of high doses chemotherapy with stem cell rescue in ependymomas. Gross total resection significantly improves survival rates[80, 81]. Administration of postoperative chemotherapy to children with subtotally resected tumors improves the likelihood of a complete resection at second look surgery[81]. Adjuvant radiation is considered standard therapy for older children with ependymomas. As such routine neuraxis radiation is not recommended unless leptomeningeal disease is demonstrated at diagnosis[78, 80]. In the presence of widespread disease craniospinal radiation is desirable. Recent studies have identified prognostic factors. Poor prognostic factors include age younger than 2 to 5 years, incomplete resection, short duration of symptoms before diagnosis, brainstem invasion and radiation dose less than 4500 Gy. Paradoxically degree of malignancy and presence of leptomeningeal disease at diagnosis are not significant factors in some studies. Good prognostic factors are gross total resection and age greater than 3 years. 5 year survival rates of 90 % have been reported in such patients. In contrast poor risk group have 5 year survival rates of 25%[76, 77, 82].

The role of adjuvant chemotherapy is still controversial. Post operative chemotherapy regimen consisting of cyclophosphamide and vincristine for newly diagnosed children less than 3 years of age was associated with a 48 % response rate. Transient responses to chemotherapy especially cisplatin have been shown in recurrent tumors. The children's cancer study group trial of surgery and radiotherapy with or without CCNU, vincristine or prednisone found no difference in outcome between the two arms. It must be recognized that ependymomas tend to recur late therefore promising early results must be viewed with caution[77, 82].

In summary radical resection plus local radiation is the most effective treatment at this time. Further studies of adjuvant chemotherapy to improve the likelihood of gross total resection at second look surgery are in progress.

Brainstem tumors

Epidemiology

Approximately 10 to 20 % of brainstem tumors in pediatric age group are found in the brainstem[83]. These tumors occupy the region of

the brain traversed by the fourth ventricle and aqueduct of Sylvius. Brainstem gliomas constitute 15% of all brain tumors. In children, brainstem glioma represents 25-30% of all brain tumors. Most brainstem gliomas are low-grade astrocytoma. Stereotactic biopsy is the procedure of choice because of fear of damaging vital brainstem structures and the possibility of brainstem swelling. Small biopsies cannot be viewed as definitive, as sampling error and potential for malignant dedifferentiation may complicate interpretation. These considerations led many authors to reject the need for pathologic confirmation. Conversely, others have thought that because most patients have pilocytic tumors that are uniform in nature with little regional variation, sampling error may not be a problem and biopsy is worthwhile[84, 85, 86]. Few are present in an exophytic location (i.e. the floor of the fourth ventricle, the lateral recess, the cerebellopontine angle, or the cervicomedullary junction). Evacuation of the tumor cysts found in low grade astrocytomas may be associated with long term cures and relief of symptoms[86].

Brainstem tumors are progressive and invariably have a fatal outcome. The five year survival rates range from 5 to 30%. Prognosis depends on location of tumor and histologic diagnosis and duration of symptoms. Children with signs and symptoms of less than 6 month duration, tumors located in pons, and 2 or 3 brainstem signs have the worst prognosis. Conversely lesions that are focal or exophytic or that originating in cerebellar peduncles or cervicomedullary junction tend to have a better prognosis and may be amenable to surgery[84-87]. Tumors located in the midbrain (tectal, pretectal or tegmental) tend to have a benign course and produce obstructive hydrocephalus[85, 86, 88].

Diagnosis

On CT, brainstem tumors may be isodense, cystic, necrotic or calcified. Low density lesions with and without contrast enhancement are more likely to behave in a malignant fashion[89]. MRI more accurately delineates the location and extent of tumor (Fig.4). Infrequent brainstem lesions are hemangioma, cavernous hemangioma, telangiectasia of the pons or hamartoma[86, 89].

Management

Stereotactic biopsy of the mass minimizes surgical morbidity. With the advent of better anaesthesia, agents to control edema and microsurgery there is a growing tendency towards surgical exploration and biopsy. Surgery avoids wrong diagnosis, allows the removal of exophytic lesion and decompresses the cyst contents[90, 91, 92]. Epstein and others[86, 91, 92] suggested that prognosis and treatment may be determined on the basis of anatomic localization. Four categories of brainstem tumors have been defined-diffuse, focal, cystic, cervicomedullary. Exophytic brainstem lesions or the tumors at cervicomedullary junction are the most amenable to surgery. Surgery in these patients offers long term remission. Another group of patients having favorable prognosis are those with neurofibromatosis. Brainstem tumors in these patients have different biological behavior and long term survival[91].

Primary treatment of most brainstem tumors is radiotherapy. Five year survival rates is less than 30 %[92, 93]. For children with diffuse pontine gliomas survival rates are less than 10%. Radiation in doses of 5500 Gy over 5 to 6 weeks is recommended. Hyperfractionated radiation has been used as an alternative to conventional radiation. Hyperfractionated protocols using radiation schedules from 6400Gy to as high as 7500Gy have demonstrated trends of increased survival[93, 94]. Long term toxicity has not been assessed because almost all children have died of progressive disease. Chemotherapy has not been proven successful. Overall survival of children with brainstem gliomas remains a therapeutic challenge. Even with gloomy prognosis there remains a subgroup of patients who have favorable prognosis: those with focal, cystic, exophytic, or cervical medullary lesions and those associated with neurofibromatosis. A child with diffuse abnormalities on MRI or CT, short clinical course carries a poor prognosis[93, 94, 95].

Choroid plexus tumors

Choroid plexus papilloma and carcinoma represent 0.4-0.6% of all intracranial tumors. The

third ventricle and cerebellopontine angle are rare locations for this tumor. Surgery is the mainstay of treatment. In most of cases, CSF analysis demonstrates increased protein, xanthochromia, or both. Choroid plexus papilloma (WHO grade I) is the most common variety whereas choroid plexus carcinoma (WHO grade III) is malignant but rare variant[96].

Atypical Rhabdoid teratoid tumors (ATRT)

It is a very aggressive embryonic malignancy that occurs predominantly in children younger than 5 years of age and can occur at any location in the neuraxis. The histology demonstrates a heterogeneous pattern of cells including rhabdoid cells that express epithelial membrane antigen and neurofilament antigen[97, 98, 99].

Ependymoblastomas and medullomyoblastomas are very rare but highly malignant tumors of childhood[9, 16].

Metastatic tumors

Metastatic spread of ALL and NHL can be seen uncommonly in any part of CNS[9]. Three percent of all cranial metastatic lesions occur in the brainstem and 18% occur in the cerebellum. The site of origin includes breast, lung, skin, and kidney. Solitary metastasis is better treated by surgical removal before radiation therapy.

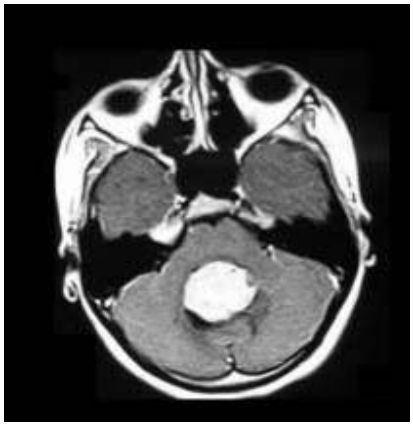

Fig. 1. Axial T_1-weighted contrast enhanced MR image showing a intensely enhancing medulloblastoma occupying the fourth ventricle

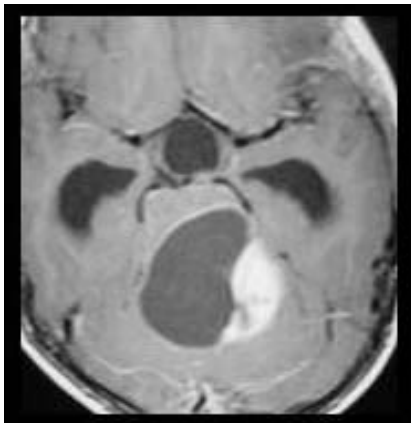

Fig. 2. Axial T_1-weighted MR image showing a large vermian cyst with a mural nodule

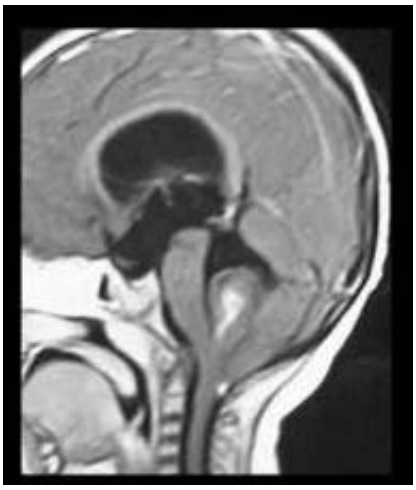

Fig. 3. Sagittal T_1-weighted contrast enhanced MR image showing an enhancing fourth ventricular ependymoma with inferior extension

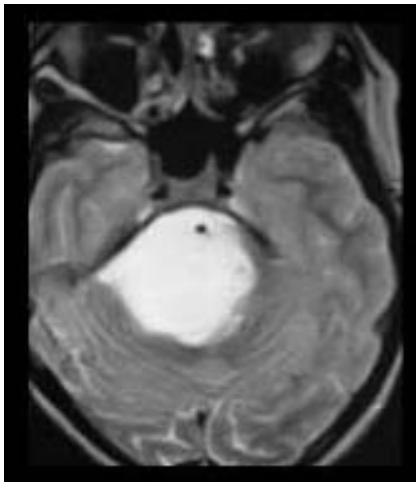

Fig. 4. Axial T_2-weighted MR image showing a diffuse pontine glioma

Surgery also should be considered in case of radiosensitive original tumors or when the primary source is unknown.

Dermoid tumors

Dermoid tumors arise from incomplete separation of epithelial ectoderm from neuroectoderm at the region of the anterior neuropore; this usually occurs during the fourth week of gestation. The cyst grows slowly and gradually becomes filled by desquamated epithelium, sweat, and sebaceous materials. Aseptic meningitis is a sequela of cyst rupture. More commonly, the cyst occurs in the posterior fossa, at or near the midline. It may be extradural, vermian, or intraventricular. A dermal sinus may be connected to the mass. It may be detected clinically or by MRI[1,4,8,9].

Hemangioblastoma

Hemangioblastoma represents about 7-12% of all posterior fossa tumors, being more common in males. About 70% of hemangioblastomas occurring in the cerebellum are cystic and are usually associated with von Hippel-Lindau disease[1,4,8,9].

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