Pediatric Brain Tumors

35

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Pediatric brain tumors (PBT) are the most common solid malignancy in childhood, and the second most common cause of cancer-related mortality after leukemia in this age group [1–3]. The incidence is about 4 per 100,000 children each year and is slightly more common in boys particularly for medulloblastoma, germ cell tumors, and ependymoma. Astrocytomas are the most common primary intra-axial brain tumor in children, constituting approximately three-quarters of all primary glial neoplasms, followed by medulloblastoma, ependymoma, craniopharyngioma, and germ cell tumors [1–5]. The majority of PBTs are infratentorial involving the cerebellum, brain stem, and fourth ventricle affecting all pediatric age groups, while supratentorial tumors are more common in children under 3 years of age [6, 7].

The location of brain tumor may be related to its cell of origin; for example germ cell tumors develop in the midline. Tumor location is also responsible for the presenting symptoms; for example sellar and suprasellar lesions (e.g., craniopharyngioma) may produce hormonal disturbance, visual abnormalities, and hydrocephalus. Anatomy likewise plays a role in the determination of treatment and prognosis. For instance, cerebral or cerebellar pilocytic astrocytomas are often completely resected, whereas those in the diencephalon or brain stem can less easily be resected and may require radiotherapy or chemotherapy [7, 8].

Patients with ependymoma, or embryonal and germ cell tumors involving the ventricles, may require postoperative irradiation of the craniospinal axis as the cerebrospinal fluid (CSF) is an important route for tumor dissemination [9].

Anatomic location appears to be also a significant factor in the biologic behavior of childhood gliomas. Cerebellar astrocytomas have a much more favorable prognosis than histologically similar astrocytomas in the cerebral hemispheres [10]. Medulloblastoma of the cerebellum and pineoblastoma are regarded as the

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prototypes of primitive neuroectodermal tumor (PNET). Although the 5-year survival is roughly two-thirds of all patients, however, survivors suffer from neurologic, cognitive, psychologic, and endocrinologic sequelae as a result of both the disease and its treatment [6, 11].

This chapter focuses on clinical presentation, diagnosis, management, and outcome of treatment of frequently encountered PBTs.

35.1 Classification of Brain Tumors

There are several grading and classification systems of brain tumors. Since 2007, the World Health Organization (WHO) three-tiered grading system has been the most widely used classification system [12]. In 2016, neuropathologists classified central nervous system (CNS) tumors using microscopic examination along with molecular parameters defining more tumor entities, and removed some. They integrated phenotypic and genotypic parameters which would lead to greater diagnostic accuracy and improve patient treatment with more accurate determinations of prognosis and management response [13]. This has allowed better understanding of the molecular oncogenesis of brain tumors, and improved treatment options including gene therapy and precision therapeutics. This has also led to finding of a number of molecular markers with proven diagnostic, prognostic, or therapeutic significance in PBT. For example, combined deletion of chromosomes 1p/19q is associated with improved prognosis and response to therapy in anaplastic oligodendroglioma and with superior overall survival and progression-free survival in low-grade gliomas, especially gliomas with an oligodendroglial component [14].

Based on the WHO classification of brain tumors (Table 35.1), the traditional principle of the diagnosis is based on the microscopic features, which has relied heavily on recognition of morphologic patterns and immunohistochemical identification of different antigens [12].

35.2 Pathogenesis of PBTs

The pathogenesis of PBTs, particularly gliomas, involves alterations in genes mediating initiation, differentiation, and proliferation of tumor cells. Alterations involving oncogenes (overexpression) result in gain of function, while inactivation of tumor-suppressor genes (deletion, translocation) results in loss of function. Familial tumor syndromes are linked to germline mutations [9, 15].

Pediatric gliomas are intrinsic tumors and generally do not relapse or recur far from the primary site after resection. Malignant neoplasms such as medulloblastomas, ATRT, pineoblastoma, supratentorial PNET, germ cell tumors, and anaplastic ependymoma can spread through the CSF and metastasize along the meninges or spine. It is particularly common for medulloblastoma to metastasize to involve the meninges or spinal cord or cauda equina. Metastasis outside the CNS is rare and

Table 35.1 Classification of brain tumors

Astrocytic tumors	Pilocytic astrocytoma
	Pilomyxoid astrocytoma
	Pleomorphic xanthoastrocytoma
	Diffuse astrocytoma
	Anaplastic astrocytoma
	Glioblastoma
	Giant-cell glioblastoma
	Gliosarcoma
	Gliomatosis cerebri
Oligodendroglial tumors	Oligodendroglioma
	Anaplastic oligodendroglioma
	Oligoastrocytoma
	Anaplastic oligoastrocytoma
Ependymal tumors	Ependymoma
	Anaplastic ependymoma
	Subependymoma
Choroid plexus tumors	Choroid plexus papilloma
	Atypical choroid plexus papilloma
	Choroid plexus carcinoma
Other neuroepithelial tumors	Astroblastoma
	Choroid glioma of the third ventricle
	Angiocentric glioma
Neuronal and mixed neuronal-glial tumors	Ganglioglioma and gangliocytoma
	Desmoplastic infantile astrocytoma and ganglioglioma
	Central neurocytoma and extraventricular neurocytoma
	Cerebellar liponeurocytoma
	Papillary glioneuronal tumor (PGNT)
Tumors of the pineal region	Pineocytoma
	Pineal parenchymal tumor of intermediate differentiation
	Pineoblastoma
	Papillary tumor of the pineal region
Embryonal tumors	Medulloblastoma
	CNS primitive neuroectodermal tumor (PNET)
	Medulloepithelioma
	Ependymoblastoma
	Atypical teratoid-rhabdoid tumor
Tumors of the cranial nerves	Schwannoma
	Neurofibroma
	Perineurioma
	Malignant peripheral nerve sheath tumor (MPNST)
Meningeal tumors	Meningiomas
Mesenchymal, non-meningothelial tumors	Hemangiopericytoma
	Melanocytic lesions
	Hemangioblastoma

(continued)

Table 35.1 (continued)

Tumors of the hematopoietic system	Malignant lymphomas
	Histiocytic tumors
Germ cell tumors	CNS germ cell tumors
Familial tumor syndrome	Neurofibromatosis type 1
	Neurofibromatosis type 2
	Schwannomatosis
	Von Hippel–Lindau disease and hemangioblastoma
	Tuberous sclerosis complex and subependymal giant-cell astrocytoma
	Li–Fraumeni syndrome and TP53 germline mutations
	Cowden disease and dysplastic gangliocytoma of the cerebellum
	Lhermitte-Duclos disease
	Turcot syndrome
	Nevoid basal cell carcinoma syndrome
	Rhabdoid tumor predisposition syndrome
Tumors of the sellar region	Pituitary adenoma
	Craniopharyngioma
	Granular cell tumor of the neurohypophysis
	Pituicytoma
	Spindle cell oncocytoma of the adenohypophysis
Metastatic tumors of the CNS	Brain metastasis

thought to be through unfiltered shunts before chemotherapy was used to treat malignant brain tumors [2, 3, 9, 16, 17].

35.3 Clinical Features of PBT

Clinical diagnosis of PBT is challenging, as symptoms and signs may be mistaken for viral illness or gastroenteritis, and lead sometimes to significant delay in the diagnosis. This needs a high index of suspicion among pediatricians, careful history taking, and appropriate neurological examination [18, 19].

Symptoms and signs of PBT depend on the anatomic location, biological behavior of the tumor, presence or absence of hydrocephalus, and age of the patient. They may be nonspecific, related to increased intracranial pressure (ICP), e.g., headache, nausea, and vomiting; subtle developmental delay; and behavioral changes. In infants with open cranial sutures, a tumor may reach a large size with a gradual increase in head circumference without other or minimal symptoms. Focal neurological symptoms depend mainly on the location of the tumor, and may include hemiparesis, monoparesis, hemisensory loss, dysphasia, aphasia, and recent memory impairment [18–21].

Tumors involving optic pathways may present with visual field restriction (quadrantanopsia, homonymous hemianopsia), or cortical blindness, in cases with bilateral occipital lobe involvement. Seizure is the major presenting feature of PBT, seen

Table 35.2 Frequent symptoms and signs of PBT

Infants	Children
Failure to thrive	Headaches
Bulging anterior fontanelle	Nausea and vomiting
Arrested development	Lethargy
Head nodding	Ataxia
Nystagmus	Cranial nerve palsies
	Seizures
	Visual field abnormalities

in more than 50% of children with hemispheric tumors [22]. The majority of patients with tumor-associated epilepsy harbor slow-growing neoplasms such as low-grade gliomas. Rapidly growing lesions are more likely to produce complex partial motor or sensory seizures, although generalized tonic-clonic seizures are also common. Malignant gliomas are less frequently associated with seizures and are more likely to cause focal neurologic deficits, mainly due to infiltration of normal brain tissue, or by local mass effect [23] (Table 35.2).

Brain tumor may arise at any part of the brain within the cranial cavity which has two main compartments: supratentorial including cerebral hemispheres, diencephalon, optic pathway, and pituitary fossa, and infratentorial region includes cerebellar hemispheres and brain stem.

In general, a high proportion of PBTs do not present with increased ICP, and initial neurological features are usually nonspecific, with visual symptoms, weight loss, enlarging head, failure to thrive, and precocious puberty being some of the most common. It may be helpful to involve a pediatric neurologist or pediatric neurosurgeon during the diagnostic phase, particularly if there is a complex neurological presentation or abnormal brain image. There may be associated medical problems, or developmental and behavioral changes that mask the original cause of symptoms. To achieve an upward learning curve, an open line of communication must be established with pediatric neurologists and pediatric neurosurgeons [8, 18, 19].

35.4 Supratentorial Tumors

Supratentorial tumors often present with localizing symptoms and signs, in addition to raised ICP. These symptoms can vary from relentless course to an acute presentation based on the tumor growth rate and the presence of hydrocephalus. In children, supratentorial tumors are either gliomas affecting cerebral hemispheres, diencephalon, thalamus, hypothalamus, and optic pathway or craniopharyngioma of the sella and parasellar region or intraventricular as choroid plexus papilloma, and ependymomas, or in the pineal region like germinoma and less commonly pinealoma [8, 19].

Optic pathway tumors cause visual symptoms; unilateral visual deficit, afferent pupillary defect (Marcus Gunn phenomenon), and blindness. Other common

findings are proptosis and squint. Suprasellar tumors also cause pituitary endocrinopathy, particularly growth hormone deficiency and precocious puberty. Failure to thrive and emaciation are found in diencephalic syndrome due to hypothalamic tumors [24].

Children with pineal region tumors present with Parinaud's syndrome (upward gaze palsy, abnormal pupillary response, eyelid retraction, and nystagmus) [2, 25].

35.5 Infratentorial Tumors

Infratentorial tumors in children are more common than supratentorial tumors. They arise in the cerebellum or brain stem. In general, patients with posterior fossa tumor may present with subtle cerebellar manifestations till they develop obstructive hydrocephalus and raised ICP, presenting with morning headache, projectile vomiting, bilateral papilledema, and limitation of the lateral eye gaze due to sixth nerve palsy. Acute obstructive hydrocephalus causes rapid increase in the ICP leading to altered level of consciousness. This usually takes place in rapidly growing midline posterior fossa tumor [8, 19]. Tumors involve cerebellar hemisphere causing cerebellar signs, such as truncal ataxia, dysarthria, nystagmus, and dysmetria, while brain stem tumors present with cranial neuropathies including facial asymmetry, absent corneal reflex, weak gag reflex, difficult swallowing, and hearing loss. Motor deficits may involve any or all of the extremities [26].

35.6 Neonatal Brain Tumors

Clinical presentations of infantile brain tumors are generally vague and nonspecific including irritability, poor feeding, failure to thrive or regression of acquired milestones, vomiting, and hypotonia. Macrocrania, full and bulging anterior fontanelle, and sunset eyes are seen in large tumors or in case of associated hydrocephalus [27, 28].

Antenatal diagnosis by fetal ultrasound or MRI scan is possible. Prognosis is generally poor particularly in malignant tumors as it affects the brain formation and function [29].

35.7 Genetic Tumors

Several genetic syndromes are associated with brain tumors. Physicians should be familiar with clinical stigmata of these syndromes, e.g., *neurofibromatosis type 1 (NF 1)* characterized by café au lait spots, axillary freckling, and Lisch nodules of the iris. The majority of these patients have optic pathway glioma, and hamartomas [30]. Children with *tuberous sclerosis* (autosomal dominant) present with seizures, developmental delay, and adenoma sebaceum.

These patients develop subependymal giant-cell astrocytomas (SEGA), and malignant gliomas [31]. Patients with *Li–Fraumeni syndrome* may have brain tumors and those with *bilateral retinoblastoma* are at risk of developing pineal region tumors [32].

35.8 Diagnostic Imaging of PBT

Magnetic resonance imaging (MRI) and computed tomography (CT) are the main imaging modalities in the diagnosis of PBT. CT is quick and generally available in most health facilities. MRI has no radiation hazard and provides higher sensitivity in differentiating tumor tissue from normal brain, allowing more detailed anatomic characterization of the lesion, and should be obtained in all children with a diagnosis of a brain tumor. A complete series usually include T1-weighted (without and with contrast), T2-weighted, and fluid-attenuated inversion recovery (FLAIR). Other sequences such as fat suppression, MR angiography (MRA), MR spectroscopy (MRS), functional MRI, perfusion measurements, and neuronavigation protocol studies may also be required in specific situations [33, 34].

CT or MRI is indicated whenever a new neurological deficit arises, whether cranial nerve related, motor weakness, or an abnormal ophthalmological finding. Unexplained new-onset torticollis may be a sign of a posterior fossa tumor or craniocervical lesion. It is also indicated for enlarging head circumferences beyond the growth curve, suggesting hydrocephalus or intracranial mass. New-onset seizure is also an indication of brain imaging. It is important to obtain whole-spine MRI at the same time for all children diagnosed to have brain tumor to rule out leptomeningeal dissemination and spine metastasis [33, 34].

MR spectroscopy is indicated in PBTs to suggest the grade of the tumor by assessing the metabolites in both brain parenchyma and tumor. Most commonly are choline, creatinine, N-acetylaspartate (NAA), and lactate. In brain tumors choline increases and NAA decreases. Lactate peak usually reflects areas of ischemia and necrosis within the tumor, suggesting a higher grade tumor, while lipid peak is related to cell proliferation, which is usually present in high-grade tumors [35].

Functional MRI sequence is used to give information about the involvement of eloquent areas of the brain. The principle of fMRI is based on increase of oxygen consumption in the brain area used for a particular activity and is carried out with the child awake and able to collaborate [36, 37].

Diffusion tensor imaging (DTI) also known as tractography study is used alone or in association with fMRI to determine the degree of white matter tract involvement by a brain tumor, which is very useful during surgical resection and planning for radiation therapy treatment [37].

Positron-emission tomography (PET) and single-photon emission computerized tomography (SPECT) are used to evaluate brain tumor recurrence or metastasis and radiation-related necrosis [Fig. 35.1] [38].

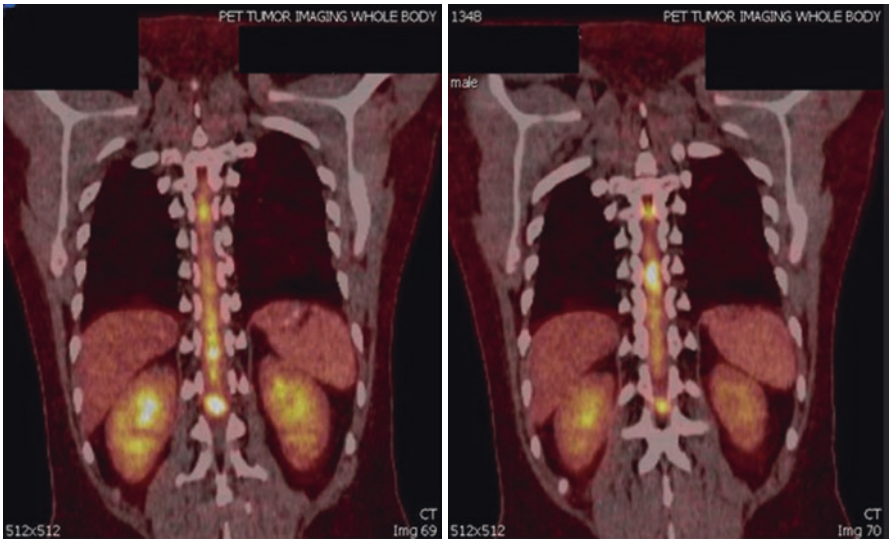


Fig. 35.1 Anteroposterior (positron-emission tomography) PET/CT fused whole-spine image showing extensive multifocal FDG-avid deposits along the neuroaxis in the spinal cord and in the epidural space with variable FDG uptake representing multiple levels of metastases from recurrent cerebral GBM in 15-year-old boy

35.9 Other Diagnostic Investigations

This includes serum and CSF tumor markers, in germ cell tumor such as alpha-fetoprotein (αFP), beta-human chorionic gonadotrophin (β-hCG), and placental alkaline phosphatase. The presence of these markers is diagnostic, and helps in decision-making for treatment protocols as well as a baseline marker for follow-up [39].

35.10 Gliomas

Pediatric gliomas include pilocytic and fibrillary low-grade astrocytomas, anaplastic astrocytoma, glioblastoma and its variants, and less commonly pleomorphic xanthoastrocytoma (PXA), SEGA, ganglioglioma and desmoplastic infantile ganglioglioma, astroblastoma, ependymoma, oligodendroglioma, pilomyxoid astrocytoma, and gliomatosis cerebri [40].

35.11 Low-Grade Astrocytomas

Low-grade astrocytomas (WHO grade I and II) are the most frequent brain tumors in children. They constitute a heterogeneous group of tumors, both in histological appearance and prognosis. The most common subtype is juvenile pilocytic astrocytoma (WHO grade I), accounting for approximately 20% of PBTs, and most often occur in the posterior fossa. Although infiltrating astrocytomas are low-grade tumors, they tend to dedifferentiate into higher grade [41].

35.12 Pilocytic Astrocytomas

Pilocytic astrocytomas are the most common pediatric glioma, commonly present in the cerebellum or midline along the hypothalamus and optic pathways. Pilocytic astrocytomas are well circumscribed, often cystic, and could be solid lesions. They are (WHO I) tumors, microscopically composed of a compact fibrillary component that neighbors a spongy microcystic element (Fig. 35.2). Cerebellar pilocytic astrocytomas often present with ataxia, vomiting, or headache and raised ICP. Optic pathway glioma can present with proptosis or gradual visual deterioration. Children with NF-1 are susceptible to developing optic pathway gliomas [41–43].

Juvenile pilocytic astrocytoma appears in MRI as a well-circumscribed enhancing lesion that is bright on T2 imaging. Cystic areas are commonly seen. Very little surrounding edema is seen on FLAIR imaging (Fig. 35.3). Occasionally low-grade tumors in the posterior fossa can result in thinning of the occipital skull bone as they slowly grow over long periods [42, 43].

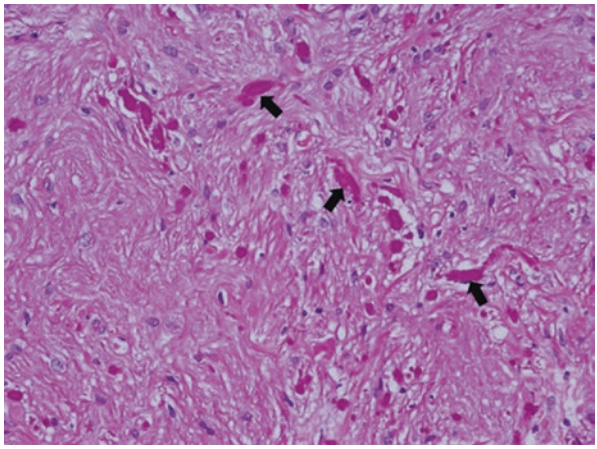


Fig. 35.2 Pilocytic astrocytoma WHO grade I (H&E). Note that the piloid bipolar cells and Rosenthal fibers are seen in the compact area (arrows)

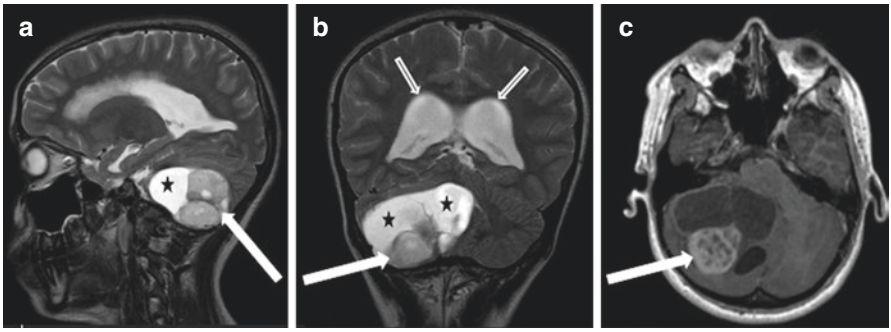


Fig. 35.3 MRI of 11-year-old patient with right cerebellar juvenile pilocytic astrocytoma: (**a**) sagittal T2-WI, (**b**) coronal T2-WI, and (**c**) postcontrast axial views, showing solid component of the tumor (solid arrow) and cystic part (star). The tumor distorted and displaced the fourth ventricle causing obstructive hydrocephalus (empty arrows)

Pilocytic astrocytoma may affect any part of the brain, and third ventricle is a common site. Symptoms are always related to raised ICP caused by obstructive hydrocephalus when the tumor and its cyst obstruct the foramen of Monro (Fig. 35.4a, b). Treatment of pilocytic astrocytomas is always by surgical excision.

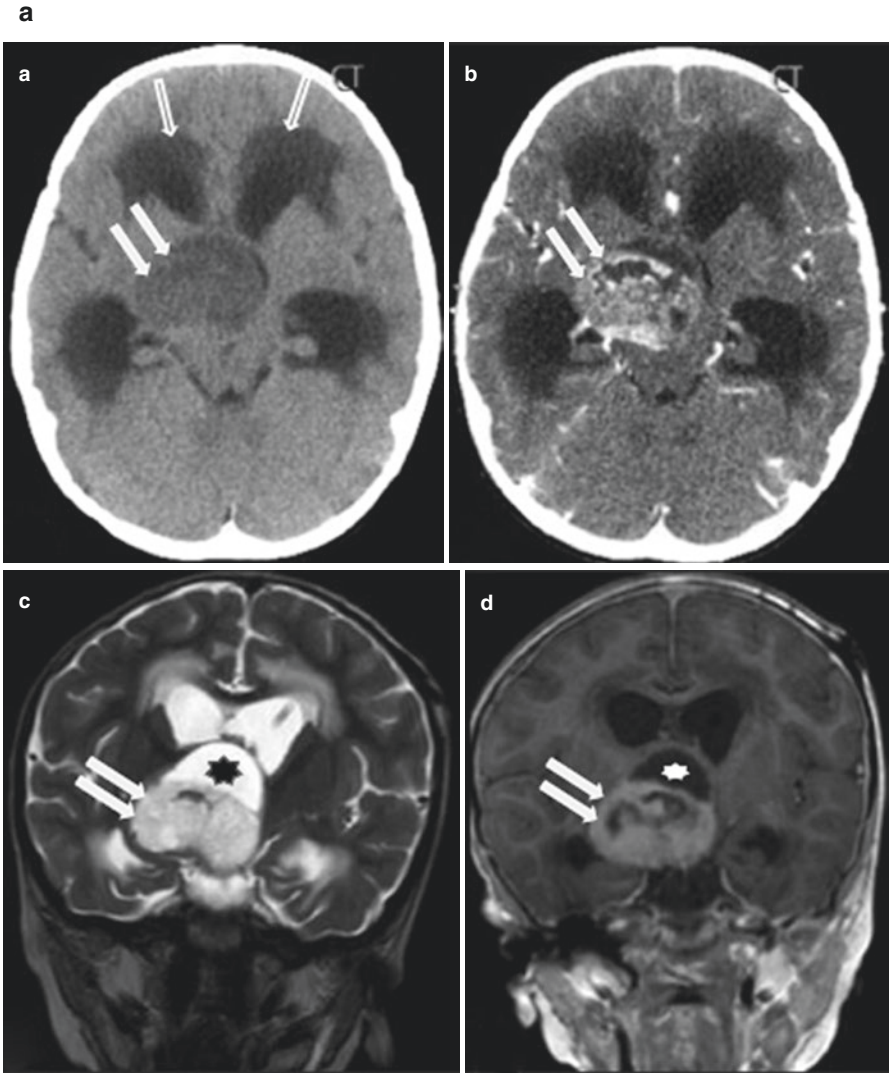
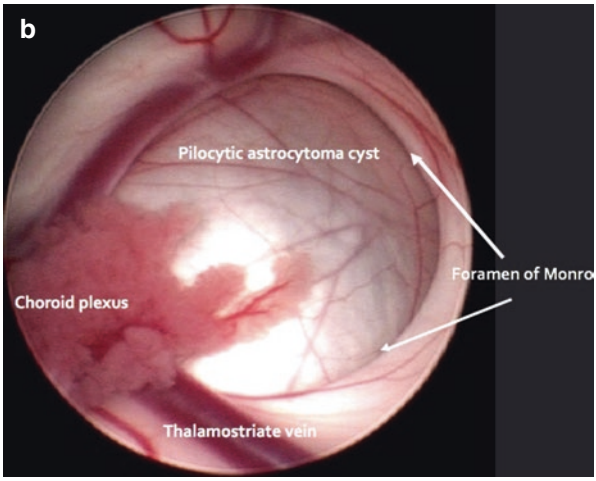


Fig. 35.4 (**a**) Brain CT scan (**a**) without and (**b**) with contrast of a 3-year-old child presented with repeated vomiting and irritability, showing hypodense mass filling the third ventricle and growing more toward the right, heterogeneously enhancing with contrast (arrows), causing obstructive hydrocephalus. Note periventricular edema (empty arrow). MRI of the same child coronal views (c) T2-WI and (d) T1 with contrast showing solid part (arrows) and cystic component (star). (**b**) Endoscopic view of third ventricular pilocytic astrocytoma showing the cyst projecting through and obstructing the foramen of Monro

Fig. 35.4 (continued)



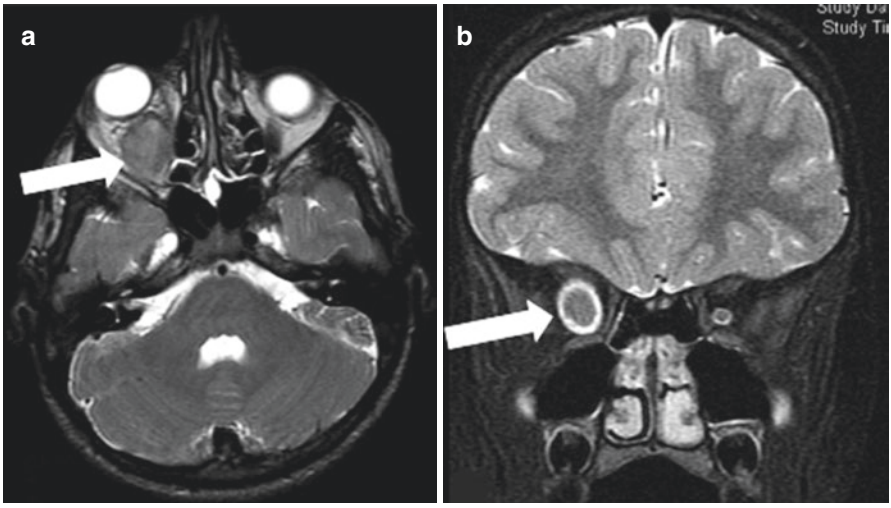


Fig. 35.5 MRI scan T2-WI: (**a**) axial and (**b**) coronal views showing optic nerve glioma (arrow) arising in the orbit. Note that the other optic nerve is intact

Pilocytic astrocytomas generally occur in one location and do not tend to spread throughout the CSF. Excision is curative when surgically accessible. On the other hand, optic pathway gliomas are not surgically resectable without compromising the child's vision, and biopsy can also be risky. Optic pathway gliomas can be diagnosed based on its characteristic appearance in the MRI (Fig. 35.5).

Although most low-grade astrocytomas will respond to radiation therapy, it is better to avoid its long-term side effects in young children. In older children, radiation is generally tolerated better and can be quite effective in treating a growing

unresectable lesion. However, there is always a theoretical risk of malignant transformation of these tumors when exposed to radiation. Nowadays, most progressive, unresectable low-grade astrocytomas are treated by chemotherapy for a period of up to 1 year [44, 45].

Prognosis is very good, and the overall survival at 5 years is greater than 90%. Even after gross total resection, children should be followed up regularly with MRI scans for a few years after surgery. Children with residual tumor will need close follow-up, to assist in the decision of when to start treatment [46].

35.13 Other Low-Grade Gliomas

A variety of other, less common low-grade glial tumors are seen in children, including pleomorphic xanthoastrocytoma (PXA), subependymal giant-cell astrocytoma (SEGA), ganglioglioma and desmoplastic infantile ganglioglioma, astroblastoma, ependymoma, and oligodendroglioma [46–48].

35.14 Pleomorphic Xanthoastrocytoma (PXA)

Pleomorphic xanthoastrocytoma is typically a well-circumscribed tumor that tends to be superficially located, usually in the temporal lobe, in children with intractable seizures, and rendered seizure free after gross total resection or within 1 year of surgery. PXA cyst typically appears hypointense in T1-WI with enhancing mural nodule and hyperintense in T2-WI, with suppression of cyst content in FLAIR images (Fig. 35.6).

Histologically, PXA is of a low-grade subtype, (WHO grade II); however it mimics GBM in its pleomorphic cells, but lacks mitotic figures with absent vascular proliferation and necrosis. Its characteristic signature is the presence of eosinophilic granular bodies (EGBs). Another diagnostic finding of PXA is dense intercellular and pericellular reticulin and perivascular lymphocytic infiltrates. Xanthomatous change is also found in the cytoplasm of pleomorphic, giant, and multinucleated cells because of intracellular accumulation of lipids. Approximately 15% of PXA will recur after surgery and undergo anaplastic progression to high-grade diffuse astrocytoma (Fig. 35.6) [47].

35.15 Subependymal Giant-Cell Astrocytoma (SEGA)

Subependymal giant-cell astrocytomas (WHO grade I) are intraventricular tumors invariably almost associated with tuberous sclerosis. Tuberous sclerosis is an autosomal dominant disease linked to two genes, TSC1 (chromosome 9) and TSC2 (chromosome 16). It is characterized by widespread benign hamartomas that arise in many organs, including the brain, kidneys, skin, eyes, lungs, heart, and liver [48, 49].

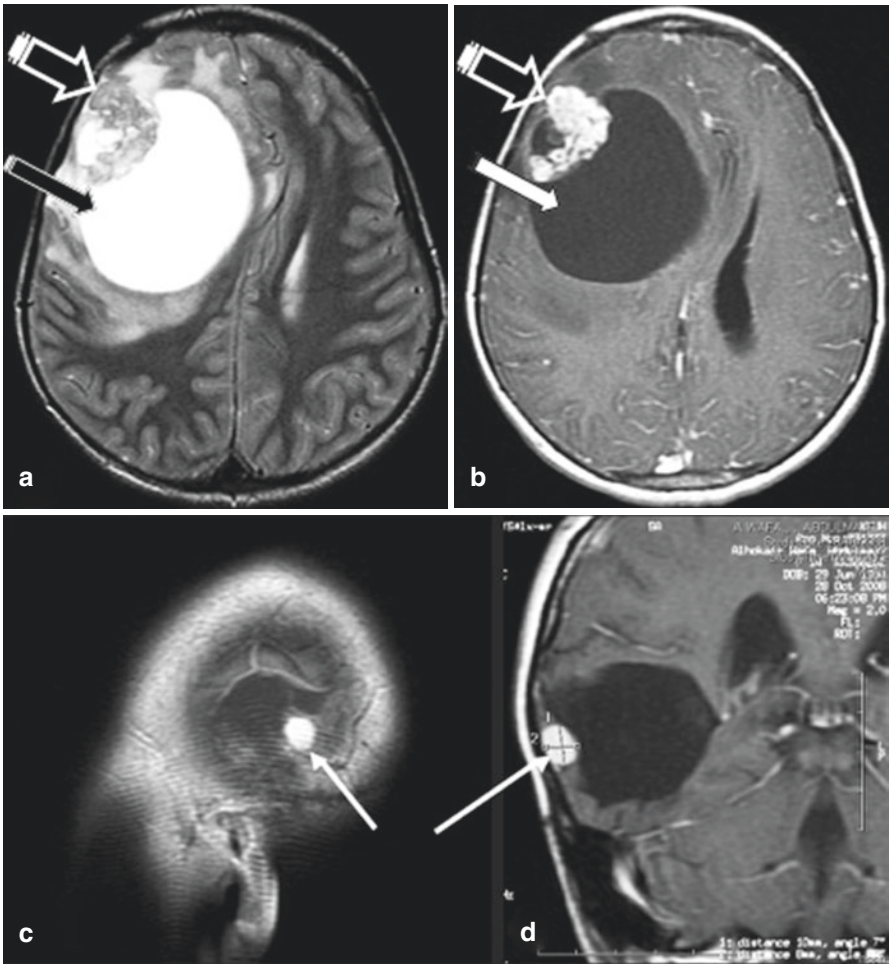


Fig. 35.6 MRI scan of a child with PXA: (**a**) axial T2-WI and (**b**) postcontrast view showing large cystic tumor (narrow arrow) with solid enhancing mural nodule (broad arrow) causing shift of midline structures of the brain. (**c**) Sagittal and coronal (**d**) MRI after 2 years of total surgical excision showed evidence of tumor recurrence (arrow)

SEGA can be seen in any location inside cerebral ventricles; those near foramen of Monro can cause life-threatening symptoms, e.g., hydrocephalus requiring emergency surgery (Fig. 35.7). The most common manifestations of SEGA are epilepsy, intellectual disability, cognitive delay and seizures. SEGAs are also accompanied by cardiac rhabdomyoma in the newborn which may lead to arrhythmia that can be life threatening at the time of surgery for the SEGA. SEGA responds to therapy by mammalian target of rapamycin inhibition, and in symptomatic large SEGA surgical resection is curative [48–50].

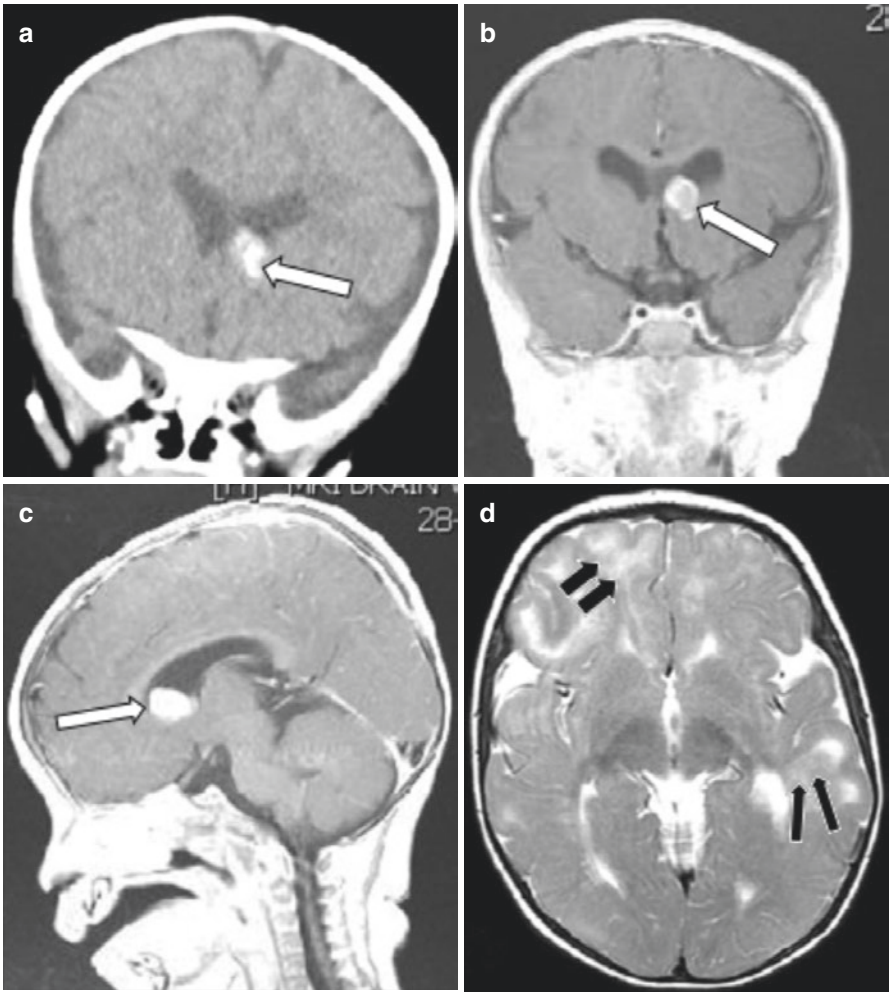


Fig. 35.7 Postcontrast CT scan coronal view (**a**) showing typical appearances of tuberous sclerosis with enhancing SEGA close to the left foramen magnum. It has the same appearance in postcontrast coronal MRI: (**b**) sagittal contrast-enhancing MRI (**c**) with SEGA in the frontal horn. Axial T2-WI MRI (**d**) with high-signal right frontal and left temporal multiple hamartomas (black arrows)

35.16 Desmoplastic Infantile Astrocytoma

Desmoplastic infantile astrocytoma (WHO grade I) is a rare infantile tumor-simulating desmoplastic infantile ganglioglioma in morphology and clinical features. Both share a cerebral cortical location, large size, circumscribed growth pattern, and development during infancy. Surgical resection is the treatment of choice, and the prognosis is generally favorable [51].

35.17 Pilomyxoid Astrocytoma

Pilomyxoid astrocytoma (WHO grade II) is similar to pilocytic astrocytoma in its gross appearance and microscopic features. It occurs most commonly in the midline, predominantly in the hypothalamic or chiasmatic region. It has been found to be clinically more aggressive than ordinary pilocytic astrocytoma, with increased tendency to recur and less favorable prognosis. Grossly, pilomyxoid astrocytomas are well-circumscribed, solid, gelatinous, or cystic lesions. Unlike pilocytic astrocytomas, in pilomyxoid astrocytoma, Rosenthal fibers and eosinophilic granular bodies (EGBs) are either very sparse or absent [52].

35.18 Optic Pathway Glioma

Optic nerve gliomas are rare low-grade tumors, accounting for 3–5% of gliomas in children. Seventy-five percent of optic gliomas present during the first decade of life. They present with slowly progressive visual loss, painless proptosis, and decreased color vision of the affected eye (Fig. 35.6). Children with large optic glioma present with symptoms of raised ICP, e.g., headache, eye pain, hemiplegia, and dementia. About 50% of patients with optic gliomas have NF1. Gliomas in NF1 are characterized by being multifocal affecting both optic nerves and sparing optic chiasm [24, 53, 54].

35.19 Neurofibromatosis Type 1 (NF-1, von Recklinghausen's Diseases)

Neurofibromatosis type 1 is a relatively common autosomal dominant genetic disorder. It involves a mutation of the gene neurofibromin in chromosome 17. Children with neurofibromatosis type 1 are prone to develop café au lait spots (Fig. 35.8), Lisch nodules (hamartomas of the iris), neurofibromas, axillary freckling, and bony abnormalities. During their lifetime, approximately 15% of patients with NF-1 will develop optic glioma [30, 51, 56].

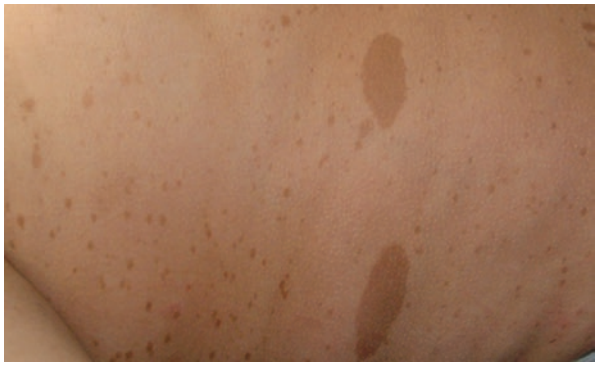


Fig. 35.8 Multiple café au lait spots in a child with neurofibromatosis type I

In NF-1, optic gliomas usually have a benign course and occasionally regress spontaneously. There is a theoretical risk of malignant transformation as well as radiation-induced vasculopathies, e.g., moyamoya disease. NF-1 patients may also develop other tumors throughout the CNS. Therefore, MRI brain and spine should be done for all NF-1 patients [30, 51, 55].

35.20 Brain Stem Gliomas

Brain stem gliomas are usually diagnosed by CT or MRI in a child with squint, ataxia, and weakness of rapid onset or over few weeks or several months. They represent about 10–20% of PBTs, and are found in 4–18% of NF-1 patients. They range from low-grade (WHO grade I, II) to high-grade (WHO grade 3, 4) astrocytomas, and prognosis is relatively poor for high grades. There are four categories including diffuse, focal, exophytic, and cervicomedullary junction [10, 57].

In MRI, the tumor appears as a large expansile brain stem mass involving the majority of the pons. There may be an exophytic component. Diffuse pontine gliomas are hypo- or isointense in T1-WI and hyperintense in T2-WI, and frequently appear relatively homogeneous in FLAIR sequences. Tiny hemorrhages are not uncommon. Contrast enhancement is variable, but these lesions frequently do not significantly enhance at diagnosis (Fig. 35.9).

Focal brain stem tumors, exophytic and cervicomedullary, are typically of low grade, and are amenable to surgical resection; this can be safely achieved with image guidance and intraoperative neurophysiological monitoring. Surgical intervention plays no rule in diffuse pontine gliomas. Most brain stem gliomas in NF1 patients either remain stable, decrease in size, or spontaneously resolve after an average follow-up of several years. Obstructive hydrocephalus can be treated by ETV or insertion of ventriculoperitoneal shunt [57].

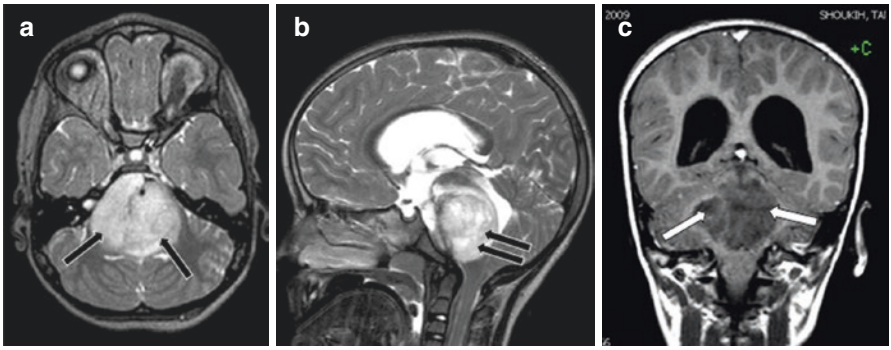


Fig. 35.9 Typical MRI appearance of diffuse intrinsic pontine glioma: (**a**) axial T2-WI, (**b**) sagittal T2, and (**c**) T1-WI postcontrast

35.21 High-Grade Gliomas (Anaplastic Astrocytoma and Glioblastoma Multiforme)

Pediatric high-grade gliomas consist of anaplastic astrocytoma [WHO grade III], and glioblastoma multiforme (GBM; WHO grade IV) represent the most common high-grade glial tumors in childhood. They occur most commonly in the supratentorial region or in the brain stem. The median age at diagnosis is 9–10 years for high-grade glioma and 6–7 years for pontine glioma, and there is a predilection for GBM in adolescence [58]. Symptoms and signs manifest rapidly and can be related to increased ICP in the form of headaches, seizures, or contralateral weakness. Children with diffuse pontine glioma can present with unsteadiness and lower cranial neuropathies [18, 58].

On CT and MRI, high-grade gliomas appear with ill-defined margins, usually surrounded by marked edema, mass effect, and heterogeneous enhancement (Fig. 35.10). These tumors show restricted diffusion on diffusion coefficient on MRI and a marked increase in choline levels with a reduction in N-acetyl aspartate on MR spectroscopy. On perfusion imaging, these tumors tend to have high relative cerebral blood volume values. Diffuse pontine gliomas are characterized by diffuse expansion of the pons which is isointense or hypointense in T1 and bright in T2 sequences [17, 58].

GBM is the most malignant glial tumor and is characterized by poorly differentiated astrocytes. Histologically it appears with cellular polymorphism, nuclear atypia, mitotic activity, vascular proliferation, and necrosis (Fig. 35.11) [58, 59].

The standard treatment for anaplastic astrocytoma and GBM typically includes radiotherapy and chemotherapy. The prognosis is generally poor, and long-term survivors, particularly GBM, usually have significant cognitive impairment and

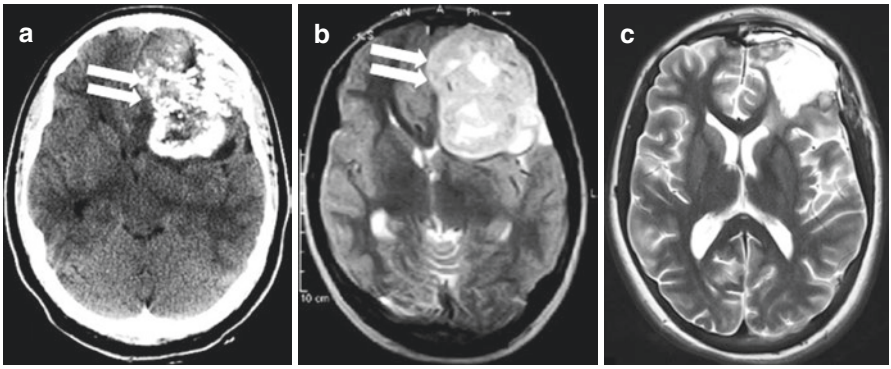


Fig. 35.10 The images illustrate a case of glioblastoma multiforme in 14-year-old patient, presented with seizures. Plain CT scan (**a**) demonstrated left frontal heterogenous mass with areas of dense calcification. In MRI FLAIR view (**b**) seen of mixed intensity hyperintense with multiple cavities or areas of necrosis. In most cases there is a cleavage plane between the brain and tumor and gross total removal can be achieved (**c**)

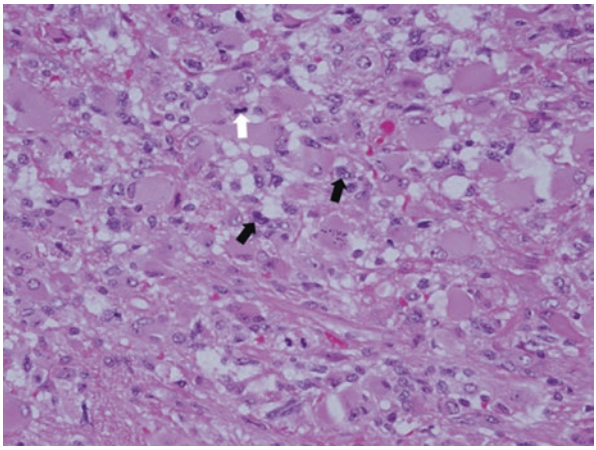


Fig. 35.11 Epithelioid subtype of glioblastoma multiforme consists of tumor cells with abundant eosinophilic cytoplasm, vesicular nuclei with prominent nucleoli (black arrows), distinct cytoplasmic borders, and mitotic figures (white arrow). The cells are arranged in cohesive patternless sheets

neurological deficits attributed to the disease and treatment, and most of the patients die from their disease [58, 59].

35.22 Medulloblastoma

Medulloblastoma is the most common intracranial embryonal tumor in children. It usually arises in the cerebellar vermis, and comprises approximately 20% of PBTs. The peak incidence is at 7 years, and up to one-third are associated with dissemination beyond the primary site at the time of diagnosis. Although the majority of cases occur as sporadic cases, hereditary conditions have been associated with medulloblastoma, including Gorlin syndrome (nevoid basal cell carcinoma syndrome) and Turcot syndrome (e.g., glioma polyposis syndrome) [60].

Most medulloblastomas are relatively circumscribed mass; histologically they are classified into various subtypes: classic, nodular/desmoplastic, and large cell/anaplastic. These subtypes are related to prognosis, and basically used to guide treatment. The new molecular classification has shown that there are different molecular subtypes and genetic patterns of medulloblastoma that are able to predict the outcomes. Medulloblastoma is composed of sheets of densely packed small round cell, with abundant mitotic figures, and vascular proliferation and necrosis with pseudopalisading are uncommon (Fig. 35.12) [60–62].

Clinical presentation of posterior fossa medulloblastoma includes headache, vomiting, unsteadiness, and symptoms related to increased ICP due to obstructive hydrocephalus. Treating these children as cases of viral illness or gastroenteritis always lead to delay in the diagnosis [60].

Medulloblastomas in CT scan appear as hyperdense midline posterior fossa tumor usually involving the vermis. In MRI they appear hypointense or isointense in T1-WI and typically hyperintense in T2-WI, and usually enhance after intravenous injection of gadolinium (Fig. 35.13) [62, 63].

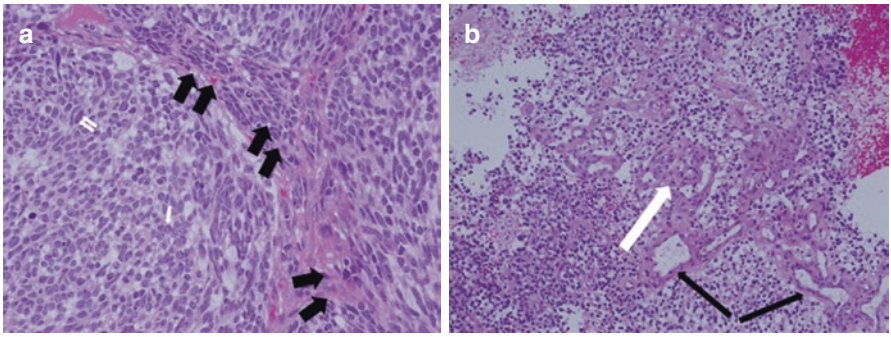


Fig. 35.12 Nodular (desmoplastic) medulloblastoma (**a**) with multiple nodules. Note small round blue cells with high nuclear cytoplasmic ratio (white arrow) and mitosis (double white arrows), and the abundant intervening less differentiated internodular region (black arrows). The tumor is extremely cellular, with sheets of anaplastic cells, with little cytoplasm and hyperchromatic nuclei. Note that mitoses are abundant. True rosettes (black arrow), capillaries and vascular profilation (white arrow) (**b**)

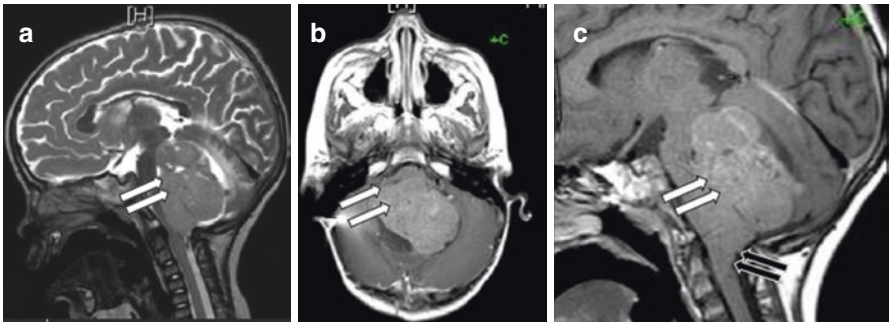


Fig. 35.13 MRI scan midsagittal view T2-WI (**a**) of a 3-year-old child with slightly hyperintense medulloblastoma filling the fourth ventricle (arrows). Postcontrast (**b**) axial and (**c**) sagittal views showing subtle enhancement of the medulloblastoma. Note herniation of cerebellar tonsil through the foramen magnum (black arrows) caused by the mass effect of the medulloblastoma

Treatment of medulloblastoma is generally by surgical removal with attempt for gross total resection, followed by craniospinal axis radiation. A temporary EVD is usually placed during surgery to treat hydrocephalus. Persistent hydrocephalus is treated by ETV or permanent VP shunt [63].

About 20% of patients undergo resection of medulloblastoma and develop cerebellar mutism soon after surgery; they become unable to speak or express themselves and generally have pronounced mood of dysregulation and hypotonia. Almost all will demonstrate a slow steady recovery [64].

Poor prognostic factors include children younger than 3 years, incomplete removal, distant metastases, and diffuse anaplasia in the histologic specimen. Nowadays, craniospinal radiation is followed by chemotherapy for both average (defined as gross totally resected tumor without severe anaplasia, and no

metastases) and high-risk children aged 3 and older. The 5-year survival exceeds 80% after gross total removal followed by radiotherapy and chemotherapy [65].

35.23 Ependymoma

Ependymoma is the third most common PBT, after astrocytoma and medulloblastoma, accounting for about 10% of PBTs. These tumors typically arise from the ependymal cell layer of the cerebral ventricles. Ependymomas are seen mainly in children at 4–6 years with about one-third diagnosed before the age of 3. Two-thirds of ependymomas are infratentorial, and one-third are supratentorial. There is evidence of leptomeningeal dissemination at the time of diagnosis in 5% of patients [17, 66, 67].

Ependymoma is a slowly growing intraventricular tumor, most commonly in the fourth ventricle, but may occur in the brain parenchyma outside the ventricles. Ependymoma is grossly characterized by sharply demarcated edges and histologically is moderately cellular and composed of oval cells with monomorphic nuclei and tapering eosinophilic cytoplasm. The presence of perivascular pseudorosette (perivascular radiating tumor cell cytoplasmic processes) is diagnostic. Anaplastic ependymomas (WHO grade III) can be extremely invasive and are poorly differentiated. They demonstrate clear evidence of malignancy in the form of increased mitotic activity, and cellularity with microvascular proliferation and pseudopalisading necrosis [3, 67].

In general, ependymoma has less infiltrative growth pattern that predisposes to surgical resection. Ependymomas usually grow out of the fourth ventricle via the foramina of Luschka and Magendie toward the cerebellopontine angle and through the foramen magnum into the upper cervical canal around the spinal cord.

On CT scan ependymoma appears iso- to hypodense enhancing peri- or intraventricular mass lesion with different degrees of calcifications, and necrotic and cystic changes. However in MRI it is iso- to hypointense in T1-WI and hyperintense in T2-WI (Fig. 35.14). Hemorrhage is reported in 10% of cases [3, 17].

The current treatment of ependymoma is gross total resection, followed by local therapy (chemotherapy for children below 3 years of age, and radiotherapy for children 3 years or older). Proton beam radiotherapy has played an important role in young children. The most important prognostic factor is gross total resection (Fig. 35.15) [68].

35.24 Choroid Plexus Tumors

Choroid plexus tumors represent 2–4% of all PBTs, and 10–20% of infantile brain tumors. They are choroid plexus papilloma (WHO grade I), atypical choroid plexus papilloma (WHO grade II), and choroid plexus carcinoma (WHO grade III). Choroid plexus tumors originate from epithelial layer of choroid plexus of cerebral

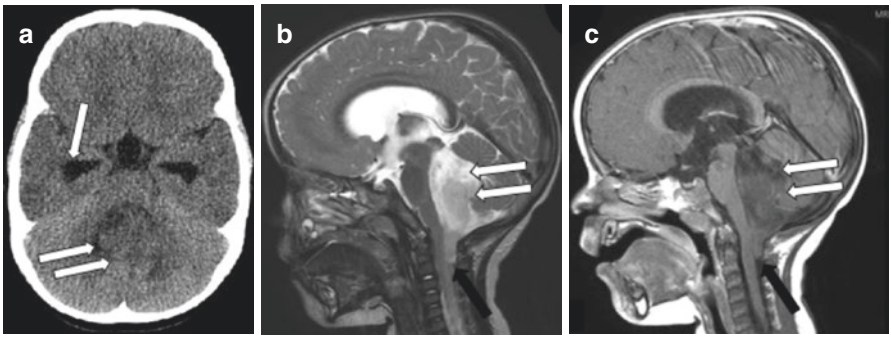


Fig. 35.14 (**a**) Axial CT scan of a 2-year-old child with fourth ventricular ependymoma (white arrows) causing early obstructive hydrocephalus with prominent temporal horn (single white arrow). Ependymoma appears hyperintense in sagittal T2-WI (**b**) with subtle enhancement after contrast (**c**). Note tonsillar herniation caused by mass effect of the tumor (black arrow)

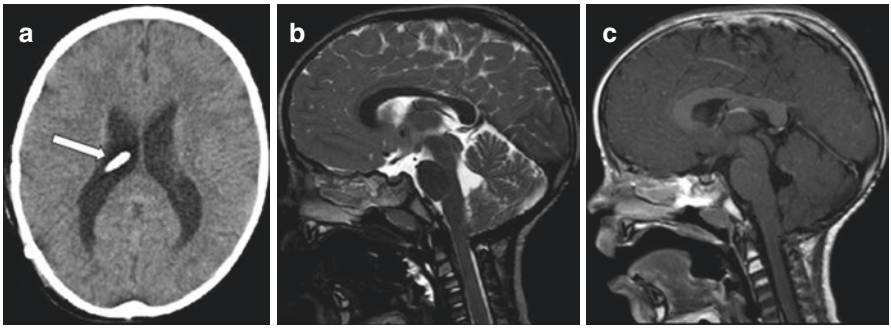


Fig. 35.15 Postoperative images of the same child 2 years after gross total removal of the tumor and proton beam radiotherapy. Persistent hydrocephalus treated by insertion of VP shunt (white arrow) seen in (**a**) axial CT scan image. Sagittal T2-WI (**b**) and postcontrast sagittal (**c**) views, showing no evidence of tumor recurrence

ventricles, mainly lateral ventricles in children and adolescents. In general choroid plexus papillomas are five times more common than choroid plexus carcinoma [69].

Choroid plexus tumors present at birth with increased ICP from hydrocephalus, usually of communicating type resulting from excessive production of CSF, but obstructive hydrocephalus may result from obstruction of the ventricular foramen. Older children present with nausea, vomiting, diplopia, papilledema, headaches, and weakness. Diagnosis is usually made by CT or MRI where multilobular, calcified, contrast-enhancing intraventricular masses associated with hydrocephalus are seen [69, 70].

Treatment is by gross total resection of this vascular tumor. Controlling blood supply of the tumor from anterior and posterior choroidal arteries is always challenging. Choroid plexus carcinomas are chemosensitive tumors, and the role of adjuvant radiation is controversial. The 5-year survival rate is 50%. Complete tumor removal completely relieves hydrocephalus without the need of a shunt [70].

35.25 Choroid Plexus Papilloma

Choroid plexus papilloma is similar to choroid plexus in its gross appearance and papillary architecture, but histologically tumor cells tend to be more crowded and columnar, as opposed to the cuboidal morphology of normal choroid plexus epithelium. Choroid plexus papilloma is a benign tumor and can be cured with surgery, but dissemination via CSF can occur in up to 20% of cases [69].

Choroid plexus papillomas are isointense in T1-WI with areas of high signal indicating hemorrhage or necrosis. Papillomas enhance brightly after administration of gadolinium, and T2-weighted images demonstrate intermediate-to-high signals (Fig. 35.16).

Children with choroid plexus papilloma often present with hydrocephalus due to overproduction of CSF, and even after surgical resection permanent VP shunt may be required [69].

35.26 Atypical Choroid Plexus Papilloma

Atypical choroid plexus papilloma differs from choroid plexus papilloma in the presence of mitotic activity. Curative surgical treatment is possible, but recurrence rate is significantly high [71].

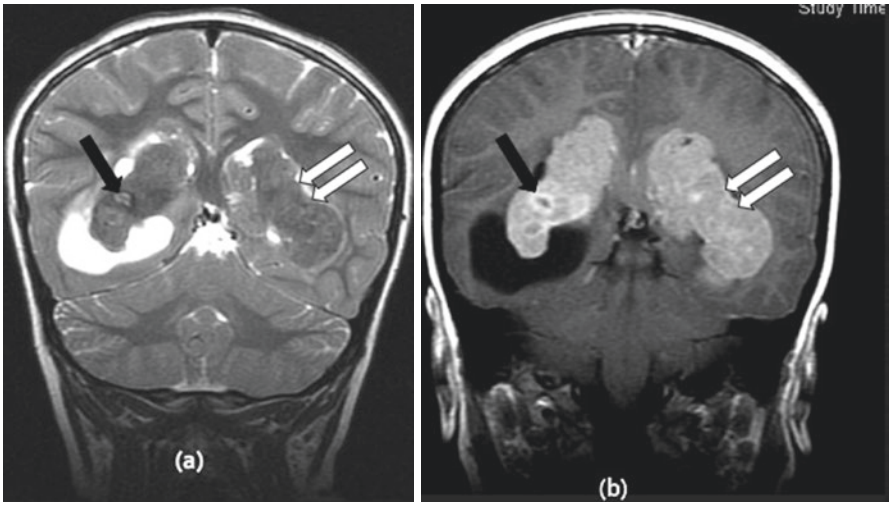


Fig. 35.16 MRI coronal views: (**a**) T2-WI and (**b**) T1 with contrast showing choroid plexus papilloma (white arrows) filling both lateral ventricles, appearing isointense in T2-WI. Papillomas enhance after contrast, and contain areas of hemorrhage or necrosis (black arrow)

35.27 Choroid Plexus Carcinoma

Choroid plexus carcinoma is an aggressive tumor that histologically shows features of malignancy, including increased cellularity, nuclear pleomorphism, mitotic activity, necrosis, frequent invasion of the adjacent brain parenchyma, and CSF dissemination. Choroid plexus carcinoma constitutes 5–10% of neonatal choroid plexus tumors. They present with macrocephaly, bulging anterior fontanel, irritability, seizures, vomiting, and lethargy. MRI is diagnostic in most cases when the tumor is large and heterogeneously enhancing after gadolinium (Fig. 35.17). Choroid plexus carcinoma is treated with surgical debulking and adjuvant chemotherapy; however, prognosis is always poor [70].

35.28 Pineal Region Tumors

Pineal region tumors are midline brain tumors, the most common are pineal parenchymal tumors and germ cell tumors. Pineal parenchymal tumors are divided into three major subgroups: pineocytoma (WHO grade I), pineal tumors of intermediate differentiation (WHO grade II/III), and pineoblastoma (WHO grade IV) [72–74].

Pediatric germ cell tumors usually present between 6 and 14 years, accounting for 35% of pineal tumors and about 2.8% of all PBTs. The majority are found in either pineal region or suprasellar region. These tumors are thought to be derived from migrated cells from the primary gonadal ridge during embryogenesis and subsequently undergo malignant transformation.

Germ cell tumors are classified into:

1. Germinomatous germ cell tumors
2. Non-germinomatous germ cell tumors:
   (a) Embryonal yolk sac tumors
   (b) Choriocarcinomas
   (c) Endodermal sinus tumors
   (d) Malignant teratomas

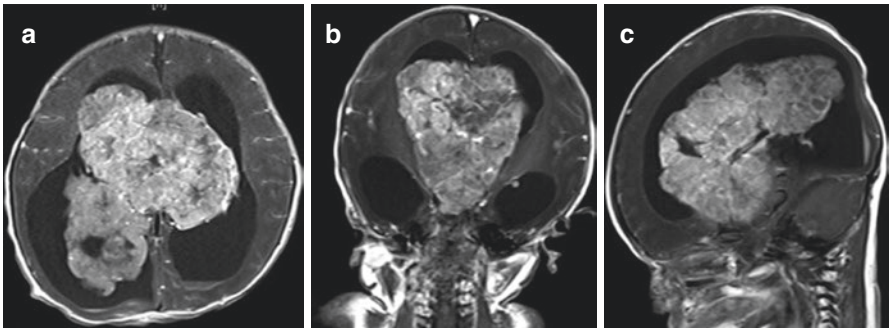


Fig. 35.17 MRI scan of a neonate; T1-WI with contrast (**a**) axial, (**b**) coronal, and (**c**) sagittal views showing heterogeneously enhancing large choroid plexus carcinoma filling most of the lateral and third ventricles with associated hydrocephalus

Symptoms usually precede the diagnosis by several months, due to the development of hydrocephalus. Children may present with visual disturbance, and endocrinopathy, altered personality or sleep pattern, dramatic weight changes, decline in school performance, or seizures. On clinical examination, patients with pineal region tumor may exhibit a characteristic Parinaud's syndrome (palsy of upward gaze, lid retraction, sunset eyes, and loss of accommodation) [72–74].

On MRI germ cell tumors appear bright in T2 and enhance with contrast with distinct margins. They can spread locally or via CSF. Spine metastases at diagnosis are not uncommon and a spine MRI should be part of the diagnostic workup (Fig. 35.18). Germ cell tumors can also be diagnosed by laboratory tests for tumor markers in the serum and CSF, including alpha-fetoprotein and beta-human chorionic gonadotropin. They are normally absent in children's CSF and serum.

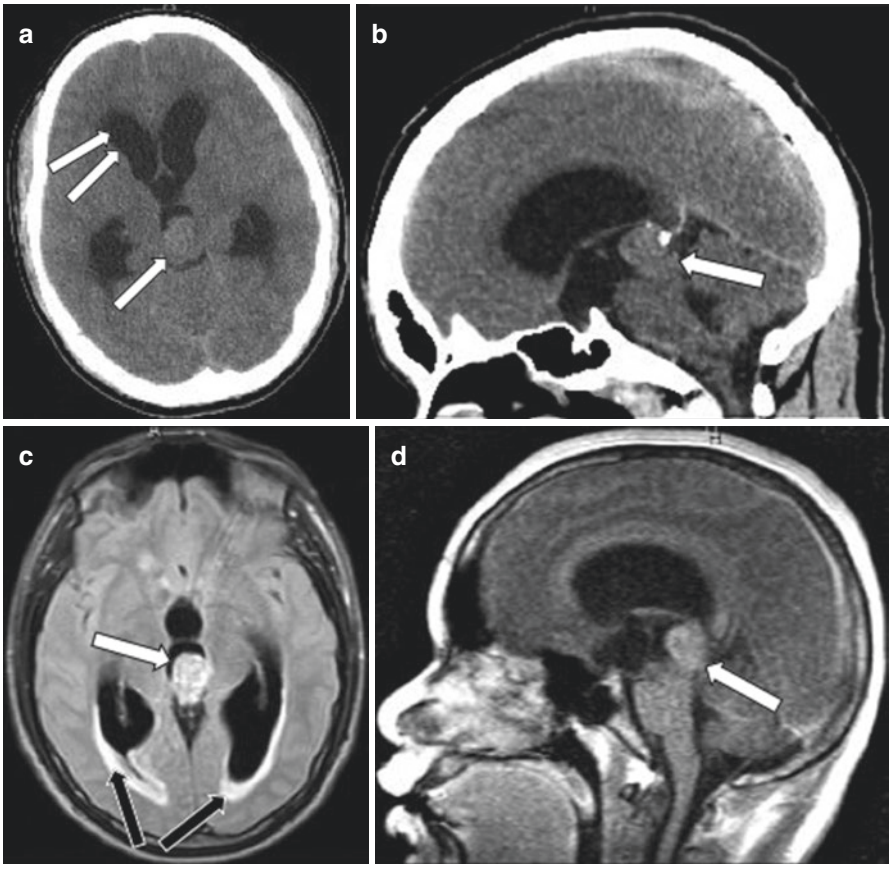


Fig. 35.18 Noncontrast (**a**) axial and (**b**) sagittal reformatting CT head showing isodense mass at the region of the pineal gland (arrow), obstructing the aqueduct of Sylvius causing hydrocephalus (double arrow). MRI (**c**) axial FLAIR and (**d**) sagittal view T1 with contrast showing a mass in the pineal region with subtle enhancement (white arrow) and periventricular edema of hydrocephalus (black arrows)

Tumor markers are usually elevated in most non-germinomatous germ cell tumors, but will be normal or very low in pure germinomas. Histologically, germinoma appears in the form of sheets of large, round cells separated by fine fibrovascular septa. The tumor cells are clear with large round irregular nuclei containing single prominent nucleolus with peripherally disturbed chromatin. Mitotic figures are seen, and there is no necrosis (Fig. 35.19) [72–74].

Overall treatment will depend on histologic diagnosis of the tumor. Gross total resection or biopsy is indicated (if assessment of tumor markers is negative), followed by radiation therapy and chemotherapy. In case of obstructive hydrocephalus; ETV and tumor biopsy can be performed at the same time (Fig. 35.20).

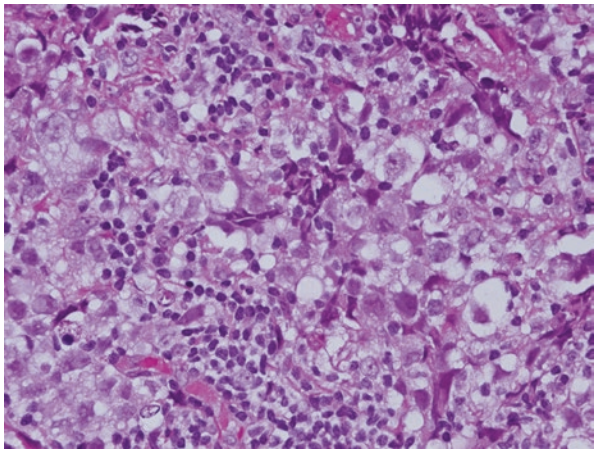


Fig. 35.19 H&E-stained section demonstrates sheets of large, round cells separated by fine fibrovascular septa. The tumor cells are clear with large round irregular nuclei containing single prominent nucleolus with peripherally disturbed chromatin. Mitotic figures are seen, and there is no necrosis

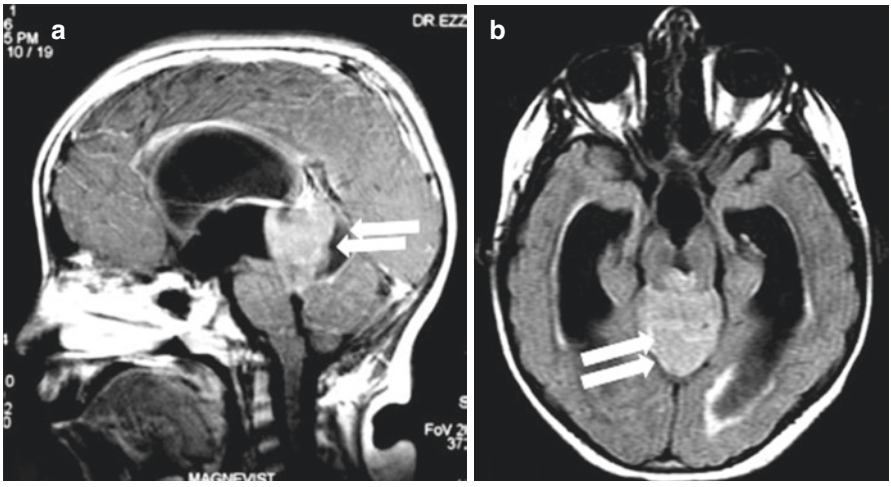


Fig. 35.20 MRI of 15-year-old boy presented with headache and vomiting: (**a**) postcontrast sagittal view showing enhancing pineal region tumor and (**b**) axial FLAIR view showing the tumor and hydrocephalus. This was treated by endoscopic third ventriculostomy and biopsy revealed germinoma

For symptomatic benign tumors (pineocytomas, pineal cysts, pilocytic astrocytomas, and teratomas), surgical resection is the definitive therapy [74].

35.29 Craniopharyngioma

Craniopharyngioma is a benign neoplasm that typically arises in sellar and suprasellar region. Pediatric craniopharyngiomas account for 1–5% of PBTs, and histologically are of adamantinomatous type. Although benign, craniopharyngiomas cause tremendous morbidity and long-term complications. They inevitably disrupt the hypothalamic–pituitary axis, which can lead to endocrinopathies, growth deficiencies, visual disturbance, headaches, or seizures [75].

Craniopharyngioma appears in CT scan as calcified heterogenous mass with cystic and solid components, or as a multicystic enhancing mass with some solid components (Fig. 35.21). In MRI craniopharyngioma appears iso- to hyperintense in T1-WI, hyperintense in T2, and vividly enhancing in contrast study (Fig. 35.22). Craniopharyngiomas do not spread throughout the CSF; therefore, routine spinal imaging or CSF collection is not essential for staging purposes. Histologically craniopharyngioma has a characteristic basal layer of small basophilic cells, with internal layer of stellate cells in loose connective matrix. A pathognomonic top layer of palisading keratinized squamous cells shed into the cyst cavity forming "wet keratin" (Fig. 35.23) [17, 75–78].

The optimal treatment of craniopharyngioma usually aims for tumor control or cure. However, attempt for gross total resection is rarely accomplished due to its proximity and adherence to the hypothalamus and optic chiasm. This tumor can also be very calcified, and stony rocklike form makes its total removal difficult. Multiple surgical approaches sometimes are needed to provide tumor control. For residual difficult-to-remove craniopharyngioma, radiation therapy may help in preventing recurrence. However, because there are many critical structures in the target field,

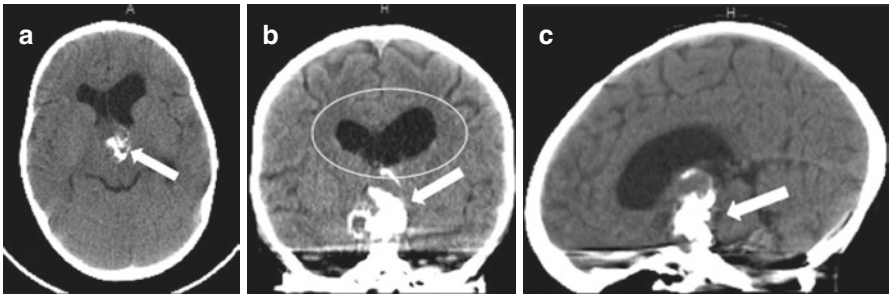


Fig. 35.21 CT scan: (**a**) axial, (**b**) coronal, and (**c**) sagittal views showing intensely calcified suprasellar craniopharyngioma (arrows). Not the associated obstructive hydrocephalus (**b**)

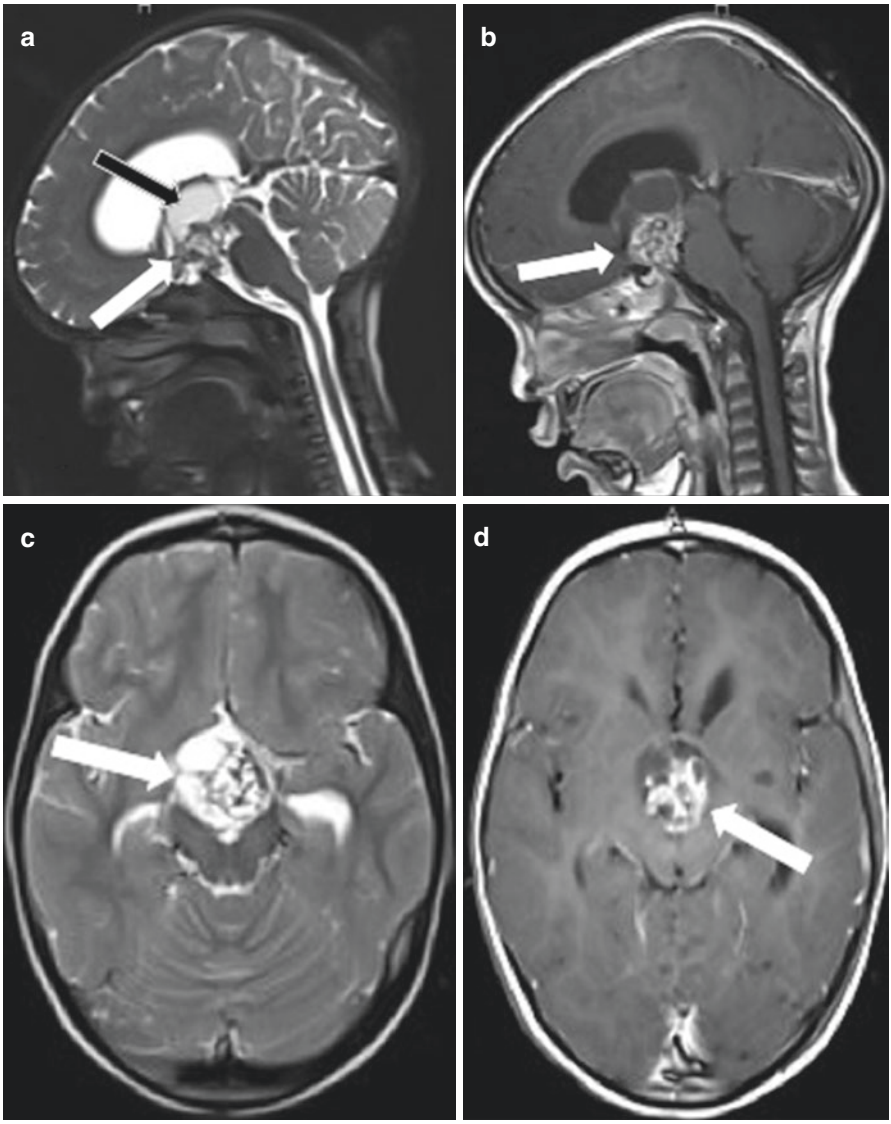


Fig. 35.22 MRI of a typical craniopharyngioma: (**a**) sagittal T2-WI. A multilobulated mass is seen in the suprasellar region partly solid (white arrow) with its cyst filling the third ventricle (black arrow). (**b**) Sagittal T1-WI following gadolinium. The suprasellar solid component enhances while the cystic area above it does not. (**c**) Axial T2-WI and (**d**) axial T1-weighted image with gadolinium

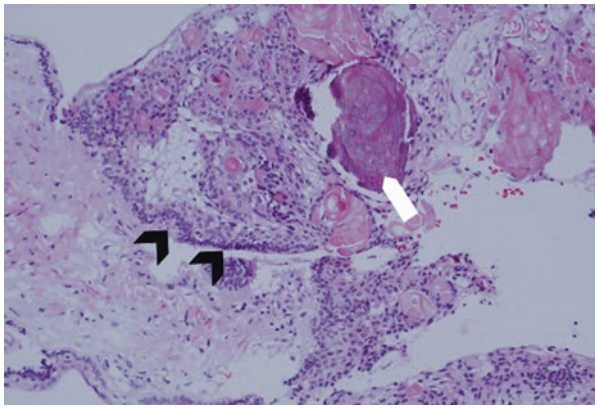


Fig. 35.23 Section of craniopharyngioma showing basal layer of small basophilic cells (black arrowheads). Internal layer of stellate cells in loose connective matrix. Top layer of palisading keratinized squamous cells that shed into the cyst cavity forming "wet keratin" (white arrow)

radiation should be delayed or spared in very young children. Modern techniques, such as 3-dimensional (conformal) radiation or proton beam therapy, may help minimize scattered and side effects of the radiation (Fig. 35.24). On the other hand, chemotherapy has no role in the treatment or stabilization of craniopharyngiomas. Some studies have suggested a benefit of injecting chemotherapy directly into the cysts. However, this approach to therapy is complicated by the presence of multiloculated cysts and the risk associated with chemotherapeutic agents leaking into the surrounding brain tissue [75–80].

35.30 Atypical Teratoid-Rhabdoid Tumor (ATRT)

Atypical teratoid-rhabdoid tumor is a malignant embryonal tumor composed predominantly of poorly differentiated elements frequently with rhabdoid cells. It is a relatively rare aggressive tumor that affects mostly infants and young children under the age of 3 years (mean age approximately 2 years). It is very rare in children older than 6 years. It is more common in males. About 50% of ATRTs arise in the posterior fossa. ATRT commonly seeds through CSF pathways. Findings on CT and MRI are similar to those seen in medulloblastoma and PNETs. Almost all ATRTs are contrast enhancing, and leptomeningeal dissemination is seen in almost 25% of cases at the time of presentation (Fig. 35.25).

Macroscopically, ATRT is large in size, and soft and fleshy in consistency, with necrotic areas. Histologically, usually a complex pattern is seen due to a combination of rhabdoid, primitive neuroepithelial, epithelial, and mesenchymal components [81–84].

Diagnosis is always made by MRI of the brain, and whole-spine MRI, CSF examination, and renal ultrasound should also be considered in all cases. There is no current standard treatment for ATRT. Multimodal treatment consists of surgery to obtain tissue diagnosis, followed by chemotherapy and radiation therapy [81–84].

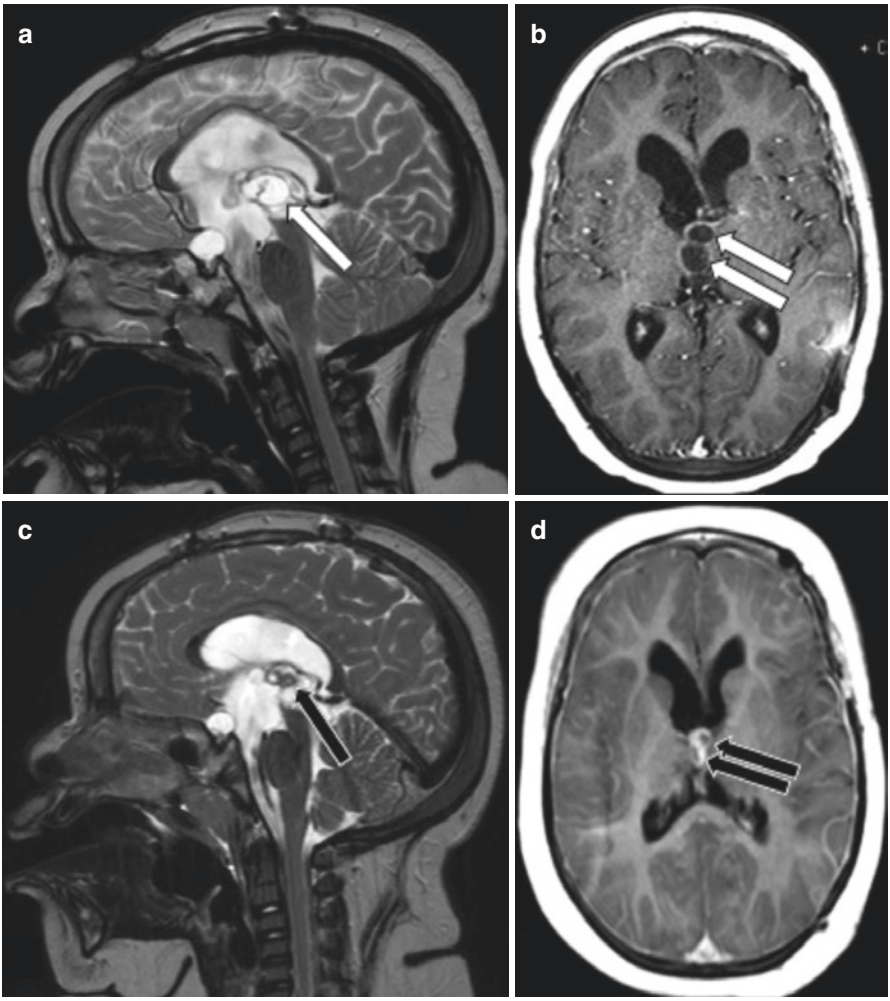


Fig. 35.24 MRI scan after surgical resection of craniopharyngioma showing small residual: (**a**) sagittal T2-WI (white arrow), enhanced after gadolinium in (**b**) axial T1-WI with contrast (double white arrows). This was treated with radiotherapy. (**c** & **d**) MRI after 2 years of treatment showing disease control with reduction in its size (black arrows)

35.31 Dysembryoplastic Neuroepithelial Tumor (DNET)

DNETs are benign, supratentorial, cortical tumors, accounting for about 1% of PBTs, and typically associated with intractable focal epilepsy. Neurological examination of those patients is usually unremarkable. They are considered the second most common surgically resectable epileptic tumors and found in about one-fifth of patients who undergo surgery for the treatment of intractable epilepsy [85].

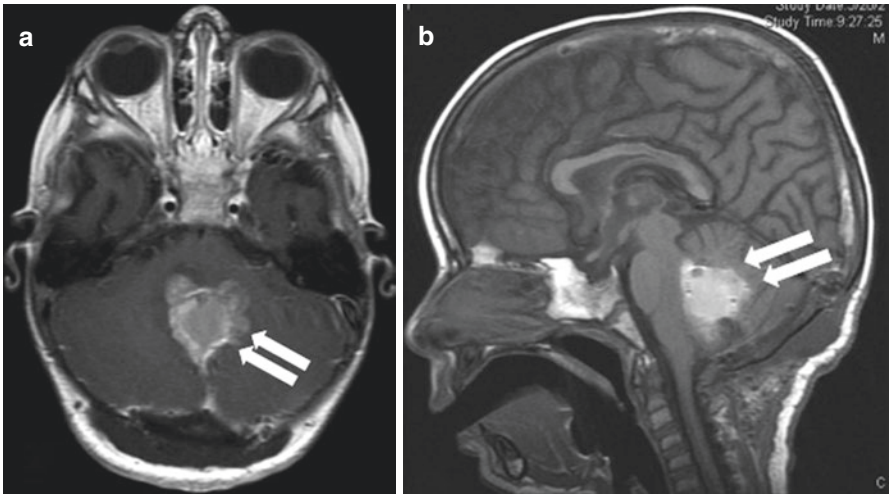


Fig. 35.25 T1-weighted postcontrast: (**a**) axial and (**b**) sagittal MRI of an irregular enhancing posterior fossa atypical teratoid rhabdoid tumor (ATRT) filling the fourth ventricle (arrows) in a 3-month-old child presenting with a facial palsy

MRI appearance of DNET is typical nodular lesion with cystic appearance, which is hypointense in T1-WI and hyperintense in T2-WI and FLAIR. Scalloping of the overlying skull is also seen in slow-growing tumor [Fig. 35.26]. Pathological findings of DNETs include the presence of columns of oligodendroglioma-like cells and floating neurons, along with nodular structures. Surgical resection is curative for seizures in most cases [86, 87].

35.32 Ganglioglioma

Gangliogliomas are well-differentiated, slowly growing tumors, composed of neoplastic, mature ganglion and glial cells. Gangliogliomas are benign tumors (WHO grade I), but malignant transformations to anaplastic ganglioglioma, WHO grade III, have been reported. Ganglioglioma comprises about 40% of all tumors associated with intractable seizures. The mean age at presentation is 8.5 years, and there is slight male predominance. Gangliogliomas predominantly arise in the cerebral hemispheres, predominantly localize to the temporal lobe, but also occur in the cerebellum, ventricles, or brain stem. Meningeal or leptomeningeal spread is rare [88].

New-onset seizures and refractory epilepsy are the most common presentation. Other common symptoms include raised ICP and focal neurologic deficits. Gangliogliomas appear hypointense in T1-WI and hyperintense in T2-WI circumscribed mass lesions, with variable enhancement and appearance as solid, rim, or nodular (Fig. 35.27) [88].

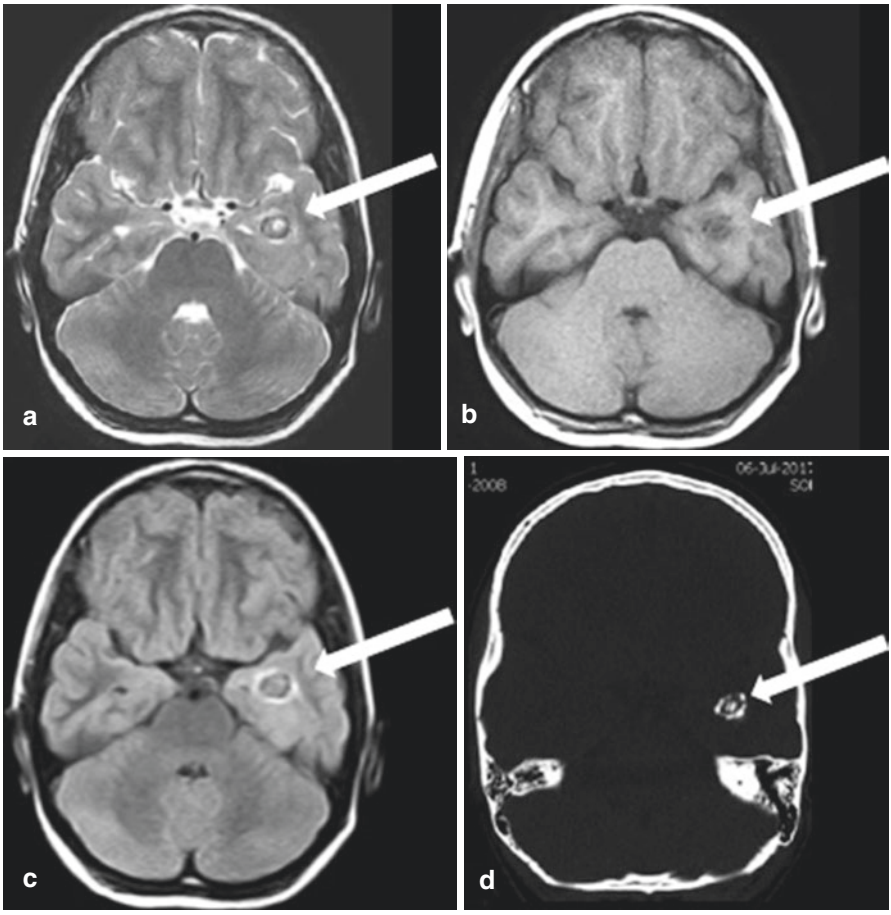


Fig. 35.26 Axial T2-WI (**a**), FLAIR (**b**), T1-WI (**c**), and MRI scan of DNET showing 1.5 cm ovoid heterogeneous focus, located along the anterior margin of the left temporal horn abutting the amygdala and head of the hippocampal formation period. The lesion is surrounded by faint edema. Axial CT scan bone window view showing the main lesion appearing as a calcified ring with central calcified nidus

Histologically, gangliogliomas are composed of clusters of large cells representing neurons, fibrosis, and calcification. Binucleate neurons are diagnostic, but evident in less than half of the cases. Lymphocytic or plasma cell infiltrates are common (Fig. 35.28).

Good prognostic factors include temporal localization, complete surgical resection, and long-standing epilepsy. The 5-year survival rate is 93% for cerebral lesions [88].

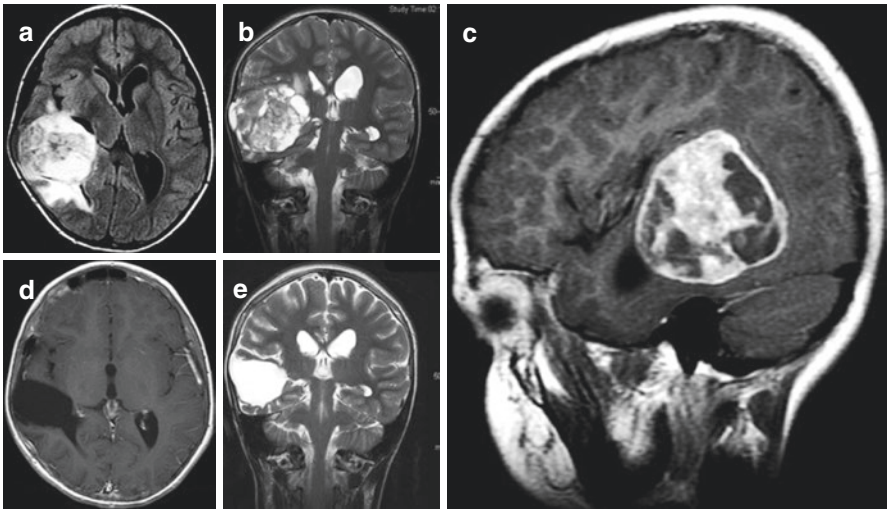


Fig. 35.27 MRI scans of 8-year-old boy presented with intractable epilepsy showing large histologically proved ganglioglioma: (**a**) axial FLAIR, (**b**) coronal T2-WI, and (**c**) sagittal with contrast. Seizures controlled after gross total removal: (**d**) postcontrast axial view and (**e**) coronal T2-WI

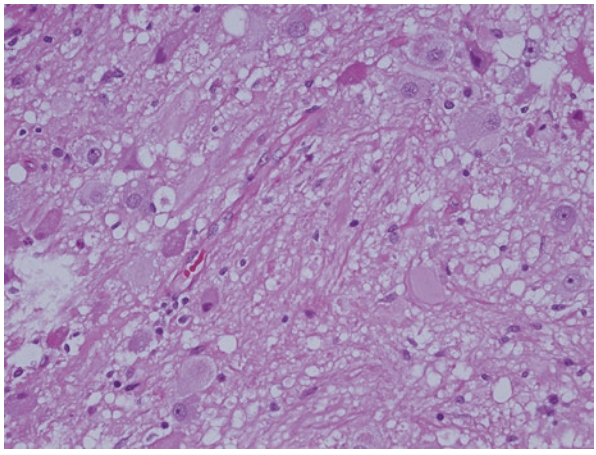


Fig. 35.28 Histopathology picture of ganglioglioma showing a compact growth pattern with clusters of neoplastic ganglion cells with loss of cytoarchitectural organization. Large bi- or multinucleated neurons with prominent nucleoli

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