

# Pediatric Pineal Region Tumors

Ulrike Löbel and Andrea Rossi

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Abstract

Tumors of the pineal gland region in children include pineal parenchymal tumors (mostly represented by pineoblastoma, a variant of primitive neuroectodermal tumors) and germ cell tumors (mostly represented by germinomas), with a handful of other rarer tumors and tumor-like masses. Germinomas are, by far, the most common pineal gland tumor and may also involve other areas simultaneously, such as the suprasellar region in the typical “bifocal” germinoma. Germ cell tumors may secrete tumor markers in the serum and/or CSF, and these may greatly facilitate the diagnosis and obviate the need for a biopsy. Pineal gland cyst is, by far, the most common pineal region mass in children. They are benign and usually do not require long-term follow-up.

Introduction

The pineal region is a central midline intracranial location that includes the pineal gland, the surrounding cisterns of the quadrigeminal plate and velum interpositum, the posterior third ventricle, and the adjacent nervous tissues of the brain stem, thalami, and callosal splenium. Tumors of this region account for 3–8% of intracranial tumors in children (Smirniotopoulos et al. 1992). In the past, pineal region tumors were believed to be of pineal parenchymal origin and were collectively called “pinealomas.” However, with the advent of immunohistochemical and electron microscopy studies, it has become clear that most pineal region masses are malignant germ cell tumors (GCTs), among which germinoma is the most common (Smirniotopoulos et al. 1992). Together with pineal parenchymal tumors and gliomas, GCTs account for about 85% of tumors in this area. Whereas GCTs predominate in males, pineal parenchymal tumors show an equal sex incidence.

Clinical presentations of pineal region tumors depend on lesion size and patient age. The anatomic relationship between pineal gland and quadrigeminal plate, third ventricle, and deep venous structures accounts for most of the symptoms associated with pineal region tumors. Clinical signs related to obstructive hydrocephalus usually become evident with large tumors occluding the cerebral aqueduct or posterior third ventricle. Invasion of the midbrain may produce two similar, albeit not identical, clinical syndromes, depending on the degree of infiltration: (1) the Parinaud syndrome (paralysis of upward gaze, varying degrees of paralysis of convergence, and pupillary constriction) is caused by compression or invasion of the mesencephalon ventral to the aqueduct and caudal to the posterior part of the third ventricle; and (2) the Sylvian aqueduct syndrome (impairment of upward gaze, abnormalities of the pupil, paralysis or spasm of convergence, and nystagmus retractorius) may occur if the superior colliculus and pretectal areas are involved.

Masses of the pineal region may also cause precocious puberty, which may be explained by interference with the normal antigonadotropic effect of the gland, secondary invasion into the diencephalon with destruction of the median eminence, and ectopic production of gonadotropins by the neoplasm (Smirniotopoulos et al. 1992). Diabetes insipidus has also been found in patients with isolated, or
apparently isolated, pineal region tumors, perhaps indicating that germinomatous
tissue also is present on the floor of the third ventricle despite negative neuroradio-
logical findings or that hypothalamic function is impaired as a secondary effect of
hydrocephalus.

Because the different pineal tumors require different combinations of surgery,
chemotherapeutic drugs, and radiation, accurate assessment of tumor histology and
response to therapy is essential. Unfortunately, although both CT and MRI are
highly sensitive in the detection of pineal region tumors, only very rarely is the
histological diagnosis deduced on the basis of neuroradiological findings. When the
disease presents as bifocal masses (i.e., with simultaneous pineal and hypothalamic
involvement), germinoma is the most likely diagnosis; however, we also observed
bifocal mixed germ cell tumors. Furthermore, when the lesion contains calcified,
fatty, and parenchymatous (solid) portions, a mature teratoma is extremely likely.
Diffusion-weighted imaging (DWI) is useful to estimate the cellularity of the
lesions and, thus, whether the tumor is likely to be low or high grade.

In many clinical situations, biopsy of the intracranial tumor may be required for
specific diagnosis. Calcification of the pineal gland is a useful clue to the diagnosis,
since approximately 70 % of patients with pineal region tumors have calcifications,
whereas physiological calcification is thoroughly absent before age 6 years and is
found in a minority of children 7–14 years old (Zimmerman and Bilaniuk 1982).
Although most calcifications seen in association with pineal region neoplasms
occur within the gland rather than as calcium deposits within the neoplasm,
GCTs (especially teratomas) may have tumoral calcifications. The normal pineal
calcification lies in the midline; germ cell tumors typically engulf the calcified
gland, whereas an off-midline, or exploded, pineal calcification is highly suspicious
for a mass (usually a pineal parenchymal tumor) that displaces it to the periphery.

**Pineal Parenchymal Tumors**

Pineal parenchymal tumors account for about 15–20 % of all pineal tumors and are
represented by pineocytoma (WHO grade I), parenchymal tumor of intermediate
differentiation (WHO grade II–III), pineoblastoma (WHO grade IV), and papillary
tumor of the pineal region. Unlike GCTs, they do not show sexual predilection and
usually are found in older children or adolescents.

**Pineocytoma**

**Epidemiology and Clinical Picture**
The pineocytoma, composed of well-differentiated mature cells, presents in all age
groups but mainly in adults with an average age at diagnosis of ca. 50 years
(Dumrongpisutikul et al. 2012; Kakigi et al. 2014); sometimes it represents an
occasional finding at autopsy. It is a rare tumor in children (Engel et al. 2000) but
represents 14–30 % of pineal tumors (Dumrongpisutikul et al. 2012). It is usually a
well-marginated, unencapsulated, slow-growing, noninvasive lesion. Cysts and calcifications are commonly found; hemorrhage may be present as well. Although frequently solid, the tumor may appear predominantly, or even purely, cystic (Engel et al. 2000). Dissemination to the CSF and tumor recurrence usually do not occur after gross-total resection or radiosurgery alone; however, diffuse leptomeningeal relapse has been reported in a single adult patient 10 years after diagnosis (Gomez et al. 2011).

**Biological Behavior and Neuropathology**

Histologically, pineocytomas are moderately cellular lesions composed of round cells with hyperchromatic, moderately pleomorphic nuclei, resembling pineocytes and being virtually indistinguishable from the normal pineal parenchyma (Smirniotopoulos et al. 1992). The cells form sheets or lobules, and the tumor cell processes form pineocytomatous rosettes (Borit et al. 1980). Immunohistochemistry shows strong positivity for synaptophysin, neuron-specific enolase, and neurofilament protein.

**Imaging Studies**

On CT, pineocytomas have been described as isodense or slightly hyperdense, with predominantly peripheral calcification and strong contrast enhancement (CE) (Chiechi et al. 1995; Nakamura et al. 2000). Hydrocephalus is usually present due to compression of the cerebral aqueduct (Louis et al. 2007).

The MRI features are nonspecific. Pineocytomas have been frequently described as solid, partly cystic, or purely cystic masses, and their differentiation from germinomas may not be feasible (Nakamura et al. 2000). The solid portion is described as hypointense on T1-weighted images and isointense on T2-weighted images; CE has been variably described as homogeneous (Nakamura et al. 2000) or heterogeneous (Chiechi et al. 1995). The differentiation of these lesions from pineal cysts or other tumors may be difficult on a single examination, and short- to medium-term follow-up with MRI is strongly suggested in order to detect lesion growth. Advanced imaging techniques are inconsistent in differentiating pineal parenchymal lesions from germ cell tumors. However, margins that are well defined, smooth, and thinner than 2 mm are believed to be strongly related to benign pineal cysts (Engel et al. 2000). Furthermore, a normal pineal gland should not exceed 5–9 mm in length, 3–6 mm in width, and 3–5 mm in height (Zimmerman and Bilaniuk 1982).

**Pineal Parenchymal Tumor of Intermediate Differentiation**

**Epidemiology and Clinical Picture**

The pineal parenchymal tumor of intermediate differentiation (PPTID) was first included into the WHO classification of brain tumors in 2007. Based on the tumor’s mitotic activity and immunoreactivity to neurofilament protein, PPTIDs
are classified as WHO grade II or III lesions, between pineocytoma and pineoblastoma. However, their classification is not yet definite. The reported 5-year survival ranges from 39% to 74% (Louis et al. 2007). Overall, the clinical course of the lesion is difficult to predict; therefore, they should be treated as high-grade lesions (Behari et al. 2011). PPTID represents 20–62% of pineal lesions in children and adults (Dumrongpisutikul et al. 2012). It usually presents in older children (mean, 12.1 years; range, 4.5–18 years) (Komakula et al. 2011). Leptomeningeal dissemination is more common in high-grade tumors (ca. 30%) (Dumrongpisutikul et al. 2012).

**Biological Behavior and Neuropathology**
PPTID shows moderately high cellularity, mild to moderate nuclear atypia, and low to moderate mitotic activity.

**Imaging Studies**
CT may show calcification described as “exploded” and typical for pineal parenchymal tumors. Hemorrhage was identified in 9% of patients (Komakula et al. 2011).

On MRI, the tumor has a bulky appearance and invades the surrounding parenchyma in 82% of patients. It is usually hypointense on T1-weighted images and hyperintense on T2-weighted images. There is usually marked homogeneous or heterogeneous contrast enhancement DWI can show restricted diffusion, correlating with the moderately high cellularity typical of this tumor (Fig. 1).

**Pineoblastoma**

**Epidemiology and Clinical Picture**
Pineoblastomas represent 24–50% of pineal tumors (Dumrongpisutikul et al. 2012). They are highly malignant tumors composed of undifferentiated, immature cells. Nearly all patients present with hydrocephalus due to compression of the aqueduct. Dissemination may occur in up to 45% of patients (Dumrongpisutikul et al. 2012), and osseous metastases have been reported (Constantine et al. 2005).

**Biological Behavior and Neuropathology**
Unlike pineocytomas, they are heterogeneous, ill-marginated, invasive tumors, often characterized by necrotic-degenerative changes. They usually are irregular in shape and larger (>4 cm) than other pineal tumors (Tien et al. 1990); they may invade the adjacent brain and spread by CSF seeding. They resemble medulloblastoma and supratentorial PNET on histopathology, but their outcome differs compared to supratentorial PNET; therefore, they are believed to be biologically distinct tumors (Dhall et al. 2010). The outcome depends largely on patient age, because radiation therapy is usually not performed in children younger than 3 years of age. Therefore, the outcome of children with pineoblastoma younger than 3 years...
is worse, while that of patients older than 3 years is better compared to supratentorial PNETs (Dhall et al. 2010). Neuronal maturation following chemotherapy has been described (Nozza et al. 2010).

**Imaging Studies**

Overall, imaging findings of pineoblastoma are nonspecific. On CT, the presence of “exploded” calcifications is relatively characteristic.

On MRI, owing to their hypercellular nature, these tumors usually show iso- to hypointense solid components both on T1- and T2-weighted images (Fig. 2). Enhancement is variable (Nakamura et al. 2000), confined to solid portions, and can be completely absent (Fig. 3). Cysts are rare. However, calcification and size are not believed to represent useful differentiating signs from pineocytomas (Dumrongpisutikul et al. 2012; Nakamura et al. 2000). Diffusion-weighted imaging typically shows restricted diffusion with low ADC values of the solid portions.
owing to their hypercellular nature; however, this is not a mandatory rule, and ADC values may be similar to those of normal brain (Fig. 4).

Papillary Tumor of the Pineal Gland

Epidemiology and Clinical Picture
The papillary tumor of the pineal gland (PTPG) was first described in 2003 (Jouvet et al. 2003) and are most likely WHO grade II or III lesions with a risk of dissemination in up to 7% (Dumrongpisutikul et al. 2012). To date, 70 cases, including seven pediatric patients, have been reported (Chang et al. 2008). Patients seem to present with hydrocephalus frequently. Treatment includes tumor resection, chemotherapy, and radiation. Currently, the outcome has been significantly impacted only by the extent of tumor resection (Abela et al. 2013).

Biological Behavior and Neuropathology
Histopathologically, these lesions are believed to originate from subcommissural ependymal cells. They show characteristic papillary features and dense cellular areas, forming true rosettes and tubes (Louis et al. 2007). Necrosis may be present.
Immunohistochemistry is positive for CK18, S100, NCAM, neuron-specific enolase, and vimentin (Abela et al. 2013).

**Imaging Studies**

On MRI, the tumor presents as large, well-circumscribed lesion with cystic components, characterized by inhomogeneous contrast enhancement (Fig. 5). A study of four adult patients found that all tumors were hyperintense on T1-weighted images. No hypointensity on susceptibility-weighted images was observed (Chang et al. 2008). However, larger studies are needed to confirm this finding as specific for PTPG.

**Retinoblastoma**

Retinoblastomas (RBs) belong to the PNET family. Isolated intracranial RBs have been described only exceptionally (Al Omari et al. 1999), whereas the so-called “trilateral” RB (Bader et al. 1980) is a multifocal lesion involving both ocular globes and the pineal gland.

Intracranial RBs show neuroradiological features that mirror those of their intraocular counterparts (Bagley et al. 1996). These lesions usually are coarsely

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**Fig. 3** Pineoblastoma in a 2-year-old boy. (a) Sagittal T2-weighted and (b) sagittal T1-weighted images show pineal mass (open arrows) plugging the cerebral aqueduct (thin arrow) and causing obstructive hydrocephalus; (c) contrast-enhanced sagittal T1-weighted image shows the mass does not enhance (open arrow). There is an incidental cyst of the pars intermedia of the pituitary gland. (d) Diffusion-weighted image and (e) corresponding ADC map show the lesion has restricted diffusion (arrowhead) due to elevated cellularity. Low signal intensity on axial T2-weighted image (arrowhead, f) and increased density on unenhanced CT (arrowhead, g) are also consistent with a solid, hypercellular tumor.
calcified, and an apparently innocuous, early pineal calcification in a small infant without associated signs of a pineal mass may be the initial manifestation.

MRI typically shows a solid mass that is isointense with gray matter on T1-weighted images and hypointense on T2-weighted images, shows restricted diffusion on DWI, and enhances markedly with gadolinium. Areas of lower signal intensity on T2-weighted images may reflect calcified spots within the mass. Subarachnoid seeding is a common feature; therefore, imaging of the whole neuraxis is mandatory in all patients with trilateral RB.

In addition to their relationship to pineoblastomas, RBs may also be associated with pineal cysts (Beck Popovic et al. 2006). However, a more recent review suggests that the incidence of pineal cysts in hereditary retinoblastoma is not higher than in the healthy population (Rodjan et al. 2010).

**Germ Cell Tumors**

Up to 50–75 % of pineal tumors are of germ cell lineage: 65–76 % of them are germinomas, 10–26 % are nongerminomatous, and 9–13.5 % are mixed (Al-Hussaini et al. 2009). Intracranial GCTs vary in their geographic incidence;
in Western series, they constitute anywhere between 0.4 % and 3.4 % of patients with primary CNS tumors, whereas in series reviewing patients in Japan and the Far East, the incidence of GCTs is fivefold to eightfold greater (Packer et al. 2000; Sumida et al. 1995). The most recent WHO classification of GCTs (Louis et al. 2007) is reported in Table 1.

**Table 1** Germ cell tumors according to the WHO classification 2007 and cells of origin

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<th>WHO classification of germ cell tumors</th>
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<tr>
<td>Germinoma</td>
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<tr>
<td>Teratoma</td>
</tr>
<tr>
<td>Mature</td>
</tr>
<tr>
<td>Immature</td>
</tr>
<tr>
<td>Teratoma with malignant transformation</td>
</tr>
<tr>
<td>Embryonal carcinoma</td>
</tr>
<tr>
<td>Endodermal sinus (Yolk sac) tumor</td>
</tr>
<tr>
<td>Choriocarcinoma</td>
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<tr>
<td>Mixed germ cell tumors</td>
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**Fig. 5** Papillary tumor of the pineal gland in a 12-year-old girl. (a) Sagittal T2 DRIVE sequence, (b) sagittal T1-weighted image, and (c) contrast-enhanced sagittal T1-weighted image show a mass lesion centered in the pineal region, with a partially cystic structure and showing enhancement of solid portions. (d) Axial diffusion-weighted image and (e) corresponding ADC map show diffusivity comparable to that of normal brain. (f) Axial FLAIR image and (g) contrast-enhanced axial T1-weighted image show tumor sitting in the posterior third ventricle and causing obstructive hydrocephalus.
GCTs most frequently arise in the pineal and suprasellar region, and, in general, GCTs of the pineal region outnumber suprasellar GCTs by a ratio of 2:1 (Packer et al. 2000). Less frequently, they involve the thalamus and basal ganglia. The preferential location in the pineal or suprasellar regions possibly accounts for the relatively significant amount of associated congenital midline abnormalities, such as falx sinus, callosal dysgenesis, and the Chiari I malformation, that are found in these patients. Primordial germ cells develop from embryonic cells of the yolk sac wall; these cells migrate from their original location near the allantois to the genital ridges, where they invaginate during the sixth gestational week. Because this movement occurs simultaneously with the development of the diencephalon and pineal gland, it is possible that misguided germ cells may remain trapped within the pineal gland, hypothalamus, and thalamus, thus explaining why GCTs preferentially arise in these locations (Smirniotopoulos et al. 1992).

Males are approximately twice as likely as females to develop GCTs, especially nongerminomatous variants. The male predominance of germinomas is limited to the pineal region, whereas suprasellar germinomas are more frequent in females. GCTs peak in incidence near the time of puberty. Nongerminomatous GCTs are more frequently diagnosed earlier in life, whereas germinomas usually are diagnosed between 10 and 21 years of age (Packer et al. 2000).

The presence, or absence, of specific protein markers, produced and/or secreted by tumor cells, is an important adjunct in the diagnosis of GCTs (Allen et al. 1979). At high levels, these protein markers can be measured in the serum, although CSF levels are a more sensitive and reliable measure of tumor presence (Packer et al. 2000; Table 2). Serum and CSF levels of α-fetoprotein and human β-gonadotropin (β-HCG) are now routinely analyzed. Elevation of one of both markers highly suggests a germ cell neoplasm and may point to a specific subgroup (e.g., α-fetoprotein, yolk sac tumor, teratoma; β-HCG, choriocarcinoma) (Louis et al. 2007). In addition, placental alkaline phosphatase, c-kit and OCT-4, and human placental lactogen may be elevated in germ cell tumors (Behari et al. 2011). Persistence of elevated tumor markers after surgical and adjuvant treatment is associated with poor prognosis (Drummond and Rosenfeld 1999).

<table>
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<th>Tumor</th>
<th>β-HCG</th>
<th>αFP</th>
<th>PLAP</th>
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<tr>
<td>Teratoma</td>
<td>−</td>
<td>−</td>
<td>±</td>
</tr>
<tr>
<td>Germinoma (pure)</td>
<td>± (weak)</td>
<td>−</td>
<td>±</td>
</tr>
<tr>
<td>Germinoma (syncytiotrophoblastic)</td>
<td>+</td>
<td>−</td>
<td>±</td>
</tr>
<tr>
<td>Choriocarcinoma</td>
<td>++</td>
<td>−</td>
<td>±</td>
</tr>
<tr>
<td>Mixed germ cell</td>
<td>++</td>
<td>++</td>
<td>±</td>
</tr>
<tr>
<td>Endodermal sinus (Yolk sac) tumor</td>
<td>±</td>
<td>++</td>
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<tr>
<td>Embryonal carcinoma</td>
<td>±</td>
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β-HCG beta-human-chorionic gonadotropin, αFP alpha-fetoprotein, PLAP placental alkaline phosphatase
Germinoma

Epidemiology and Clinical Picture
Germinomas are the most common type of pineal region mass (50–75 %) and account for two-thirds of GCTs (Smirniotopoulos et al. 1992). About 57 % of intracranial germinomas arise in the pineal region, whereas 32 % involve the suprasellar region and 9 % the basal nuclei (Wang et al. 2010). Germinomas arising from other sites, such as the brain stem or spinal cord, have only exceptionally been reported (Nakajima et al. 2000). As previously stated, germinomas are thought to arise from a midline stream of totipotential cells during the early stages of rostral neural tube development.

Clinically, compression of the cerebral aqueduct and invasion of the mesencephalic tectum result in hydrocephalus and the Parinaud syndrome, although precocious puberty is also frequently associated.

Biological Behavior and Neuropathology
Histologically, germinomas are malignant tumors composed of an admixture of large multipotential primitive germ cells and smaller lymphocyte-like cells (Smirniotopoulos et al. 1992). Laboratory tests display mildly increased serum levels of β-HCG and placental alkaline phosphatase (Tien et al. 1990).

Generally, germinomas respond markedly to chemotherapy and irradiation; therefore, surgery is contraindicated as a first option. However, a negative correlation between tumor response to radiation therapy and the presence of intratumoral cysts was recently demonstrated, with partly cystic tumors responding less rapidly and effectively than purely solid tumors. This probably is due to the fact that solid tumors have more viable tumor cells, better vascular supply, and higher oxygen tension than cystic tumors (Moon et al. 1999).

Because germinomas are not encapsulated, they are prone to invade the adjacent brain and CSF (22 %) (Keene et al. 2007). Therefore, both intracranial and spinal leptomeningeal metastases may be found at presentation. Contrast-enhanced spinal MRI is mandatory in order to detect possible drop metastases (Tien et al. 1990). Overall, the outcome is favorable with a 5-year survival rate of above 90 % (Borja et al. 2013).

Imaging Studies
On CT (Fig. 6), germinomas characteristically appear as homogeneous masses showing iso- or high density compared with the surrounding brain and a strong enhancement (Sumida et al. 1995; Fujimaki et al. 1994; Hoffman et al. 1991). Calcification is common and may result either from engulfment of the normal pineal gland by the tumor (Higano et al. 1994) or from calcification within the substance of the tumor, which usually results in small to medium, sometimes multiple, hyperdense foci (Fujimaki et al. 1994).

On MRI (Fig. 6), germinomas appear as well-delineated masses, either homogeneous or multilobular. They may show cystic-hemorrhagic components in up to 25 % (Figs. 7 and 8) and calcification in 19 % (Wang et al. 2010). They usually are
iso- to hypointense to gray matter on T1-weighted images and iso- to hyperintense on T2-weighted images (Wang et al. 2010). Intense and homogeneous enhancement is generally described for pineal germinomas (Smirniotopoulos et al. 1992; Sumida et al. 1995 Neuroradiology), while it may be more heterogeneous in a suprasellar location (Wang et al. 2010). Pineal germinoma may be bifocal, i.e., there is simultaneous hypothalamic involvement, in 2–20 % of cases (Wang et al. 2010; Cuccia and Alderete 2010) (Figs. 7 and 8). The differentiation of bifocal GCT from a unilateral disseminated lesion may require confirmation by endoscopy (Cuccia and Alderete 2010). Secondary intraventricular and leptomeningeal spread is common, with a preference for the frontal horns of the lateral ventricle (Figs. 9 and 10). The outcome of bifocal GCT seems to be similar to unifocal lesions. Although low ADC values of germinomas (Borja et al. 2013; Dumrongpisutikul et al. 2012) would be expected based on their high cellularity, a recent study suggested that ADC values and FDG-PET did not differ significantly between germinomas and pineal parenchymal tumors (Kakigi et al. 2014). In our experience, MR spectroscopy reveals an increased choline/NAA ratio with respect to normal brain and the possible presence of lipid resonance, consistent with necrosis (Fig. 9).
Fig. 7  Bifocal germinoma in a 15-year-old boy. (a) Axial CT and (b) axial FLAIR image show large mass sitting in the posterior third ventricle, with a markedly inhomogeneous structure due to coexistent solid and necrotic-cystic components and with evidence of calcification (arrows, a) and chronic intracystic hemorrhage (arrowhead, b). (c) Sagittal T2-weighted and (d) contrast-enhanced sagittal T1-weighted images show additional localization involving the median eminence of the hypothalamus (arrows). (e) Axial SWI image shows diffuse petechial hemorrhages (arrows) and confirms position-dependent intracystic layering from old hemorrhage (arrowhead), while (f) contrast-enhanced axial T1-weighted image shows multiple cystic components as nonenhancing against the background of enhancing solid tumor tissue. (g) Axial diffusion-weighted image and (h) corresponding ADC map show restricted diffusivity of the solid portions due to elevated cellularity.
Embryonal Carcinoma

The embryonal carcinoma is the most undifferentiated among the GCTs, being composed of malignant embryonal-type epithelial cells, and has been regarded as a precursor of teratomas (Smirniotopoulos et al. 1992). Embryonal carcinomas often represent the most aggressive portion of mixed GCTs and may produce metastases. The diagnosis may be facilitated when CSF and plasma levels of both β-HCG and α-fetoprotein are elevated; however, secretion of these chemicals is not a consistent feature.

Embryonal carcinomas do not show peculiar CT and MRI features, and the diagnosis is usually histological.

Teratoma

Teratomas are the second most common pineal tumor, accounting for approximately 15 % of all masses (Smirniotopoulos et al. 1992). They are more frequent in males, and they are the most common form of congenital brain tumor, accounting
Fig. 9 Disseminated pineal germinoma in a 9-year-old boy. (a) Axial diffusion-weighted image, (b) corresponding ADC map, and (c) axial T2-weighted image show hypercellular solid mass in the pineal region, engulfing the pineal calcification and surrounded by perifocal edema. (d, f) Contrast-enhanced sagittal T1-weighted images show the principal mass, causing obstruction of the cerebral aqueduct, as well as secondary dissemination in the frontal horn (arrows, f). (e) MR spectroscopy (PRESS, TE 144 ms) centered in the lesion shows elevated choline/NAA ratio and the presence of lipid resonances (arrow).
for approximately half of all reported cases (Severino et al. 2010). Teratomas are neoplasms of multipotential cells that recapitulate normal organogenesis, usually producing tissues that represent an admixture of two or more of the embryological layers of ectoderm, mesoderm, and endoderm (Smirniotopoulos et al. 1992). Therefore, the differentiation spectrum in teratomas may be extremely diverse and range from a multicystic mass composed primarily of ectodermal derivatives to a complex mass with additional endodermal and mesodermal tissues, to a primitive or abortive attempt at twinning (so-called fetus in fetu) (Smirniotopoulos et al. 1992). The degree of tissue differentiation may range from benign to immature. Malignant teratomas may either spontaneously differentiate into more benign tissue or, alternatively, behave aggressively and metastasize. Increased serum carcinoembryonic antigen (CEA) is commonly found in affected patients.

Benign (mature) teratomas typically are heterogeneous due to coexistent enhancing solid portions, cystic portions, fatty tissue, and calcification (Tien et al. 1990; Fujimaki et al. 1994). CT shows mixed density lesions with markedly hypodense fatty components and also exquisitely depicts calcified portions, which are often multiple and may sometimes reflect the presence of the bone or teeth (Fujimaki et al. 1994). Diffusion-weighted imaging is especially sensitive to epidermoid components within heterogeneous masses (Fig. 11). The association of fat, calcification, and solid tissue in a pineal region tumor is notably absent from all other tumor types in this area and therefore is strongly suggestive of a teratoma. Fat-suppression MRI techniques and CT may be useful in the differentiation of fat from hemorrhage. CE usually is heterogeneous, either limited to the solid tissue areas or involving the walls lining the cystic spaces (Smirniotopoulos et al. 1992).

Malignant (immature) teratomas show less defined margins and fewer cysts and calcifications and cannot be differentiated from other pineal tumors. Highly
Fig. 11  Mature teratoma in a 6-year-old boy with long-standing headaches. (a) Axial CT scan shows a heterogeneous mass containing calcified spots (thin arrow) and marginal hyperdense components, consistent with hemorrhaging (empty arrow); (b) axial T1-weighted and (c) axial T2-weighted images confirm fresh hemorrhagic component (empty arrows). (d) Contrast-enhanced axial T1-weighted image shows heterogeneous enhancement, with optimal delineation of cystic components. (e) Sagittal T2-weighted image and (f) contrast-enhanced sagittal T1-weighted image show the lesion involves the pineal region and protrudes in the posterior third ventricle, causing obstructive hydrocephalus. (g) Axial diffusion-weighted image and (h) corresponding ADC map reveal epidermoid cyst component (arrowhead).
malignant teratomas are large, quite homogeneous masses, usually lacking calcifications or fat (Tien et al. 1990). The mesencephalic tectum and tegmentum commonly are invaded, and large tumors may infiltrate the cerebellum, thalamus, and cerebral hemispheres (Tien et al. 1990). Perifocal edema may be observed, contrary to mature teratomas (Fujimaki et al. 1994). CSF metastases also are common.

The vast majority of intracranial teratomas occur in the pineal region; other midline locations may be involved less frequently, such as the suprasellar region, the ventricles (Bavbek et al. 1999; Srinivasan and Joseph 1999), and the posterior fossa. It should be pointed out that congenital teratomas may involve the brain more extensively (Fig. 12) than pineal teratomas of older children, although a preferential location in the midline is retained. These congenital teratomas carry a poor prognosis because of the rapid, invasive growth of the tumors and destruction of the surrounding brain (Storr et al. 1997). They may also present with unusual appearance on MRI (i.e., mimicking a parietal encephalocele) (Baykaner et al. 2007).

**Endodermal Sinus Tumor (Yolk Sac Tumor)**

This tumor is another example of differentiation of totipotential germ cells from extraembryonic tissues into cell lineages that have histological features of both yolk sac endoderm and mesoblasts (Smirniotopoulos et al. 1992). These uncommon tumors often occur as mixed tumors combined with other germ cell elements; elevated $\alpha$-fetoprotein in both CSF and plasma generally is found. Another possible location of these tumors is the sacrum.

As is the case with embryonal carcinoma, endodermal sinus tumors do not show peculiar CT and MRI features that may permit differentiation from germinomas. Both CT and MRI display intense, mostly homogeneous enhancement.

**Choriocarcinoma**

Choriocarcinomas account for less than 5% of all pineal masses and have a male predilection (Smirniotopoulos et al. 1992). They result from differentiation of ectopic pluripotential germ cells into placenta-like tissue. Choriocarcinomas may be associated with elevated $\beta$-HCG in both CSF and plasma.

Choriocarcinomas are more likely to present with precocious puberty than any other type of GCT (Packer et al. 2000); they also commonly present with intratumoral subacute hemorrhage due to their prominent vascularity.

Although their appearance on CT and MRI may be aspecific, the presence of hemorrhage is considered to be strongly suggestive of this oncotype. However, pineal germinomas and glioblastomas may show the same behavior. On CT, hemorrhagic portions will be depicted as hyperdense areas showing attenuation values consistent with blood, whereas the appearance on MRI depends on the age of the clot, related to the different paramagnetic properties of hemoglobin byproducts.
Angiography may show neovascularity with small multiple areas of aneurysmal dilation (Tien et al. 1990).

Fig. 12 Congenital immature teratoma. (a) Sagittal and (b) axial T2-weighted images obtained with fetal MRI at 31 gestational weeks show a huge, heterogeneous mass replacing the larger part of the brain and severely distorting the normal anatomy. (c) Sagittal and (d) axial T2-weighted images obtained on postnatal day 1 confirm the presence of a giant mass, with profound structural heterogeneity, causing severe distortion and compression of adjacent structure, including displacement of the hindbrain (arrows, c) and right lateral ventricle (arrow, d). There are large marginal cystic components, which are shown to be hyperproteic due to hemorrhaging on the corresponding (e) axial T1-weighted image (asterisks). (f) Axial SWI image shows diffuse hemorrhagic texture and also reveals a central vascular hilus (arrowhead). (g) Contrast-enhanced axial T1-weighted image shows the mass enhances irregularly and also reveals relatively well-defined tumor margins despite the size of the mass. (h) Axial CT scan shows isolated calcified spot (arrow)

Angiography may show neovascularity with small multiple areas of aneurysmal dilation (Tien et al. 1990).
Mixed Germ Cell Tumors

Around 9–13.5 % of germ cell tumors have mixed histology (Al-Hussaini et al. 2009). Embryonal carcinomas represent the most aggressive portion of these tumors and may produce metastases. The diagnosis is not possible on imaging and is based on histological examination.

Other Pineal Tumors

Gliomas

Most pineal region gliomas are astrocytomas and originate from astrocytes, a normal component of the pineal parenchyma. However, gliomas of the quadrigeminal plate may be difficult to differentiate from purely pineal tumors when the mass is large. Histologically, most gliomas of the pineal region are pilocytic astrocytomas; they may arise independently or within the setting of neurofibromatosis type 1. However, pleomorphic xanthoastrocytomas (Thakar et al. 2012) and glioblastomas do occur in this region (Fig. 13). Ependymomas may originate from the ependymal epithelium of the third ventricle, which is in close proximity to the pineal body (Hoffman et al. 1994).

Epidermoids

Localization of epidermoids to the pineal region is rare, accounting for 1.6 % of pineal region masses and 6 % of intracranial epidermoids in the general population (MacKay et al. 1999). The clinical presentation may include hydrocephalus and the Parinaud syndrome. Aseptic meningitis may ensue as a complication of leakage or rupture of the cyst.

Epidermoids of the pineal region are iso- or slightly higher density than CSF on CT, whereas they are typically characterized by signal intensity comparable to or slightly higher than that of CSF on both T1-weighted and T2-weighted MR images (MacKay et al. 1999). As with other, more typical intracranial locations, the principal neuroradiological differential diagnosis on MRI is that of an arachnoid cyst, whereas a pineal cyst or a dilated suprapineal recess of the third ventricle usually is easier to exclude. The differentiation of epidermoid cysts from arachnoid cysts relies on DWI (Kuzma and Goodman 1997): epidermoids give restricted diffusion, whereas arachnoid cysts are isointense with CSF.

Rare Tumors and Nonneoplastic Mass Lesions

Meningiomas and choroid plexus papillomas may arise from arachnoidal elements around the pineal body and have been reported in this region (Hoffman et al. 1994;
Fig. 13  Glioblastoma in a 5-year-old boy. (a) Axial CT and (b) axial FLAIR image show neoplasm of the pineal gland that is faintly hypodense on CT (arrows, a) and hyperintense on FLAIR (b). (c) Sagittal T2-weighted image shows an inhomogeneous signal intensity (arrows) suggesting an infiltrative pattern of growth. (e) Diffusion-weighted image and (f) corresponding ADC map reveal increased diffusivity, despite the histological nature of the lesion, highlighting difficulties in correlating ADC values with grading in adult-type pediatric gliomas. (g) Axial T1-weighted image shows a specific hypointensity, whereas (d) sagittal and (h) axial contrast-enhanced T1-weighted images show intense, slightly heterogeneous enhancement.
Sasani et al. 2014); however, they are exceedingly rare in children. Hemangiopericytomas, malignant melanomas, dermoids, lymphomas, adenocarcinomas, and nonneoplastic masses, such as cavernous hemangiomas, sarcoidosis, tuberculomas (Fig. 14), and parasitic cysts, may also rarely involve the pineal region (Behari et al. 2011; Hoffman et al. 1994). In addition, a series of atypical teratoid rhabdoid tumors reported pineal location in 4 of 11 patients (Chen et al. 2005).

Benign Pineal Cysts

Epidemiology and Clinical Picture

These idiopathic lesions are a casual finding in 25–40 % of unselected MRI examinations. They have been found in 1.4–4.3 % of healthy subjects (Mamourian and Yarnell1991) and in as many as 40 % of autopsy studies. However, they are rare in young children with an incidence of 2 % in children below the age of five (Al-Holou et al. 2009) and none identified in 73 children below the age of 10 years (Sawamura et al. 1995).

They are well depicted by midsagittal MR images as rounded, cystic, usually solitary lesions that often replace the pineal gland completely. Usually, pineal cysts are asymptomatic (Engel et al. 2000); despite the fact that some cysts may exceed a diameter of 1 cm and that the quadrigeminal plate and superior cerebral aqueduct may be slightly compressed, hydrocephalus and the Parinaud syndrome characteristically do not appear, unlike with true pineal region tumors.

Biological Behavior and Neuropathology

Histologically, pineal cysts show a three-layered wall composed of an inner gliotic layer with a high number of Rosenthal fibers, a middle layer with columns of pineal parenchyma, and a thin fibrous external layer (Engel et al. 2000). Such features could support the theory that pineal cysts originate from necrosis within a glial plaque (Golzarian et al. 1993). Alternative hypotheses could be related to sequestration, within the pineal gland, of portions of the diverticulum created from proliferation of parenchymal cells arising from the neuroectoderm of the roof of the third ventricle and the pia of the tela choroidea or to degeneration of those cells that differentiate into ependyma or neuroglia (Hayman and Hinck 1992).

Imaging Studies

On MRI (Fig. 15), pineal cysts usually are iso- to slightly hyperintense to CSF on T1-weighted, T2-weighted, and FLAIR images. Slight hyperintensity relative to CSF is due to increased protein content as well as immobility of the fluid within the cyst (Smirniotopoulos et al. 1992; Mamourian and Yarnell 1991; Golzarian et al. 1993). Cysts may be solitary or multiple, the latter usually resulting from septa separating a large cyst into multiple cavities. The cyst wall is well defined and smooth and does not exceed 2 mm in thickness (Barboriak et al. 2001); it is exquisitely depicted by high-resolution heavily T2-weighted sequences, such as DRIVE or equivalent. Hemorrhage is a rare finding (Fakhran and Escott 2008) and
Fig. 14 Pineal tuberculoma in a 2-year-old boy. (a) Sagittal T2-weighted image shows pineal mass composed of a conglomeration of hypointense nodules (arrows) with surrounding edema. (b) Sagittal and (c) axial contrast-enhanced T1-weighted images show multiple nodules with peripheral, rim-like enhancement consistent with a conglomeration of granulomas, extending to the left ambient cistern (arrowhead, c). (d) Axial ADC map shows central reduced diffusivity (arrow) with peripheral edema, while (e) MR spectroscopy at TE 32 ms shows prominent lipid peak (arrow), consistent with necrosis.
can give rise to position-dependent intracystic layering (Fig. 16). Homogeneous enhancement of the cyst margins is a common feature, related to the presence of pineal parenchymal tissue which physiologically lacks a blood-brain barrier. Faint central enhancement may be observed on late contrast-enhanced T1-weighted sequences, possibly related to active secretion (Fig. 17); therefore, it is recommended to acquire the T1-weighted images immediately after contrast injection (Fakhran and Escott 2008). Pineal cysts may sometimes be associated with other midline abnormalities, such as dysgenesis of corpus callosum.

Follow-up of pineal gland cysts is a debated topic. It was initially suggested that pineocytomas may mimic pineal cysts; however, this could not be confirmed by a thorough literature review (Fakhran and Escott 2008). Commonly, follow-up is advised when the cyst exceeds 10 mm in maximum diameter (Fig. 18); however, one report found that young age was the only significant predictor of cyst growth, whereas initial cyst size or morphology was not (Al-Holou et al. 2010).
Fig. 16 Hemorrhagic pineal gland cyst in an 8-year-old boy. (a) Axial T1-weighted and (b) axial T2-weighted images show dependent layering due to intracystic hemorrhage (arrows). (c) Contrast-enhanced sagittal T1-weighted image shows peripheral enhancement (arrowhead) due to displaced gland parenchyma. (d, e) Sagittal T2 DRIVE images show with a greater detail both the intracystic fluid-fluid level (arrows, d) and the peripheral parenchymal tissue (arrowheads, e)
Fig. 17 Late enhancement of a pineal gland cyst in a 17-year-old girl. (a) Sagittal T2 DRIVE and (b) sagittal T1-weighted images show multicystic appearance of the pineal gland. (c) Contrast-enhanced sagittal T1-weighted image acquired 3 min after intravenous gadolinium chelate administration shows essentially unenhancing gland (arrows). (d) Contrast-enhanced sagittal T1-weighted image acquired after 15 min shows intracystic contrast material leakage (arrows).
Fig. 18  Giant pineal gland cyst in a 12-year-old boy. (a) Sagittal T2 DRIVE image shows giant pineal gland cyst, with a maximum anteroposterior diameter measuring 19 mm. Despite its size and the fact that the cerebral aqueduct appears to be compressed (arrow), the third ventricle (asterisk) is not significantly enlarged. (b) Contrast-enhanced sagittal T1-weighted image shows enhancement of the gland parenchyma at the margins of the cyst and within intracystic septa (arrowheads)
References


