Posterior Fossa Tumors

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INTRODUCTION
Pediatric brain tumors are the leading cause of death from solid tumors in childhood.\textsuperscript{1,2} The most common posterior fossa tumors in children are medulloblastoma (MB), atypical teratoid/rhabdoid tumor (ATRT), cerebellar pilocytic astrocytoma (CPA), ependymoma, and brainstem glioma (BG). Location, as well as imaging findings on computed tomography (CT) and conventional magnetic resonance (cMR) imaging may provide important clues to the most likely diagnosis. Moreover, information obtained from advanced MR imaging techniques, such as diffusion-weighted imaging (DWI), MR spectroscopy (MRS), perfusion-weighted imaging, and dynamic contrast-enhanced (DCE) studies, increase diagnostic confidence and help distinguish between different histologic tumor types.

Here we discuss the most common posterior fossa tumors in children, including typical imaging findings on CT, cMR imaging, and advanced MR imaging studies.

MEDULLOBLASTOMA
Medulloblastoma (MB), a highly malignant neoplasm, is the most common posterior fossa...
neoplasm in children, representing 15% to 20% of all pediatric brain tumors and 30% to 40% of posterior fossa neoplasms. Medulloblastomas are classified as embryonal tumors, the largest group of malignant tumors in the pediatric population. This highly malignant neoplasm occurs more frequently in boys, usually before 10 years of age. Although less common, the disease may also occur in adults, usually in the third and fourth decades of life.

**Clinical Picture and Treatment**

Clinical symptoms and signs are generally brief, typically less than 3 months in duration, and reflect the strong predilection of this tumor to arise within the cerebellum, most often in the vermis. Symptoms may include headache, general malaise, failure to thrive, vomiting, and clumsiness, among other presentations that mimic common and benign childhood pathologies seen in primary care. Typically, the treatment strategies for MB are threefold: maximal safe resection (which may include cerebrospinal fluid [CSF] diversion), neuraxis radiotherapy, and chemotherapy.

**Location**

The tumor usually arises at the midline within the vermis and exhibits growth into the fourth ventricle. Less typical locations include nonventricular superior or inferior vermic tumor, cerebellar hemispheric lesions, and extension into the foramina of Magendie and foramina of Luschka to the cerebellopontine angle (CPA).

**Computed Tomography and Conventional MR Imaging**

On unenhanced CT, the tumor is usually characterized as hyperdense (Fig. 2), and on T2 images, as isointense to hypointense compared with gray matter (Fig. 3). These imaging findings are likely secondary to high cell density and high nuclear-to-cytoplasmic ratio. The tumor typically may appear heterogeneous on imaging, with findings related to cyst formation and hemorrhage on MR, and calcification seen on CT (see Fig. 3A–C). Intratumoral cyst or necrosis is observed in 40% to 50% of cases. MBs typically enhance. Atypical imaging findings, such as high signal intensity compared with the cerebellar cortex on T2, as well as no enhancement may be demonstrated (Fig. 4). Sometimes the tumor presents with an infiltrative pattern instead of a solid solitary mass (Fig. 5).

Evidence of leptomeningeal metastatic spread is present in 33% of all cases at the time of diagnosis and is well evaluated with contrast-enhanced MR imaging of the brain and the spine. MR imaging is more sensitive than CSF studies for the detection of CSF spread of primary brain tumors. Metastases may be leptomeningeal, dural-based, intraventricular, adherent to the spinal roots, or even to the liver (Fig. 6).

Metastasis to the brain parenchyma may bleed, resembling cavernoma (Fig. 7).

**Diffusion-Weighted MR Imaging**

Apparent diffusion coefficient (ADC) values are significantly lower in MBs than in all other posterior...
fossa tumors ($P<.001$) related to high cell density (Fig. 8, see also Figs. 3D, E and 5E).21–23

A study by Jaremko and colleagues21 confirmed that diffusion imaging is the single most useful sequence for differentiating pediatric posterior fossa tumors and that, as expected, diffusion restriction is rare in grade 1 tumors and common in grade 4 tumors. The optimal threshold for distinguishing MB and juvenile pilocytic astrocytomas (JPAs), ADC minimum = 800 × 10^{-6} \text{mm}^2/\text{s}, was lower than the threshold of 900 × 10^{-6} \text{mm}^2/\text{s} used by Rumboldt and colleagues,22 likely because they used ADC mean rather than ADC minimum.

Desmoplastic medulloblastoma, a histologically less aggressive subtype with better prognosis than the classic type, is expected to have less highly restricted diffusion than the classic type. Some of these tumors present with no restricted diffusion at all (Fig. 9).21

**Proton Magnetic Resonance Spectroscopy**

**Choline**

On MRS, MBs usually demonstrate a significant elevation of the choline (Cho) peak related to high cell density and elevated Cho/Cr and Cho/N-acetyl-aspartate (NAA) ratios, reflecting its malignant nature (Fig. 10, see also Figs. 3F and 5F).2,24–26

High Cho has been previously reported as a characteristic finding of embryonal tumors.12,27

Elevation of the Cho peak is useful in distinguishing between MB and L’Hermitte-Duclos disease (LDD), as MBs occasionally may present with a laminated appearance, and with no contrast enhancement, mimicking LDD. The Cho peak is typically elevated in patients with MB when compared with patients with LDD.8

Desmoplastic MBs may present with no elevation of the choline in the spectra. In these tumors, a huge myo-inositol peak may be seen related to the desmoplastic nature (Lara A. Brandão, MD, personal communication, 2013) (Fig. 11).

**Taurine**

Spectra with a short echo time (TE) show a significantly elevated taurine (Tau) concentration at 3.3 ppm in patients with MB when compared with other tumors (see Fig. 10).24,28–32 Furthermore, at a TE of 30 ms, the Tau peak projects above the baseline; whereas, at a TE of 144 ms, the Tau peak occurs below the baseline.28

Tau has been established as an important biomarker in distinguishing MBs from other common pediatric brain tumors, such as cerebellar astrocytomas.24,28,31,33,34 Higher Tau levels are associated with increased cellular proliferation and tumoral aggressiveness.23,24,28,29,35

**Glutamine and glutamate and alanine**

In a study of 60 children with untreated brain tumors, Panigrahy and colleagues24 measured the highest glutamate (Glu) concentrations in pineal germinoma
Fig. 3. MB: MR imaging. Same patient as Fig. 1. A 6-year old girl complaining of neck pain, presenting with walking difficulty and ataxia. There is a well-circumscribed lesion in the midline vermis, with growth into the fourth ventricle. Some cysts with high signal intensity on T2 (A: coronal and B: axial) as well as some foci of low signal intensity on the gradient echo (C) that may be related to calcification or blood are demonstrated within the lesion. The solid portion is isointense to the cerebellar cortex on T2, due to high cell density along with high nuclear-cytoplasmic ratio, also responsible for the restricted diffusion (D: DWI, E: ADC map) and high Cho peak (F) demonstrated in the lesion. There is significant enhancement (G: axial T1 with contrast) and no elevation of the blood volume (H: rCBV map) in the perfusion study.

Fig. 4. MB: high signal on T2 and no enhancement. An 8-year old boy presenting with headaches and vomiting. There is a solid MB within the inferior vermis growing into the fourth ventricle, with no enhancement (A: sagittal, B: axial T1 with contrast) presenting with high signal intensity compared with the cerebellar cortex on T2 (C: axial T2).
and in MB (see Fig. 10B). Specifically, the MB, pineal germinoma, and astrocytoma showed mean glutamine and glutamate (Glx) concentrations above the mean in all tumors; whereas, Glx concentration was low in both the choroid plexus papilloma and carcinoma. The quantitation of these metabolites proved useful in separating either MB or astrocytoma from choroid plexus papilloma. Panigrahy and colleagues have also reported the highest mean alanine (Ala) concentration among posterior fossa tumors in MBs.

Lipids and lactate
Prominent lipid (Lip) resonances can be observed in some, but not all, spectra of malignant MB (see Fig. 11B). High lactate (Lac) values are usually found in the spectra of MB. Panigrahy and colleagues have also reported the highest mean alanine (Ala) concentration among posterior fossa tumors in MBs.

Magnetic resonance spectroscopy in metastatic versus localized medulloblastomas
Metastatic MBs are characterized by higher total Cho (tCho), which is consistent with increased cell turnover and tumor growth, a finding substantiated by a significant positive correlation between tCho and the Ki67 index. Tau is present in both metastatic and localized tumors, although higher levels are typically found in metastatic tumors, which is consistent with previous findings in neuroblastoma (ie, Tau is a reliable biomarker for more aggressive subtypes of neural tumors). The fact that higher mobile Lip levels are observed in localized tumors may also reflect a higher proportion of necrotic tumor in these cases.

Dynamic Susceptibility Contrast and Dynamic Contrast-Enhanced MR Imaging
There can be variable perfusion and permeability characteristics in MB, with some lesions showing elevated perfusion and permeability and others not (Fig. 12, see also Fig. 3H).

Important considerations
Radiologic-pathologic correlation The World Health Organization (WHO) classification system
2007 uses histology to classify MBs into 4 major groups, including classic, desmoplastic, MB with extensive nodularity (MBEN), and large cell/anaplastic MB subtypes:\textsuperscript{3,40}

**Classic** Classic MB represents the most common histologic subtype and is composed of sheets of densely packed small round blue cells (basophilic) with a high nuclear-to-cytoplasmic ratio, mitotic and apoptotic activity, and may occur in the midline.\textsuperscript{3}

Elevation of Tau is seen specifically in this histologic subtype.

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**Fig. 6.** MB: metastasis. (A, B) A 26-year-old woman treated for MB at the age of 8. Now presenting with ataxia and incoordination. Enhancing leptomeningeal metastases are demonstrated surrounding the brainstem, basal cisterns, temporal lobes, and occipital lobes (A, B: axial T1 with contrast). (C, D) A 20-year-old man treated for MB 2 years ago. MR imaging shows dural-based metastasis in the temporal and frontal basal regions, isointense to the cortex on T2 (C: axial) with solid enhancement (D: axial T1 with contrast). Metastasis also may compromise the ventricular system (E), the spinal roots, which may look thickened (F), as well as the liver (G).
Fig. 7. MB: parenchymal metastasis resembling cavernoma. A 7-year-old girl presenting with headaches and paresthesia on the right. A solid lesion is demonstrated in the left frontal region, which is heterogeneous, hypointense on T2 (A: axial T2), has significant low signal on the gradient echo image (B: axial gradient echo [GRE]) and some enhancement (C: axial T1 with contrast). Lesion was diagnosed as cavernoma. Two months later (D, E: axial T1 with contrast) dural-based, as well as leptomeningeal metastasis are demonstrated with final diagnosis of metastatic MB.

Fig. 8. MB-restricted diffusion. Patient diagnosed with MB, presenting with dizziness and nausea in the previous 2 months. There is a solid lesion in the midline vermis, mostly isointense to the cerebellar cortex on T2 (A: axial T2), presenting with restricted diffusion (B: DWI, C: ADC map).
Fig. 9. MB: no restricted diffusion. A 51-year-old man diagnosed with desmoplastic MB, presenting with headaches and nausea in the preceding 3 months. There is an infiltrative lesion compromising most of the cerebellar parenchyma, presenting with mild high signal intensity on T2 (A: coronal, B: axial T2), and no restricted diffusion (C: ADC map). The lesion does not enhance (D: axial T1 with contrast).

Fig. 10. MB: MRS. Same patient as in Fig. 8. There is a solid enhancing MB in the cerebellar vermis (A: sagittal T1 with contrast), presenting with very high Cho as well as Tau peak in the spectra (B: MRS). NAA is very low and there is elevation of Glx as well as presence of Ala and lactate.
Desmoplastic This subtype is hypocellular, presents with lower Tau concentration compared with the classic subtype and carries a favorable prognosis.3,41 This histologic subtype is often found in adult patients with MB, demonstrating a cerebellar hemispheric mass extending to the overlying meninges, with desmoplastic reaction evoked by prominent leptomeningeal involvement (Fig. 13).19

Anaplastic Anaplastic MBs (15%) are characterized by marked nuclear pleomorphism, nuclear molding, and cell–cell wrapping, and the large cell variant (2%–4%) displays a monomorphous population of large cells whose nuclei exhibit prominent nucleoli.3,42 Both variants are characterized by a very high proliferative activity, abundant apoptosis, and a much poorer prognosis.3,43,44 This is the most aggressive subtype, characterized by presence of necrosis. Extensively nodular MBENs tend to develop in the vermis in children younger than 3 years in most cases and is frequently represented as a nodular enhancing appearance on CT scans or MR images. Prognosis is better than for the classic MB.19,41

Molecular subgroups More recently there has been the development of a classification of 4 main subgroups of MBs based on molecular profiling.42,45–51 The WNT and SHH groups were named after the predominant signaling pathways thought to be

Fig. 11. MB: no elevation of Cho. Patient diagnosed with desmoplastic MB. MRS (A: voxel placement-axial T2) demonstrates no elevation of the Cho peak (B-curve). The most striking finding is elevation of the myo-inositol peak (ml).

Fig. 12. MB: low blood volume, no significant permeability. Same patient as in Figs. 8 and 10. There is a solid enhancing MB in the cerebellar vermis (A: axial T1 with contrast), showing no elevation of the blood volume (B: rCBV map), as well as no significant elevation of the permeability (C: maximum slope of increase map).
affected in their pathogenesis. Less is known currently regarding the pathogenesis of groups 3 (tending to harbor MYC amplification) and 4 (tending to have isochromosome 17q) and therefore generic names were chosen until they are better understood.45

The SHH group has become of increasing interest because of the availability and

![Fig. 13. MB: desmoplastic type. A 64-year-old woman presenting with numbness and reduced consciousness. There is an infiltrative cerebellar lesion in the left cerebellar hemisphere, extending laterally to the cerebellopontine angle, hyperintense on T2 (A, B: axial T2) with a laminated appearance. There is no restricted diffusion, which may be demonstrated in desmoplastic MBs (C: ADC map). There is nonhomogeneous enhancement in the lesion, associated with thickening of the adjacent meninges due to desmoplastic reaction (D, E: axial, F: coronal T1 with contrast).](image13)

![Fig. 14. ATRT: CT. ATRT hyperdense on noncontrast CT (A), with enhancement in the contrast-enhanced study (B). (Courtesy of A. James Barkovich, MD, San Francisco, CA.)](image14)
temporary success of small molecule inhibitors to
smoothened (SMO), which is part of the SHH
pathway.

For a detailed comprehensive review on the mo-
lecular subgroups of MB, see the consensus
article by Taylor and colleagues.52

MB is the most common malignant brain
tumor in children and, as such, has been the
focus of tremendous efforts to genomically
characterize it.53

What was once thought to be a single disease
has been divided into multiple, molecularly
unique subgroups through gene expression
profiling. Each subgroup is not only unique in its
origin and pathogenesis, but also in the prognosis
and potential therapeutic options. The molecular

Fig. 15. ATRT: MR imaging. A 5-year-old girl with irritability and hypersexuality, sent to a psychiatrist. There is a
nonhomogeneous lesion presenting with a solid component isointense to the cerebellar cortex on T2 (A: coronal
and B–D: axial). Cysts are demonstrated within and adjacent to the solid component. The lesion is located off
midline and extends to the CPA on the right, which favors ATRT instead of MB. Some low signal intensity foci
are demonstrated within the solid portion, which may be related to blood products (E: axial GRE). There is het-
erogeneous enhancement (F: axial T1 with contrast) and significant restricted diffusion (G: DWI, H: ADC map).
classification system has a potential use in developing prognostic models as well as for the advancement of targeted therapeutic interventions.

MB is currently stratified into 4 molecular variants through the advances in transcriptional profiling. They include sonic hedgehog (SHH), wingless (WNT), Group III, and Group IV.

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**Fig. 16.** PA: location and signal on T2. (A, B) A 9-year-old girl presenting with headaches, neck pain, ataxia, and vomiting. There is a PA in the left cerebellar hemisphere, compressing and displacing the fourth ventricle (A: coronal and B: axial T2). The solid component is hyperintense to the cerebellar cortex on T2. (C, D) Children diagnosed with MB. The lesion is located in the midline vermis, filling the fourth ventricle. The solid component of MB is usually isointense to the cerebellar cortex on T2 (C). Some MBs may present with high signal intensity on T2 (D), resembling a PA.
SHH (sonic hedgehog) medulloblastomas SHH tumors are thought to account for 28% of all medulloblastomas. They have an intermediate prognosis between good prognosis WNT tumors and poor prognosis group 3 tumors, and may be similar in prognosis to group 4. SHH MBs show a dichotomous age distribution being more common in both infants (<4 years) and adults (>16 years).

Most tumors in this group are of the desmoplastic subtype, located in the cerebellar hemisphere more often than in the midline.

WNT (wingless) medulloblastomas (~10%) WNT tumors are thought to be the rarest subgroup of medulloblastoma, accounting for 11% of these tumors, but they have probably been the most studied and have a very good long-term prognosis with overall survivals reaching 90%.

WNT tumors also show a specific age distribution being almost absent in infants (aged <4 years) but predominantly affecting children with a peak incidence of 10 to 12 years. Most (97%) WNT MBs show classic histology; however, rarely, they are phenotypically large cell/anaplastic and may remarkably retain their relatively good prognosis with this phenotype. They tend to occur in the middle cerebellar peduncle/cerebellopontine angle.

Group 3 Group 3 tumors account for 28% of all MBs. They are associated with the worst prognosis of all the subgroups and are frequently

Fig. 17. PA: multinodular/multicystic appearance. PA presenting with multiple enhancing nodules (A: coronal, B: axial T1 with contrast) hyperintense on T2 (C: axial T2), as well as multiple cystic nonenhancing components.

Fig. 18. PA: striking solid enhancement. Same patient as in Fig. 16A, B. The solid portion of the PA presents with striking enhancement. (A) Coronal and (B) axial T1 with contrast.
metastatic. Group 3 tumors are found in infants and children but very rarely in adults. Group 3 MBs are mostly classic or large cell/anaplastic morphology. MYC amplification appears to be highly associated with group 3 tumors and is associated with a worse prognosis. The tumors in this subgroup tend to be ill-defined on imaging.

**Group 4** Group 4 MBs are thought to be the most common “typical” subgroup of MB, accounting for approximately 34%, and can be thought of conceptually as being associated with isochromosome 17q. Group 4 medulloblastomas rarely affect infants (0–3 years) and mainly affect children, with a peak age of 10 years.

Although they frequently metastasize, they still have an intermediate prognosis compared with the poor prognosis of group 3.

The vast majority of group 4 MBs have a classic histology.

All histologic subtypes can present with this molecular profile, except the desmoplastic one.

These tumors tend to have minimal or no enhancement.

**Molecular profiling: implications in treatment** The identification of different molecular pathways involved in the pathogenesis of MBs provides new therapeutic targets for drug development.

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**Fig. 19.** PA: peripheral enhancement. (A) Axial T1 with contrast, (B) axial T2: Patient diagnosed with PA. There is a large round lesion in the right cerebellar hemisphere presenting with marginal enhancement (A) and mild peripheral edema (B). (C, D) Child diagnosed with right cerebellar abscess presenting with peripheral enhancement (C: axial T1 with contrast). There is significant diffusion restriction (D: DWI) not typically found in PA.
Medulloblastomas and associated syndromes

**Basal cell nevus syndrome (Gorlin syndrome)*** This is a rare autosomal dominant disorder with high incidence of neoplasms, notably MB. Ten percent of these patients will develop MBs, usually desmoplastic. Falcine calcification in children with MB may be a marker for basal cell nevus syndrome.64,65

**Turcot syndrome*** Turcot syndrome is associated with familial colonic polyposis, with high incidence of brain tumors, such as MB and glioma.66

**Li-Fraumeni** Germline mutations of the p-53 tumor suppressor gene predisposes to different types of cancer in patients, especially soft tissue sarcomas. Ten percent of these patients develop MB.67

**Key points to remember**
- MB is the most common posterior fossa tumor in children
- MB affects mainly boys before 10 years of age
- There is a second peak in adults

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**Fig. 20.** PA: DWI. (A, B) Same patient as Fig. 16A, B. There is no restricted diffusion in the solid component of the PA (A: DWI and B: ADC map), which helps distinguish PAs from MBs, which typically present with restricted diffusion, due to high cell density (C: DWI and D: ADC map, same patient as Fig. 16C).
Lesion is often located in the midline vermis and presents with hyperattenuation on CT, isointense to hypointense on T2, restricted diffusion and high Cho and taurine on MRS.

Perfusion and permeability values are variable.

Look for CSF spread!

There are imaging features associated with molecular subgroups: SHH involves the cerebellar hemisphere, the WNT pathway involves cerebellar peduncle/CPA cistern, group 3 tumors are ill-defined on imaging, and group 4 tumors have minimal or no enhancement.

Fig. 21. Infiltrative rather than well circumscribed PA. A 23-month-old boy with developmental delay, low stature and low weight for his age. There is a PA infiltrating the left cerebellar hemisphere and vermis, extending anteriorly to the left cerebellopontine angle, compressing the fourth ventricle (A: coronal T2, B, C: axial T2). There is an associated cystic component in the right cerebellar hemisphere. There is striking enhancement in the solid component (D: axial T1 with contrast) and no restricted diffusion (E: ADC map). MRS (F, G) demonstrates a large choline peak, along with reduced NAA and Cr, as well as high lipids, very consistent with the diagnosis of PA.
ATYPICAL TERATOID RHABDOID TUMORS

ATRTs are classified as part of the embryonal tumor group of central nervous system (CNS) tumors. ATRT is a highly malignant CNS neoplasm that most often occurs in children younger than 2 years. ATRTs represent 1.3% of CNS primary brain tumors in the pediatric population, but if one considers only children younger than 3, prevalence rises to 20%. ATRTs are more common in girls than in boys, with 94% in an intra-axial location. A review of 14 histologically confirmed cases of ATRTs demonstrated equal preference for the supratentorial and infratentorial compartments.

These tumors are aggressive lesions with a dismal prognosis, and a 2-year survival of only 17%. Survival improves if the patient is older than 3 years.

Poor prognosis is related to the young age of the affected patients as well as the high propensity for CSF tumor spread. Metastasis to the lungs and abdomen also may be demonstrated.

Imaging Findings

On unenhanced CT, the tumor is usually characterized as hyperdense (Fig. 14) and on T2 images, as isointense to hypointense compared with gray matter (Fig. 15). These imaging findings are likely secondary to high cell density and high nuclear-to-cytoplasmic ratio and overlap with those described for MBs.

Enhancement is demonstrated in approximately 89% of the cases (see Fig. 15F).

Due to high cell density, as well as high nuclear-to-cytoplasmic ratio, restricted diffusion is typically seen (see Fig. 15G, H).

MRS shows elevated Cho and reduced NAA as well as a prominent Lip peak. However, there are no reports in the literature that quantify these values.
changes or address the presence or size of Tau peaks.4,36

Atypical Teratoid Rhabdoid Tumors Versus Medulloblastoma

The main differential diagnosis for posterior fossa ATRT is MB. If the patient is younger than 3 years, if tumor is located off midline, extending to the CPA, and if blood products are demonstrated in the lesion, one should consider ATRT as the most likely diagnosis.74

However, the precise distinction can be made only through immunohistochemistry and genetic analyses. ATRTs frequently demonstrate deletions of chromosome 22q with inactivation of the INI1/hSNF5, thought to be a tumor suppressor gene. Loss of the INI1 gene product is used to diagnose ATRT, although it is not present in all ATRT tumors.75,76

CEREBELLAR PILOCYTIC ASTROCYTOMA

CPA and MB each constitute approximately 35% of all posterior fossa masses in children.77

Pilocytic astrocytomas (PAs) are low-grade (grade I) tumors, most often located in the posterior fossa (60%), with 40% involving the cerebellum and 20% involving the brainstem.4

CPA has excellent survival after gross total surgical resection.2,4,78

Differential diagnosis between PA and MB in the posterior fossa is crucial; the former is a low-grade (WHO grade I) tumor, with excellent prognosis, whereas MB is a grade IV tumor, with poorer prognosis.36,79

Location

Predilection for the cerebellar hemisphere instead of the cerebellar vermis is typically demonstrated.

Fig. 23. PA versus ependymoma: MRS. (A, B) Same patient as Fig. 18 diagnosed with PA. Spectra from the lesion (A, B) demonstrates very high Cho peak, reduced NAA and Cr peaks, along with presence of lipids and lactate, typical of PA. (C, D) A 3-year-old boy diagnosed with grade II ependymoma. Spectra from the tumor demonstrates significant elevation of the ml peak as the most striking finding.
The lesion displaces and compresses the fourth ventricle (Fig. 16A, B), as opposed to what is typically demonstrated in MB that usually compromises the cerebellar vermis, filling the fourth ventricle (Fig. 16C, D).²,⁴,⁷⁹

**Imaging Findings**

CPA often presents with a solid component that is hyperintense to the cerebellar cortex on T2 due to high water content as well as low cell density (see Fig. 16A, B).²,⁴,⁷⁹ By contrast, the solid component of MBs is usually isointense or hypointense to normal cerebellar parenchyma on T2 images (see Fig. 16C).²,⁴ However, higher-grade astrocytomas may manifest lower signal intensity on T2-weighted images, effectively mimicking MBs.⁴ On the other hand, some MBs may present with high signal intensity on T2, resembling PA (see Fig. 16D).¹⁸

Cysts associated with PAs are usually larger than those demonstrated in MBs (compare Fig. 16 A, B vs C).⁷⁹

Some tumors may present with multiple solid and/or cystic components (multinodular/multicystic appearance) (Fig. 17).

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**Fig. 24.** PA: high perfusion blood volumes. (A, B) Same patient as Fig. 18. The solid enhancing PA (A: axial T1 with contrast) demonstrates high blood volume on the DCE perfusion study (B: rCBV map). (C, D): Same patient as Fig. 22. The solid enhancing PA (C: axial T1 with contrast) presents with high blood volumes (D: rCBV map).
Despite being low-grade (grade I) tumors, striking solid enhancement is characteristic (Fig. 18). The amount of gadolinium enhancement matches the T2 abnormality.\textsuperscript{79} Some lesions will present with peripheral enhancement resembling abscesses (Fig. 19). Diffusion may help in the differential diagnosis in these cases.\textsuperscript{21} The solid component of PAs has higher ADC values than do other cerebellar tumors, such as MB and ATRT (Fig. 20).\textsuperscript{21–23} The typical imaging features described previously may be useful to suggest the diagnosis of a pilocytic tumor and to distinguish this tumor from more aggressive tumors, such as MBs. However, the following are some imaging findings rarely seen that can be considered atypical.\textsuperscript{79}

**Infiltrative, rather than well-circumscribed lesion**

CPAs are typically well-circumscribed, localized lesions. However, sometimes the tumor may be infiltrative, presenting with ill-defined margins, and hence complete surgical resection is very difficult (Fig. 21).

**Presence of blood products**

CPAs, despite being grade I (low-grade) tumors may bleed (Fig. 22). Knowledge of this “unexpected” finding is essential so as not to change the diagnosis in these cases.

**Restricted diffusion**

Diffusion is typically not restricted in PAs (see Fig. 20A, B), because these are low cell density lesions.\textsuperscript{21–23} Approximately 7% of these tumors may present with restricted diffusion.\textsuperscript{21}

**Very high Cho along with presence of lipids and lactate in the magnetic resonance spectroscopy**

Brain metabolites may be useful to suggest tumor grade. Among these, Cho is typically related to tumor cell density and, hence, higher Cho/creatinine and Cho/NAA ratios are typically demonstrated in higher grade (grade III) than in lower grade (grade II) gliomas. However, tCho is not an effective or accurate biomarker for grade I PAs.\textsuperscript{36} Choline is typically very high in pilocytic tumors, despite the benign clinical course for tumors of this type (Fig. 23A, B).\textsuperscript{2,4,26,36,80} Due to the very high Cho peak, the spectral pattern of PAs may overlap with that from MB (see Fig. 10).\textsuperscript{79} However, the Tau peak, considered very characteristic of MBs, is not typically demonstrated in PAs.\textsuperscript{33} Lipids and lactate are also usually demonstrated in the spectra of PA.\textsuperscript{26,79}

The spectral pattern of PAs may be used to distinguish between these tumors and grade II ependymomas (Fig. 23C, D).\textsuperscript{79}

**High blood volumes in the perfusion study**

Despite being low grade (grade I tumors), PAs may present with high blood volumes on dynamic

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**Fig. 25.** PA: CSF tumor spread. (A, B) An 8-year-old girl treated for PA, now presenting with CSF tumor spread with multiple ependymal enhancing nodules in both frontal horns (A: axial T1 with contrast) better demonstrated in the axial T2 fluid-attenuated inversion recovery (FLAIR) with contrast (B). There is also involvement of the ependyma of the third ventricle and the atrium bilaterally. (C) A 6-year-old boy treated for PA presenting with CSF spread. Enhancing nodules are demonstrated adjacent to the conus medullaris (C: sagittal T1 with contrast).
susceptibility contrast studies (Fig. 24).\textsuperscript{79,81–83} This finding is not related to aggressiveness in these lesions.

\textbf{Cerebrospinal fluid spread}

Despite the low malignancy grade, PA may spread via CSF dissemination (Fig. 25).\textsuperscript{4,79}

\section*{Ependymomas}

Ependymomas are characterized by perivascular arrangement of tumor cells.\textsuperscript{3} These tumors are most often seen in children younger than 5, with a second peak in adults in the fourth decade.\textsuperscript{2,4}

Ependymomas are the fourth most common posterior fossa tumors in children after MB, cerebellar astrocytoma, and BG.\textsuperscript{2,4}

There are genetically distinct subgroups that have been identified by genomic studies based on locations in classic grade II and III ependymomas. They are supratentorial ependymomas with C11 or f95-RELA fusion or YAP1 fusion, infratentorial ependymomas

\begin{figure}[h]
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\includegraphics[width=\textwidth]{Fig_26.png}
\caption{Ependymoma in the fourth ventricle. Fourth ventricular mass, extending though the foramina of Luschka on the left to the left cerebellopontine angle (CPA). (A) Coronal T2, (B, C) axial T1 with contrast.}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{Fig_27.png}
\caption{Ependymoma in the foramina of Luschka. A 4-year-old boy with ataxia and hearing loss. Ependymoma growing in the foramina of Luschka on the right, displacing the medulla and pons. Lesion was mistaken for exo-phytic BG. (A) Coronal T1 with contrast, (B, C) axial T2.}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{Fig_28.png}
\caption{Ependymoma: calcification. Ependymoma located in the fourth ventricle, presenting with multiple foci of calcification. (Courtesy of A. James Barkovich, MD, San Francisco, CA.)}
\end{figure}
with or without a hypermethylated phenotype (CIMP), and spinal cord ependymomas.\textsuperscript{84}

Seventy percent of all ependymomas are in the posterior fossa, with 90% involving the ventricular ependyma (Fig. 26).\textsuperscript{2} Ependymomas may also spread through the foramina of Luschka and Magendie (Fig. 27). Punctate calcification is demonstrated in 50% of ependymoma cases on CT (Fig. 28).\textsuperscript{4} Calcification is most often seen in ependymomas than in any other posterior fossa tumor in children.

These tumors are heterogeneous on MR imaging (see Fig. 28, see also Fig. 27), reflecting a combination of solid tumor, cyst, calcification, necrosis, edema, or hemorrhage.\textsuperscript{4}

The most important imaging finding in identifying an ependymoma is extension of the tumor through the fourth ventricular outflow.

\textbf{Fig. 29.} Ependymoma: MR imaging. MR imaging after surgical resection of an ependymoma in a 3-year old boy demonstrates residual tumor in the fourth ventricle, extending through the foramina of Luschka on the left, encasing the vertebral and basilar arteries, as well as extending inferiorly through the foramina of Magendie and foramen magnum. The lesion is isointense to the cerebellar cortex on T2 (A: sagittal, B, C: axial T2) and presents with a cystic component. High-resolution T2 (D, E) demonstrates encasement of the basilar artery, extension to the left internal auditory canal (IAC) and to left Meckel cave (arrow in E). There is heterogeneous enhancement (F) and a punctate hypointensity likely representing calcification is demonstrated within the lesion (arrow in G).
foramina (see Fig. 26; and Fig. 29); however, this feature is not entirely pathognomonic, as some MBs may extend through the fourth ventricular exit foramina. In addition, they usually show more bulbous extension and restricted diffusion rather than small amounts of tissue through the foramina that is characteristic of an ependymoma. Siderosis may be demonstrated associated with ependymomas.

**Diffusion-Weighted Imaging**

Most ependymomas in the posterior fossa are classic (grade II) ependymomas. These tumors usually present with no or mild restricted diffusion (Fig. 30). Jaremko and colleagues demonstrated an overlap between ADC values of the classic type (WHO grade 2, one-half of tumors demonstrating restricted diffusion) and anaplastic type (WHO grade 3, two-thirds of tumors demonstrating restricted diffusion). Given the wide histologic and prognostic spectrum of ependymoma, diffusion characteristics of ependymoma also have a wide range overlapping other tumor types, such as MB. Because ependymoma shows no distant disease in more than 90% of cases, metastasis favors MB.

![Fig. 30. Ependymoma: DWI. (A, B) Same patient as Fig. 29. There is mild restricted diffusion in the lesion (A: axial T2, B: ADC map).](image)

![Fig. 31. Ependymoma: MRS. Same patient as Fig. 26. Classic grade II ependymomas typically demonstrate high ml in the spectra (A: axial FLAIR, B: spectroscopy).](image)
**Magnetic Resonance Spectroscopy**

High myo-inositol (ml) levels are typically demonstrated in classic grade II ependymomas.\(^{36,61}\) In a study by Harris and colleagues,\(^{88}\) the presence of high ml levels strongly suggested a diagnosis of ependymoma when short TE is used at 1.5 T (Fig. 31 see also Fig. 23 C, D). Schneider and colleagues\(^{29}\) also demonstrated that ependymomas are characterized by an elevation in ml and Glx.

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**Perfusion and Permeability Studies**

Ependymomas generally demonstrate markedly elevated relative cerebral blood volume (rCBV) (Fig. 32) and, unlike many other glial neoplasms, a poor return to baseline that may be attributable to fenestrated blood vessels and an incomplete blood brain barrier (BBB) (see Fig. 32 C).\(^{89-91}\) This behavior, although very characteristic of ependymomas, is not entirely pathognomonic and also may be demonstrated in other tumors, such as...

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*Fig. 32. Ependymoma: perfusion. Same patient as Fig. 26 diagnosed with ependymoma. There is a solid enhancing tumor in the fourth ventricle (A: axial T1 with contrast) presenting with significant elevation of rCBV on perfusion imaging (B: rCBV map) with poor return of the perfusion curve to the baseline (arrows in C: perfusion curve).*
embryonal tumors (Fig. 33) (Lara A. Brandão, MD, personal communication, 2013).

For the same reason stated previously (fenestrated blood vessels and an incomplete BBB), ependymomas tend to present with very high permeability (Fig. 34) (Lara A. Brandão, MD, personal communication, 2013).

BRAINSTEM GLIOMA AND OTHER BRAINSTEM TUMORS

One narrowly defined group of tumors primarily occurring in children (but sometimes in adults too) is characterized by K27M mutations in the histone H3 gene H3F3A, or less commonly in the related HIST1H3B gene, a diffuse growth pattern, and a midline location (e.g., thalamus, brainstem, and spinal cord). This newly defined entity is termed diffuse midline glioma, H3 K27M–mutant and includes tumors previously referred to as diffuse intrinsic pontine glioma. Most of these tumors have poor prognosis but exceptions have been reported.

The identification of this phenotypically and molecularly defined set of tumors provides a
Fig. 34. Ependymoma: permeability (DCE study). Same patient as Figs. 26, 31, and 32. There is an enhancing fourth ventricular ependymoma (A: axial T1 with contrast) with significant elevation of the permeability (B: maximum slope of increase map, C: curves; region of interest [ROI] 1, from the jugular vein; 2, from the tumor; 3, from the cerebellar white matter; 4, from the cerebellar cortex).
rationale for therapies directed against the effects of these mutations.

Brainstem tumors represent 10% to 20% of all CNS tumors in childhood.2 Most BGs are diffuse and involve the pons.4 Diagnosis is based on the characteristic changes on MR imaging of diffuse T2 hyperintense expansion of the brainstem without biopsy (Figs. 35 and 36).2,4 Enhancement is typically absent (see Fig. 35B) or restricted to a small portion of the lesion (Fig. 36D).

Five-year survival is related to location, with midbrain lesions having the best outcome (72%–100% of patients alive in 5 years) and pontine lesions having the worst (18% alive in 5 years).92 Tumor extension also influences survival, with diffuse lesions having the worst survival rates (18%–20%) and focal lesions having the best (56%–199%).92

**Diffusion-Weighted Imaging**

Areas of restricted diffusion may be demonstrated within a pontine glioma, indicating higher cell density and the best place for biopsy (Fig. 37).79

ADC measurements in these tumors are closely related to prognosis and survival with lower ADC values associated with poorer survival.92,93

**Magnetic Resonance Spectroscopy**

Single-voxel MRS (SV-MRS) or multivoxel spectroscopy (chemical shift imaging) can be used to evaluate BGs.36,94 Proton MRS and perfusion imaging may be useful in differentiating low-grade (usually focal) pontine tumors, which have lower Cho peaks (as well as Cho/Cr and Cho/NAA ratios) and lower blood volumes, from high-grade tumors in which the Cho/Cr ratio is usually higher (Fig. 38).36 A citrate peak can be demonstrated at approximately 2.6 ppm and can be used to follow tumor progression (Fig. 39).95–97 Reduced citrate levels may indicate malignant transformation of these tumors, or may be related to chronic administration of steroids, RT, and/or chemotherapy.96 Although the citrate signal is most prominent and most often observed in diffuse midline gliomas of the pons, it is also noted in other common pediatric brain tumors and in the developing brain of infants younger than 6 months.97 Some studies suggest that MRS might be a useful early predictor of disease progression in BGs, preceding clinical and radiological deterioration.95,96,98 Metabolic changes indicative of malignant transformation include increased levels of tCho, decreased metabolite ratios of NAA/tCho and Cr/tCho, and increased levels of Lips. In addition, a significant reduction in the “apparent” citrate levels also may be associated with malignant transformation.97

**Perfusion and Permeability Studies**

Available literature suggests that at least a subset of diffuse midline gliomas of the pons...
is histologically low grade (WHO grade II) at initial clinical presentation, but rapidly evolves into high-grade neoplasms, with most found to be glioblastoma at postmortem examination.96,99–105

Perfusion and permeability are related to tumor grade, with areas of higher blood volumes and higher permeability indicating aggressiveness and the best site for biopsy (Fig. 40).91

**Treatment considerations**
Radiation therapy is the most used therapy for BGs, with very good response in some patients, especially in those with low cell density tumors (Fig. 41). Enlargement of a pontine glioma during radiation therapy plus chemotherapy and or immunotherapy is not necessarily related to treatment failure and may represent pseudoprogression especially with immunotherapy treatments.108,107

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*Fig. 36.* BG: MR imaging. A 4-year-old girl presenting with headaches in the previous 3 months, strabismus, and ataxia. There is a midline diffuse glioma with high signal intensity on T2 (A: sagittal, B: coronal, C: axial T2) expanding the pons, compressing the fourth ventricle and encasing the basilar artery. A small area of enhancement is demonstrated in the lesion (arrow in D: axial T1 with contrast).
Fig. 37. BG: DWI. Same patient as Fig. 36. An area of restricted diffusion is demonstrated in the lateral portion of the lesion (arrow in A: DWI, B: ADC map) indicating high cell density.

Fig. 38. Focal versus diffuse BG: MRS. (A, B) Focal BG presenting with more preserved NAA and higher ml than the infiltrative more aggressive pontine glioma (C, D). Cho/Cr and Cho/NAA ratios are also higher in the diffuse glioma versus the focal less aggressive one.
Other brainstem tumors
Tumors in the midbrain and medulla are most often PAs on histology, with a better prognosis than the diffuse midline glioma.2,4

Ganglioglioma is another diagnostic consideration for tumors located in the brainstem.

Posterior fossa gangliogliomas (PF GGs) occur less often than supratentorial gangliogliomas (ST GGs).108

On imaging, PF GGs are most often infiltrative and expansile solid masses with dorsal predominant “paintbrush” enhancement (Fig. 42).

**Fig. 39.** BG: MRS. Same patient as Figs. 36 and 37. MRS (A: voxel, B, curve) shows high Cho along with citrate peak in 2.6 ppm.

**Fig. 40.** BG: perfusion and permeability. Same patient as Fig. 36. An area of high rCBV is demonstrated in the lateral portion of the lesion (arrow in A: rCBV map). There is no significant elevation of the permeability (B: maximum slope of increase map).
Fig. 41. BG: good response to RT. Same patient as Fig. 35. A 5-year-old boy presenting with headaches and diplopia, diagnosed with diffuse midline glioma of the pons (A: axial T2). There is no restricted diffusion in the lesion, indicating low cell density (B: ADC map). After RT (C: axial T2) the lesion is smaller and less hyperintense, indicating therapeutic response.

Fig. 42. Brainstem ganglioglioma. A 5-year-old boy presenting with hypotonia. There is an infiltrative expansile ganglioglioma at the cervicomedullary junction, with an exophytic component in the left foramina of Luschka, hyperintense on T2 (A: sagittal, B: coronal, C: axial T2) with no restricted diffusion (D: ADC map). There is dorsal linear enhancement, as well as multiple enhancing nodules within the lesion (E: sagittal, F: coronal T1 with contrast).
PF GGs are not amenable to gross total resection, and have worse progression-free survival and mortality, compared with ST GGs.\textsuperscript{107}

These tumors can be grade I or II and have a higher propensity to CSF spread than PA.\textsuperscript{109}

If there is evidence of high cell density within the tumor, with restricted diffusion and high Cho in the spectra, one should consider embryonal tumor in the differential diagnosis (Figs. 43 and 44).\textsuperscript{110}

**EMBRYONAL TUMOR WITH MULTILAYERED ROSETTES C19MC-ALTERED**

A new entity, embryonal tumor with multilayered rosettes (ETMR) C19MC-altered, was recently described in children younger than 3 years.\textsuperscript{51}

The spectrum of morphologic patterns in this entity includes the following:

- ETANRT (embryonal tumors with abundant neuropil & true rosettes) with variable numbers of rosettes, small blue cells
- Ependymoblastoma (diagnosis removed from WHO 2016)

These are usually large bulk tumors in the supratentorial compartment, but also may be found in the posterior fossa.

They are usually heterogeneous and can have little edema for their size.

A small percentage of pontine gliomas may be diagnosed as ETMR.

Prognosis is dismal despite radiation therapy.

**SUMMARY**

 Pediatric brain tumors are the most common solid tumor in children and the leading cause of death in
this patient population. The primary objective of this article was to offer a detailed overview of the most common brain tumors affecting the posterior fossa in children. The respective imaging features on CT, cMR imaging, and advanced MR imaging studies, may help suggest the most likely diagnosis leading to early and appropriate treatment.

REFERENCES

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Fig. 44. Embryonal tumor. Same patient as Fig. 33, diagnosed with embryonal tumor. A 13-year-old girl with headaches, ataxia, and diplopia. There is a solid lesion centered in the medulla, hypointense on T2 (A: sagittal, B: axial T2) extending to the left cerebellopontine angle (arrow in B), presenting with significant enhancement (C: axial T1 with contrast). Restricted diffusion is demonstrated (D: DWI, E: ADC map), indicating high cell density.


