Infratentorial brain tumors in children: The role of conventional and advanced magnetic resonance imaging (MRI).

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Learning objectives

The aim of this exhibit is to review the principal infratentorial neoplasms in pediatric age and to illustrate their most specific conventional and advance magnetic resonance imaging (MRI) findings and their main differential diagnosis.

Also we review the role of these imaging techniques in prognosis and monitoring treatment response.

Background

Brain tumors are the most common solid tumor in children and the second most common neoplasm in childhood after hematological malignancies (1-3/100,000 children); however they are the leading cause of morbidity and mortality.

Up to 60-70% are infratentorial, being this location most common in children from 4 to 11 years.

Some authors proposed that these pediatric tumors derive from the transformation of stem cell with the capacity to differentiate into neuronal or glial cells, so they can present multiple different cell types and they appear frequently in periventricular areas, where these stem cells are located.

Tumor location determines the neurological signs and symptoms: diplopia, nystagmus and ataxia (cerebellus involvement); weakness, spasticity and cranial nerves palsies (brainstem) and increased intracranial pressure causes headache, vomiting, papilledema and macrocephaly in infants.

Common posterior fossa brain tumors in children include juvenile pilocytic astrocytoma (JPA), medulloblastoma (MB), ependymoma and brainstem gliomas.

Because these various tumors require very different treatment approaches and have significantly different natural histories and outcomes, an accurate and specific diagnosis is mandatory. Conventional and advanced MR imaging techniques (perfusion imaging, diffusion-weighted imaging, and MR spectroscopy) are the corner stone in the initial evaluation of pediatric brain tumors.

Findings and procedure details

Although the definitive diagnosis is obtained by histological analysis, imaging techniques provides valuable information about the location and extent of the tumor and, sometimes,
neuroimaging findings are pathognomonic, so biopsy is not necessary if tumor is not accessible or not approachable for surgical resection.

Computed tomography (CT) is probably the imaging technique used most commonly for the initial diagnosis of intracranial neoplasms, but magnetic resonance imaging (MRI) is now the study of choice because the multiplanar imaging capability is extremely useful in determining the exact extent of the tumor and its relationship to surrounding normal structures.

The standard sequence is sagittal T1-weighted images followed by axial T2-weighted spin echo or fluid attenuated inversion recovery (FLAIR) images. Supplemental images in either coronal or axial plane should be obtained to better define its extent, but postcontrast images should then be obtained in three planes.

Advanced MR imaging techniques include diffusion and perfusion weighted images and proton spectroscopy:

- Diffusion weighted images and apparent diffusion coefficient (ADC) maps are useful in assessing tumoral cellularity: very cellular tumors will show diffusion characteristics similar or greater to gray matter in solid portions but increased diffusion in necrotic or cystic regions.

- Perfusion imaging may be useful for differentiating lower grade glial neoplasms (low blood volume) from higher grade glial neoplasms (high blood volume) and for finding the region of a mass that is of a highest histologic grade (stereotactic biopsy).

It is also useful in post-therapy evaluation to differentiate hypovascular radiation injury from hypervascular tumor recurrence.

- Spectroscopy is utilized in our hospital in the preoperative analysis of brain tumors. The spectral pattern of neuroectodermally derived tumors appears to be fairly characteristic, showing elevation of choline levels, reduced N-acetyl aspartate (NAA) and creatine, and sometimes increased lipid and lactate. A low NAA/choline ratio is sign of tumor and the larger the choline peak, the more likely the tumor is to be of a high grade.

Finally MRI can also be used in conjunction with computerized navigation techniques that greatly facilitate tumor resection.

We reviewed all the pediatric posterior fossa tumors diagnosed in our hospital from 2005 to 2012, and we founded 28 patients (15 male, 54% and 13 female, 46%), whom their age ranged from 0 - 8 years old with the mean age 7.5 years.
The MRI evaluation and histopathological reports showed 13 MBs (46%), 7 JPAs (25%), 4 brainstem gliomas (15%), 2 atypical teratoid-rhabdoid tumors (7%), 1 case of infratentorial ependymoma (3%) and 1 case of ganglioglioma (3%).

**MEDULLOBLASTOMA**

*(Primitive Neuroectodermal Tumor of the posterior Fossa, PNET)*

It is a highly malignant tumor composed of undifferentiated cells, being the most common posterior fossa tumor in children (30-40%), slightly more common that the cerebellar astrocytoma. It is also the most common tumor in 6-11 years old children and males are affected twice to four times as frequently as females.

Also medulloblastomas can be found in adults, being 14-30% out of overall medulloblastomas and being more frequent in younger adults.

Because of his fast growth, clinical symptoms mostly develop rapidly and are tipically related to intracranial hipertension and cerebellar ataxia. There are also nausea and vomiting when the tumor grown in proximity to the emetic center of the brain, which is located near the inferior aspect of the fourth ventricle.

75-90% of medulloblastomas in childrens occur in the midline, in vermis, in contrast with adolescent and adults, in whom they are most often located in the cerebellar hemispheres (10-15%). The tumor usually forms a well defined vermian mass widening the space between the cerebellar tonsils: it impinges anteriorly upon the roof of the 4th ventricle causing obstruction to CSF flow and posteriorly, it may project into the cisterna magna and extend to the upper cervical spinal cord.

Dissemination along the cranioespinal axis is found in approximately 11-43% of patients and it is one of the most important predictors of outcome so it is mandatory to schedule MRI of the spine before surgical treatment.

On CT, medulloblastoma appears as midline, well-defined, homogeneus and hyper-isodense mass, with mild-moderate perilesional edema in 90-95% of patients. Enhancement, most commonly diffuse but sometimes patchy because of cysts or nonenhancing necrotic regions, is seen in greater than 90% of medulloblastomas. Calcifications can be found in up to 20% of cases.

On MRI the appareance is variable, tipically it appears as round slightly lobulated and T1 iso/hypointense mass, being heterogeneus and iso/hypointense compared with the gray matter in T2-weighted images. It also shows reduced diffusion.

All these findings are related to the hight cellularity of the tumor (low signal intensity and reduced diffusion) and to cyst and calcifications (signal heterogeneity); hemorrhage is not a frequent finding.
As on CT, the enhancement pattern of this tumor after intravenous infusion of paramagnetic contrast is variable, ranging from diffuse and homogeneous to local and patchy.

Spectroscopy shows decreased NAA/Cho and Cr/Cho ratios while low grade astrocytomas and ependymomas have values between those of medulloblastomas and those of normal cerebellum. Accordingly spectroscopy may be useful in prospectively differential diagnosis.

Dissemination to the cerebrospinal fluid (CSF) is common and can be best seen on T1-weighted sequences after injection of paramagnetic contrast. They can be located intracranial (vermis, basal cisterns and lateral and third ventricle most frequently) or in the spinal cord, being difficult to distinguish from debris and blood or subdural and extradural bleedings in the first weeks after surgery.

Treatment of medulloblastoma includes surgery, radiotherapy and chemotherapy in all cases but the intensity of the treatment (particularly the craniospinal radiation) depends of patient own risk. Medulloblastoma risk classification is based on the presence or absence of disseminated disease based on MRI findings and CSF cytology, degree of tumor resection and patient’s age at diagnosis. Accordingly, we can differentiate high risk patients (survival rate of 20% at 5 years) or standard risk patients (54-100% at 5 years depending of cytogenetic and molecular markers).

ASTROCYTOMA

Astrocytomas are the second most frequent brain tumor in children (30-35%) and approximately 60% of them are located in the posterior fossa. Cerebellar astrocytomas are more frequent at the age of 5-13 years and occur equally frequent in boys and girls.

They are usually sporadic but association with neurofibromatosis type 1, TURCOT syndrome, Ollier’s disease and others has been reported.

Most of them are of a specific histological type called Juvenile Pilocytic Astrocytoma (JPA) which is considered a unique tumor and is the most benign astroglial tumors of the CNS. Malignant astrocytomas can occur in children and they have a very poor prognosis.

Approximately half of JPAs are purely midline tumors and they extend into the cerebellar hemispheres in 30% of cases. Because of their slow growing the children usually present a long story of waxing and waning signs of increased cranial pressure. The incidence peak is in 2 years old.

They can be cystic, solid or solid with necrotic center; approximately 40-45% of the tumors are composed of a rim of solid tumor with a cyst-like necrotic center, and only the 10% of all JPAs do not present necrotic regions.
On CT the typical appearance of the JPAs is a large and predominantly cystic mass arising from the vermis cerebelli or the cerebellar hemispheres. The solid part are usually hypodense in contrast with high-grade gliomas which can be hyperdense on CT.

On T1-weighted MRI the solid component of JPAs is usually hypo to isointense compared to the gray matter and their signal intensity can be homogeneous or heterogeneous (if they have necrotic and/or cystic areas). On T2-weighted images this solid component appears hyperintense to the gray matter and slightly hypointense/isointense compared to CSF. Enhancement pattern is also variable but mostly heterogeneous because of cysts and central necrotic nonenhanced areas, while the solid component tend to enhance prominently and homogeneously. Enhancement of the cyst walls indicates tumor infiltration or intralesional hemorrhage.

Because of the cystic and necrotic regions JPAs do not restrict in diffusion sequences. Spectroscopy shows an aggressive metabolic pattern with low NAA and creatine levels and increase of choline peak; Although JPAs are low grade tumors they present a low NAA/Cho ratio and usually have lactate, which is generally considered to be a sign of high grade neoplasm.

They have an excellent prognosis (survival rate of 25 years close to 90%) and it depends particularly on the complete or uncomplete resection of the tumor and his characteristics (location, structure and size). Complete resection, hemispheric location, cystic component and small size are favorable prognostic factors.

Malignant or high grade astrocytomas arising in the posterior fossa are uncommon, only 10% of all pediatric high-grade gliomas. They can be sporadic but they occur particularly with genetic disorders like TURCOT syndrome or Ollier’s disease.

They usually occur in older children than JPAs and, because to the higher growth rate, the time interval between onset of symptoms and diagnosis is shorter.

On MR imaging, high-grade cerebellar astrocytomas are more hypointense on T2 weighted images and more heterogeneous, they usually present rim-like enhancement with poorly defined margins. Presence of extraaxial metastases or dissemination through the subarachnoid spaces is also more frequent than in other posterior fossa tumors.

**EPENDYMOMA**

Ependymomas are the fourth most common posterior fossa tumors in children (8-15%), being more frequent infra (70%) than supratentorial (30%) in pediatric age. The peak of incidence occur between the ages of 1 - 5 years and it is equally prevalent in both sex, with minimum predilection for boys.
Patients usually present a long clinical history of nausea and vomiting resulting from hydrocephalus and increased intracranial pressure from tumor obstructing the 4th ventricle (90%). They also can present torticollis, ataxia and lower cranial neuropathies.

Ependymomas derive from differentiated ependymal cells that line the floor and roof of the 4th ventricle extending into both lateral recesses and into foramina of Luschka. Also additional ependymal cell rests are sometimes found far from the ventricular linings, so this tumor may originate from any of these locations.

They are usually well-demarcated tumors which progressively fill out the 4th ventricle and extend through the foramina of Magendie and Luschka into the perimedullary cisterns and upper cervical spinal canal, surrounding the brainstem and the main vessels of the posterior cerebral circulation. Infiltration of adjacent brain is uncommon.

Histologically most of ependymomas of the posterior fossa are low-grade or WHO grade II (70%). Anaplastic ependymomas (30%) is the malignant variant or WHO grade III because of his fast growth, high mitotic rate and necrosis, and it is more common in younger children and in supratentorial location.

On CT ependymoma appear as iso/hyperdense mass filling and distending 4th ventricle, with heterogeneous contrast enhancement. Up to 50% present multiple and punctuate calcifications.

On MRI, infratentorial ependymomas mostly present as a homogeneous mass which is T1-iso/hypointense and T2-hypointense. Signal heterogeneity can occur, more commonly in supra than in infratentorial ependymomas due to myxoid accumulation and cyst components. In addition to calcifications we can also found old hemorrhages result in focal hypointensities.

15% extend laterally into the cerebelopontine angles by means of the foramina of Luschka and 60% extend through the foramen of Magendie into the cisterna magna and through the foramen magnum into the upper cervical spinal canal.

MR spectroscopy yield high choline peak and decreased levels of creatine and NAA. As low-grade astrocytomas, NAA/Cho and Cr/Cho ratios are between those of medulloblastoma and those of normal cerebellum.

Subarachnoid dissemination along the CSF is uncommon (10-12%) so when it is present the presence of an anaplastic variant must be suggested. Complete spine imaging is mandatory.

According to the pattern of extension there is two types of ependymomas, lateral-type, present a lateral displacement of brainstem while the another one, the midfloor-type displace anteriorly the brainstem. This clasification is important because the lateral-type has higher risk of residual tumor after treatment, being necessary more intensive treatment.
Accordingly, tumor’s location is sometimes more important than his histology for prognosis and treatment of the patient who will receive surgery +/- radiotherapy depending on complete or uncomplete tumor resection.

**BRAINSTEM GLIOMAS**

Gliomas of the posterior fossa account for 5-11% of all intracranial tumors in children and 15-30% of infratentorial tumors. They can occur at any age of childhood but the peak of incidence is between the ages of 6 and 8 years, with an equal distribution for boys and girls.

Depending on the primary anatomical location we can establish three groups: diffuse intrinsic gliomas, exophytic gliomas of the lower brainstem or tectal gliomas; all of them with very different clinical presentation, prognosis and treatment.

Focal neoplasms have a better prognosis than diffuse intrinsic gliomas which are often not approachable for surgical resection due to the location and their infiltrative nature.

**Diffuse intrinsic brainstem gliomas** (60-75% of the posterior fossa gliomas) tipically involve more than 50-75% of the cross sectional area of the brainstem on initially diagnosis and present poor-defined margins.

They usually infiltrates diffusely the pons respecting the anatomical borders of the brainstem, with midly compressed 4th ventricle, so obstructive hidrocephalus usually appears late during disease progression.

Children usually present a short story of cranial nerve palsies (V-VII), pyramidal signs and/or ataxia.

On CT appear as a hypodense mass centered in an expanded pons with occasionally a cystic component. They are T1-iso/hypointense an T2 heterogeneously hyperintense on MRI with variably gadolinium enhancement.

These tumors have and extremely poor prognosis, being the median survival time 9-12 months with intensive radio and chemotherapy.

**Exophytic gliomas of the lower brainstem**

They arise from the dorsal surface of the lower brainstem and they tend to extent exophytically into the 4th ventricle or perimedullary cisterns.

On CT, they appear as a sharply demarcated iso to hypodense mass lesions originating from the dorsal contour of the lower brainstem. On MRI, these tumors are T1-hypointense
and T2-hyperintense. They show a moderate-strong and homo or heterogeneous enhancement in both imaging techniques.

They are usually low-grade gliomas and their typical exophytic growth makes these tumors approachable for surgical resection, so prognosis is excellent.

**Tectal gliomas**

They are centered to the tectal plate and because of their close proximity to the Sylvian aqueduct, children usually present with a history of increased intracranial pressure due to an obstructive hydrocephalus. They can remain stables for ages.

On CT, tectal gliomas present as small nonenhancing, hypodense focal mass lesions centered within the tectal plate. On MRI, they are T1-hypointense and T2-hyperintense. They do not usually present peritumoral edema and contrast enhancement is typically uniform. Because these tectal gliomas may be small or compressed due to hydrocephalus they can easily be missed on initial imaging, becoming more apparent after shunting/decompression of the hydrocephalus.

Next to previously described tumors, a wide variety of less frequent tumors may be encountered in the posterior fossa: atypical rhabdoid-teratoid tumor, hemangioblastoma, dermoids, schwannoma of the VIIIth cranial nerve, gangliocytoma, meningioma, high grade gliomas and metastases.

**Images for this section:**
Fig. 1: 8 years-old boy which presented with vomiting and nausea, frontal headache and self-limited episode of blindness since 1 week ago. MRI showed a right cerebellar mass that compresses the bulb and obliterates the 4th ventricle, hypointense on T1 weighted images and heterogeneous with punctate hyperintense areas (necrotic areas) on T2. Tumor shows restricted diffusion and slight enhancement after contrast administration.
Fig. 2: MRI spectroscopy showed NAA decrease with increasing Cholina, there was also a lactate peak.
Fig. 3: JPA in 6 years-old boy with headache and vomiting since 1 month ago. Coronal T1 and T2 weighted images shows heterogeneous mass located in left cerebellar hemisphere that collapses basal cisterns and compresses IV ventricle producing triventricular hydrocephalus and herniation of cerebellar tonsils. Tumor is predominantly cystic and it presents a solid nodule located on the anterior and left lateral of the mass.
**Fig. 4:** Axial FLAIR and Axial T1 after contrast administration. Intense enhancement of septations and the solid region of the tumor. Cystic portion of the tumor shows no restriction on diffusion weighted images.
Fig. 5: MRI finding in 2 years-old boy with history of ataxia. Axial T1 and T2 weighted images show slightly hyperdense and heterogeneous mass that partially fills the 4th ventricle extending to the cerebellopontine angle, with punctate calcifications inside. It also presents T2-hyperintense areas poorly defined in the posterior and right lateral region (necrotic areas). After contrast administration it present heterogeneous peripheral enhancement. Tetraventricular hydrocephalus with signs of transependymal resorption is also seen.
Fig. 6: Low-grade brainstem glioma. T1- hypointese and T2- hyperintense well defined mass located in bulb and protuberance.
Fig. 7: Diffuse brainstem glioma. Heterogeneous mass with T1- hyperintenses and T2-hypointenses areas inside located on protuberance, midbrain and diencephalon. After contrast administration we found a irregular and rim enhancement.
**Fig. 8:** 7 years-old child with left hearing loss and ataxia. T1- hypointense and T2-heterogeneous mass located in the left cerebellopontine angle. It shifts brainstem and compresses 4th ventricle extending through internal auditory canal. It shows heterogeneous enhancement after contrast administration.
**Fig. 9:** Mass showed restricted diffusion.
Conclusion

Magnetic resonance imaging is the primary imaging modality used for the assessment of posterior fossa tumors in pediatric age because it provides superior delineation of their location, characterization and extension pattern.

Although the definitive diagnosis is obtained by histological analysis, advanced MRI techniques such as diffusion and perfusion weighted images and spectroscopy provides additional presurgically important information.

Knowledge of their characteristic findings is essential to get to an accurate diagnosis and to monitorize treatment response.

Personal information

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