ORIGINAL REPORT

Magnetic resonance imaging of infratentorial anaplastic ependymoma in children

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KEYWORDS
Ependymoma; Anaplastic ependymoma; Magnetic resonance imaging

Abstract
Objective: To show the main findings for anaplastic ependymoma on MRI.
Material and methods: We reviewed all patients diagnosed with anaplastic ependymoma at our tertiary hospital during a six-year period.

We recorded the MRI findings for this type of tumor (on conventional sequences following the protocol for the study of CNS tumors, diffusion-weighted imaging, contrast-enhanced sequences, and MR spectroscopy).

Results: Our series comprises seven children with infratentorial anaplastic ependymoma. We found no definitive characteristics to distinguish between grade II and grade III tumors before histology, as none of the lesions had spread to the cerebrospinal fluid at diagnosis or showed increased restriction in the diffusion-weighted sequence.

Conclusions: The MRI characteristics cannot definitively distinguish between grade II ependymomas and anaplastic grade III ependymomas. Only a few details about diffusion and dissemination to the cerebrospinal fluid, if present, can distinguish between these types at imaging.

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PALABRAS CLAVE
Ependimoma; Ependimoma anaplásico; Resonancia magnética

Resonancia magnética en el ependimoma anaplásico infratentorial pediátrico

Resumen
Objetivo: El objetivo es mostrar las principales características radiológicas que el ependimoma anaplásico puede presentar en las imágenes de resonancia magnética (RM).

Material y métodos: Se recogen los pacientes diagnosticados de ependimoma infratentorial de tipo anaplásico en los últimos 6 a años en nuestro hospital terciario.

Se estudian las características de imagen mediante RM (secuencias convencionales protocolizadas para estudio tumoral del SNC, difusión, estudio con contraste, espectroscopia) de este tipo tumoral.

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Introduction

Anaplastic ependymoma is a high-grade malignant tumor, World Health Organization (WHO) grade III,1 whose histopathological description is controversial due to the lack of consensus, which results in a more difficult clinical assessment and therapeutic management. The grade of the ependymoma and the extent of surgical resection are the primary determinants of survival.2

Ependymomas may arise from an infratentorial, supratentorial or spinal location. From an imaging point of view, it is important to know that most pediatric ependymomas are infratentorial, that infratentorial tumors show overlapping imaging features with medulloblastoma (the main differential diagnosis at this age), and that anaplastic ependymomas have a greater tendency to spread in the cerebrospinal fluid (CSF) than other types of ependymoma. Initial diagnosis and follow-up evaluation should therefore include magnetic resonance imaging (MRI) of the neuraxis.

The aim of this review is to examine the main distinctive imaging features of anaplastic ependymoma on MRI.

Materials and method

We performed a retrospective study of the cases of pediatric infratentorial ependymomas diagnosed at our tertiary children hospital between 2004 and 2010. Seventy percent of the total pediatric infratentorial ependymomas were classified as WHO grade III (7/10).

An additional pathological review of those ependymomas classified as grades II and III was conducted based on current pathological diagnostic criteria, and there was no modification of the grades previously assigned.1,3

Once we had knowledge of the assigned histological grade, we carried out a retrospective review of the MRI studies of the 7 anaplastic tumors. All patients were studied according to the protocol for pediatric central nervous system (CNS) tumors, with unenhanced and contrast-enhanced MRI sequences of the brain and neuraxis. Scans were performed on a Philips 1.5 Tesla and a General Electric 1.5 Tesla MR system, assessing the semiologic data from the MRI of brain and neuraxis in order to differentiate between anaplastic ependymomas and grade II ependymomas, with a particular focus on diffusion data and spinal dissemination.

Results (Table 1)

We present 7 patients diagnosed with infratentorial anaplastic ependymoma, with ages ranging from 6 months to 5 years (Table 1).

All ependymomas were located in the midline of the cerebellum. All, except one contained within the fourth ventricle, extended into the adjacent cisterns (pontocerebellar, perimedullary and/or superior vermian) through the foramen of Luschka, Magendie and/or magnum (Fig. 1). The average tumor size, estimated in relation to the maximum diameter, was 4.7 cm (4–5 cm).

In some cases (2/7), the tumors presented as a predominantly solid mass, but the dominant pattern was solid-cystic (5/7), leading to marked signal heterogeneity on the different sequences (Fig. 1). Six of the 7 ependymomas demonstrated similar or slightly high T1, significantly high T2, and intermediate FLAIR signal intensity relative to gray matter. Only one heavily calcified tumor, seen on emergency CT scan, appeared hypointense on all MRI sequences, which may be attributable to the extensive calcification.

Contrast enhancement varied widely: moderate and heterogeneous in 3 tumors, intense but heterogeneous in 2, and very mild in 2 (Fig. 2).

In the diffusion-weighted sequences, moderate restriction was seen in 4 of the 7 studies performed (Fig. 3).

MR spectroscopy was performed in 3 patients and demonstrated unspecific data, with reduced N-acetylaspartate and elevated choline.

Dissemination into the neuraxis was not detected in any of the patients at initial diagnosis or during follow-up. The neuraxis was studied following an MRI protocol (sagittal fatsuppressed T1- and T2-weighted and contrast-enhanced T1 sequences. Diffusion MRI was not performed).

The treatment of the 3 younger patients included surgery and chemotherapy for the six-month-old patient: chemotherapy for the nine-month old, and surgery for the 12-month-old patient, who was moved to another center and lost to follow-up. Radiation therapy was included in the treatment of the 4 older patients.

Residual tumor was found in all but one of the patients after surgery. All patients underwent single-stage surgery and none of them underwent a second surgery.

One patient died during follow-up and the remaining 6 patients were followed up during a period ranging 9 months to 6 years (one was moved to another center after surgery).
Magnetic resonance imaging of infratentorial anaplastic ependymoma in children

Table 1  Summary of the characteristics of the infratentorial anaplastic ependymomas in our series.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age/sex</th>
<th>Infratentorial location</th>
<th>Maximum diameter and internal structure</th>
<th>Post paramagnetic contrast enhancement pattern</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>3 years/M</td>
<td>In IV v, extension into foramen magnum and perimedullary cistern</td>
<td>5 cm</td>
<td>Intense and heterogeneous</td>
<td>Surgery and radiation</td>
<td>Residual tumor</td>
</tr>
<tr>
<td>Patient 2</td>
<td>2 years/M</td>
<td>In IV v, extension into foramen magnum</td>
<td>4 cm</td>
<td>Heterogeneous</td>
<td>Surgery, chemotherapy and radiation</td>
<td>No residual tumor</td>
</tr>
<tr>
<td>Patient 3</td>
<td>12 months/F</td>
<td>In IV v, extension into perimedullary cisterns</td>
<td>Solid</td>
<td>Mild</td>
<td>Surgery</td>
<td>Lost to follow-up</td>
</tr>
<tr>
<td>Patient 4</td>
<td>5 years/M</td>
<td>In IV v, extension into foramen magnum and superior vermian cistern</td>
<td>5.5 cm</td>
<td>Intense and heterogeneous</td>
<td>Surgery, chemotherapy and radiation</td>
<td>Residual tumor</td>
</tr>
<tr>
<td>Patient 5</td>
<td>4 years/M</td>
<td>In IV v, extension into foramen magnum and superior vermian cistern</td>
<td>Solid-cystic</td>
<td>Heterogeneous</td>
<td>Radiation</td>
<td>Residual tumor</td>
</tr>
<tr>
<td>Patient 6</td>
<td>9 months/M</td>
<td>In IV v, extension into foramen magnum and midbrain perimedullary cisterns, infiltrates brain stem</td>
<td>Solid-cystic, with calcifications</td>
<td>Heterogeneous</td>
<td>Chemotherapy</td>
<td>Death</td>
</tr>
<tr>
<td>Patient 7</td>
<td>6 months/F</td>
<td>In IV v, extension into perimedullary, pontocerebellar cisterns and foramen magnum</td>
<td>Solid-cystic, with many hemorrhage and calcium foci</td>
<td>Minimal</td>
<td>Surgery and chemotherapy</td>
<td>Residual tumor</td>
</tr>
</tbody>
</table>

F: female; M: male; v: ventricle.

Figure 1  Classic appearance of ependymoma. These images correspond to an anaplastic ependymoma. (A) Unenhanced CT scan shows a midline infratentorial mass with epicenter at the fourth ventricle, with multiple foci of calcification. The lesion causes obstructive hydrocephalus with ventricular distension and periependymal hypodensity secondary to transependymal migration of CSF. (B) Sagittal unenhanced T1-weighted image shows hypo-isointense mass relative to gray matter that extends through the foramen magnum as a “thin tongue” and passes the medullary-spinal junction (arrow). (C) Axial T2-weighted image shows a markedly heterogeneous mass, predominantly hyperintense that engulfs and lateralizes the basilar artery (arrow), extends into the cistern of the right pontocerebellar angle infiltrating the adjacent brainstem. (D) Coronal FLAIR sequence shows heterogeneity and intermediate signal intensity. Obstructive supratentorial hydrocephalus with transependymal edema.
ependymomas arise from ependymal cells that line the fourth ventricle and the foramina of Luschka. They tend to distend the fourth ventricle resulting in hydrocephalus and hydrocephalus-related complications in 90% patients.\(^5\) In our series, 6 of the 7 patients required a permanent ventriculoperitoneal shunt.

Anaplastic ependymomas are less common than grade II ependymomas,\(^6\) and have greater incidence of CSF dissemination and worse prognosis.\(^5\) In our series, however, anaplastic ependymomas were more common than grade II tumors, and none of these grade III tumors had neuraxial dissemination at the time of diagnosis or during follow-up. These findings are in contrast to those reported in the literature. Maybe, placing pediatric and adult ependymomas into the same group, grouping together all the possible localizations (spinal, supra and infratentorial), and the fact that histological criteria have not yet been determined may help explain this dissociation of results.

Clinical signs and symptoms of anaplastic ependymomas are similar to those for grade II tumors, but the former tend to develop earlier.\(^1\) We were not able, however, to verify this fact as we did not compare anaplastic with ‘non anaplastic’ ependymomas.

Infratentorial ependymomas generally demonstrate heterogeneous appearance on MRI with low T1, high T2 and intermediate FLAIR signal intensity. These characteristics have been attributed to the high proportion of ependymomas with intracellular myxoid accumulation and cyst formation. For this reason, they are conspicuous on T2-weighted and FLAIR sequences and even visible on unenhanced T1-weighted sequences.\(^2,5\) Ependymomas are generally heterogeneous, particularly supratentorial ependymomas.\(^5\) In our series, all the infratentorial anaplastic tumors showed solid enhancement and heterogeneity to a greater or lesser degree.

Calcifications and old hemorrhage demonstrate very low signal on all MRI sequences.\(^3\) It is a known fact that, in children, ependymoma is the first differential diagnosis for an infratentorial mass with hyperdensity on CT, secondary to its

Figure 2  Variable enhancement pattern in an infratentorial anaplastic ependymoma. (A) Axial gadolinium-enhanced T1-weighted sequence shows marked and heterogeneous tumor enhancement. (B) Axial gadolinium-enhanced T1-weighted sequence shows tumor with cystic-necrotic areas of peripheral, thick and irregular enhancement in the posterior portion, and a more homogeneous and moderate enhancement in the anterior and right cisternal portions. (C) Axial gadolinium-enhanced T1-weighted image shows anaplastic ependymoma with little enhancement after contrast material administration. (Predominantly hypointense mass because of the extensive calcification.)

Figure 3  Diffusion-weighted imaging. Intraventricular infratentorial mass with vermal extension and intermediate-to-high signal intensity on T2-weighted sequence. The diffusion-weighted sequence in the same plane shows moderate restricted diffusion.

Discussion

Ependymomas account for only 3–9% of all brain tumors. However, they are the third most common brain tumor in children after medulloblastoma and astrocytoma.\(^2,6\)

The group of tumors exhibiting ependymal differentiation includes\(^1,4,5,7,:\)

1. Subependymoma (grade I).
2. Myxopapillary ependymoma (grade I).
3. Grade II ependymoma; variants including cellular, papillary, clear cell, tanacytic. WHO grades I and II are low-grade ependymomas.
4. Anaplastic ependymoma (grade III), classified as high-grade.

Approximately, 70% of ependymomas are infratentorial with the rest being supratentorial and spinal. Cerebellar...
tendency to exhibit calcium. The presence of calcium was constant in the 7 cases of our series. In this regard, extensive calcification was present in patient 7 and, to a lesser extent, in the rest of patients.

A typical feature is the morphological "plasticity" of these tumors, which leads to foraminal and cisternal extension. Some medulloblastomas, the main differential diagnosis for infratentorial ependymoma, may extend through the exit foramina of the fourth ventricle showing more round or "bulbous" extension rather than "tongue"-like extension as in ependymomas.5

Ependymomas demonstrate intense but heterogeneous enhancement, in line with the heterogeneity of the solid mass.5 The heterogeneous pattern with mild intensity was predominant in our series. Only 2 cases with extensive calcifications showed lower enhancement.

Diffusion values of ependymomas are between those of pilocytic astrocytomas and medulloblastomas, but variations in diffusion have been described for the different histological types of ependymomas.4,9-10 An increase in restricted diffusion has been reported in two-thirds of anaplastic ependymomas and in half of grade II ependymomas.9,10 However, the diffusion values in our series were not consistent with the published literature since all tumors were anaplastic ependymomas but none of them showed increased restricted diffusion. This information was, therefore, of no help in the preoperative differentiation between anaplastic ependymomas and ependymomas of lower grade.

MR spectroscopy usually demonstrates elevated choline and reduced N-acetylaspartate, as in other tumors.5,10 Although MR spectroscopy may be useful in the differentiation of ependymoma from medulloblastoma, there is overlap in a considerable number of measurements. Therefore, spectroscopy is used primarily to differentiate tumor recurrence from postradiation changes.5

Perfusion MRI of ependymoma usually demonstrates markedly elevated cerebral blood volume and, unlike other glial neoplasms, poor return to baseline that may be attributable to fenestrated blood vessels and an incomplete blood–brain barrier (BBB).5 As with MR spectroscopy, perfusion MR is used primarily to differentiate post-treatment changes from tumor recurrence since this technique has a more limited use in children than in adults.5

Despite their location in the ependymal surfaces of the ventricles and canal of the spinal cord, that could make us suspect increased tumor exfoliation into the subarachnoid space, leptomeningeal dissemination of ependymomas is relatively uncommon in comparison to other pediatric central nervous system tumors such as medulloblastoma and high-grade astrocytoma.7,11 In general, CSF spread of intracranial ependymomas is more common in anaplastic tumors, infratentorial tumors (against supratentorial) and in younger children.4,5,12 However, none of the anaplastic ependymomas in our series showed CSF dissemination.

Characteristics of anaplastic histology include hypercellularity, pleomorphism, atypia and microvascular proliferation.5,2 Perivascular pseudorosettes and true rosettes are histological features of these tumors2,4,7,11 (Fig. 4). The focal nature of the anaplasia makes interpretation difficult. No criteria regarding the number of foci or their size have been established. In this respect, for some authors occasional foci of anaplasia are allowed in grade II ependymomas.2

Conventional treatment includes surgical resection and radiation therapy. Chemotherapy plays a role in younger children to avoid or delay the use of radiation, may improve surgical resectability and may be used in recurrent tumors.7,10,13,14

According to the literature, the 5-year survival rate for patients with anaplastic or high-grade ependymoma is 10–47%.5,14 Four of our patients are alive with the disease, one is alive with no disease, one died and one was lost to follow-up.

As determined by this review, that despite including a small number of cases could be another representative sample of anaplastic tumors, there are no definitive imaging features that help distinguish grade II ependymomas from grade III anaplastic ependymomas, each requiring a different clinical, therapeutic and prognostic management. From an imaging point of view, only a few details regarding diffusion and a higher tendency to CSF dissemination, if present, may help in their differentiation.

A deeper insight into the immunohistochemistry and molecular pathology of ependymoma will improve the
histological grading of these tumors, and as a result, their prognostic differentiation.\(^2,^3,^7\)

**Authorship**

1. Responsible for the integrity of the study: MIML.
2. Conception of the study: MIML.
3. Design: MIML.
4. Acquisition of data: MIML, MVD, BWL.
5. Analysis and interpretation of data: MIML, BWL.
6. Statistical analysis: MIML, BWL.
7. Bibliographic search: MIML, MVD, BWL.
8. Drafting of the manuscript: MIML.
9. Critical review with intellectually relevant contributions: MIML, WBL.
10. Approval of the final version: MIML, MVD, BWL.

**Conflict of interest**

The authors declare not having any conflict of interest.

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