MR Manifestations of Subependymomas

C. Hoeffel, M. Boukobza, M. Polivka, G. Lot, J. P. Guichard, F. Lafitte, D. Reizine, and J. J. Merland

PURPOSE: To provide a description of the MR and enhanced MR appearances of subependymomas. METHODS: We reviewed the MR examinations of eight cases of pathologically proved subependymomas and correlated them with operative and pathologic reports, and also reviewed the previous published cases of subependymomas documented by MR. Gadopentetate dimeglumine–enhanced MR examination was performed in seven cases. RESULTS: One patient presented with four subependymomas, two patients had subependymomas of the cervical spine, and the others were intraventricular with no transependymal extension. They were isointense to hypointense relative to normal white matter on T1-weighted images, heterogeneous in five cases. Minimal (n = 1) or no (n = 3) enhancement was noted in four cases, and moderate or marked enhancement was noted in three cases. CONCLUSION: We conclude that even though there is no specific sign of subependymomas, when confronted with a complete intraventricular lesion or with a spinal lesion causing little or no edema which is minimally enhancing or nonenhancing, one must consider the diagnosis of subependymoma.

Index terms: Ependymoma; Brain neoplasms, magnetic resonance; Spinal cord, neoplasms


Subependymomas are rare, benign, slow-growing, generally well-circumscribed, and sometimes multiple lesions, most frequently located in the fourth ventricle (1–4). They have a distinctive histologic appearance, but their histogenesis and exact nature still are controversial (5). Their differential diagnosis from other tumors, mainly ependymomas, may have some therapeutic implications (6). Computed tomography and angiographic findings of intracerebral subependymomas are well known (2). There is limited description of magnetic resonance (MR) features of adequate material in the literature; 10 cases have been studied with enhanced MR (7–14). To define the most common appearance of subependymomas, we report eight cases of pathologically proved subependymomas that have been studied with MR.

We also review the previous published cases of subependymomas documented by MR.

Material and Methods

The MR studies of eight patients with subependymomas were retrospectively and independently analyzed by two senior radiologists. In all cases, the histopathologic findings were reviewed and correlated with the MR findings. The operative and clinical data were reviewed retrospectively. The imaging and clinical follow-up data also are reported.

The patients ranged in age from 17 to 73 years (mean, 50 years). MR examinations were performed in all cases at initial presentation. Six of these patients were imaged again postoperatively by MR (one 7 years after surgery and others at a mean time interval of 1 year after surgery, ranging from 1 month to 2 years). Five preoperative examinations were performed at 0.5 T, one at 0.35 T, one at 1 T, and one at 1.5 T. T1-weighted images were acquired in all cases, either using inversion-recovery sequences (n = 1), spin-echo sequences (n = 4), or gradient-echo sequences (n = 4). T2-weighted images were obtained in six cases, using spin-echo sequences. Enhanced gadopentetate dimeglumine images were obtained in seven cases. Computed tomography was performed in five patients, and intravenous contrast material was administered in three cases.
MR findings in subependymomas

<table>
<thead>
<tr>
<th>Case</th>
<th>Age, y/Sex</th>
<th>Location</th>
<th>Extent and Routes of Extension</th>
<th>Consistency</th>
<th>Signal of Solid Tumor Relative to White Matter</th>
<th>Signal-Intensity Heterogeneity</th>
<th>Margins</th>
<th>Edema</th>
<th>Enhancement</th>
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Note.—T1 indicates T1-weighted images; T2, T2-weighted images; PD, proton density-weighted images; V4, fourth ventricle; SP, septum pellucidum; SC, spinal cord; IM, intramedullary; EM, extramedullary; LPCA, left pontocerebellar angle; V3, third ventricle; PCA, Monro, Luschka, Magendie, and magnum, tumor extending in pontocerebellar angle or through foramen of Monro, of Luschka, of Magendie, and magnum; VL, lateral ventricle; CSC, cervicospinal cord; mixed, solid and cystic components; =, isointense; −, hypointense; +, hyperintense; min, minimal; and mod, moderate. Margins were moderately well (Mod), poorly (Poor), or well delineated (Well).

Pathology

Surgical specimens were fixed in Bouin’s fixative embedded in paraffin. Five-μm-thick sections were obtained and stained with hematein eosin and Masson’s trichrome. In one case (case 8, Fig 6), immunohistochemical study was performed with anti–glial fibrillary acidic protein and anti–neurone specific enolase polyclonal antibody (Dako, Trappes, France) diluted at 1/1000 and 1/100, respectively, with avidin-biotin complex method and horseradish peroxidase, and diaminobasydine used as chromogene. In three cases (cases 4, 5, and 8), parts of the specimen were fixed in glutaraldehyde and processed routinely for electron microscopy.

Results

The data for location, extent, and routes of extension of the tumor are tabulated (Table). Three subependymomas were medullary, located at the level of the cervical spine, and one patient presented with four subependymomas, one of which could not be seen on MR and was located on the tentorium. In two patients, there was extension of the tumor into the foramen of Luschka, as determined surgically, but it was not seen preoperatively. Consistency, signal-intensity heterogeneity, and the signal intensity of solid tumor also are listed in the Table. Most of the tumors (n = 6) were heterogeneous. Completely solid tumors and the solid component of mixed solid and cystic neoplasms were isointense (n = 2) to hypointense (n = 6) on T1-weighted images, and hyperintense relative to white matter on T2-weighted images in all instances. Precise correlation with pathologic findings revealed that regions of necrosis (n = 1), calcification (n = 2), tumor vascularity, microcystic structures or cystic spaces (n = 4), and chronic hemorrhage (n = 1) accounted for heterogeneous signal intensity. Edema was present in just one case (case 5).

Detail of delineations is noted in the Table. The differentiation of neoplasm from surrounding structures on T1-weighted images was improved after administration of gadopentetate dimeglumine in only one case (case 4). After intravenous administration of gadopentetate dimeglumine, five lesions in three patients demonstrated no enhancement (case 3, Fig 3; cases 5 and 6). In one patient, there was partial and minimal enhancement surrounding a probable small cystic area (case 1, Fig 1). In three patients, the enhancement was moderate (case 2, Fig 2) or marked case 7, Fig 4; case 4, Fig 5). In the latter, the enhancement was heterogeneous and partial. There was nonuniformity of enhancement related both to cystic or calcified areas and to nonenhancing solid tumor.

In four patients, encasement or displacement of normal vessels was well demonstrated by
MR. At surgery, even when the arteries were involved, tumor was easily dissected off these structures. A crisp demarcation line between the lesion and the surrounding structures allowed total resection in four cases. However, in one case, there was infiltration of the cerebellar peduncle, and in three cases, the potential risks of total resection curtailed excision. In case 4, laminectomy at the level of C-1 and suboccipital craniectomy revealed a grayish tumor observed as an extramedullary lesion compressing the spinal cord to the right, extending cranially and attached in a small region to the spinal cord, but with no intramedullary component. Follow-up revealed recurrence in only one case (case 3) 7 years after surgery. One patient died of postoperative causes.

Histologic examination of the specimens showed similar appearances in all cases; they were all pure subependymomas. The features consisted of a matrix of dense fibrillar material (glial fibers) that contained scattered clusters of uniform cells with oval nuclei (Figs 6 and 7). There were no atypias, mitoses, rosette formation, or abnormal vascularization. In one case (case 4, Fig 5), astrocytic differentiation was noted. Immunohistochemistry showed positivity of the fibrillary background with glial fibrillary acidic protein. At electron microscopy, most cells had purely astrocytic differentiation. In one case, a cavernous angioma, already seen at MR, could be identified next to the subependymomas.

Discussion

Characteristics of subependymomas include their indolent growth that accounts for the frequency with which this tumor is found at autopsy (1). This slow progression differentiates subependymomas from other more common tumors of the ventricles. It is thus useful to make the correct diagnosis preoperatively. As a matter of fact, in cases in which surgery is risky, one may not operate and just perform a close follow-up (depending on the symptoms). In addition, tumor removal in critical regions should not be performed too vigorously, because even
subtotal removal results in a favorable outcome in most cases. On the other hand, in some cases in which surgery is controversial because of a tumor located in a critical region, it may be important for the neurosurgeon to know that this tumor, if it is a subependymoma, is likely to be removed radically without removing normal contiguous tissues (2). Suspecting a subependymoma also can be of importance for the selection of technique of resection (6), laser being used in case of infiltrative lesions. As far as spinal subependymomas are concerned, the prognosis is difficult to establish because of the small numbers of reported cases, and we do not know whether spinal cord subependymomas are as benign as intracranial subependymomas (7, 15). Pagni (7) indicates that his case did not show recurrence 5 years after a radical excision.

In our series, it is noteworthy that a recurrence was seen 7 years after apparent total removal. Subependymomas have a distinctive microscopic appearance (16), but their origin has been a matter of some controversy. This is reflected in the varied nomenclature found in the earlier literature (subependymal glioma, subependymal glomerate astrocytoma). Chason (3) suggested mixed astrocytic and ependymal origin; ultrastructural observations (17) demonstrated both ependymal and astrocytic features, and Moss (18) suggested an origin from ependymoglial cells of the subependymal layer. Regardless of the origin, there exists a histologic gradation ranging from the pure subependymoma (largely astrocytic) to a mixed tumor type, exhibiting areas composed of both subependymoma and classic ependymoma. The
Fig 3. Case 3. 33-year-old man.
A, Imaged at initial presentation at 0.35-T. Sagittal T1-weighted image shows an enlarged cord from the medullar to C-5 level with a solid portion (thick arrow) and what appears as superior and inferior cystic portions (small and curved arrows).
B, Imaged at the time of recurrence 7 years later (postoperative MR). Sagittal T1-weighted image (400/14/2) shows cord enlargement from the level of the medulla oblongata to the level of C-4, along with ill-defined areas of hypointensity superiorly and inferiorly and an isointense homogeneous area (T). What appeared to be cystic portions were only detached portions from the rest of the surrounding tissue but no T2-weighted images were available.
C, Enhanced sagittal T1-weighted image (400/15/2) shows no enhancement of the central portion (arrow).
D, Axial T1-weighted image (400/14/2) shows intramedullary hypointense mass (N) relative to surrounding tissue.
E, Enhanced axial T1-weighted image at the same level demonstrates no enhancement (arrow).
ependymomatous portion of the mixed type shows increased cellularity, both ependymal rosettes and perivascular pseudorosette formations, foci of necrosis, and abundant vascularity (16). The mixed type is known to pursue a more malignant course than the pure subependymoma; however, infiltrative growth is possible in the case of pure subependymoma, even though it is rather unusual (6).

Computed tomography features are well known (2). Although Lobato et al (2) indicate that contrast enhancement is almost always the rule in both ependymomas and subependymomas, the suspicion of subependymoma should arise when an adult patient presents with an intraventricular tumor that is isodense or hypodense and shows minimal or no enhancement. As far as MR is concerned, 20 cases of intrace- rebral subependymomas have been reported (5, 6, 8–12, 19–23), but without full character- ization. Ten lesions (7–14) were imaged with MR after administration of intravenous contrast material. As for the intramedullary subependymoma, 7 cases of the reported 15 cases have been imaged with MR (7, 13, 15, 24–26).

Very unusual findings, such as spinal extramedullary subarachnoid and multiple subependymomas, were present in our series. Two cases of electron microscopy spinal subependymomas have been reported (4, 27). Our findings of a totally subarachnoid extramedul- lary lesion, either with a good cleavage plane from the medulla (case 4, Fig 5) or with dense adherence to the medulla (case 5), support the heterotopic cell origin theory, described and supported by many authors (28–31). The main hypothesis is that the tumor originates from leptomeningeal heterotopic glial tissue (32) and secondarily attaches to the surface of the spinal cord (1, 16). No recurrence of our two cases
was seen at clinical follow-up 3 and 4 years after surgery, respectively.

Our patients with intracerebral subependymomas always had an epicenter within a ventricle and were completely intraventricular, with no transependymal extension to the parenchyma, consistent with the majority of subependymomas reported. Two reports, though (11, 12), list cases of subependymomas located in a ventricle and invading the brain parenchyma. The multiplanar imaging capability of MR was quite valuable in assessing the location and full extent of these tumors. Our findings of a heterogeneous tumor (62%), predominantly isointense or hypointense on T1-weighted images and hyperintense on T2-weighted images, are similar to other intracranial tumors and consistent with the literature. Two reports (5, 14), though, indicate that subependymomas displayed high signal intensity on T1-weighted images without giving further details. None of the neoplasms contained areas characteristic of fat or hemorrhage in our series, whereas two reports (11, 20) mention the presence of areas of subacute hemorrhage (20) or of foci of hypersignal on T1-weighted images (11). Intratumoral bleeding is infrequent in subependymomas, with a prevalence of 12% (11).

The enhancing characteristics of subependymomas after intravenous administration of gadopentetate dimeglumine remain unclear. In the literature, of the 10 lesions examined with enhanced MR, 6 demonstrated minimal (n = 2) (11, 13) or no (n = 4) (8–10, 14) enhancement and 4 showed marked enhancement (7, 8, 12, 13). In our series, minimal (n = 1; case 1, Fig 1) or no (n = 3; case 3, Fig 3; cases 5 and 6) enhancement was noted in 4 cases (6 lesions), and moderate (n = 1; case 2, Fig 2) or marked
enhancement in 3 cases. Even when enhancement was present, it always was partial, in an irregular pattern with areas of nonenhancing solid tumor. Edema is not a common feature (17%, according to Yamasaki’s report [11]), and it was present in just one case in our series (case 5).

Margins of the tumor most often are well defined (10, 12, 19, 22, 23), as was the situation in our patients.

The differential diagnosis of intracranial subependymoma depends on the location of the tumor and on the age of the patient (22, 23). In our series, all patients were older than 30 years, which narrows the differential diagnosis. Signal-intensity characteristics do not distinguish subependymomas from ependymomas or from

Fig 6. Case 8. A, This section shows the sharp delineation with cerebellar cortex (top) (hematoxylin and eosin, magnification ×75). B, Clusters of small round nuclei (thin arrow) on a fibrillary background (thick arrow), low cellular density, and no atypias or mitoses (hematoxylin and eosin, magnification ×350). C, This picture shows distended capillaries inside the tumor (arrow) (hematoxylin and eosin, magnification ×175).

Fig 7. Case 7. This section shows clusters of small round nuclei scattered on a fibrillary background. Abundant vascularization, with some hyalinized vessel walls, is present (arrow) (hematoxylin and eosin, magnification ×120).
other intracranial gliomas, whereas the intra-ventricular or periventricular location and morphology of the former do help in the differential diagnosis. Subependymoma is almost always totally intraventricular, whereas ependymoma commonly has a transependymal extension. Presence of edema also seems to be a more common feature in ependymoma than in subependymoma. One criterion that also may help to distinguish subependymomas is the appearance after administration of gadopentetate dimeglumine. According to Jelinek (23), lateral ventricular brain tumors always show enhancement. The only nonenhancing tumor he noticed was a subependymoma. Lobato (2) indicates that ependymomas display more frequent and marked enhancement than subependymomas do. Of the 19 lesions examined with enhanced T1-weighted sequences in both the literature and our series, 12 showed no (n = 9) or minimal (n = 3) enhancement, and 7 lesions demonstrated moderate or marked enhancement that in most cases was irregular and partial.

We conclude that suspicion of subependymomas should arise when a completely intraventricular lesion with no transependymal extension causes little or no edema, and minimal or no enhancement is present.

References