Neuroradiology (2005) 47: 183–188
DOI 10.1007/s00234-005-1342-3

TJ Rath
PC Sundgren
B Brahma
AP Lieberman
WF Chandler
SS Gebarski

Massive symptomatic subependymoma of the lateral ventricles: case report and review of the literature

Received: 30 July 2004
Accepted: 14 December 2004
Published online: 9 February 2005

T. Rath · P. Sundgren (✉)
S. Gebarski
Department of Radiology,
University of Michigan Health Systems,
1500 E Medical Center Drive,
Ann Arbor, MI 48109-0030, USA
E-mail: sundgren@umich.edu
Tel.: +1-734-7633253
Fax: +1-734-7642412

B. Brahma · W. Chandler
Department of Neurosurgery,
University of Michigan Health Systems,
1500 E Medical Center Drive,
Ann Arbor, MI, 48109-0030, USA

A. Lieberman
Department of Pathology,
University of Michigan Health Systems,
1500 E Medical Center Drive,
Ann Arbor, MI 48109-0030, USA

Abstract Subependymomas are benign intraventricular tumors with an indolent growth pattern, which are usually asymptomatic, and most commonly occur in the fourth and lateral ventricles. When symptomatic, subependymomas often obstruct critical portions of the cerebrospinal fluid (CSF) pathway, causing hydrocephalus, and range from 3 cm to 5 cm in size. We report a case of an unusually massive subependymoma of the lateral ventricles treated with subtotal resection, ventriculoperitoneal shunt, and post-surgical radiation. The clinical course, radiographic and pathologic characteristics of this massive intraventricular subependymoma are discussed, as well as the differential diagnosis of lateral ventricular masses and a review of the literature concerning subependymomas.

Keywords MRI · Brain Subependymoma · Intraventricular mass

Introduction

Subependymoma is a rare, benign, slow-growing neoplasm that was first described by Scheinker [1] in 1945 as a tumor arising from the subependymal cell plate. Subependymomas are most commonly located in the fourth and lateral ventricles, but have also been reported arising in the third ventricle, septum pellucidum, and the spinal canal [2–9]. Since its original description, more than 100 case reports of intracranial subependymomas have been described. Due to its rarity and variable imaging characteristics, reliable pre-operative diagnosis remains challenging [10].

The indolent growth of subependymomas is reflected by the fact that most subependymomas are asymptomatic, often incidentally discovered at autopsy [2]. It has been reported that there is a 0.7% incidence of subependymoma among 1,000 patients with pathologically proven intracranial neoplasms versus an incidence of only 0.4% among 1,000 asymptomatic patients at autopsy [11]. Subependymomas are more common in males. Patients with symptomatic subependymomas usually present between the fourth and sixth decades of life with symptoms related to increased intracranial pressure [2]. The most common symptoms include headache, gait ataxia, vertigo or dizziness, nausea, and

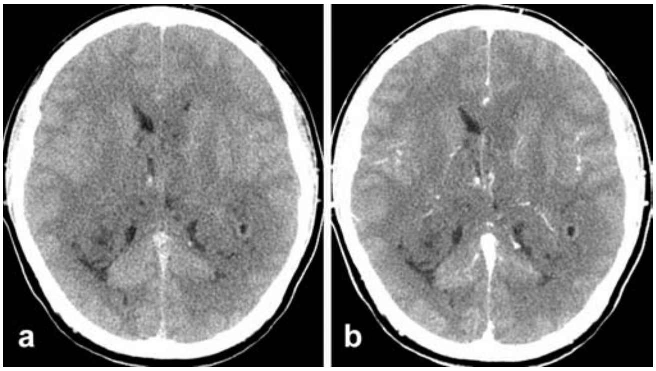


Fig. 1 Axial pre- (**a**) and post- (**b**) contrast-enhanced computed tomography (CT) of the head shows a large symmetric isodense intraventricular mass without calcifications filling the lateral ventricles and extending into the temporal horns

vomiting [8]. We present a young male with a large symptomatic intraventricular subependymoma, discuss the clinical course, differential diagnosis, and provide a review of the literature concerning intraventricular subependymomas.

Case report

A 20-year-old Chinese male attending college in the United States presented with a complaint of intermittent severe occipital headaches for 2 years that had become more frequent and debilitating in nature. He did not have visual symptoms, nausea, or vomiting. On physical examination, visual acuity was 20/70 OU with horizontal end gaze nystagmus to both sides with a latent component. Funduscopic exam was notable for chronic papilledema. The rest of the physical and neurological examination was normal.

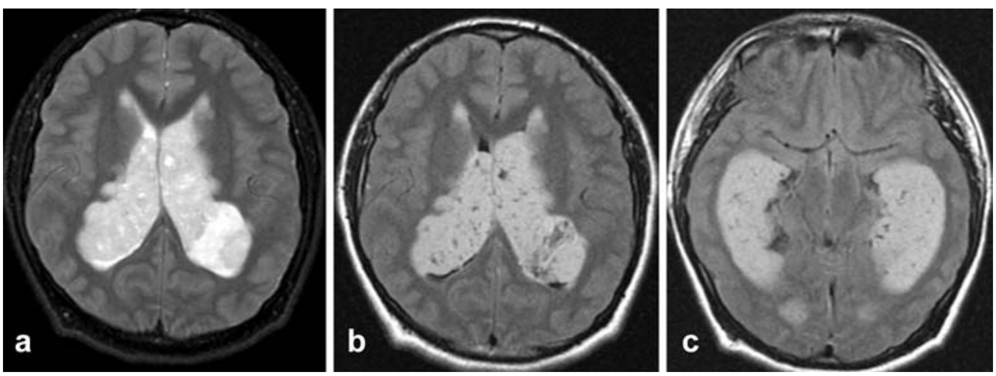
A non-contrast head computed tomography (CT) revealed a large symmetric isodense intraventricular mass without calcification occupying the right and left lateral ventricles, extending into the temporal horns (Fig. 1). A subsequent magnetic resonance imaging (MRI) scan demonstrated this mass to be primarily isointense to gray matter on T1-weighted images and hyperintense on T2-weighted images, with minimal enhancement after administration of dimeglumine gadopentetate (Figs. 2 and 3). The mass caused expansion and scalloping of the lateral ventricles. The third and fourth ventricles were of normal size.

In 2001, a stereotactic biopsy was performed via a right frontal bur hole. Several specimens were taken at various depths and trajectories within the tumor. Histological examination of the biopsy revealed choroid plexus with xanthoma cells but no cholesterol clefts or granulomatous inflammation, and the diagnosis of probable xanthogranuloma was made. Because of the benign nature of this lesion, the lack of obstruction of the cerebrospinal fluid (CSF) pathway, and the patient's report of a decrease in his symptoms after biopsy, a decision was made to monitor the patient's symptoms and follow this lesion clinically and with imaging.

The patient remained relatively asymptomatic for approximately 18 months, taking acetaminophen for his headaches with relief. MRI evaluation at 6, 12, and 18 months demonstrated slow interval growth in the intraventricular mass with development of cerebellar tonsillar ectopia, but no evidence of CSF outflow obstruction. While traveling abroad, his headaches worsened and he visited an emergency room where a head CT scan demonstrated little change in the size of the tumor, but was concerning for the increasing encroachment of the uncus onto the basal cisterns. He was placed on acetazolamide in order to decrease the production of CSF and, again, he symptomatically improved.

The patient did well for approximately another 6 months and then presented to the emergency room with a 3-h history of severe headache and altered mental status. On physical examination, the patient was unable to follow verbal commands but localized briskly. A subsequent noncontrast head CT scan demonstrated a stable appearance of the large intraventricular mass. A right frontal ventriculostomy catheter was immediately placed. The extent of the large intraventricular mass

Fig. 2 Axial T2-weighted (**a**) and fluid attenuation inversion recovery (FLAIR) images (**b**, **c**) show a large symmetric hyperintense intraventricular mass that fills the lateral ventricles (**a**, **b**) and the temporal horns (**c**)



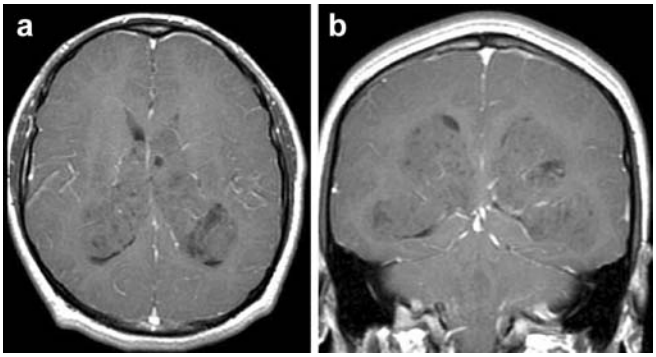


Fig. 3 Axial (**a**) and coronal T1-weighted (**b**) post-contrast-enhanced images demonstrate an intraventricular mass with minimal enhancement occupying the lateral ventricles and extending into the temporal horns

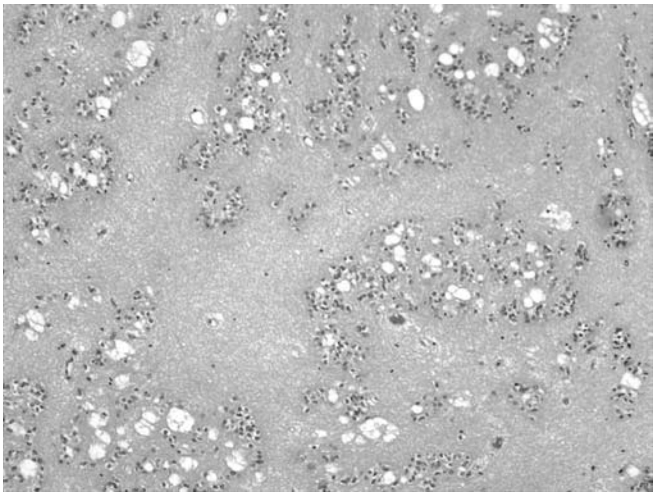


Fig. 4 Resection specimen reveals a subependymoma, as characterized by nests of tumor cell nuclei and microcysts in a fibrillary stroma

precluded total resection, which would require bilateral craniotomies, a high-risk procedure. Consequently, the patient was taken urgently to the operating room for a right frontal craniotomy with an interhemispheric transcallosal approach for tumor debulking. The tumor was resected from the frontal horn and the body of both the right and left lateral ventricles. The Foramen of Monro was identified and decompressed bilaterally. A ventriculostomy catheter was left in place in order to drain cerebrospinal fluid and monitor intracranial pressure. It was estimated that 10–15% of the mass was resected. Histopathologic evaluation demonstrated features compatible with subependymoma, including a hypocellular tumor with a dense pink fibrillary matrix and microcysts. Glial fibrillary acid protein stain was faintly positive and the MIB-1 index was near zero. No mitotic figures were present (Fig. 4).

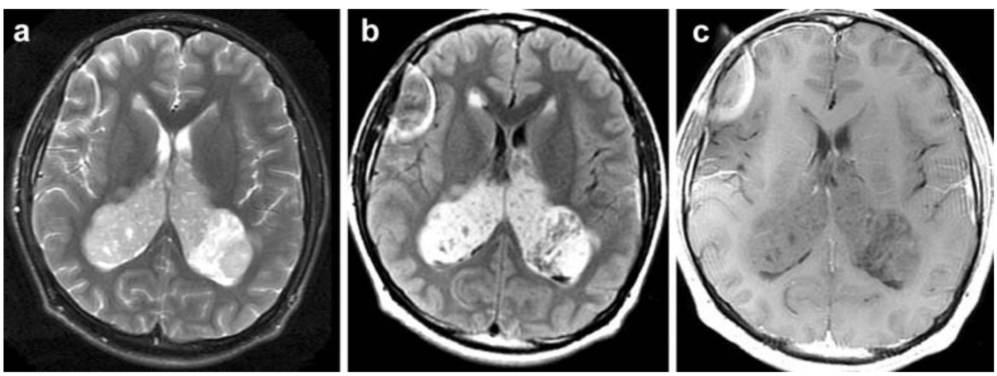
After surgery, the patient improved and was able to follow commands by the second post-operative day. However, the patient's intracranial pressure remained elevated and he required a ventriculoperitoneal shunt which was placed into the right frontal horn with an adjustable valve set to the highest setting.

Due to the large residual tumor burden and prior reports of some beneficial response to radiation therapy [5], the patient underwent radiation therapy with the goal of preventing any further tumor progression. Whole ventricular radiation therapy was performed using a three-field technique to a total dose of 45 Gy in addition to a 5.4 Gy boost in areas of bulky remaining disease. The patient tolerated radiation therapy well and remains highly functional, having recently completed graduate school and reporting no changes in vision or memory. Follow-up MRI at 6 months shows no evidence of interval increase in the large residual intraventricular tumor (Fig. 5). Further surgical intervention will only be considered if the patient develops evidence of tumor progression.

Discussion

Subependymoma is a rare, usually asymptomatic benign neoplasm that occurs more often in males than females. The presence of symptoms has been shown to directly correlate with tumor size, with the majority of symp-

Fig. 5 Axial T2-weighted (**a**), FLAIR (**b**), and T1-weighted (**c**) post-contrast-enhanced images demonstrate a slight debulking of the tumor after surgery with CSF present in the frontal horns of the lateral ventricle. The patient has a right frontal ventriculoperitoneal shunt catheter in place and is presently asymptomatic



tomatic subependymomas measuring 3–5 cm or greater in size [2, 6]. Symptom occurrence has also been shown to be dependent upon tumor location, with supratentorial lesions more often symptomatic than fourth-ventricle tumors [2]. In symptomatic patients with subependymomas of a smaller size, the tumor was often obstructing a critical part of the cerebrospinal fluid (CSF) pathway [6]. Two previous reports have found the presence of hydrocephalus to be critical to and correlate with symptomatology. In both studies, 88% of symptomatic patients demonstrated hydrocephalus [2, 6], while hydrocephalus was absent in 47 cases of asymptomatic subependymomas [2].

The World Health Organization classifies subependymoma as a grade 1 neoplasm. The tumor was originally described as consisting of primarily ectodermal elements derived from the subependymal glia [1]. However, the histological origin of subependymoma has remained controversial, reflected in the multitude of names previously ascribed to this tumor, including subependymal astrocytoma, subependymal glomerate astrocytoma, and subependymal mixed glioma [12–14]. In the 1970s, electron microscopy of subependymoma demonstrated a mixed population of ependymal cells, astrocytes, and intermediate morphology bipotential cells with the capability of differentiating into ependymal cells or astrocytes [12, 13]. The presence of a mixed population of cells within subependymoma has led to multiple hypotheses over the years regarding its origin, including arguments that it is truly an ependymal neoplasm with a reactive astrocytic component [12] versus an overlap neoplasm of astrocytoma and ependymoma [15] versus a hamartomatous lesion arising from mature subependymal tissue with neoplastic potential [13]. Others have argued that subependymoma represents a unique tumor that arises from an ependymal glial precursor cell [14]. A recent report has suggested that the bland microscopic appearance and low MIB-1 labeling index of subependymoma support the hypothesis that it may actually represent a hamartoma rather than a neoplasm [8].

Light microscopy characteristics of subependymoma include a hypocellular tumor with isomorphic clusters of subependymal cells within a dense glial fibrillary matrix. Microcystic degeneration is frequent and most subependymomas are hypovascular. Common degenerative changes such as vascular sclerosis, calcium deposition, hemosiderin deposition, and thrombosis are more likely to occur in longstanding or large tumors [2, 5, 8]. Mitoses are rare and the slow growth of this neoplasm is evidenced by its low MIB-1 labeling index [8].

Computed tomography (CT) characteristics of subependymoma most commonly include a lobulated, well defined intraventricular mass that is hypodense or isodense to brain parenchyma with no paraventricular extension [5, 9, 16, 17]. Rarely, hyperdense subependymomas have been reported [6, 7]. The majority of subependymomas are solid or solid with areas of cystic degeneration [11, 16, 17]. Calcification is common, occurring in 32% of cases [16]. CT enhancement characteristics of subependymoma are variable, with no enhancement, minimal enhancement, heterogeneous enhancement, and marked enhancement having all been reported [3–5, 9, 11, 16].

Magnetic resonance imaging (MRI) characteristics commonly include a well defined solid or mixed solid and cystic intraventricular mass, the solid component of which is hypo or isointense on T1-weighted images and hyperintense on T2-weighted images [5, 7, 9, 11, 17–20]. The heterogenous signal commonly seen in subependymomas correlates well with histopathologic findings, including necrosis, calcification, microcystic change, and hemorrhage [19, 21]. Peritumoral edema is an infrequent feature. Similar to CT, MRI enhancement characteristics are variable, including no enhancement, minimal, heterogeneous, or intense enhancement [7, 17, 19, 20]. A previous study evaluating the MRI characteristics of 19 reported subependymomas found that 12 of the 19 tumors demonstrated no or minimal enhancement, while 7 of the tumors demonstrated moderate or marked enhancement that was often partial or irregular [19]. MRI has proven most useful in defining the size and extent of the tumor, as well as its relationship to other anatomical structures, such as vasculature, playing a critical role in pre-operative planning.

Included in the differential diagnosis of lateral ventricular masses are choroid plexus papilloma, central neurocytoma, subependymal giant cell astrocytcoma, meningioma, metastasis, subependymoma, and ependymoma. Age, location, and some imaging features are helpful in narrowing this large differential diagnosis. Choroid plexus papillomas most commonly occur in young patients and intensely enhance after contrast administration [10]. Central neurocytomas are similar to subependymomas in their cystic appearance but are usually isointense with grey matter on both T1- and T2-weighted sequences, whereas subependymomas are almost always hyperintense on T2-weighted images [7]. Subependymal giant cell astrocytomas always occur near the Foramen of Monro, calcify frequently, intensely enhance, and are often associated with ventricular wall calcification [7, 10, 16]. Meningiomas, similarly, frequently calcify and intensely enhance. Metastasis and malignant gliomas are more likely to grow rapidly and often lack calcification [3].

Lateral intraventricular subependymomas appear to have some distinguishing features, often including poor contrast enhancement [6, 22] and lack of calcification [6]. In contrast to lateral ventricular subependymomas, fourth-ventricle subependymomas are more likely to have calcification and contrast enhancement, precluding distinction from ependymoma [6]. Age may be helpful in this regard as only 18% of symptomatic subependymomas occurred in patients less than 15-years-old in one study, while ependymomas more commonly occur in children and young adults [16]. In addition, ependymoma is more likely to be hyperdense on precontrast CT than subependymoma [16].

The distinction between supratentorial subependymomas from ependymomas is less difficult. Supratentorial ependymomas are often paraventricular compared to subependymomas, which are usually entirely intraventricular. Because subependymomas are usually intraventricular, they are also more often associated with hydrocephalus than ependymomas [16]. As previously discussed, on precontrast CT, ependymomas are more likely to be hyperdense and, though both supratentorial ependymoma and subependymoma may have calcification, cyst formation, and contrast enhancement, these features more commonly occur in supratentorial ependymomas [16].

Optimal therapy for symptomatic subependymomas is complete surgical excision. This can often be achieved with supratentorial subependymomas, given that these tumors are usually well demarcated, avascular, and noninvasive [5, 11, 16]. Fourth-ventricle subependymomas, however, frequently arise from the floor of the fourth ventricle and the likelihood of cranial nerve injury often precludes complete surgical resection [3, 5, 11, 20]. Perioperative mortality rates as high as 42% have been reported with surgical resection of fourth-ventricle subependymomas [3]. At the Mayo Clinic between 1975 and 1989, the need for post-operative tracheostomy decreased from 50% to 15%, and the perioperative mortality rate decreased from 25% to 0% when compared to patients operated on from 1950 to 1974 [16]. In cases of symptomatic fourth-ventricle subependymomas where complete resection cannot be achieved, surgery should be directed towards debulking and improving CSF outflow [3, 5, 17].

Most authors do not advocate post-operative radiation therapy after complete surgical resection of pure subependymoma as there is a good prognosis with surgery alone [5, 9, 16, 17]. Lombardi et al. reported follow-up data in 21 patients who underwent surgery for subependymoma and found that, of the 19 patients who survived the perioperative period, 12 underwent gross total resection with no evidence of tumor recurrence or tumor-related death [5]. The remaining seven patients were treated with radiation therapy and follow-up imaging demonstrated a greater radiographic response at doses of 5,000 cGy or greater, supporting an argument for radiation therapy in patients with residual tumor or evidence or tumor progression [5]. More recently, a rare instance of subependymal seeding after subtotal resection and radiosurgery has been suggested to account for intraventricular tumor spread in one case. However, we have no evidence to support seeding in our patient [23].

We conclude that intraventricular subependymomas are rare, often asymptomatic masses. When they are large, they become symptomatic due to CSF outflow obstruction causing hydrocephalus. Intraventricular subependymomas have some distinguishing MRI and CT features that make them unique from other lateral ventricular masses. The best treatment for a symptomatic subependymoma is total resection and, if this is not possible, debulking of the tumor followed by radiation therapy. As in this situation, some patients will require shunting for unresolved hydrocephalus.

References

1. Scheinker IM (1945) Subependymoma: a newly recognized tumor of subependymal derivation. J Neurosurg 2:232–240
2. Scheithauer BW (1978) Symptomatic subependymoma: report of 21 cases with review of the literature. J Neurosurg 49:689–696
3. Jooma R, Torrens MJ, Bradshaw J, Brownell B (1985) Subependymomas of the fourth ventricle: surgical treatment in 12 cases. J Neurosurg 62:508–512
4. Artico M, Bardella L, Ciappetta P, Raco A (1989) Surgical treatment of subependymomas of the central nervous system: report of 8 cases and review of the literature. Acta Neurochir 98:25–31
5. Lombardi D, Scheithauer BW, Meyer FB, Forbes GS, Shaw EG, Gibney DJ, Katzmann JA (1991) Symptomatic subependymoma: a clinicopathological and flow cytometric study. J Neurosurg 75:583–588
6. Chiechi MV, Smirniotopoulos JG, Jones RV (1995) Intracranial subependymomas: CT and MR imaging features in 24 cases. Am J Roentgenol 165:1245–1250
7. Maiuri F, Gangemi M, Iaconetta G, Signorelli F, Del Basso De Caro M (1997) Symptomatic subependymomas of the lateral ventricles. Report of eight cases. Clin Neurol Neurosur 99:17–22
8. Prayson RA, Suh JH (1999) Subependymomas: clinicopathologic study of 14 tumors, including comparative MIB-1 immunohistochemical analysis with other ependymal neoplasms. Arch Pathol Lab Med 123:306–309
9. Im SH, Paek SH, Choi YL, Chi JG, Kim DG, Jung HW, Cho BK (2003) Clinicopathological study of seven cases of symptomatic supratentorial subependymoma. J Neuro-Oncol 61:57–67
10. Koeller KK, Sandberg GD (2002) Cerebral intraventricular neoplasms: radiologic–pathologic correlation. Radiographics 22:1473–1505

11. Matsumara A, Ahyai A, Hori A, Schaake T (1989) Intracerebral subependymomas: clinical and neuropathological analyses with special reference to the possible existence of a less benign variant. Acta Neurochir 96:15–25
12. Fu Y, Chen AT, Kay S, Young H (1974) Is subependymoma (subependymal glomerate astrocytoma) an astroctyoma or ependymoma? A comparative ultrastructural and tissue culture study. Cancer 34:1992–2008
13. Azzarelli B, Rekate HL, Roessmann U (1977) Subependymoma: a case report with ultrastructural study. Acta Neuropathol 40:279–282
14. Moss TH (1984) Observation on the nature of subependymoma: an electron microscopic study. Neuropathol Appl Neurobiol 10:63–75
15. Friede RL, Pollak A (1978) The cytogenetic basis for classifying ependymomas. J Neuropathol Exp Neurol 37:103–118
16. Lobato RD, Sarabia M, Castro S, Esparza J, Cordobes F, Portillo JM, Rivas JJ (1986) Symptomatic subependymoma: report of four new cases studied with computed tomography and review of the literature. Neurosurgery 19:594–598
17. Nishio S, Morioka T, Mihara F, Fukui M (2000) Subependymoma of the lateral ventricles. Neurosurg Rev 23:98–103
18. Kim DG, Han MH, Lee SH, Chi JG, Cho KJ, Kim JH, Choi KS, Han DH (1993) MRI of intracranial subependymoma: report of a case. Neuroradiology 35:185–186
19. Hoeffel C, Boukobza M, Polivka M, Lot G, Guichard JP, Lafitte F, Reizine D, Merland JJ (1995) MR manifestations of subependymomas. Am J Neuroradiol 16:2121–2129
20. Silverstein JE, Lenchik L, Stanciu MG, Shimkin PM (1995) MRI of intracranial subependymomas. J Comput Assist Tomogr 19:264–267
21. Yamasaki T, Kikuchi H, Higashi T, Yamabe H, Moritake K (1990) Two surgically cured cases of subependymoma with emphasis on magnetic resonance imaging. Surg Neurol 33:329–335
22. Jelinek J, Smirniotopoulos JG, Parisi JE, Kanzer M (1990) Lateral ventricular neoplasms of the brain: differential diagnosis based on clinical, CT, and MR findings. Am J Roentgenol 155:365–372
23. Seol HJ, Hwang SK, Choi YL, Chi JG, Jung HW (2003) A case of recurrent subependymoma with subependymal seeding: case report. J Neuro-Oncol 62: 315–320