# Diagnosis of symmetric bilateral lateral ventricular subependymomas: A case report

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**Abstract.** Subependymomas are rare benign tumors that are hypovascular and noninvasive. Subependymomas tend to present as solitary lesions in the fourth ventricle or the frontal horn of the lateral ventricle. When multiple lesions are present, determining the correct diagnosis between subependymoma and other intraventricular neoplasms can be challenging. The characterization of imaging features and enhancement patterns can help narrow down the list of potential differential diagnoses. In this article, we describe a case of bilateral subependymomas in the lateral ventricles in a 40-year-old Asian man, including the clinical features, imaging results from conventional magnetic resonance imaging, magnetic resonance spectroscopy, and magnetic resonance perfusion, histological outcomes, and the disease management approach.

## Introduction

Although the first description of subependymoma was reported by Scheinker in 1945, the exact histogenesis remains unknown (1,2). Subependymoma occurs more commonly in men and those who are middle-aged or older (3,4). The vast majority of subependymoma cases are asymptomatic and detected only as incidental findings. Symptomatic subependymomas are typically associated with cerebral spinal fluid (CSF) obstructions, which lead to intracranial hypertension symptoms (such as headache, vomiting, papilledema, and impaired consciousness) or symptoms caused by the compression of nerve structures (such as convulsions, motor paralysis, and sensory disturbances) (2,4). Subependymomas commonly present as isolated lesions that arise in the fourth ventricle or the frontal horn of the lateral ventricle (3,5). To our knowledge, few studies have reported the use of magnetic resonance perfusion (MRP) or magnetic resonance spectroscopy (MRS) in the assessment of subependymoma. In this article, we describe a case presenting with bilateral subependymomas in the lateral ventricles, including the clinical features, imaging results from conventional magnetic resonance imaging (MRI), MRS, and MRP, histological outcomes, and the disease management approach.

## Case report

A 40-year-old Asian man presented at our institution complaining of a bilateral parietal-occipital headache and dizziness that lasted for 6 months. He denied experiencing vomiting or nausea. Upon physical examination, the patient was completely conscious, with a Glasgow Coma Scale score of 15. No symptoms of motor paralysis, sensory disturbances, or visual problems were documented, and laboratory tests were within normal limits.

On MRI, we detected 2 large, well-defined, lobulated masses located at the trigone and the occipital horn of the bilateral lateral ventricles; the right lesion measured 42x18x19 mm, and the left lesion measured 43x21x25 mm. Both masses displayed similar signal intensity as the normal gray matter on T1-weighted (T1W) imaging, showed heterogeneous hyperintensity on T2-weighted (T2W) imaging and fluid-attenuated inversion recovery (FLAIR) imaging, displayed no evidence of restriction on diffusion-weighted imaging (DWI), and were not enhanced by the use of a contrast agent. Some small intramural cysts were observed, but no evidence of calcification, hemorrhage, or hydrocephalus was noted. The adjacent brain parenchyma showed no evidence of paraventricular extension or infiltration. (Fig. 1A-F).

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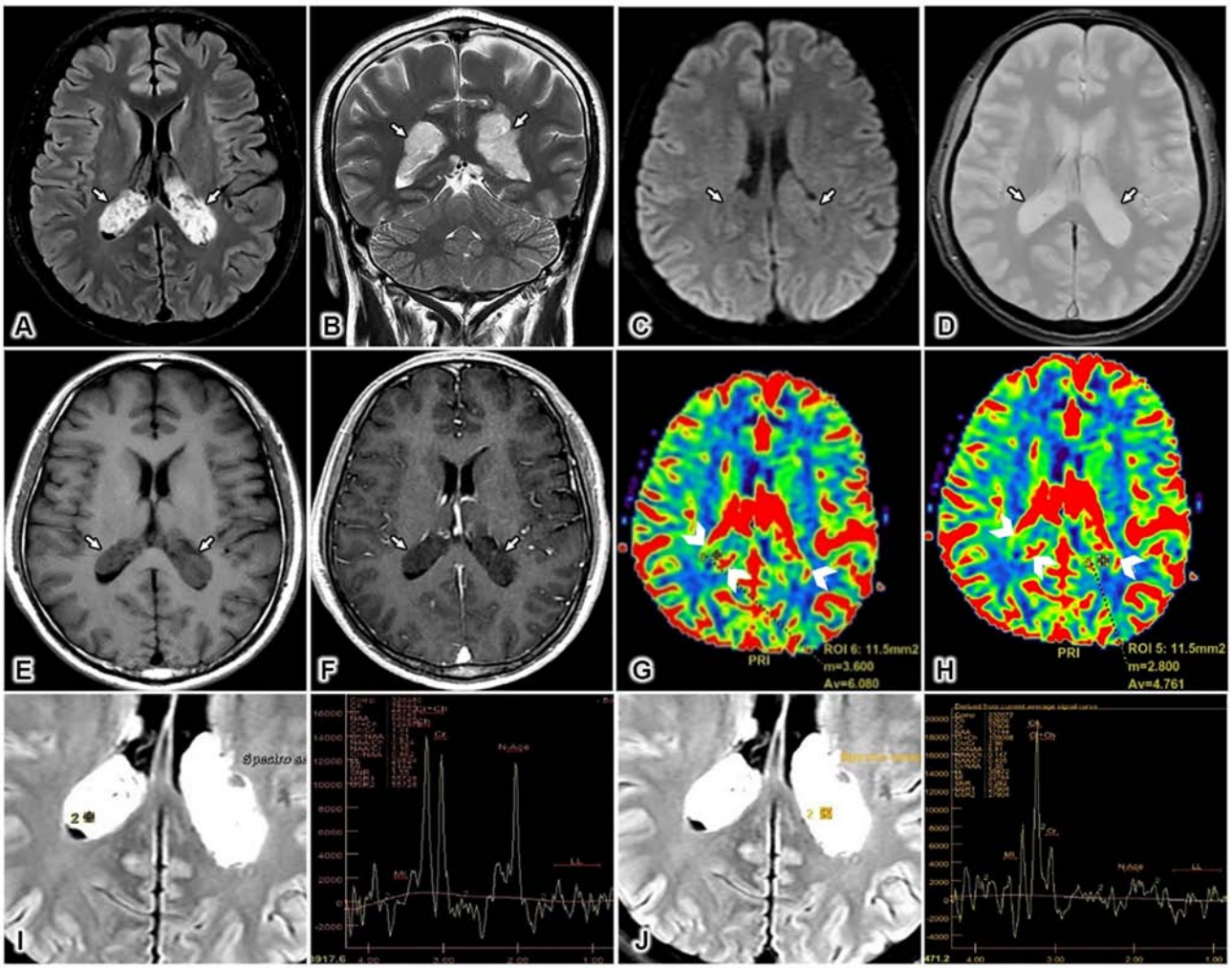


Figure 1. Imaging results. Magnetic resonance imaging (MRI) sequences, including (A) axial fluid-attenuated inversion recovery (FLAIR), (B) coronal T2-weighted (T2W), (C) axial diffusion-weighted imaging (DWI), (D) axial T2*, (E) axial T1-weighted (T1W) non-contrast, and (F) axial T1W post-contrast, show bilateral lateral ventricular masses (white arrows in A-F), which appeared hyperintense on FLAIR and T2W sequences. The masses were characterized by small regions of cystic degeneration, no surrounding edema, no diffusion restriction, no intratumoral hemorrhage, and no contrast enhancement. (G and H) Perfusion images revealed some intratumoral areas of hyperperfusion (arrowheads). (I and J) Magnetic resonance spectroscopy (MRS) multivoxel images show an increase in choline (Cho) peaks and a decrease in N-acetyl aspartate (NAA) peaks for both the right and left masses.

MRP revealed high cerebral blood volume (CBV) in some areas within these lesions. The relative CBV (rCBV) of the right lesion was 1.97, and the rCBV of the left lesion was 1.3 (Fig. 1G and H). On multivoxel MRS, both lesions showed high choline (Cho) and low N-acetyl aspartate (NAA) peaks, but the Cho/NAA ratio of the left mass was 1.21, whereas the same ratio in the right mass was 6.81. (Fig. 1I and J).

Several days after admission, the patient underwent partial resection surgery for the left ventricular tumor. A postoperative computed tomography (CT) image demonstrated a large isointense mass without evidence of calcification or hemorrhage in the trigone and occipital horn of the right lateral ventricle, with no signs of parenchymal invasion. A mixed-density mass was observed in the trigone and occipital horn of the left lateral ventricle, with hyperintense areas due to hemorrhage, and evidence of postoperative paraventricular edema (Fig. 2).

Histopathologically, the macroscopic image showed a soft tissue mass with pinkish surface color and no hemorrhage. Microscopically, the tumor was composed of a cluster of epithelial cells with round, basophilic nuclei and a few thick, hyalinized vessels (Fig. 3A). Immunohistochemical staining showed that the tumor cells were positive for epithelial membrane antigen (EMA) and negative for oligodendrocyte transcription factor 2 (OLIG2) and glial fibrillary acidic protein (GFAP) (Fig. 3B-D). The histopathological and immunohistochemical results were consistent with a diagnosis of subependymoma.

## Discussion

Subependymomas are uncommon benign tumors of the central nervous system (WHO grade I) (6) and account for 0.2-0.7% of all intracranial tumors (7). Subependymomas tend to occur in older individuals, typically presenting between the ages of 60 and 80 years, with a slight male predominance (male to female ratio of 2.3 to 1) (3,8). Typically, subependymomas (<2 cm), sharply demarcated nodules, are identified as incidental findings associated with subtle to no clinical symptoms. Unfortunately, during operation, there were no macroscopic photographs obtained for this case to contribute to medical

Table I. Reported cases of bilateral subependymoma in the literature.

| Number | Authors (Refs.) | Year of publication | Sex of patients | Age of patient (years) | Clinical symptoms |
|---|---|---|---|---|---|
| 1 | Rath *et al* (9) | 2005 | Male | 20 | Severe headache and altered mental status |
| 2 | Kumar *et al* (11) | 2012 | Male | 25 | No information available |
| 3 | Miguel *et al* (4) | 2015 | Female | 69 | Headache, ataxia, apraxia, right-sided weakness, and neglect |
| 4 | Moinuddin *et al* (12) | 2017 | Male | 48 | Seizure |
| 5 | Clinical case | 2022 | Male | 40 | Headache, vertigo |

Figure 2. Postoperative, axial, non-enhanced computed tomography (CT). Imaging shows a hemorrhagic area (curved arrow) in the left ventricle. A large isointense mass (white arrow) without calcification or hemorrhage was observed in the right lateral ventricle, without parenchymal invasion.

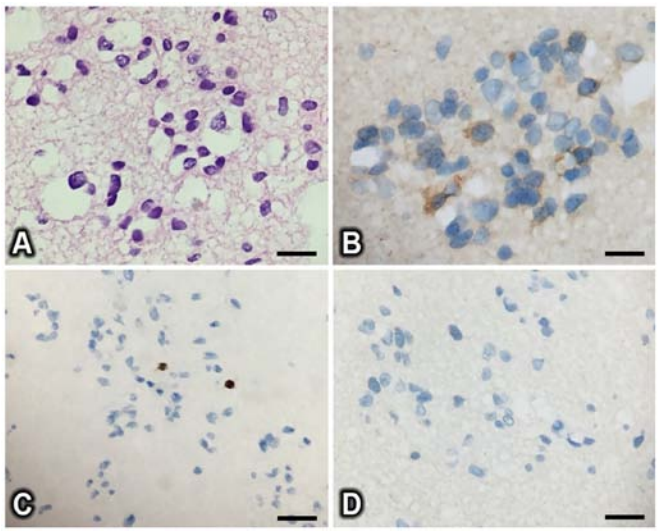


Figure 3. Microscopic images. (A) Hematoxylin and eosin staining, x400 magnification. Tumor cells are concentrated in small clusters, and the nuclei are relatively monomorphous. (B-D) Immunohistochemical imaging. (B) Epithelial membrane antigen (EMA) staining, x400 magnification, shows that tumor cells are positive for the cytoplasmic EMA marker. (C) Oligodendrocyte transcription factor 2 (OLIG2) staining, x200 magnification, shows multiple tumor cells negative for the OLIG2 marker. (D) Glial fibrillary acidic protein (GFAP) staining, x200 magnification, shows tumor cells were negative for the cytoplasmic GFAP marker.

literature. Symptomatic subependymomas are generally larger lesions (3-5 cm) or small neoplasms that obstruct the flow of cerebral spinal fluid (CSF), resulting in hydrocephalus (5,9).

Subependymomas are most commonly detected in the fourth ventricle (50-60% of cases) or the lateral ventricle (30-40% of cases), predominantly in the frontal horn (3,5). Occasionally, subependymomas are detected in the third ventricle, cerebellar pontine angle, or intraparenchymal and intraspinal regions (7,10). Isolated subependymomas are the most frequently detected type, whereas bilateral subependymomas are uncommon. In our search of the literature, only 4 cases of bilateral subependymomas have been reported (Table I) (4,9,11,12).

Upon CT, subependymomas typically present as lobulated, well-defined masses that are hypointense or isointense relative to the normal brain parenchyma, and extra-ventricular invasion is uncommonly observed (9). Hydrocephalus presents in 85% of cases (5). Cystic degeneration and calcification are also common characteristics, particularly for infratentorial neoplasms (3,13). Upon magnetic resonance imaging (MRI), subependymomas are characterized by hypointensity or isointensity on T1W (compared with the normal white matter), hyperintensity on T2W, and no evidence of restricted diffusion on DWI. Histological examination often reveals that the heterogeneous signals observed on MRI are due to necrosis, calcification, tiny areas of cystic degeneration, and hemorrhage. Peritumoral edema tends to be absent. Following the administration of a contrast agent (gadolinium), variable enhancement patterns have been described for subependymomas. Supratentorial subependymomas are often poorly enhanced or not enhanced, whereas infratentorial masses display heterogeneous enhancement (3,13). Our patient displayed similar enhancing features to the patients described by Rath *et al* and Kumar *et al* (9,11). Similar to reports by Miguel *et al* and Moinuddin *et al*, our patient showed no evidence of hemorrhage (4,12).

The performance of magnetic resonance perfusion (MRP) or magnetic resonance spectroscopy (MRS) for the diagnosis

of subependymomas has not been frequently reported. A previous study by Rumboldt concluded that subependymomas are typically characterized by hypoperfusion (14). Hyperperfusion of subependymomas reported in this case was in contrast to the common hypoperfusion characteristic of subependymoma described by Rumboldt (14). In 2012, Abdel-Aal *et al* (13) reported an intraventricular subependymoma in the left lateral ventricle. The authors noticed several areas characterized by hyperperfusion, with an rCBV value of 3.91. Our findings were consistent with the results reported by Abdel-Aal *et al*, as the rCBV value of the left tumor was 2, and that of the right tumor was 1.3. Abdel-Aal *et al* (13) speculate that hyperperfusion in subependymomas may be caused by the presence of thick hyalinized vessels rather than the neoangiogenesis observed in typical high-grade tumors. MRS results in low-grade tumors are generally characterized by normal choline (Cho) levels and slightly reduced N-acetyl aspartate (NAA) levels (7). Several differences were observed between the 2 neoplasms in our case. The right-sided mass showed slightly high Cho and low NAA levels (Cho/NAA ratio of 1.21), whereas the left-sided mass showed high Cho and low NAA levels (Cho/NAA ratio of 6.81). Both tumors manifested appeared to present high Cho values due to increased cellular activity.

Choroid plexus xanthogranuloma (CPX), choroid plexus papillomas (CPP), choroid plexus carcinomas (CPC), and metastasis are possible differential diagnoses for bilateral subependymomas. CPP and CPC are less likely due to the patient's age, as these entities are most often detected in children, and these entities tend to display enhancing features (15). CPX is typically smaller than 1 cm, appears strongly restricted on DWI, and presents with either heterogeneous or rim-like enhancement on the post-contrast sequence (16). Ventricular metastasis typically presents with vivid enhancement and surrounding vasogenic edema (3). Our patient was younger than the typical age group associated with subependymoma occurrence, and the trigone and occipital horn are not common locations for subependymomas. However, based on the other imaging characteristics and the lack of post-contrast enhancement, subependymoma was our initial diagnosis.

The microscopic appearance of subependymomas is characterized by multiple clusters of cells embedded in a dense gliofibrillary matrix with cystic degeneration, and hyalinized vessels are not rare findings (2,7,13). Immunohistologically, subependymomas are commonly positive for oligodendrocyte transcription factor 2 (OLIG2) and glial fibrillary acidic protein (GFAP) and negative for epithelial membrane antigen (EMA) (2,13). Although most of these typical features were demonstrated in our case, GFAP and OLIG2 staining were negative. Our results were similar to the findings obtained by Belgian authors in 2015, in which 2 of 43 individuals were negative for GFAP and 1 of 43 individuals were negative for OLIG2 (10). By contrast, similar to our findings, the report by Moinuddin *et al* described EMA positivity (12). The origins of subependymomas remain controversial. Several prior theories have suggested that subependymomas arise from subependymal glia, astrocytes of the subependymal plate, or ependymal cells. Due to the lack of clear cellular origins, no immunohistological classifications have been defined for the identification of subependymoma (2). We believe that the pathological findings for the left-sided mass removed from our patient are most consistent with a diagnosis of typical subependymoma.

Generally, the prognosis of subependymomas is good. Subependymomas identified on incidental findings can be managed by conservative treatment. Individuals with symptomatic subependymomas are commonly treated by total surgical excision. However, when a subependymoma appears in some critical areas, partial resection could also be a favorable approach, and the maintenance of CSF flow should be prioritized (2). To our knowledge, radiotherapy and chemotherapy are unnecessary, even when only a partial resection can be performed (8,9). The recurrence rate of subependymoma is 7.9% (10). Varma *et al* (8) concluded that few patients exhibit any recurrent masses following subependymoma resection on MRI imaging after medium- to long-term follow-up, suggesting that shorter follow-up times may be sufficient.

In conclusion, the classical appearance of subependymoma is an isolated lesion arising from the fourth ventricle and the frontal horn of the lateral ventricle. However, atypical subependymomas presenting as bilateral intraventricular neoplasms in the lateral ventricles can result in diagnostic challenges. By focusing on the enhancing features, MRS and MRP can be useful for providing accurate diagnoses and facilitating better treatment planning.

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**Availability of data and materials**

All data generated or analyzed during this study are included in this published article.

**Authors' contributions**

NDM and NDH contributed equally to this article as co-first authors. NDM, NDH, and NMD were the patient's physicians, reviewed the literature and contributed to acquisition, analysis and interpretation of data and manuscript drafting. NDH and NMD contributed to manuscript drafting and acquisition of data. DTG, NQD, and PNH analyzed and interpreted the imaging findings. NDH and NMD reviewed the literature, and contributed to conception and design of the study, analysis and interpretation of data, and drafted, reviewed and edited the manuscript. NDM and NDH confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

**Ethics approval and consent to participate**

Not applicable.

## Patient consent for publication

Written informed consent for patient information to be published in this article was obtained.

## Competing interests

The authors declare that they have no competing interests.

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