

Case Report

Meningeal Supratentorial Hemangioblastoma in a Patient with Von Hippel-Lindau Disease Mimicking Angioblastic Meningioma

Hoon Kim, M.D., Ik-Seong Park, M.D., Ph.D., Kwang Wook Jo, M.D.

Department of Neurosurgery, The Catholic University of Korea College of Medicine, Bucheon St. Mary's Hospital, Bucheon, Korea

Hemangioblastomas are sporadic tumors found in the cerebellum or spinal cord. Supratentorial hemangioblastomas are rare, and those with meningeal involvement are extremely rare and have been reported in only approximately 130 patients. Here, we report the case of a 51-year-old female patient with supratentorial meningeal hemangioblastoma detected 5 years after surgical resection of an infratentorial hemangioblastoma associated with von Hippel-Lindau disease. Patients with von Hippel-Lindau syndrome are at risk for developing multiple hemangioblastomas, with new tumor formation and growth and possible meningeal infiltration. Regular lifelong follow-up in at-risk patients is recommended and should include the differential diagnosis of dural-based tumors such as angioblastic meningioma and metastatic renal cell carcinoma.

Key Words : Angioblastic meningioma · Hemangioblastoma · Supratentorial · Von Hippel-Lindau disease.

INTRODUCTION

Hemangioblastomas (HBs) are highly vascular benign tumors composed of neoplastic stromal cells with rich capillary networks³¹. They develop sporadically in 67% of all cases and in 33% of cases as a feature of von Hippel-Lindau (VHL) disease^{22,23,31}. HBs may arise in any part of the central nervous system, but are found most frequently in the posterior fossa or spinal cord. HBs in a supratentorial location are rare and have been found in approximately 130 patients, but very limited information on their natural history, incidence, clinical effects, and optimal management is available²¹. Among these patients, 60% received a diagnosis of VHL disease, whereas infratentorial HB occurs in only 33% of patients with VHL¹⁹. Furthermore, supratentorial HB with meningeal involvement is extremely rare.

This case report describes the case of a supratentorial meningeal HB mimicking angioblastic meningioma detected 5 years after surgical resection of an infratentorial HB in a patient with VHL disease.

CASE REPORT

A 51-year-old female patient presented to our hospital with severe dizziness and right facial paresthesia. Five years previously, magnetic resonance imaging (MRI) had shown 2 small masses on the right cerebellum and 1 large mass on the left cerebellum. At that time, lateral vertebral artery digital subtraction angiography (DSA) had shown a highly vascular tumor nodule supplied by the posterior inferior cerebellar artery. Lateral internal carotid artery (ICA) and external carotid artery (ECA) DSA had shown no vascular abnormalities. T1-weighted gadolinium enhancement MRI had shown no abnormal findings in the supratentorial region (Fig. 1A-D). The patient had undergone craniotomy, and the left cerebellar tumor was removed. The pathological diagnosis was HB. Abdominal computed tomography, an evaluation of the patient's family history, and genetic screening had been employed to evaluate the presence of VHL disease. Computed tomography had revealed cysts in the pancreas, liver, and both kidneys. Three of the patient's 6 siblings and 1 of her 2 children were diagnosed with VHL disease.

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• Address for reprints : Kwang Wook Jo, M.D.

Department of Neurosurgery, The Catholic University of Korea College of Medicine, Bucheon St. Mary's Hospital, 327 Sosa-ro, Wonmi-gu, Bucheon 420-717, Korea
Tel : +82-32-340-2259, Fax : +82-32-340-7391, E-mail : jkw94@naver.com

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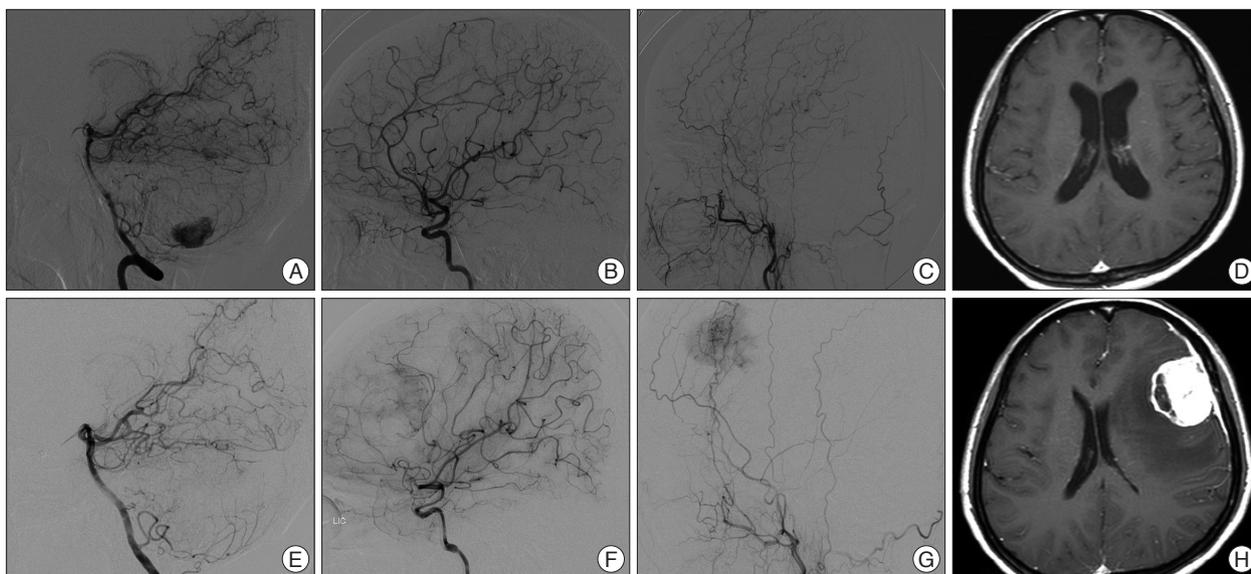


Fig. 1. Initial digital subtraction angiography (DSA) and magnetic resonance image (MRI). A : Lateral vertebral artery (VA) DSA shows a highly vascular tumor nodule supplied by the posterior inferior cerebellar artery. B and C : Lateral internal carotid artery (ICA) and external carotid artery (ECA) DSA show no vascular abnormality. D : No abnormal findings are observed in the supratentorial region on an enhanced T1-weighted image. DSA and MRI images at 5 years after the operation. E : Lateral VA DSA shows complete resection of the cerebellar tumor after the previous surgery. F : Left ICA DSA shows pial blood supply to the rim of the tumor. G : Left ECA DSA shows tumor stain from the middle meningeal artery. H : A 4.0×3.6×4.0-cm strongly enhanced dural-based tumor and peritumoral edema are observed in the left frontal lobe on an enhanced T1-weighted image.

Genetic analysis had shown the presence of a VHL gene mutation; thus, the patient's condition had been diagnosed as HB associated with VHL disease.

Follow-up MRI performed 1 and 12 months after the first operation had shown no evidence of recurrence or abnormal findings in the supratentorial region. However, MRI performed 5 years after the first operation showed a 4.0×3.6×4.0-cm cystic mass with strong enhancement, dural base thickening, and peritumoral edema on the left frontal surface. However, no tumor recurrence was observed in the cerebellum. Left ICA DSA showed pial blood supply to the rim of the tumor. Left ECA DSA showed tumor staining from the middle meningeal artery (Fig. 1E-H).

The tumor was completely removed after preoperative embolization. It was a vascular tumor with extensive dural attachment. Histopathological examination with hematoxylin and eosin staining showed lipid-containing vacuoles and abundant vascular cells (Fig. 2A). The tumor cells were negative for epithelial membrane antigen (EMA), glial fibrillary acidic protein (GFAP), CD34, and S100, but positive for neuron-specific enolase (NSE) and vimentin (Fig. 2B-E). The patient was definitively diagnosed with HB with meningeal involvement. The patient's dizziness resolved postoperatively. There was no recurrence of the supratentorial tumor or change in the size of the multiple small right cerebellar tumors during the 12-month follow-up period.

DISCUSSION

HBs are benign tumors of vascular origin that develop in the central nervous system. They account for 2% of all intracranial tumors and 5-15% of posterior fossa tumors in adults^{4,17}. HBs

primarily arise in the cerebellum and are rarely found in the supratentorial region.

Supratentorial HB was first described by Bielschowsky in 1902²⁶. Approximately 130 cases of supratentorial HB have been reported. HB tumors are frequently found in the cerebrum and sellar/suprasellar and intraventricular regions. In order of frequency, they are found in the frontal, parietal, and temporal lobes of the cerebrum, and there are a few reports of congenital HB^{11,24}. Among patients with supratentorial HB, 60% were diagnosed with VHL disease, and this condition is more common in VHL disease than infratentorial HB (33%)^{22,23,31}. A significant association was found between HB tumors located in the sellar/suprasellar region and a diagnosis of VHL disease¹⁹. HBs may present as either isolated or multiple lesions. Most reported HBs were solid tumors, whereas one-third were found to be cystic.

However, meningeal HBs in a supratentorial location are extremely rare. Only 16 patients with meningeal involvement of HB have been described in the literature (Table 1). The sex ratio is equal, and the patient age range is 10-72 years. Tumors are mostly located in the frontal lobe, but they are also found in the parietal lobe. All these HBs had a solid consistency, and only 2 were associated with VHL disease, including the case reported here (12.5%). Four patients had multiple lesions and 3 had infratentorial HB, 2 of whom had VHL disease.

Ammerman et al.² reported that "Long-term natural history of hemangioblastomas in patients with von Hippel-Lindau disease", excluding those in a supratentorial location, had a stuttering or stepwise growth pattern. In addition, approximately 45% of symptomatic HBs were not visible on the initial MRI. Wanebo et al.³² reported that 44% of infratentorial and spinal cord HBs

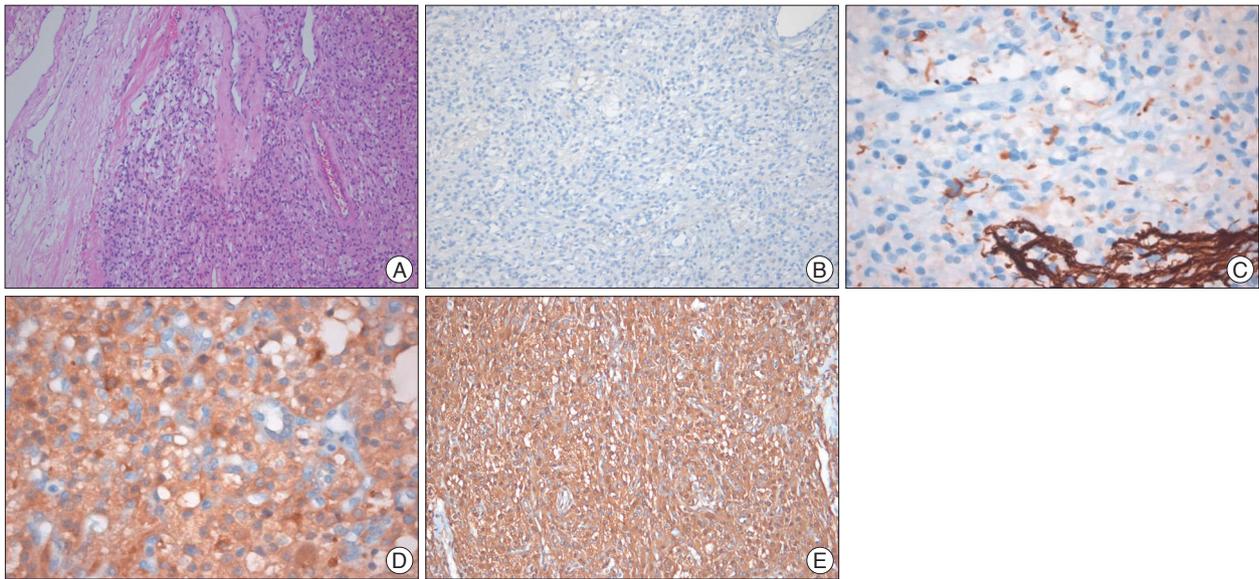


Fig. 2. A : Photomicrograph shows large vessels, lipid-containing vacuoles, and abundant vascular cells adhered to the dura basement (hematoxylin and eosin staining, $\times 100$). B and C : Immunohistochemical staining for epithelial membrane antigen and glial fibrillary acidic protein is negative. D and E : Staining for neuron-specific enolase and vimentin is positive.

Table 1. Reported cases of supratentorial meningeal hemangioblastoma

Author	Sex	Age	Location	Gross appearance	VHL	Multiple	Infratentorial hemangioblastoma
Zeitlin ³³⁾	M	54	Parasagittal	Solid	-	-	-
Rivera and Chason ²⁵⁾	M	16	Parietal	Solid	-	-	-
Ishwar et al. ¹²⁾	F	62	Falx	Occipital	Solid	-	+
Lee et al. ¹⁸⁾	M	46	Frontal	Solid	+	+	+
Sharma et al. ²⁶⁾	M	72	Parietal	Solid	-	-	-
Choi et al. ⁵⁾	F	26	Parietal	Solid	-	-	-
Kim et al. ¹⁶⁾	M	45	Convexity	Frontal	Solid	-	+
Agostinelli et al. ¹⁾	F	10	Convexity	Frontal	Solid	-	-
Iyigun et al. ¹³⁾	M	61	Convexity	Frontal	Solid	-	-
Cosar et al. ⁷⁾	M	50	Parasagittal	Parietal	Solid	-	-
Murali et al. ²⁰⁾	M	57	Parasagittal				
Takeuchi et al. ²⁹⁾	M	58	Parasagittal	Frontal	Solid	-	-
Sherman et al. ²⁷⁾	F	52	Convexity	Frontal	Solid	-	-
Jang et al. ¹⁴⁾	F	68	Convexity	Frontal	Solid	-	-
Elguezabal et al. ⁸⁾	F	67	Falx	Frontal	Solid	-	-
Kaloostian and Taylor ¹⁵⁾	F	49	Falx	Frontal	Solid	-	-
Present study	F	51	Convexity	Frontal	Solid	+	+

VHL : von Hippel-Lindau

seemed to grow during the follow-up period. In addition, Peyre et al.²¹⁾ reported that “Natural history of supratentorial hemangioblastomas in von Hippel-Lindau disease”, of 11 supratentorial HBs followed-up with serial MRI for at least 6 months, 10 enlarged and 1 remained stable. Enlarged tumors showed either continuous (n=7) or intermittent (n=3) growth patterns. Furthermore, 7 tumors were followed-up for more than 24 months. Five of these tumors showed a rapid increase in size after 24 months. Thus, supratentorial HBs (92.9%) show a higher incidence of tu-

mor growth during follow-up than infratentorial and spinal cord HBs (44%). Nevertheless, the natural history of supratentorial meningeal HBs is unclear because it is extremely rare.

It is difficult to make a diagnosis of supratentorial meningeal HB by preoperative neuroimaging or microscopic observation of the tumor during surgery. The main differential diagnoses of supratentorial meningeal HB include angioblastic meningioma, hemangiopericytoma, and metastatic renal cell carcinoma. The HBs show variable cellularity and consist of 2 major compo-

nents (vascular channels and stromal cells) that stain negative for epithelial markers such as EMA and vascular markers such as CD34. Therefore, EMA immunostaining can especially help distinguish supratentorial meningeal HB from meningioma with the former being negative for EMA staining²⁰. In addition, CD34 immunochemical activity is positive in some cases of HB but shows more focal, heterogeneous, weak staining of tumor cells in meningioma and hemangiopericytoma^{7,10,29}. Furthermore, HB tumors are generally negative for GFAP and positive for NSE. Additionally, S-100 protein showed a variable immunoreactivity among neuroectodermal markers^{3,9,30}. Finally, vimentin, the most widely distributed intermediate filament expressed in virtually all mesenchyma and corresponding tumors, is positive in HB tumors, supporting the hypothesis that HBs originate from the mesenchyme. In our case, the tumor was negative for EMA, but positive for NSE and vimentin. Recently, inhibin- α has been described as a useful marker for distinguishing HB from angiomatous meningioma²⁸. In addition, histologically, HB may be difficult to distinguish from renal cell carcinoma because both tumors are highly vascular and contain cells with pale cytoplasm. Immunohistochemically, renal cell carcinomas stain positive for EMA whereas HB are EMA negative⁶.

The treatment of choice for supratentorial meningeal HB is surgical resection. Mills et al.¹⁹ reported that patients with supratentorial HB undergoing gross total tumor resection (GTR) experienced a significant improvement in progression-free survival (PFS) compared with those receiving subtotal resection (STR) (5-year PFS : GTR, 100% vs. STR, 53%). However, treatment modality and the literature are not definitive because of the rarity of supratentorial meningeal HBs. In our opinion, total resection of the tumor prevents recurrence and postoperative hemorrhage and radiotherapy may be an alternative or adjuvant therapy for multiple, subtotally resected, and recurrent tumors.

CONCLUSION

We reported a rare case of supratentorial meningeal HB that was detected 5 years after surgery for cerebellar HB in a patient with VHL disease. Although supratentorial meningeal HBs are extremely rare tumors, differential diagnosis of meningioma and other meningeal-based tumors should be investigated. Pathological and immunohistochemical techniques are helpful for such diagnoses. Definitive treatment for these lesions is surgical resection. Accordingly, physician should be aware that supratentorial meningeal HBs can be developed in patient with VHL disease and regular follow-up are mandatory.

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