



Usefulness of neuroimaging and immunohistochemical study for accurate diagnosis of parasagittal hemangioblastoma arising in the supratentorial region: a case report and review of the literature

Kota Kanehisa¹, Akihiro Inoue^{1^}, Hideaki Watanabe¹, Kosuke Kusakabe¹, Mashio Taniwaki², Seiji Shigekawa¹, Riko Kitazawa², Takeharu Kunieda¹

¹Department of Neurosurgery, Ehime University School of Medicine, Toon, Japan; ²Division of Diagnostic Pathology, Ehime University Hospital, Toon, Japan

Correspondence to: Akihiro Inoue, MD, PhD. Department of Neurosurgery, Ehime University School of Medicine, 454 Shitsukawa, Toon, Ehime 791-0295, Japan. Email: iakihiro3@gmail.com.

Background: Hemangioblastoma originates in the central nervous system (CNS), usually in the cerebellum, and sporadic cases in the supratentorial region are extremely rare. In addition, there have been no previous reports of cases showing hyperintensity on diffusion weighted image (DWI) on magnetic resonance imaging (MRI) and negative immunostaining for inhibin- α . Here, we report a rare case of sporadic supratentorial hemangioblastoma arising in the parasagittal region and suggest a useful indicator for the exact diagnosis and pitfalls for surgical procedures.

Case Description: A 66-year-old woman was admitted to our hospital with a 6-month history of progressive numbness in the right lower extremities and gait disturbance. Neurological findings on admission revealed mild right-sided hemiparesis of the lower limbs (manual muscle test: 4/V). Neuroimaging demonstrated an abnormal lesion with clear boundaries in the left frontal lobe appearing hypointense on T1-weighted image (WI), hyperintense on T2-WI, and hyperintense on DWI, with strong enhancement on gadolinium (Gd)-enhanced T1-WI. Computed tomography (CT) showed no calcification, and cerebral angiography revealed strong staining from bilateral middle meningeal arteries and the left anterior cerebral artery (ACA). Surgical excision of the lesion was performed and gross total resection was achieved. Histological findings revealed a marked increase in vascular structures, and the round stroma contained tumor cells. Silver impregnation stains demonstrated abundant reticulin fibers. In addition, immunohistochemistry revealed that most tumor cells stained negatively for epithelial membrane antigen (EMA) and inhibin- α , and positively stained for podoplanin (D2-40), and the tumor was diagnosed as hemangioblastoma. The postoperative course was uneventful and follow-up neuroimaging after one year revealed no signs of recurrence.

Conclusions: Supratentorial hemangioblastomas are extremely rare and display a strong infiltrative and aggressive nature. Careful identification from preoperative image and histopathological study for appropriate treatment selection are warranted for supratentorial hemangioblastoma.

Keywords: Hemangioblastoma; supratentorial region; sporadic; reticulin; case report

Submitted Mar 30, 2022. Accepted for publication Oct 13, 2022.

doi: 10.21037/tcr-22-851

View this article at: <https://dx.doi.org/10.21037/tcr-22-851>

[^] ORCID: 0000-0002-7438-2369.

Introduction

Hemangioblastomas are benign tumors of vascular origin that arise in the central nervous system (CNS), newly proposed in the World Health Organization (WHO) classification of the CNS in 2016 (1,2). These tumors can occur in any part of the CNS, but are more common in the posterior fossa, accounting for 5–15% of tumors in this region (3). The next most common site is the spinal cord, and other sites such as the brainstem and supratentorial compartments are less frequent. Cases occurring in the supratentorial region appear to be extremely rare (4). In addition, these tumors may infiltrate adjacent structures such as the meninges or blood vessels, in which case surgical resection has been reported to be difficult and may require caution (5). Therefore, recognizing the characteristic features of supratentorial hemangioblastomas is very important, including the form of clinical onset, neuroimaging, pathological findings and the risks of surgical operations. However, there have been no previous reports of cases showing hyperintensity on diffusion weighted image (DWI) on magnetic resonance imaging (MRI) and negative immunostaining for inhibin- α . Therefore, it is extremely important to understand the imaging and immunohistochemical features as above. Here, we report an extremely rare case of sporadic hemangioblastoma occurring in the parasagittal supratentorial region, and we suggest useful indicators for the exact diagnosis and pitfalls for surgical procedures of this rare entity. We present the following case in accordance with the CARE reporting checklist (available at <https://tcr.amegroups.com/article/view/10.21037/tcr-22-851/coif>).

Case presentation

A 66-year-old woman presented to our department on August 13, 2020, with mild motor weakness of the right lower extremity and gait disturbance. She had no family history of von Hippel-Lindau (VHL) disease and no medical history of note. Neurological findings on admission showed mild right-sided hemiparesis of the lower limbs (manual muscle test: right 4/V). MRI of the brain demonstrated solid masses with clear boundaries in the left frontal lobe appearing hypointense on T1-weighted image (WI), hyperintense on T2-WI and fluid attenuating inversion recovery (FLAIR), and hyperintense on DWI, and homogeneously enhanced to a high degree with gadolinium (Gd), but cystic formation was not observed (*Figure 1A-1E*). Computed tomography

(CT) showed no calcification (*Figure 1F*); however, it was not recognized as a solid mass on CT on March 29, 2012. Cerebral angiography revealed strong staining from the bilateral middle meningeal artery (MMA) and left anterior cerebral artery (ACA). No obstruction of the superior sagittal sinus (SSS) was identified (*Figure 2*). The preoperative differential diagnosis included meningioma arising at the parasagittal region. Surgery was performed to obtain the definitive histological diagnosis on September 14, 2020. She underwent left frontal craniotomy, allowing gross total tumor excision after transarterial embolization of bilateral MMAs and the left ACA using Embosphere® (Biosphere Medical, Rockland, MA, USA) and n-butyl-2-cyanoacrylate. Intraoperative findings demonstrated an extra-axial, solid, yellowish-looking tumor close to the SSS and adjacent dura. Histopathological findings obtained from hematoxylin and eosin staining revealed a marked increase in vascular structures, and the round stroma contained tumor cells (*Figure 3A*). Vascular elements occupied less than 50% of the total tumor area. Silver impregnation staining demonstrated abundant reticulin fibers, which were closely associated with vascular channels and intermingled with clusters of stromal cells (*Figure 3B*). Immunohistochemistry demonstrated that most tumor cells did not stain for epithelial membrane antigen (EMA), inhibin- α and cluster of differentiation 34 (CD34) (*Figure 3C*), but showed positive staining for podoplanin (D2-40) (*Figure 3D*). The Ki-67 (MIB-1) proliferation-related labeling index was low, at 2.0%, and the tumor was diagnosed as hemangioblastoma. Postoperatively, a slight worsening of the right hemiparesis of her lower extremities was recognized (manual muscle test: right 3+/V), but improvement was noted within one week. Otherwise, seizures were not observed and the postoperative course was uneventful. Follow-up neuroimaging on MRI on December 7, 2021, revealed no signs of recurrence (*Figure 4*). In addition, neurological findings returned to near-normal.

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

After a review of literature in PubMed, we found that there

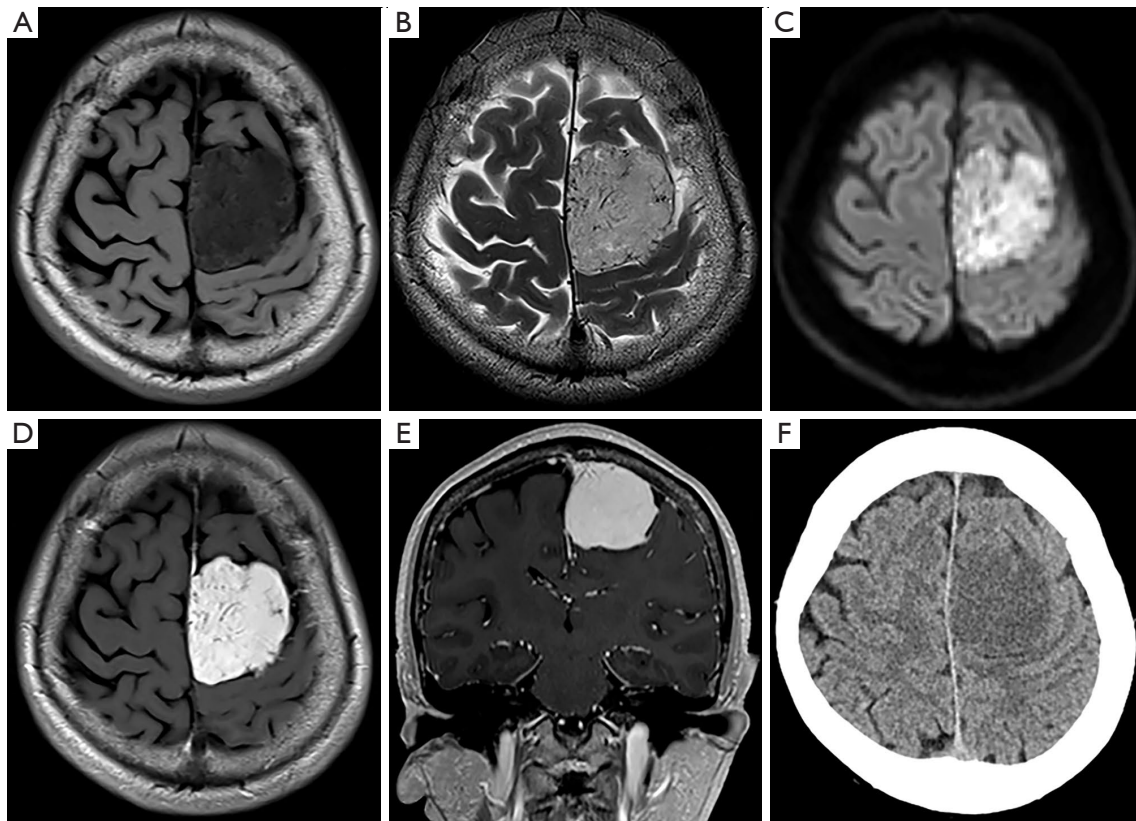


Figure 1 Preoperative MRI and CT imaging. Preoperative T1-WI (A), T2-WI (B), DWI (C), and Gd-enhanced T1-WI (D: axial view, E: coronal view) on MRI show a solid tumor in the left frontal lobe. In addition, no tumor calcification is evident on CT (F). MRI, magnetic resonance imaging; CT, computed tomography; WI, weighted image; DWI, diffusion weighted image; Gd, gadolinium.

were only 33 patients of supratentorial hemangioblastoma with meningeal involvement reported in English language literature from 1942 to 2021. The following discussion is based on the cumulative data of 34 cases (33 reported cases and one current our case).

Hemangioblastomas occurring at the supratentorial region are rare tumors that account for 1–2% of all hemangioblastomas (1). In particular, cases that develop in areas adjacent to the parasagittal regions or involving meningeal structures involved with the SSS are even rarer. However, the epidemiology is unclear because of the low incidence of this entity. Sánchez-Ortega *et al.* stated that a total of only 33 cases of supratentorial hemangioblastoma with meningeal involvement had been reported previously (5). According to that report, supratentorial hemangioblastomas occurred mainly in adults, with a mean age of 49.4 years (range, 9–77 years) at the time of diagnosis. A slight male predominance (51.5%) was suggested. Of these 33 patients, 31 tumors (94%) were located in the cerebral

hemispheres, most frequently in the frontal lobe, while two (6%) were located in the sellar or parasellar region (5). In these patients, 60% were diagnosed with VHL disease or showed a positive genetic result for *VHL* gene mutation (6,7). Clinically, invasion of this tumor into adjacent structures such as meninges or blood vessels is rare (5). However, for cases arising in the parasagittal region, tumor cells tend to invade meninges where the SSS may be involved and can present with aggressive features. In such cases, *en-bloc* surgical resection is very difficult and the probability of recurrence is higher (5). In our present case, the patient was relatively old, at 67 years, and the absence of VHL disease was atypical for supratentorial hemangioblastoma. Even in elderly patients and those with no family history of VHL, the possibility of supratentorial hemangioblastoma should be suspected.

Differential diagnoses of supratentorial hemangioblastoma include other tumors such as meningiomas, solitary fibrous tumors, and metastatic renal cell carcinomas. In

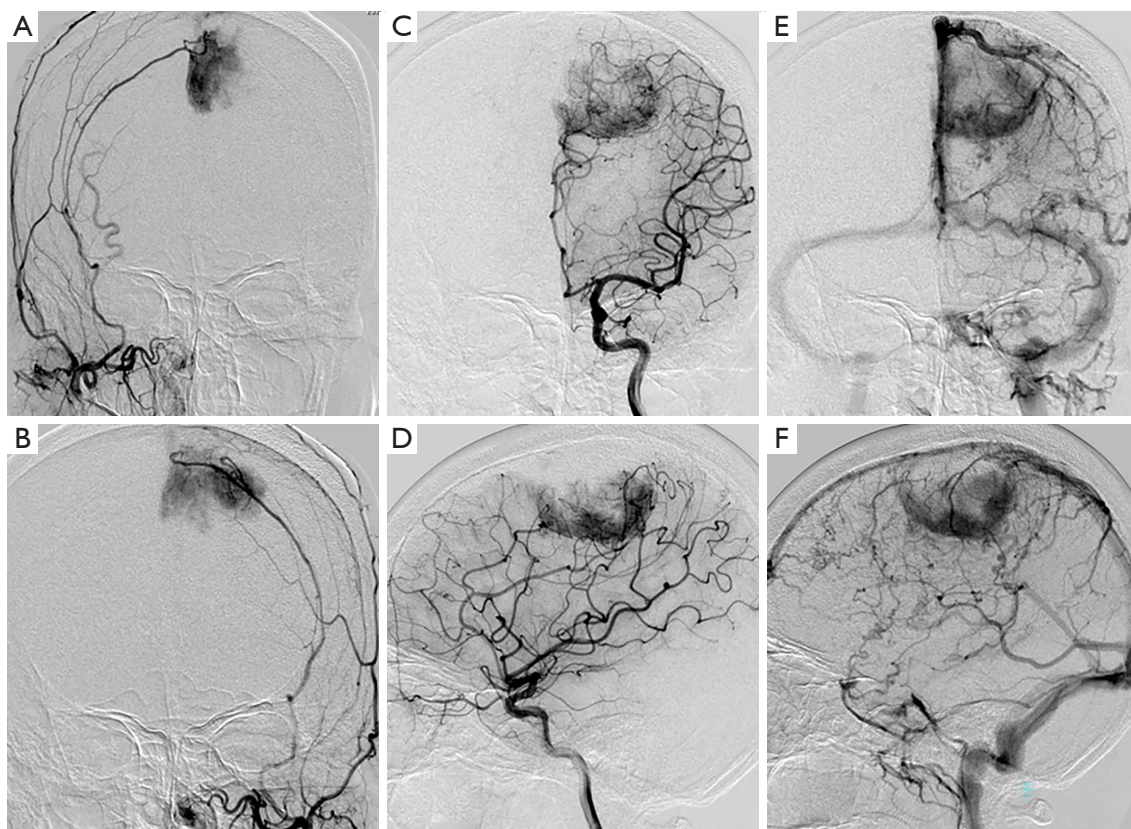


Figure 2 Preoperative cerebral angiography. (A,B) External carotid angiography (anterior-posterior view) (A: right, B: left) shows tumor staining via the MMA. (C,D) Left ICAG (arterial phase) (C: anterior-posterior view, D: lateral view) reveals a hypervascular appearance via the left ACA. (E,F) Left ICAG (venous phase) (E: anterior-posterior view, F: lateral view) demonstrates no obstruction of the SSS. MMA, middle meningeal artery; ICAG, internal carotid angiography; ACA, anterior cerebral artery; SSS, superior sagittal sinus.

particular, this tumor has many radiological similarities with angiomatous meningiomas (4). In a previous report, Liu *et al.* revealed that angiomatous meningiomas were hypointense on T1-WI, hyperintense on T2-WI and slightly hypointense on DWI (8). In our present case, the tumor appeared as a hyperintense mass on DWI, in addition to demonstrating very strong contrast enhancement from Gd. This high-intensity description on DWI is extremely interesting and appears to represent a key finding for the preoperative accurate diagnosis of supratentorial hemangioblastoma.

On the other hand, clinically, preoperative identification of supratentorial hemangioblastoma may be very difficult and the confirmation of this tumor is only possible through histological analysis. Hemangioblastomas are benign tumors classified as WHO grade I and highly vascularized tumors (2). Macroscopically, solid masses are well circumscribed with a yellowish appearance due

to lipid-rich components and a small mural nodule. Microscopically, hemangioblastomas consist of a network of capillaries surrounded by a layer of endothelium and reticulin fibers. This capillary network is composed of two cellular components: vascular cells; and stromal cells. The latter show a polygonal morphology with clear cytoplasm and abundant lipid deposits. With immunohistochemical analysis, hemangioblastomas are strongly positive for inhibin- α , D2-40, glucose transporter 1 and vimentin. On the contrary, these tumors reveal negative reactivity for cytokeratin, glial fibrillary acidic protein and EMA (9). On histological examination, the main differential diagnosis for hemangioblastoma is angiomatous meningioma. The histopathological hallmark of angiomatous meningioma is vascular elements exceeding 50% of the total tumor area and immunohistochemical analysis showing positive expression of EMA (8,10). Histologically, our case

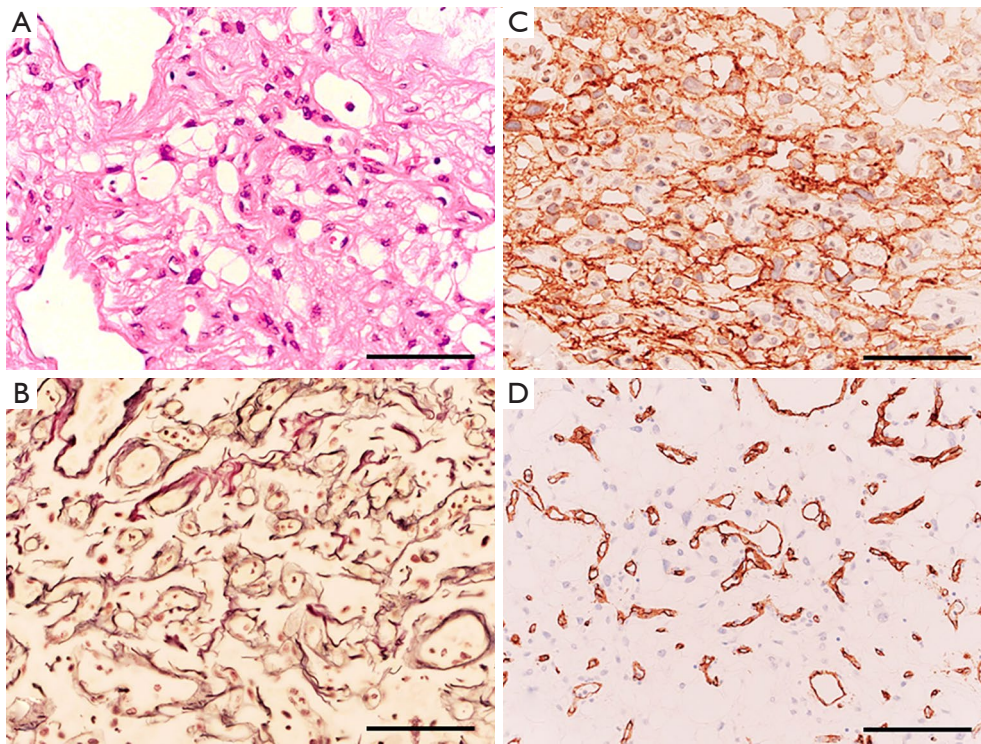


Figure 3 Histopathological findings of the resected tumor. Hematoxylin and eosin staining (A) reveals a marked increase in vascular structures, and the round stroma contains tumor cells. Silver impregnation staining (B) demonstrates abundant reticulin fibers, closely associated with vascular channels and intermingled with clusters of stromal cells. Immunohistochemical examinations show positive staining for D2-40 (C) and no staining for CD34 (D). Magnification: $\times 400$. Scale bar: 100 μm .

presented with a marked increase in vascular structures (vascular elements occupying less than 50%), and round stroma containing tumor cells with a layer of reticulin fibers. This structure was immunopositive for D2-40 and immunonegative for EMA. While immunohistochemical results for inhibin- α were negative, the overall findings were consistent with hemangioblastoma, in consideration of morphological and immunohistochemical findings, so we diagnosed hemangioblastoma in accordance with the WHO classification (2).

Surgery remains the main treatment for supratentorial hemangioblastoma and the basis of surgical procedure for this tumor is radical *en-bloc* resection. However, because of the abundant blood supply to the tumor, complete resection is often difficult. In addition, particularly for lesions in the parasagittal region, tumor cells may infiltrate the SSS, so total resection may not be possible. In cases where gross total removal proves impossible, optimal adjuvant therapy remains controversial. In previous reports of supratentorial hemangioblastomas with meningeal involvement by

Sánchez-Ortega *et al.* (5), Rivera *et al.* (11) and Ishwar *et al.* (12), recurrence was seen at 8, 2 and 10 years, respectively. Although clinical trials and reviews with sufficiently large numbers of cases are lacking in the literature, patients with partial or subtotal resection require close follow-up, even beyond 5 years. Radiosurgical treatment of small local lesions or residual tumor after incomplete resection appears to slow tumor progression and in some cases stabilize the course of the disease (13). A previous report has shown that stereotactic radiotherapy to residual tumors prevented recurrence for 5 years in 63–85% of cases, but confirmation of the effectiveness of radiotherapy is still needed (6). On the other hand, in most series of publications, complete tumor resection appeared to be superior to radiotherapy in terms of progression-free survival (5). At present time, the effectiveness of radiotherapy is unknown, and careful follow-up is needed. In the present case, the tumor originated in the parasagittal region closely attached to the SSS, and the patient is being followed-up after resection of as much of the tumor as

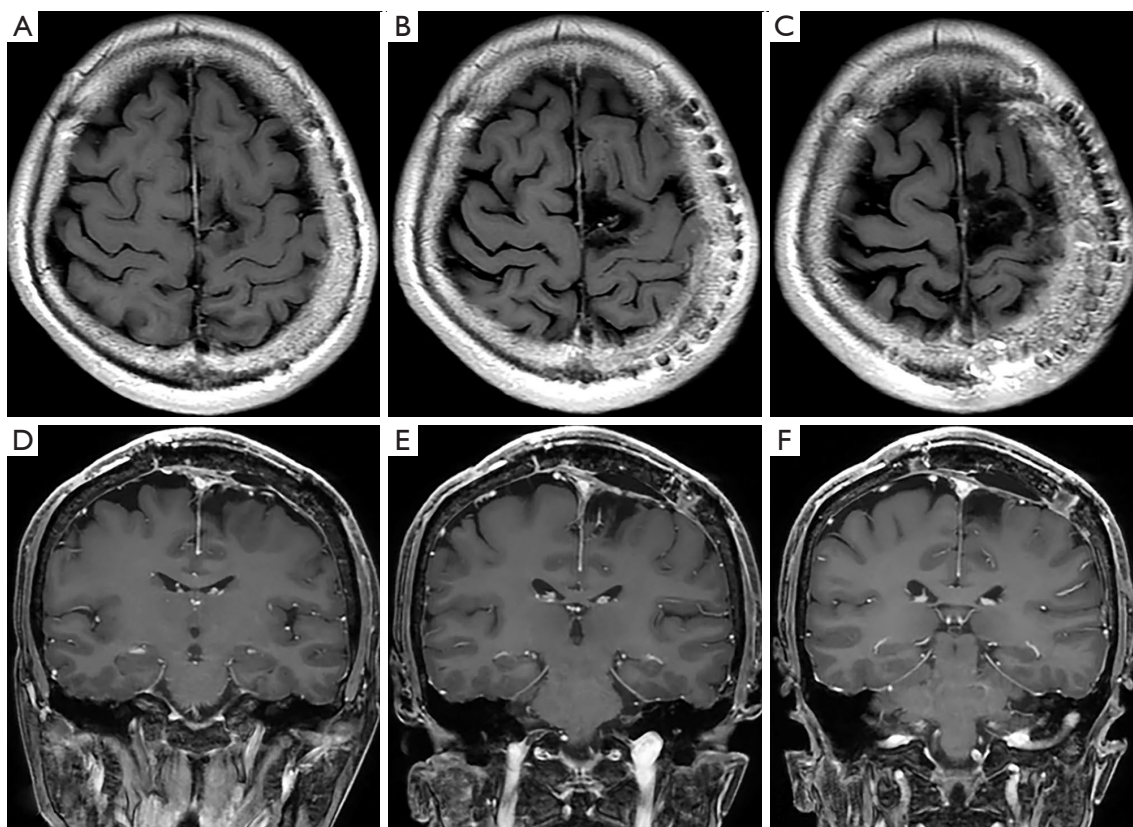


Figure 4 Gd-enhanced T1-WI (A-C: axial view, D-F: coronal view) at 12 months after tumor resection shows no residual tumor or signs of recurrence. Gd, gadolinium; WI, weighted image.

possible grossly and without radiotherapy.

Several limitations to our report must be kept in mind. At present, hemangioblastoma occurring in the parasagittal region is a rare neurological condition, and there have only been a few case reports. Therefore, further research, longer patient follow-up and accumulation of various case reports are required to obtain a better understanding of the pathological conditions and appropriate therapy associated with this entity.

In conclusion, supratentorial hemangioblastoma occurring in the parasagittal region involving the SSS region is a very rare but well-documented entity. We propose that supratentorial hemangioblastoma should be recognized as a differential diagnosis for tumors presenting in the parasagittal region because of the potential for highly aggressive and strong infiltrative natures. Detailed evaluation of radiological findings including DWI and histological studies including reticulin fiver, EMA, and D2-40 are necessary for accurate diagnosis and selection of appropriate treatments for supratentorial

hemangioblastoma.

Acknowledgments

We would like to express our gratitude to Eiji Katayama and Satsuki Myoga of the Department of Pathology, Ehime University Hospital, Japan, and to Taichi Furumochi and Yasuhiro Shiraishi of the Department of Neurology, Ehime University Hospital, Japan, for their help with pathological studies and radiological image acquisition.

Funding: None.

Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at <https://tcr.amegroups.com/article/view/10.21037/tcr-22-851/rc>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://tcr.amegroups.com>).

[com/article/view/10.21037/tcr-22-851/coif](https://doi.org/10.21037/tcr-22-851/coif)). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Open Access Statement: This is an Open Access article distributed in accordance with the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0), which permits the non-commercial replication and distribution of the article with the strict proviso that no changes or edits are made and the original work is properly cited (including links to both the formal publication through the relevant DOI and the license). See: <https://creativecommons.org/licenses/by-nc-nd/4.0/>.

References

1. Cosar M, Hatiboglu MA, Iplikcioglu AC, et al. Parasagittal leptomeningeal hemangioblastoma--case report. *Neurol Med Chir (Tokyo)* 2006;46:294-7.
2. Louis DN, Perry A, Reifenberger G, et al. The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. *Acta Neuropathol* 2016;131:803-20.
3. Hussein MR. Central nervous system capillary haemangioblastoma: the pathologist's viewpoint. *Int J Exp Pathol* 2007;88:311-24.
4. Karabagli H, Karabagli P, Alpman A, et al. Congenital supratentorial cystic hemangioblastoma. Case report and review of the literature. *J Neurosurg* 2007;107:515-8.
5. Sánchez-Ortega JF, Claramonte M, Martín M, et al. Sporadic supratentorial hemangioblastoma with meningeal affection: A case report and literature review. *Surg Neurol Int* 2021;12:394.
6. Mills SA, Oh MC, Rutkowski MJ, et al. Supratentorial hemangioblastoma: clinical features, prognosis, and predictive value of location for von Hippel-Lindau disease. *Neuro Oncol* 2012;14:1097-104.
7. Signorelli F, Piscopo G, Giraud S, et al. Von Hippel-Lindau disease: when neurosurgery meets nephrology, ophthalmology and genetics. *J Neurosurg Sci* 2019;63:548-65.
8. Liu Z, Wang C, Wang H, et al. Clinical characteristics and treatment of angiomatous meningiomas: a report of 27 cases. *Int J Clin Exp Pathol* 2013;6:695-702.
9. Takei H, Bhattacharjee MB, Rivera A, et al. New immunohistochemical markers in the evaluation of central nervous system tumors: a review of 7 selected adult and pediatric brain tumors. *Arch Pathol Lab Med* 2007;131:234-41.
10. Yang L, Ren G, Tang J. Intracranial Angiomatous Meningioma: A Clinicopathological Study of 23 Cases. *Int J Gen Med* 2020;13:1653-9.
11. Rivera E, Chason JL. Cerebral hemangioblastoma. Case report. *J Neurosurg* 1966;25:452-4.
12. Ishwar S, Taniguchi RM, Vogel FS. Multiple supratentorial hemangioblastomas. Case study and ultrastructural characteristics. *J Neurosurg* 1971;35:396-405.
13. Liebenow B, Tatter A, Dezarn WA, et al. Gamma Knife Stereotactic Radiosurgery favorably changes the clinical course of hemangioblastoma growth in von Hippel-Lindau and sporadic patients. *J Neurooncol* 2019;142:471-8.

Cite this article as: Kanehisa K, Inoue A, Watanabe H, Kusakabe K, Taniwaki M, Shigekawa S, Kitazawa R, Kunieda T. Usefulness of neuroimaging and immunohistochemical study for accurate diagnosis of parasagittal hemangioblastoma arising in the supratentorial region: a case report and review of the literature. *Transl Cancer Res* 2022;11(11):4178-4184. doi: 10.21037/tcr-22-851