

# Intratumoral Hemorrhage in a Patient With Cerebellar Hemangioblastoma

## *A Case Report and Review*

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**Abstract:** Spontaneous hemorrhage is rarely associated with hemangioblastomas. Intratumoral hemorrhage occurring in cerebellar hemangioblastomas is more rare.

A 25-year-old man was admitted to our hospital with headache. We found a round cystic lesion with solid part in the right cerebellum. The lesion was resected. The final pathological diagnosis was hemangioblastomas. The radiological features of this case were similar to normal hemangioblastomas, whereas our histological examination showed the occurrence of the intratumoral hemorrhage.

If the hemangioblastoma ruptures in our case, the outcome of the patient will be worse. It is difficult to identify the intratumoral hemorrhage of hemangioblastomas and quite dangerous if it is diagnosed late. Diagnosing an intratumoral hemorrhage of hemangioblastomas still needs a further discussion. Genetic screening may help us make an early diagnosis. Furthermore, the mechanism about intratumoral hemorrhage of hemangioblastomas remains unknown. The mutation of *D6Mit135* gene on chromosome 6 may be responsible for the vascular dilation and hemorrhage induction in the hemangioblastomas. Tumor size, upregulation of vascular endothelial growth factor, spinalradicular location, and solid type are also factors relating to the hemorrhage of hemangioblastomas.

The purpose of reporting our case is 2-fold: to remind clinicians to consider the possibility of internal hemorrhaging while diagnosing this disease, and provide a starting point to discuss mechanisms regarding the intratumoral hemorrhage of hemangioblastomas.

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**Abbreviations:** AVMs = arteriovascular malformations, CT = computed tomography, MRI = magnetic resonance imaging, VHL = Von Hippel–Lindau.

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## INTRODUCTION

Hemangioblastomas are highly vascular lesions, representing 1.5% to 2.5% of intracranial tumors and 7% to 12% of posterior fossa tumors. They can occur sporadically or as a part of Von Hippel–Lindau (VHL) disease; 76% hemangioblastomas occur in the cerebellum.<sup>1,2</sup> Hemangioblastomas are associated with intratumoral hemorrhage, which have been reported in only 4 articles.<sup>3–6</sup> Both of the patients mentioned above presented severe symptoms and typical imaging features. Herein, we report an uncommon case of cerebellar hemangioblastoma with intratumoral hemorrhaging. The symptoms of our patient were mild. However, while the radiological features of this case were similar to normal hemangioblastomas, our histological examination exposed an intratumoral hemorrhage. Although hemangioblastomas with potential for intratumoral hemorrhaging may display common radiological features and mild symptoms, they may have the risk of rupturing, even death.<sup>3</sup> It is difficult to identify the intratumoral hemorrhage of hemangioblastomas. In some articles,<sup>4,7,8</sup> hemangioblastomas were misdiagnosed as arteriovascular malformations (AVMs) or intracranial aneurysms. Therefore, neurosurgeons should pay more attention to this disease and make a diagnosis as early as possible. The mechanism of hemorrhaging within hemangioblastomas is still a mystery and needs further discussion.

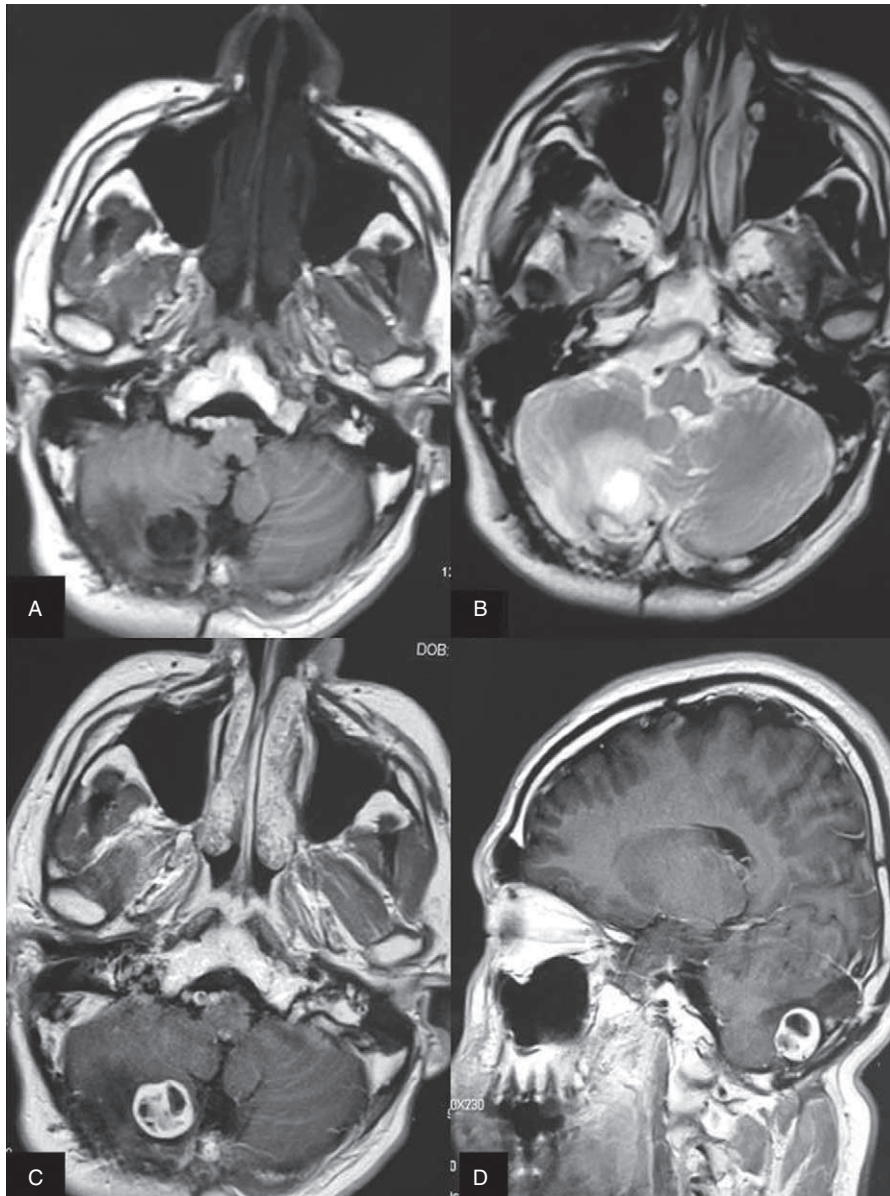
## CONSENT

The patient's parents, on behalf of the child, signed informed consent for publication of this case report and any accompanying images.

## CASE REPORT

A 25-year-old man was admitted to our hospital with a headache. However, the patient had no vomiting and convulsion of the limbs. General physical examination and neurological examination showed no abnormalities. Magnetic resonance imaging (MRI) revealed a round cystic lesion with solid part in the right cerebellum (Figure 1). The cyst appeared hypointense on T1WI and hyperintense on T2WI (Figure 1A and B). The solid part was enhanced after gadolinium administration (Figure 1C and D). After 4 days, the tumor was resected. A soft, reddish, rich blood supplied mass with integral capsule was found. Histological examination of the tumor specimen exposed a highly vascular tumor containing abundant capillary vessels and stromal cells intermingled with a large number of red blood cells that certified the occurrence of the intratumoral hemorrhage (Figure 2).

The postoperative course was uneventful. A computed tomography (CT) scan without contrast infusion was taken 1 day after the operation and presented a low-density shadow on the operative region (due to tumor resection) and no abnormal



**FIGURE 1.** Preoperative MRI. (A) Axial T1-weighted image revealed a mass in the right cerebellum with hypointense. (B) Axial T2-weighted image revealed a mass in the right cerebellum with hyperintense. (C) and (D) Axial/sagittal T1-weighted image with gadolinium administration, revealing an enhanced solid part of the tumor. MRI = magnetic resonance imaging.

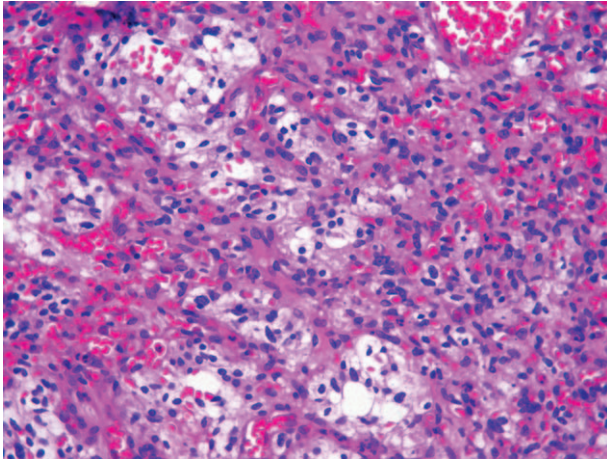
density lesions on other regions (Figure 3A). The MRI with contrast infusion revealed no enhanced lesions in the cerebellum (Figure 3B). Seven days later, the final pathological diagnosis was hemangioblastoma. The patient was discharged without discomfort.

## DISCUSSION

Hemangioblastomas are highly vascular lesions, representing 1.5% to 2.5% of intracranial tumors and 7% to 12% of posterior fossa tumors. Hemangioblastomas can occur sporadically or as a part of VHL. They are usually in the cerebellum (76%) and less common in cerebral hemispheres (9%), spinal cord (7%), and brainstem (5%).<sup>1</sup> Spontaneous hemorrhage

occurs in 1% to 5% of brain tumors, but is rarely associated with hemangioblastomas despite their rich vascular capillary networks.<sup>6</sup> There are few cases of hemorrhage from hemangioblastomas reported in the literature.<sup>9</sup> Some articles reported that intratumoral hemorrhage due to hemangioblastomas can arise from the spinal cord and cervical nerve root.<sup>4,5</sup> However, cases of cerebellar hemangioblastomas with intratumoral hemorrhage are rare. In this article, we have discussed the diagnosis of the intratumoral hemorrhage of hemangioblastomas and the mechanism of the hemorrhage.

CT and MRI are widely used in the diagnosis of hemangioblastomas that appear as cystic lesions with enhanced mural nodules. Hemangioblastomas usually occur in the posterior fossa, which is better suited for MRI than CT. In addition,

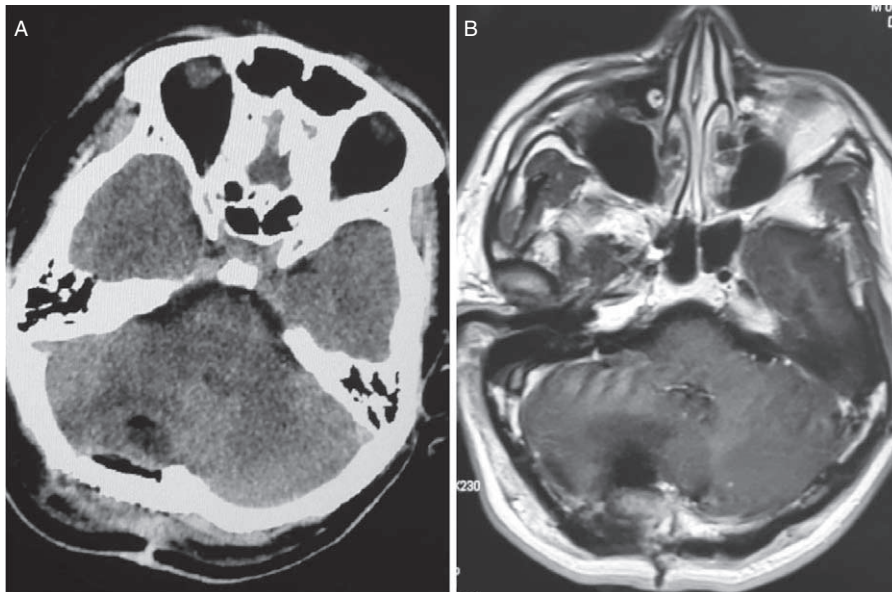


**FIGURE 2.** Histological sample with hematoxylin and eosin stain showed a highly vascular tumor, containing abundant capillary vessels and stromal cells, intermingled with a rich population of red blood cells as well (400×).

MRI can provide the best anatomic definition of these lesions. In our case, MRI revealed a round cystic lesion with enhanced solid portion in the right cerebellum. The radiological features of this case were similar to normal hemangioblastomas, whereas our histological examination uncovered the intratumoral hemorrhage. If the hemangioblastoma ruptures, the outcome of the patient will be worse. The misdiagnosis of an intratumoral hemorrhage of hemangioblastomas in a case like ours, based on its appearance in an MRI, is quite dangerous. If an MRI reveals the appearance of hemangioblastomas, we should be alerted to the possibility of an intratumoral hemorrhage. In the meantime, other examinations such as CT and histological examinations are necessary. Hemangioblastomas are also easily misdiagnosed as AVMs or intracranial aneurysms.<sup>4,7,8</sup> An AVM nidus presents a dense vascular network similar to a

hemangioblastoma nodule. Their microscopic structure and hemodynamic effects are also similar. However, the mass effect exerted by a hemangioblastoma is much more frequent and can lead to focal neurological deficits. Moreover, hemangioblastomas present a microvascular structure similar to a normal capillary bed, whereas an AVM nidus is composed of altered vessels with no actual capillary bed.<sup>7,10</sup> Angiography may be conducive to distinguishing between these 2 diseases. In Javier opinion,<sup>7</sup> hemangioblastomas may coexist with intracranial aneurysms because of the hemodynamic disturbance and the chemically modulated mechanisms. Therefore, once a hemangioblastomal hemorrhage is found, the possibility of an intracranial aneurysm should also be taken into consideration.

Meanwhile, the mechanism of hemorrhaging among hemangioblastomas is still a mystery. Gläsker et al<sup>11</sup> hold that tumor size determines the risk of hemorrhage. Hemangioblastomas that are <1.5 cm have virtually no risk of spontaneous hemorrhage. Structural fragility of tumor vessels, which is caused by the upregulation of vascular endothelial growth factor demonstrated in hemangioblastomas, is also reported as an important contributing factor for spontaneous hemorrhage of hemangioblastomas. Furthermore, spinalradicular location and solid type should be taken into consideration as well.<sup>7,9,12</sup> In cytogenetics, 23% to 34% of the hemangioblastomas, whether in VHL-associated or sporadic tumors, turn out to be associated with the loss of chromosomal arm, 6q.<sup>1,13</sup> Moreover, D6Mit135 on chromosome 6 is found responsible for vascular dilation and hemorrhage induction by Maeda et al.<sup>2</sup> We proposed that the loss of chromosomal arm 6q from hemangioblastomas may contain a mutation of D6Mit135 that induces vascular dilation and ultimately leads to the hemangioblastomal hemorrhaging. This omission of D6Mit135 may explain why hemorrhages rarely occur in hemangioblastomas. It also suggests that genetic testing may help us to make an early, accurate diagnosis. The patient in our case had a similar mass in his cerebellum 4 years ago. The mass was resected with bloody fluid found in its cystic portion (however, we lack reliable evidence other than the information gathered from surgery logs). The final pathological



**FIGURE 3.** (A) Computed tomography scan without contrast administration presents low-density shadow on the operative region. (B) Axial T1-weighted MRI with contrast infusion revealed no enhanced lesions in the cerebellum. MRI = magnetic resonance imaging.



diagnosis was hemangioblastoma as well. This suggests that the tumor in our case may have been genetically stable, which supports the proposal that we mentioned above.

### CONCLUSION

Spontaneous hemorrhaging is rarely associated with hemangioblastomas. The cerebellar hemangioblastoma with intratumoral hemorrhaging that we have reported is even more rare. We report this case in order to remind clinicians not to overlook the possibility of hemangioblastomal hemorrhaging. Our case shows that hemangioblastomas with intratumoral hemorrhage may reveal normal hemangioblastoma radiological features and mild symptoms, but have the risk of hemorrhage (even death<sup>3</sup>). Moreover, MRI, CT, and histological examination are necessary for diagnosing this disease. Tumor size, upregulation of vascular endothelial growth factor, spinalradicular location, and solid type are also the factors relating to the hemorrhage of hemangioblastomas. Genetic screening may help us make an early diagnosis, but will still require more tests for reliability in the clinical setting. Angiography can be used to identify hemangioblastomas and AVMs. The intracranial aneurysm associated with hemangioblastoma should also be taken into consideration when the hemorrhage of hemangioblastomas is found. The mutation of D6Mit135 on chromosome 6 may be responsible for vascular dilation and hemorrhage induction in hemangioblastomas, but this will require funding and extended patient stays to conduct a more thorough examination.

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