# Continuous progression of hemorrhage of sphenoid ridge meningioma causing cerebral hernia: A case report and literature review

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Abstract. The aim of the present study was to explore the clinical characteristics of repeated hemorrhages of meningioma and analyze the causes of hemorrhage. Meningiomas are mostly benign tumors that rarely manifest hemorrhagic strokes. In the present study, a case of sphenoid ridge meningioma with repeated hemorrhages is reported. Internal hemorrhage was first observed, which, on further aggravation, formed a hematoma in the brain parenchyma and finally led to the development of a hernia. No neurological deficit was present after surgery and rehabilitation. A postoperative pathological examination showed increased levels of Ki-67, abnormal blood vessels in the tumors and the presence of progesterone, which indicate possible causes of the hemorrhage. A review of associated previous studies revealed that hemorrhages originate mainly from inside the meningioma. Two cases of meningiomas with repeated hemorrhages have been reported; one in the foramen magnum region and the other in the pineal gland area. The foramen magnum tumor had an interval of 1.33 months between two hemorrhagic episodes. Collecting relevant data from the latter case was not possible. In the present case report, the interval between two bleeding episodes was 3 days. The literature review also revealed that the average age of onset of meningioma is relatively young at only 28.00±6.24 years. In conclusion, repeated hemorrhages in meningiomas are extremely rare and the causes have not yet been identified. Increased Ki-67 and abnormally proliferating blood vessels may be potential causes of hemorrhage. Early diagnosis and rapid surgical

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intervention are essential to prevent further episodes of bleeding, which may otherwise have fatal consequences for the patients.

## Introduction

Meningiomas are the most commonly occurring primary intracranial tumors, accounting for 20.0-33.8% of all intracranial tumors (1,2). According to the WHO histological classification, tumors may be classified as benign (grade 1), atypical (grade 2) or malignant (grade 3) (3,4). Atypical and malignant meningiomas account for ~5.0% of all meningiomas (2). Although meningiomas are mostly benign, the probability of an associated hemorrhage is 1.3-2.4% (5-7). Hemorrhage can occur within the tumors, surrounding the tumors, and within the brain parenchyma, subarachnoid space and subdural space (8-10). During such events, substantial bleeding may lead to severe clinical consequences. Cheng and Lin (11) reported that the mortality of hemorrhagic meningioma was as high as 38.5% in the computed tomography (CT) era and 77.8% in the pre-CT era. Bosnjak et al (12) reported that the overall mortality and morbidity rates of hemorrhagic meningioma were 21.1 and 32.6% in 2001, respectively.

The exact causes of hemorrhage in meningioma are currently unknown. The most common hypotheses are infarction of the tumor with secondary bleeding, increased density of blood vessels inside the tumor, direct tumor invasion into one of the cerebral arteries, mechanical stretching and distortion of the cortical bridging veins, and histamine-related vasodilatation or venous hypertension due to occlusion of the venous sinus (6,13).

In the present study, a case of sphenoidal ridge meningioma with repeated bleeding episodes, manifested as intratumoral parenchymal hemorrhages, is described. The progressive process eventually resulted in the formation of a cerebral hernia, which played an important role in the causal analysis of the hemorrhage. In addition, a literature review on data between 2006 and 2019 was performed to provide supplemental information on the causes of meningioma hemorrhage.

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*Key words:* meningioma, hemorrhage, magnetic resonance imaging, pathology, mortality

# **Case report**

Medical history. A 35-year-old female patient was admitted to the Sanbo Brain Hospital of the Capital Medical University (Beijing, China) on November 19, 2018, with a complaint of an intermittent week-long headache, aggravated nausea and vomiting. The patient had experienced episodes of intermittent headache 1 week prior to the aforementioned symptoms and had been admitted to a local hospital. CT examination of the head showed hemorrhagic stroke, following which, mannitol dehydration treatment (20%, once every 12 h; 125 ml each time) was applied. After 4 days, the patient started showing aggravated symptoms, accompanied by nausea and vomiting. A repeat head CT demonstrated aggravated hemorrhage. The patient was then transferred to Sanbo Brain Hospital. Upon admission, the nervous system examination results were as follows: A Glasgow Coma Scale score (14) of 13, lethargy, motor aphasia, unequal pupil size (left, 5.0 mm; right, 2.0 mm), disappearance of the left light reflex and a responsive right light reflex. The muscular strength of the right limb was grade III (Medical Research Council sum score) (15), tension was increased, deep reflex was hyperactive and right pathological reflex was positive. Admission blood tests revealed a normal platelet count, hemoglobin level, international normalized ratio and activated partial thromboplastin time.

The study was approved by the Ethics Committee of Sanbo Brain Hospital. Written informed consent for publication was obtained from the patient.

Imaging examination. On November 12, 2018, at the beginning of the onset of hemorrhage, the CT examination showed bloody high-density shadows in the left temporal region (Fig. 1A), whereas CT angiography did not show any aneurysms or arteriovenous malformations (Fig. 1D). Another CT scan performed 3 days later showed a significant increase in bleeding as compared with the previous scan, and the blood was observed to have entered the brain parenchyma and have formed a secondary temporal lobe gyrus hernia (Fig. 1B and C). A magnetic resonance imaging (MRI) scan of the head revealed that the left temporal space-occupying lesions showed isointense and hyperintense signals on T1-weighted imaging (Fig. 1E), hyperintense and hypointense signals on T2-weighted imaging and a visible liquid level (Fig. 1F) on November 19, 2018. Susceptibility-weighted imaging (SWI) showed that the hemorrhage site was located in the brain parenchyma and within and around the tumor (Fig. 1G). Enhanced scanning showed that the lesions were uniformly enhanced, whereas the surrounding hematoma was ring-enhanced and displayed the meningeal tail sign (Fig. 1H). Post-surgical CT and MRI examinations showed that the lesions had been completely removed (Fig. 1I and J).

Intraoperative and postoperative conditions. Emergency resection was performed on admission. No adherent veins were found around the tumor. The intratumoral hemorrhage that was causing blood flow into the brain parenchyma was evaluated. After the operation, the patient regained consciousness and limb function gradually recovered. After 9 days, the

patient was discharged from hospital. At the time of discharge, the patient could walk independently, but still experienced incomplete aphasia. The left pupil was large (4.5 mm), but sensitive to light reflection. The patient was then transferred to a rehabilitation hospital for recovery treatment. At the 3-month follow-up, the speech and pupil functions had recovered, and a re-examination with MRI showed no recurrence of the tumor (Fig. 1J).

*Histology*. Gross morphology of the fresh tumor tissue excised from surgery was fixed in 10% neutral buffered formalin overnight for histological examinations at room temperature (24-26°C). Furthermore, samples were specially dehydrated, paraffin embedded and sectioned at 5- $\mu$ m thickness following the procedures. After that sections were stained with hematoxylin and eosin (H&E) and/or immunohistochemical stains. The pathology result was analyzed by 2 experienced specialists in the field of neuropathology according to WHO classification of CNS tumors (2016) (4).

Immunohistochemistry. Gross morphology of the fresh tumor tissue excised from surgery was fixed in 10% neutral buffered formalin overnight for histological examinations at room temperature. Formalin-fixed sections were deparaffinized and stained with hematoxylin and eosin (H&E) and immunohistochemistry according to the manufacturers' instructions. In brief, 5- $\mu$ m sections were deparaffinized. The sections were then treated with 3% H<sub>2</sub>O<sub>2</sub> for 5 min at room temperature to block endogenous peroxidase activity. Antigen retrieval was performed by steaming the slides in target retrieval solution, citrate pH 6 (Agilent Technologies Inc.) for 15 min and then cooling for 15 min. Then, the slides were blocked with 5% fetal bovine serum (Jackson ImmunoResearch Laboratories, Inc.) diluted in wash buffer with 1% bovine serum albumin (Merk KGaA) at room temperature for 15 min and incubated with primary antibodies against epithelial membrane antigen (EMA; 1:100; cat. no. E29; DAKO, Agilent Technologies, Inc.), Ki-67 (1:50 dilution; cat. no. MIB-1; Labvision), progesterone receptor (PR; 1:150 dilution; cat. no. ab8327; Abcam); CD34 (1:100; cat. no. ab8158; Abcam); vimentin (1:150; cat. no. ab9254; Abcam) at 4°C overnight. After being washed with phosphate-buffered saline 3 times, the sections were stained with anti-mouse/rabbit polymer horse radish peroxidase-labeled secondary antibody (cat. no. PV-6000D; Zhongshan Bio-Tech Co., Ltd) for 30 min at 37°C. Then, 3,3'diaminobenzidine (DAB) was applied for color development at room temperature for 5 min and sections were subsequently counterstained with hematoxylin. Each slide was individually reviewed and scored using Faramount mounting solution (Agilent Technologies Inc.) by 2 experienced neuropathologists using light microscopy (x100-200).

Pathological findings. H&E-stained section demonstrated diffuse proliferation of spindle shaped tumor cells arranged in bundles and storiform (Fig. 2A), without necrosis, mitosis and invasion of brain tissue. Hemorrhagic and proliferative blood vessels were observed within the tumor (Fig. 2B and C). Therefore, Grade 1 fibrous meningioma was diagnosed, according to the classification criteria of 2016 WHO (4). Ki-67 expression was 5-10% (Fig. 2D). Immunohistochemical

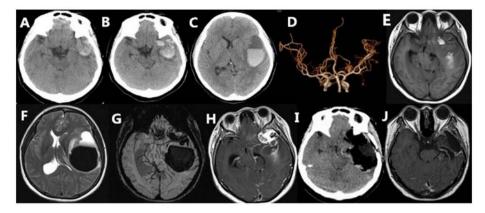


Figure 1. (A) Axial CT scanning showed bloody high-density shadows in the left temporal region, and (B and C) subsequent examination showed a marked increase in hemorrhage. (D) CT angiography revealed no aneurysms or arteriovenous malformations. On axial MRI scans, (E) isointense and hyperintense signals on T1-weighted imaging, (F) hyperintense and hypointense signals on T2-weighted imaging and a visible liquid level were noted. (H) Susceptibility-weighted imaging showed that the hemorrhage site was located in the brain parenchyma and within and around the tumor. (G) Enhanced scanning showed that the lesions were uniformly enhanced, whereas the surrounding hematoma was ring-enhanced and displayed the meningeal tail sign. (I and J) A postoperative review of axial CT and MRI showed that the lesions were completely removed. CT, computed tomography; MRI, magnetic resonance imaging.

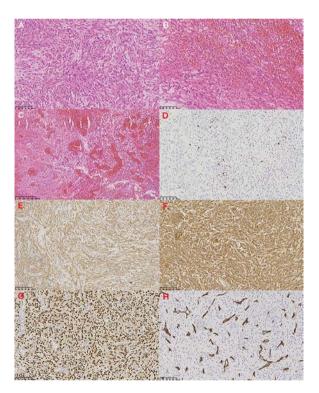


Figure 2. (A) Pathological examination (H&E staining) confirmed a fibrous meningioma. (B and C) Hemorrhagic and proliferative blood vessels were observed in H&E-stained tumors. (D) Ki-67 (5-10%). Immunohistochemical staining showed positive expression of (E) epithelial membrane antigen, (F) vimentin (F) and (G) progesterone. (H) CD34 labeling showed increased vascular density. (A), (B), (D-H)=(magnification, x200); C=(magnification, x100).

staining revealed positive expression of epithelial membrane antigens, vimentin and progesterone (Fig. 2E-G). The CD34 marker demonstrates vascular dysplasia (Fig. 2H).

Literature review on hemorrhagic meningiomas (2006-2019). A total of 40 cases of hemorrhagic meningioma were reviewed (Table I). The mean age of onset was  $56.23\pm12.91$  years, and the male to female ratio was 1:1.35. Cystic changes were observed in 5.88% (2/34) and recurrences were observed in

11.76% (4/34) of cases. The mortality rate was 9.09% (3/33). Intratumor hemorrhage accounted for 80.00% (32/40) of cases, and 37.50% (15/40) presented with solely intratumoral hemorrhage. Multiple ventricular, peritumoral and subdural hemorrhage also occurred. The proportion of solely subdural hemorrhage cases was 17.50% (7/40), and only 1 case of solely subarachnoid hemorrhage was reported (2.5%). In terms of pathological type, the meningothelial tumor occurred in 34.62% (9/26) of cases (Fig. 3A) and in 45.00% (18/40) of cases convex lesions were mostly observed (Fig. 3B).

## Discussion

Meningiomas are usually benign tumors that arise from arachnoidal cap cells and are detected by the symptoms caused by increased intracranial pressure and seizures. Progressive neurological deficits may also occur, depending on the tumor location and growth (16). Hemorrhagic meningioma is a rare disease with an incidence of 2.0-2.2% in Asia in the last two decades (6,7). Repeated hemorrhages are rare, with only 2 cases having been reported (17,18). From these cases, plus the present case, meningioma patients with repeated hemorrhages were found to be young, with the average age of onset being 28±6.24 years (Table II). One of the previous cases was in a pregnant woman, and a possible cause could be the fluctuation of hormone levels during pregnancy, a hypothesis that has also been supported by other studies (19,20). In the present study, the patient also displayed a high level of progesterone. It was also reported that the internal tumor hemorrhage progressed gradually and eventually broke into the peritumoral area and the brain parenchyma. As tumors have a higher cellular density than the brain parenchyma, it is not surprising that tumoral blood can encroach the brain parenchyma after breaking through the tumor. This may also explain why there are more peritumoral and parenchymal hemorrhages than intratumoral hemorrhages. Another possible cause of hemorrhage was found to be the high proliferation index of tumors. Niiro et al (7) reported that the MIB-1 labeling index of 5 grade I meningioma cases was 5.8±2.2. Ki-67 is known to increase with the grade of meningioma and may be

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| First author/s, year      | Age,<br>years | Sex | Hemorrhage<br>type | Pathological type      | Tumor location            | Cystic | Incentive          | Relapse | Outcome                            | (Refs.) |
|---------------------------|---------------|-----|--------------------|------------------------|---------------------------|--------|--------------------|---------|------------------------------------|---------|
| Ravindra VM, et al, 2019  | 38            | M   | HTI                | Atypical               | Saddle area               | z      | Z                  | z       | Normal                             | (56)    |
| Mandour C, et al, 2018    | 61            | М   | HVI/HTI            | Meningothelial         | Sphenoid ridge            | Z      | N                  | Z       | Hemiparesis                        | (13)    |
| Hu S, et al, 2018         | 58            | Μ   | HTI                | NA                     | Falx/sagittal sinus       | Z      | N                  | Z       | Epilepsy                           | (57)    |
| Basil G, et al, 2018      | 54            | ц   | HTI                | NA                     | Jugular foramen           | Y      | Z                  | Z       | Hoarseness/hypoglossal<br>weakness | (58)    |
| Entezami P, et al, 2018   | 49            | М   | HTI                | NA                     | Cerebellopontine<br>angle | Z      | Radiotherapy/shunt | Y       | Facial palsy/hearing<br>loss       | (59)    |
| Ravindran K, et al, 2017  | 36            | Ц   | HQS/HTI            | NA                     | Sphenoid ridge            | Z      | Postnatal          | Z       | Normal                             | (09)    |
| Byard RW, 2017            | 46            | Μ   | ITH/ICH            | Fibrous/meningothelial | Parasagittal              | Z      | N                  | Z       | Died                               | (61)    |
| Broggi M, et al, 2017     | 45            | Ц   | HT4/HT1            | Atypical               | Convex                    | Z      | N                  | Υ       | NA                                 | (62)    |
| Diehl C, et al, 2016      | 58            | Μ   | HVI/HTI            | NA                     | Ventricle                 | Z      | Thrombolytic       | Υ       | Hemiparesis                        | (49)    |
| Wang HC, et al, 2016      | 39            | Ц   | HT4/HT1            | Fibrous                | Falx                      | NA     | NA                 | NA      | Normal                             | (9)     |
| Wang HC, et al, 2016      | 45            | Μ   | HTI                | Atypical               | Parasagittal              | NA     | NA                 | NA      | Normal                             | (9)     |
| Wang HC, et al, 2016      | 51            | ц   | HT4/HT1            | Transitional           | Convex                    | NA     | NA                 | NA      | Normal                             | (9)     |
| Wang HC, et al, 2016      | 53            | ц   | HT4/HT1            | Angiomatous            | Convex                    | NA     | NA                 | NA      | Normal                             | (9)     |
| Wang HC, et al, 2016      | 59            | ц   | ITH                | Atypical               | Convex                    | NA     | NA                 | NA      | Hemiparesis                        | (9)     |
| Wang HC, et al, 2016      | 64            | М   | HT4/HT1            | Fibrous                | Parasagittal              | NA     | NA                 | NA      | Normal                             | (9)     |
| Aoyama Y, et al, 2015     | 59            | ц   | SAH                | Transitional           | Foramen magnum            | Z      | N                  | z       | NA                                 | (63)    |
| Ito Y, et al, 2015        | 78            | ц   | HTTI               | Anaplastic             | Convex                    | Z      | Anticoagulation    | Z       | Hemiparesis                        | (64)    |
| Levine AB &               | 69            | М   | HUS/HTI            | NA                     | Convex                    | Z      | Z                  | Z       | Confusion improved                 | (65)    |
| MacDougall N W, 2014      |               |     |                    |                        |                           |        |                    |         |                                    |         |
| Eljebbouri B, et al, 2014 | 51            | Σ   | HUS                | Meningothelial         | Convex                    | Z      | Ν                  | Z       | Normal                             | (99)    |
| Chonan M, et al, 2013     | 67            | ц   | SDH                | Meningothelial         | Convex                    | Z      | N                  | Z       | Normal                             | (67)    |
| Lee KH, et al, 2013       | 23            | ц   | ITH                | Chordoid               | Pineal                    | Υ      | Pregnancy          | Z       | Normal                             | (18)    |
| Sasagawa Y, et al, 2013   | 72            | ц   | ITH                | Eosinophilic           | Convex                    | Z      | Ν                  | Z       | Motor                              | (68)    |
|                           |               |     |                    |                        |                           |        |                    |         | aphasia/hemiparesis                |         |
| Rocha AJ, et al, 2013     | 52            | М   | HUS/HTI            | Meningothelial         | Convex                    | Z      | Z                  | Z       | NA                                 | (69)    |
| Kumar S, et al, 2013      | 30            | Ц   | HTTI               | Meningothelial         | Convex                    | Z      | Pregnancy          | Ζ       | NA                                 | (20)    |

| First author/s, year  | Age,<br>years       | Sex                | Hemorrhage<br>type            | Pathological type      | Tumor location            | Cystic  | Incentive                   | Relapse    | Outcome                                  | (Refs.)  |
|---|---------------------|--------------------|-------------------------------|------------------------|---------------------------|---------|-----------------------------|------------|--|----------|
| Krisht KM, et al, 2012  | 50                  | Ы                  | ITH                           | Metaplastic            | Middle cranial fossa      | Ζ       | Ν                           | Ζ          | Normal                                   | (01)     |
| Eom KS & Kim TY, 2012   | 75                  | Ц                  | HTI                           | Meningothelial         | Convex                    | Z       | Trauma                      | Z          | Consciousness not                        | (71)     |
|   |                     |                    |                               |                        |                           |         |                             |            | improved                                 |          |
| Yamaguchi S, et al, 2011  | 34                  | ц                  | ITH                           | Meningothelial         | Convex                    | Z       | Angiography                 | Z          | NA                                       | (50)     |
| Czyż M, et al, 2011   | 69                  | Ц                  | SDH                           | NA                     | Falx/sagittal sinus       | Z       | Z                           | Z          | Normal                                   | (72)     |
| Bellut D, et al, 2011   | 65                  | Ц                  | ITH/IVH                       | Transitional           | Convex                    | Z       | Z                           | Υ          | Swallowing disturbances                  | (23)     |
| Miyajima Y, et al, 2010   | 63                  | Ц                  | ITH/PTH                       | Transitional           | Convex/petrous bone       | Z       | Angiography                 | Z          | Hemiparesis                              | (51)     |
| Lakshmi Prasad G, et al, 2010   | 73                  | Σ                  | ITH/SDH                       | NA                     | Sphenoid ridge/convex     | Z       | Z                           | Z          | NA                                       | (74)     |
| Worm PV, et al, 2009  | 64                  | М                  | HQS                           | NA                     | Anterior cranial fossa    | Ζ       | Pulmonary<br>function tests | Z          | Normal                                   | (52)     |
| de Almeida JP, et al, 2009  | 99                  | Ц                  | ITH                           | NA                     | Convex                    | Z       | Z                           | Z          | Normal                                   | (53)     |
| Kashimura H, et al, 2008  | 55                  | Σ                  | SDH                           | Meningothelial         | Convex                    | Z       | Z                           | Z          | Normal                                   | (30)     |
| Miyazawa T, <i>et al</i> , 2008   | 99                  | Ц                  | ITH                           | NA                     | Falx                      | Z       | Aspirin                     | Z          | Hemiparesis                              | (75)     |
| Romeike BF, et al, 2007   | 57                  | Ц                  | ITH/IVH                       | NA                     | Ventricle                 | Z       | Z                           | Z          | Died                                     | (20)     |
| Romero JR, et al, 2007  | 99                  | Σ                  | ITH/ICH                       | NA                     | Falx                      | Z       | Warfarin                    | Z          | Died                                     | (17)     |
| Mitsuhara T, <i>et al</i> , 2006  | 60                  | Ц                  | SDH                           | Meningothelial         | Petrous bone              | Z       | Z                           | Z          | Normal                                   | (28)     |
| Ziyal IM, <i>et al</i> , 2006   | 57                  | Х                  | ITH/ICH/SDH/SAH               | Secretory              | Convex                    | Z       | Z                           | Z          | Nerve palsy/neurological status improved | (79)     |
| Di Rocco F, et al, 2006   | 72                  | Σ                  | SDH                           | NA                     | Convex                    | Z       | N                           | Z          | NA                                       | (80)     |
| M, male; F, female; Y, yes; N, no; ITH, intratumoral hemorrhage; IVH, intraventricular hemorrhage; SDH, subdural hemorrhage; ICH, intracerebral hemorrhage; PTH, peritumoral hemorrhage; SAH, subarachnoid hemorrhage; NA, not available. | o; ITH,<br>A, not a | intratı<br>vailabl | umoral hemorrhage; IVH<br>le. | , intraventricular hem | norrhage; SDH, subdural h | emorrha | ge; ICH, intraceret         | iral hemor | rhage; PTH, peritumoral hen              | orrhage; |

Table I. Continued.

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|                          |                    |            |          | Hemorrhage       | ge                |   |  |                |       |
|--------------------------|--------------------|------------|----------|------------------|-------------------|---|--|----------------|-------|
| First author/s, year     | Age, years         | Sex        | u        | Type             | Intervals         | Tumor location  | Pathological type  | Possible cause | (Refs |
| Scotti G et al, 1987     | 26                 | Ц          | 3        | SAH              | 1.33 months       | 1.33 months Foramen magnum, C1  | Papillar, epithelial, psammomatous<br>bodies (mixed ingredients) | NA             | (17)  |
| Lee KH et al, 2013       | 23                 | Ц          | NA       | HTI              | NA                | Pineal region   | Chordoid   | Pregnancy      | (18)  |
| Present case, 2019       | 35                 | Ц          | 7        | ITH, ICH         | 3 days            | Sphenoid ridge  | Fibrous  | Z              |       |
| F, female; NA, not avail | lable; N, no; SAH. | , subarach | noid hem | orrhage; ITH, in | tratumoral hemorr | F, female; NA, not available; N, no; SAH, subarachnoid hemorrhage; ITH, intratumoral hemorrhage; ICH, intracerebral hemorrhage. | orrhage.   |                |       |

Table II. Clinical features of repeated hemorrhage of meningioma

associated with the biological behavior of the invasion (21,22). Sunada *et al* (23) also reported that a high cell proliferation index may activate certain mechanisms leading to malignant tumor hemorrhage. In addition, abnormal vascular proliferation, as in the case reported in the present study, may also be one of the causes of hemorrhage (Fig. 2C and H).

A review of previous studies revealed that little research has been conducted on the imaging features of meningioma hemorrhage. In most cases, intensive MRI scans have been used; however, T1- and T2-weighted imaging can offer reference support in determining the timing of the hemorrhage. Based on the timeline, intracranial hemorrhage can be classified into hyperacute stage (the first few hours), acute stage (1-3 days), early subacute stage (3-7 days), late subacute stage (4-7 days to 1 month), and chronic stage (1 month to years) (24,25). The bleeding time of meningioma can also be evaluated by MRI signal information. The SWI MRI technique is sensitive to paramagnetic blood products, such as methemoglobin, deoxyhemoglobin, ferritin and hemosiderin. SWI is considered the most sensitive tool available for the detection of cerebral microbleeds (26-28). MRI revealed the subacute hemorrhage in the patient of the present study. The tumor diameter seemed to be unrelated to meningioma hemorrhage, and there are reports of secondary bleeding from small tumors (29,30). In addition, the literature review showed that calcification of hemorrhagic meningiomas is rare (31), which may be due to the high tumor density that makes bleeding difficult.

In 2005, Bosnjak et al (12) conducted a study on 134 cases of hemorrhagic meningioma and showed that factors that may lead to bleeding are a patient age of <30 or >70 years, convex and intraventricular lesions, and a fibrous tumor type. The mortality rate was reported to be 21.1%. In the present study, 40 cases of hemorrhagic meningioma, reported in the past 14 years, were reviewed and convex meningioma was shown to have a higher probability of hemorrhage. Although numerous pathological types of meningioma can produce hemorrhage, a meningoepithelial tumor is the type most likely to do so. Niiro et al (7) investigated 57 cases of hemorrhagic meningioma, and also showed that meningothelial is the most common pathological type, followed by fibrotic type and hemangiomas. Cystic changes are relatively rare, and were observed in 5.88% of the hemorrhagic meningioma cases. The incidence of cystic meningiomas was 1.7-10% (32). It is questionable whether the same disease occurs simultaneously into two separate processes of a rare disease progression and whether there is a correlation between these two processes. However, some reports argue that cystic meningiomas are prone to hemorrhage (33,34). With the development of imaging detection and diagnosis technologies, the mortality rate due to meningiomas has decreased. In the present study, the mortality rate was found to have decreased to 9.09% in the past 14 years (12).

The precise causes of hemorrhage in meningioma are unknown. The most regularly expounded theories are of tumor infarction with secondary bleeding, direct invasion of the tumor into a cerebral artery, mechanical stretching and distortion of the cortical bridging veins, and histamine-associated vasodilatation or venous hypertension as a result of venous sinus occlusion (13). A recent study have also found that the

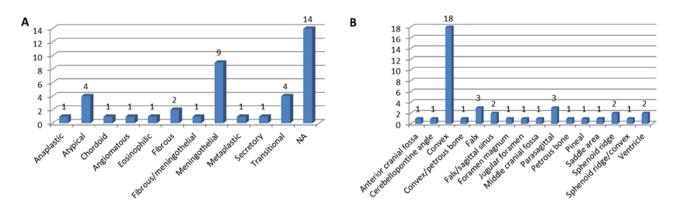


Figure 3. In the literature review, (A) the main pathological type of meningioma hemorrhage was meningothelial tumor, and (B) the location was mainly convex.

average number of undifferentiated vessels in hemorrhagic meningioma patient groups is significantly higher than that in the control groups, thereby confirming their existence as factors involved in the mechanism of hemorrhage (6). In the case report of the present study, the patient showed an onset of intratumor hemorrhage, followed by aggravated bleeding that penetrated into the brain parenchyma. Further analysis of relevant hemorrhage cases (mostly individual cases) in the past 14 years indicated that a majority of hemorrhages occur from inside the tumor, i.e., they are precipitated by an internal factor. Intratumoral hemorrhage is recorded to account for 80.00% (32/40) of cases. In such cases, it is estimated that the hemorrhage may have started inside the tumor and progressed, leading to the blood entering the peritumoral and subdural areas, and even encroaching the brain parenchyma. Due to the high density of the tumor, hemorrhage caused by an external factor, such as a peritumoral blood vessel penetrating into the brain parenchyma, is unlikely. Moreover, in the present study, the literature review focused on evaluating traceable causative factors, including embolization therapy (35-40), pregnancy (19,20), radiotherapy (41,42), air travel (43), surgery (44), trauma (8), long-term cough (45), anticoagulation therapy (46-48), thrombolytic therapy (49), cerebral angiography (50,51) and pulmonary function examination (52). Prevention and intervention targeted at these factors may reduce the probability of hemorrhage.

Hemorrhage of the meninges is often a serious event with a high mortality rate. However, several studies have reported shrinkage in tumor size following a hemorrhagic event (53). Surgical intervention for hemorrhagic meningiomas is the unanimously accepted treatment (11,54,55). In the present case, the patient had a secondary cerebral hernia, which was cured after proactive treatment. Early intervention is necessary to eliminate the risk of secondary bleeding, which can often lead to severe consequences.

In conclusion, repeated hemorrhages in meningiomas are extremely rare and the causes have not been identified yet. Increased Ki-67 and abnormally proliferating blood vessels may be potential causes of hemorrhage. Early diagnosis and rapid surgical intervention are essential to prevent further episodes of bleeding, which may have fatal consequences for the patient. A limitation of the present study is the insufficient number of studies reviewed; however, the rare case reported will add to the scant literature on such cases and will offer a basis for future research in this field.

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## Availability of data and materials

The datasets used or analyzed during the present study are available from the corresponding author on reasonable request.

#### **Authors' contributions**

CJY, CKY and SH designed the study; YKY and NL collected data and revised the manuscript for important intellectual content; XLQ performed the histological examination of the samples; ZCY analyzed the data and SH wrote the article. All authors have read and approved the final manuscript.

#### Ethics approval and consent to participate

The study was approved by the Ethics Committee of Sanbo Brain Hospital (Beijing, China).

#### Patient consent for publication

Written informed consent was obtained from the patient.

#### **Competing interests**

The authors declare that they have no competing interests.

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