Radiological classification of meningiomas with hemorrhagic onset and its clinical significance

ZUO-RUN XIE[1], HONG-CAI WANG[1], YI-LEI TONG[2], SHI-WEI LI[1], MAO-SONG CHEN[1] and BO-DING WANG[2]

[1]Department of Neurosurgery, The Affiliated Lihuili Hospital of Ningbo University; [2]Department of Neurosurgery, Hwa Mei Hospital of University of Chinese Academy of Sciences, Ningbo, Zhejiang 315040, P.R. China

Received April 14, 2022; Accepted July 7, 2022

DOI: 10.3892/ol.2022.13461

Abstract. Meningiomas are the most common benign intracranial tumors and frequently present with a gradual onset of neurological deficits; conversely, their acute presentation with hemorrhagic onset appears to be a rare event. Nonetheless, as early surgical evacuation is the foundation of treatment, a timely diagnosis of this rare type of intracranial hemorrhage is necessary. The purpose of the present single-center study was to investigate the radiological characteristics and propose a new bleeding classification for guiding the diagnosis and treatment. A total of 19 patients consecutively diagnosed with hemorrhagic meningioma were enrolled in this retrospective study. Intracranial extra-axial mass, tumor-associated hemorrhage and peritumoral brain edema were the three main radiological features of the hemorrhagic meningiomas. The site of tumor-associated hemorrhage included the peritumoral space, subarachnoid space, subdural space, brain parenchyma and/or intratumor region. Based on the anatomical relationship between meningioma and hematoma, the spontaneous hemorrhage stemming from meningiomas was further summarized into three bleeding patterns involving purely intratumoral hemorrhage (type I), purely extratumoral hemorrhage (type II) and combined intra/extratumoral hemorrhage (type III); furthermore, the type III hemorrhage usually came from type I bleeding that extended into the surrounding regions. The symptoms in type I patients were generally mild and early surgery was performed following adequate preoperative evaluations. The symptoms in type II patients were mild in certain cases and moderate to severe in others, so early or emergency surgery was chosen according to the clinical status of the patient. Almost all type III patients had moderate to severe symptoms and these patients usually required emergency surgery. In addition, patients with different bleeding types may have different pathological mechanisms underlying the tumor bleeding. Apart from being convenient for diagnosis, this concise and practical bleeding classification may aid in the selection of the treatment strategy and facilitate the understanding of the associated mechanisms.

Correspondence to: Professor Hong-Cai Wang, Department of Neurosurgery, The Affiliated Lihuili Hospital of Ningbo University, 1111 Jiangnan Road, Yinzhou, Ningbo, Zhejiang 315040, P.R. China
E-mail: roger0412@126.com

Key words: meningioma, hemorrhage, imaging, diagnosis, mechanism

Introduction

Meningiomas most frequently occur as slow-growing intracranial tumors and typically present with the symptoms of headaches, dizziness, seizures or the gradual progression of neurological deficits; however, their acute presentation with spontaneous hemorrhage appears to be a rare event (1-3). Meningioma with hemorrhagic onset usually refers to the significant intracranial hemorrhage stemming from a meningioma and results in a series of clinical symptoms, such as severe headaches, nausea and vomiting, epilepsy, hemiparesis or disturbance of consciousness (2,3). According to previously reported cases, the incidence ranges from 0.5-2.4% (3). Although rare, intracranial hemorrhage stemming from meningioma could have a detrimental effect on outcomes and may even be a life-threatening event due to acutely increased intracranial pressure (2-4). Cheng and Lin (5) reported that the mortality rate associated with hemorrhagic meningiomas was as high as 38.5% in the CT era and 77.8% in the era before CT. Bošnjak *et al* (2) reported overall mortality and morbidity rates of 21.1 and 32.6%, respectively, for hemorrhagic meningiomas in 2005. Therefore, early diagnosis and correct treatment are the key factors to improve patient outcomes.

While no difficulty is encountered in the diagnosis of a hemorrhage in a previously known brain tumor, hemorrhagic onset as the initial presentation of a brain tumor may pose diagnostic problems (6). Meningiomas with hemorrhagic onset can manifest in several ways and some of the clinical features of such a condition have been characterized; however, previous studies regarding this condition have been limited to single-case reports or small case series (2,4,7-12). The cases in the literature were reported according to the site of hemorrhage such as the subarachnoid space (8), subdural space (7,9), peritumoral space (4), brain parenchyma (2,10) or intratumor region (11,12). However, this description of tumoral bleeding

cannot reflect the association between the meningioma and the hemorrhage, and it also has no practical significance for clinical diagnosis and does not significantly contribute to guiding treatment. Furthermore, the previous studies explored the results without considering the impact of different hemorrhagic types. In the present study, a new classification system of hemorrhage associated with meningiomas that is based on a retrospective analysis of 19 cases is proposed and its clinical significance is explored.

Materials and methods

Patient selection. Following study approval by the Institutional Ethics Board of the Affiliated Li Hui Li Hospital of Ningbo University (Ningbo, China), a retrospective study was performed on the patients who underwent craniotomy for meningioma resection between July 2008 and March 2021 at the Department of Neurosurgery, The Affiliated Li Hui Li Hospital of Ningbo University (Ningbo, China). All methods were performed in accordance with the relevant guidelines and regulations. The inclusion criteria were set as follows: i) Patients meeting the diagnostic criteria of the 2016 World Health Organization (WHO) classification of meningiomas; ii) patients who underwent craniotomy for tumor resection in The Affiliated Li Hui Li Hospital of Ningbo University (Ningbo, China); iii) patients with complete clinical information and radiological data; iv) patients being diagnosed for the first time; v) follow-up data being available for ≥6 months. The exclusion criteria were as follows: i) An age of <18 years; ii) patients on a regimen of anticoagulant or antiplatelet therapy; iii) patients with serious diseases associated with the heart, lungs, kidneys, endocrine system and blood; iv) patients who had previously undergone preoperative adjuvant therapies such chemotherapy or radiotherapy; and v) hemorrhage distant from the tumor site. The patients enrolled in the study were divided into two groups according to whether or not tumor-associated hemorrhage was recorded. The patient flowchart is summarized in Fig. 1.

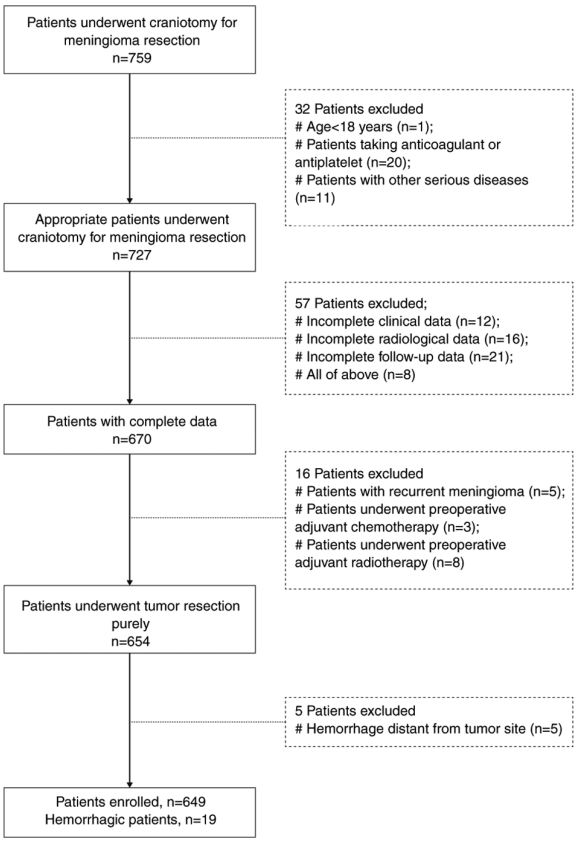

Figure 1. Flow chart of patient selection.

Data collection. This retrospective study enrolled a total of 649 consecutive patients with meningiomas who underwent craniotomy for tumor resection at the Affiliated Li Hui Li Hospital of Ningbo University (Ningbo, China), and 19 of these 649 patients presented with acute spontaneous hemorrhage stemming from a meningioma. A total of 20 cases with non-hemorrhagic meningiomas were randomly selected from the 630 patients in the same period and served as a comparison group (group 4). The clinical data, including age, sex, history of hypertension and diabetes, onset symptoms, Simpson resection grade (1) and histological variants, were extracted from the medical records. Laboratory variables, such as international normalized ratio, prothrombin time and activated partial thromboplastin time, were retrieved from the hospital database. The pre- and post-operative computed tomography (CT), magnetic resonance imaging (MRI) and/or CT angiography (CTA) data were examined via picture archiving and communication system (PACS).

Radiological evaluation. Radiological outcomes were analyzed by CT scans, MRI and/or CTA. The radiological features, including tumor location, size, signal intensity, contrast enhancement, tumor margins and hemorrhagic site, were analyzed independently by two neurosurgeons. Tumor size was determined by measuring the greatest diameter of the enhanced tumor on the preoperative CT or the contrast enhancement of T1-weighted MRI. The signal intensities of tumors on T2-weighted MRI were categorized as hypointense, isointense or hyperintense relative to that of the cortical gray matter on the same MRI. Peritumoral brain edema (PTBE) was also evaluated on T2-weighted MRI, and the extent of PTBE was assessed by calculation of the edema index (EI). The EI was calculated in this study according to the methodology previously described (13).

In order to further reflect the association between meningioma and hemorrhage, a new bleeding classification system of meningiomas was proposed and the 19 cases were correspondingly divided into three subgroups (Fig. 2): Type I bleeding was defined as the hemorrhage being purely found in the tumor (group 1); type II bleeding referred to a purely extratumoral hemorrhage, and the hemorrhage may be found in the peritumoral, subdural, subarachnoid or/and intracerebral spaces (group 2); and type III bleeding manifested as both intra-and extratumoral hemorrhages (group 3).

Treatment and prognostic assessment. Hematoma evacuation and a macroscopically complete resection of the tumor were planned for completion in one stage for all patients. The treatment strategy was performed according to the clinical status of the patients and their radiological results. The Simpson resection

Table I. Clinical features of 19meningiomas with hemorrhagic onset.

Case no.	Age, years	Sex	Symptoms	Tumor location	Bleeding type	Tumor subtype	Tumor size, mm	Resection grade	Signal intensity	Outcome
1	59	F	Headache/hemiparesis/aphasia	Convexity	I	Fibrous	65	I	Isointense	Alive/hemiparesis/no tumor recurrence
2	45	M	Headache/nausea/vomiting	Parasagital	I	Atypical	39	II	Hyperintense	Alive/tumor recurrence
3	41	M	Headache/nausea	Convexity	I	Meningothelial	22	I	Hyperintense	Alive/no tumor recurrence
4	41	M	Headache/hemiparesis	Convexity	I	Meningothelial	73	I	Hyperintense	Alive/no tumor recurrence
5	46	F	Headache	Parasagital	I	Microcystic	31	III	Hyperintense	Alive/no tumor recurrence
6	56	F	Headache/epilepsy	Convexity	I	Atypical	25	I	Isointense	Alive/no tumor recurrence
7	71	F	Headache/nausea	Middle skull base	I	Angiomatous	53	IV	Hyperintense	Alive/no tumor progression
8	63	M	Headache/vertigo/facial paralysis	Cerebellopontine angle	I	Fibrous	25	II	Hypointense	Alive/facial paralysis/no tumor recurrence
9	57	F	Headache/nausea	Convexity	II	Fibrous	43	I	Isointense	Alive/no tumor recurrence
10	71	M	Headache/drowsiness/ hemiparesis	Convexity	II	Malignant	57	I	Hyperintense	Alive/hemiparesis/no tumor recurrence
11	46	F	Headache	Parasagital	II	Angiomatous	21	II	Hyperintense	Alive/no tumor recurrence
12	71	M	Coma/epilepsy	Anterior skull base	II	Atypical	68	III	/	Alive/epilepsy/tumor recurrence
13	53	F	Headache/nausea/vomiting	Parafalx	II	Psammomatous	51	I	Hypointense	Alive/no tumor recurrence
14	19	M	Headache/drowsiness	Convexity	III	Meningothelial	45	I	Hyperintense	Alive/no tumor recurrence
15	79	M	Coma	Parasagital	III	Malignant	68	I	/	Died
16	51	F	Headache/drowsiness/ hemidysesthesia	Convexity	III	Transitional	52	I	Hyperintense	Alive/no tumor recurrence
17	53	F	Headache/drowsy/hemiparesis	Convexity	III	Angiomatous	55	I	Hyperintense	Alive/no tumor recurrence
18	64	M	Headache/hemiparesis	Parasagital	III	Fibrous	41	II	Isointense	Alive/no tumor recurrence
19	39	F	Headache/nausea/vomiting	Parafalx	III	Secretory	31	I	Hyperintense	Alive/no tumor recurrence

F, female; M, male.

Table II. Differences in sex ratio, the occurrence rate of hyperintensity on T2-weighted images, the occurrence rate of PTBE and the proportion of WHO grade I tumors among the four study groups.

	Hemorrhagic groups				
Characteristic	Group 1 (n=8)	Group 2 (n=5)	Group 3 (n=6)	Group 4[a] (n=20)	P-value
Sex					0.3429
Male	4	2	3	7	
Female	4	3	3	13	
Intensity on T2-weighted images					0.5333
Hyperintensity	5	2	4	12	
Isointensity and hypointensity	3	2	1	8	
PTBE					0.0244
Occurrence	4	4	5	8	
None	4	0	0	12	
WHO grade					0.7781
I	6	3	5	16	
II and III	2	2	1	4	

[a]Control group. WHO, World Health Organization; PTBE, peritumoral brain edema.

grade classification was used to evaluate the extent of resection on the basis of the surgical reports and the postoperative MRI within 72 h of surgery. Pathological sections of these tumors were reviewed by two independent pathologists under light microscopy, and the diagnosis was reconfirmed according to the WHO Classification of Tumors of the Central Nervous System 2016 (1). Follow-up data were collected from clinical visits and telephone interviews, with a mean follow-up time of 48.8 months [standard deviation (SD), 35.13; range, 3-125 months]. The postoperative status of the patient was investigated by physical examination and enhanced MRI. Radiological and functional assessments were usually performed preoperatively, at discharge, at 6 months postoperatively and annually thereafter. According to the Glasgow Outcome Scale (GOS; 1,2), clinical outcomes were graded from GOS 1 to 5; a good outcome was classified as GOS 4 and 5, and a poor outcome as GOS 1 to 3.

Statistical analysis. All continuous data are expressed as the mean ± SD. Statistical analysis was performed with the SAS system (version 8.1; SAS Institute, Inc.), while the statistical images were drawn using R software (version 3.5.3; R core team). Patient age, EI and tumor size among the four groups were compared using one-way analysis of variance followed by the Tukey-Kramer post-hoc test. Qualitative data, including sex ratio, the occurrence rate of hyperintensity on T2-weighted images, the occurrence rate of PTBE and the proportion of WHO Grade I tumors, were compared using Fisher's exact test. $P<0.05$ was considered to indicate a statistically significant difference.

Results

Clinical features. Of the 649 meningioma patients treated, 19 (2.9%) patients presented with hemorrhagic onset. These 19 cases had complete medical records and were included in this study. The clinical data for these cases are summarized in Table I. There were 9 males and 10 females, yielding a male-to-female ratio of 0.9:1. There was no significant difference in the clinical factor of sex ratio among these groups ($P>0.05$; Table II). The confirmed age at diagnosis ranged from 19 to 79 years old, and the mean age was 55±14.6 years old. The mean age exhibited no statistical difference among the four groups (Fig. 3; $F=0.2401$; $P>0.05$). All the patients experienced a stroke-like episode characterized by the sudden onset of acute headache, nausea and vomiting, vertigo, epileptic seizures, hemiparesis and/or altered consciousness. The above hemorrhagic symptoms were the first clinical presentations for 14 patients (73.7%). In total, 5 patients (26.3%) had initial symptoms such as mild headache, dizziness, mental disturbance or limb weakness before bleeding events, and the hemorrhagic event aggravated the initial symptoms or resulted in new symptoms. In addition, no patients with evidence of bleeding tendency and no other predisposing factors for hemorrhage were found.

Radiological characteristics. All 19 patients had preoperative CT scans, 17 patients had preoperative MRI and 7 patients had preoperative CTA according to the PACS database. Preoperative MRI was not performed in 2 cases with respective type II and type III bleeding due to severe symptoms. All patients underwent postoperative CT within 24 hand MRI scans within 72 h of surgery. Preoperative CT and MRI generally gave evidence of well-defined, dense, contoured extra-axial masses displacing the adjacent brain and acute or subacute hemorrhage associated with masses. Abnormal blood vessels, such as aneurysms or arteriovenous malformations, were not detected on CTA. According to the new bleeding classification, 8 masses manifested with type I bleeding (Fig. 4), 5 masses presented with type II bleeding (Fig. 5) and 6 masses exhibited type III

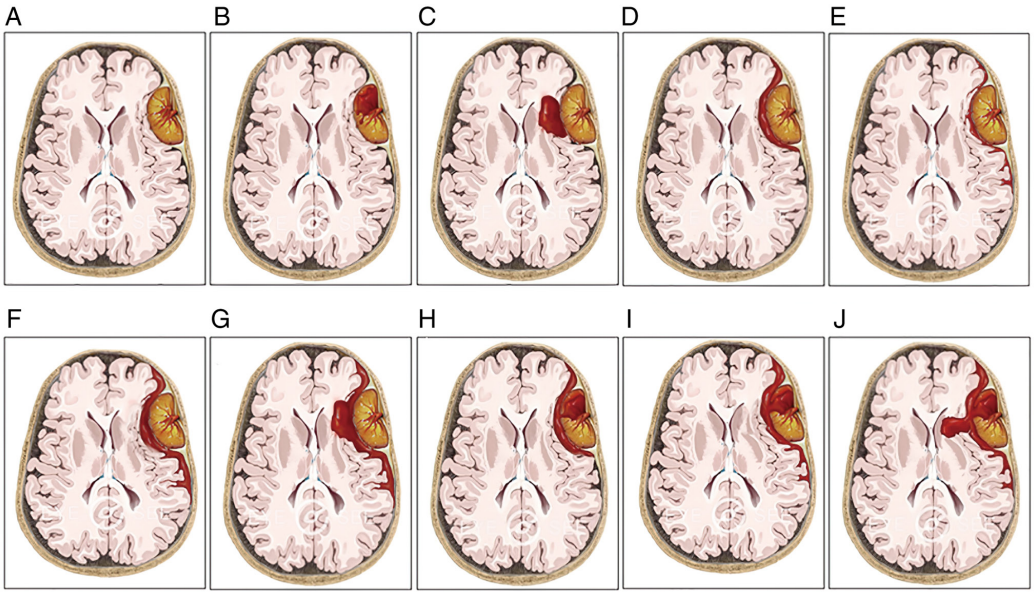

Figure 2. Illustration of different types of spontaneous hemorrhage from meningiomas. (A) A meningioma located in left temporal region. (B) The first bleeding type showing a purely intratumoral hemorrhage. (C-G) The second bleeding type showing a purely extratumoral hemorrhage, which could be located in (C) the peritumoral brain parenchyma, (D) subdural space, (E) subarachnoid space, (F) subdural space along with subarachnoid space or (G) all of the above regions. (H-J) The third bleeding type showing a combined intratumoral hemorrhage and extratumoral hemorrhage, where the extratumoral hemorrhage originated from intratumoral bleeding and the intratumoral bleeding could extend into (H) the subdural space, (I) subarachnoid space or (J) all of the above regions.

bleeding (Fig. 6). Moreover, the type I bleeding could break through the tumor and result in type III bleeding.

On MRI with gadolinium enhancement, the masses with a dural base showed moderate to strong enhancement except for the portion representing the hemorrhage. All cases in group 2 showed homogenous enhancement, while the other cases showed heterogeneous enhancement. A total of 4 masses in group 3 (80%), 5 masses in group 1 (62.5%) and 2 masses in group 2 (50%) presented as hyperintense on T2-weighted images. Although the occurrence rate of hyperintensity on T2-weighted images was not significantly different among the four groups (P>0.05; Table II), the patients in group 3 had the highest rate.

All masses in groups 2 and 3 showed PTBE on T2-weighted images; 4 masses in group 1 (50.0%) showed PTBE on T2-weighted images, and the occurrence rate was significantly different among the four groups (P<0.05; Table II). The EI was 3.12±0.97 in group 3 and 2.84±0.59 in group 2, which were both significantly higher than those in groups 1 and 4 (P<0.05; Fig. 7). The EI was not significantly different between groups 3 and 2 (P>0.05); there was also no statistical difference between groups 1 and 4 (P>0.05). The hemorrhagic masses were located at the convexity in 9 patients (47.4%), in the parasagittal areas in 5 patients (26.3%), in the parafalx in 2 patients (10.5%), at the skull base in 2 patients (10.5%) and in the cerebellopontine angle in 1 patient (5.3%); the convexity and parasagittal areas were the two most common sites for hemorrhagic meningiomas. The tumor size ranged from 2.1 to 7.3 cm (mean, 4.6±1.7 cm), with 10 tumors (52.6%) <5.0 cm and 9 tumors (47.4%) >5.0 cm in diameter. There was no statistical difference with respect to the tumor size among the four groups (F=0.4163; P>0.05; Fig. 8).

Intraoperative findings. The symptoms in most patients of group 1 (7/8 cases; 87.5%) were mild and their clinical statuses were stable, so selective surgeries were performed following adequate preoperative evaluations. The symptoms of the patients in group 2 were sometimes mild (3/5 cases; 60.0%) and sometimes moderate to severe (2/5 cases; 40.0%), so emergency or early surgeries were chosen according to the clinical status of the patient and their radiological results. Almost all patients (5/6 cases; 83.3%) in group 3 had moderate to severe symptoms, and emergency surgery was performed in these patients after the necessary examinations.

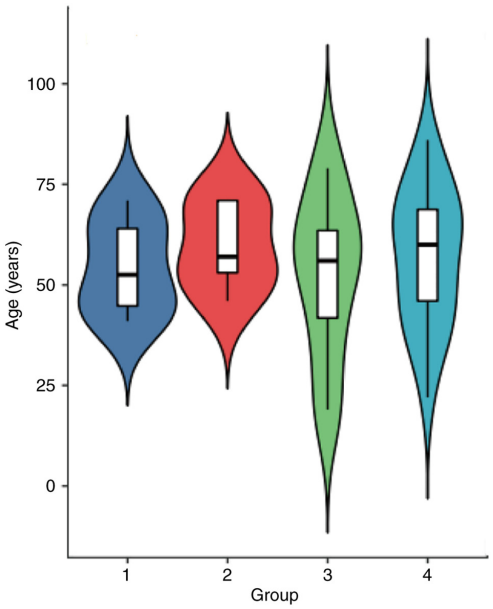

Figure 3. Difference in mean age among the four groups. The mean age was 54±11.8 years in group 1, 60±11.1 years in group 2, 52±21.1 years in group 3 and 57±17.2 years in group 4. The mean age exhibited no statistically significant difference among the four groups (P>0.05).

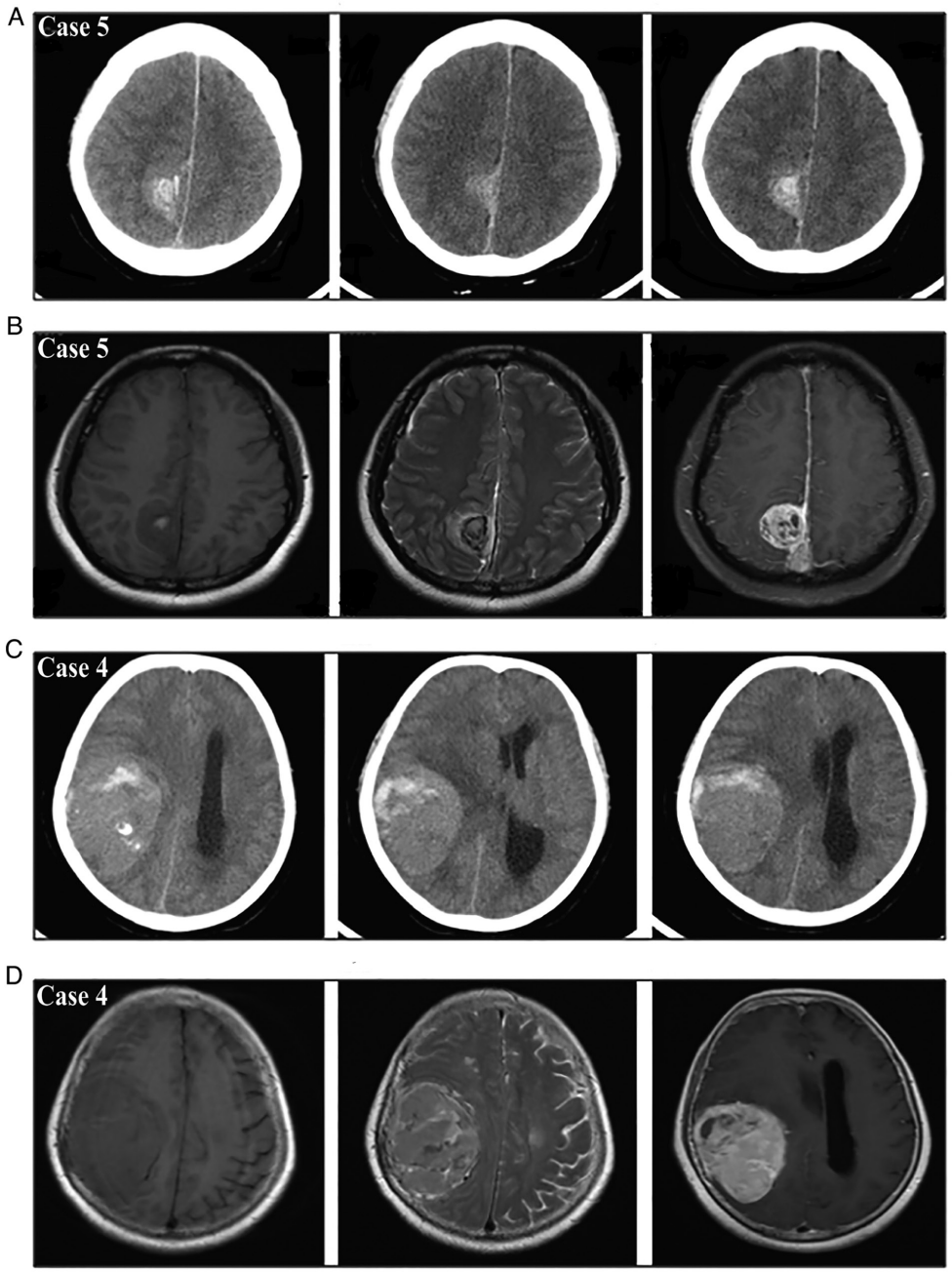

Figure 4. Radiological findings for (A and B) representative case 5 and (C and D) case 4 with solitary intratumoral hemorrhage. Preoperative brain computed tomography showing (A) a round iso-dense mass in the right parasagittal area of case 5 and (C) a large mass with high density in the right parietal region of case 4, with multi-foci of hyperdensity suggestive of intratumoral hemorrhage. Brain magnetic resonance imaging revealing (B) a dural-based mass in the right parasagittal area of case 5 and (D) a dural-based mass in the right parietal region of case 4, with heterogeneous enhancement on contrast. The peripheral area of the two masses was significantly enhanced, and the central non-enhancing area suggested acute intratumoral bleeding.

Hematoma evacuation and a macroscopically complete resection of the tumor were performed in one stage for all but 1 patient. During the operation, a solid extra parenchymal tumor attached to the dura and tumor-associated hemorrhage were found in every case; the surface of the brain contacting the tumor was intact in 12 cases and invaded by the tumor in 7 cases (2 in group1; 2 in group 2 and 3 in group 3). All tumors in group 3 (100.0%), 6 cases (75.0%) in group 1 and 2 cases (40.0%) in group 2 had a soft consistency. Of the masses in group 1, 8 had only intratumoral hemorrhage and necrotic tumor tissue was usually found. In group 2, 5 masses were only surrounded by extratumoral hemorrhage involving peritumoral, subarachnoid, subdural and/or intracerebral hemorrhage. The remaining 6 masses in group 3 included both intratumoral hemorrhage and extratumoral hemorrhage, and normal vessels with invasion by the tumor were found in 2 masses. Furthermore, tumor rupture was found in group 3 tumors and the intratumoral hemorrhage was connected with extratumoral hemorrhage. These operative results were consistent with the corresponding radiological presentations and the new bleeding classification (Fig. 9). Simpson classification of the hemorrhagic masses resulted in 63.2% grade I (n=12), 21.1% grade II (n=4), 10.5% grade III (n=2) and 5.3% grade IV (n=1) classifications.

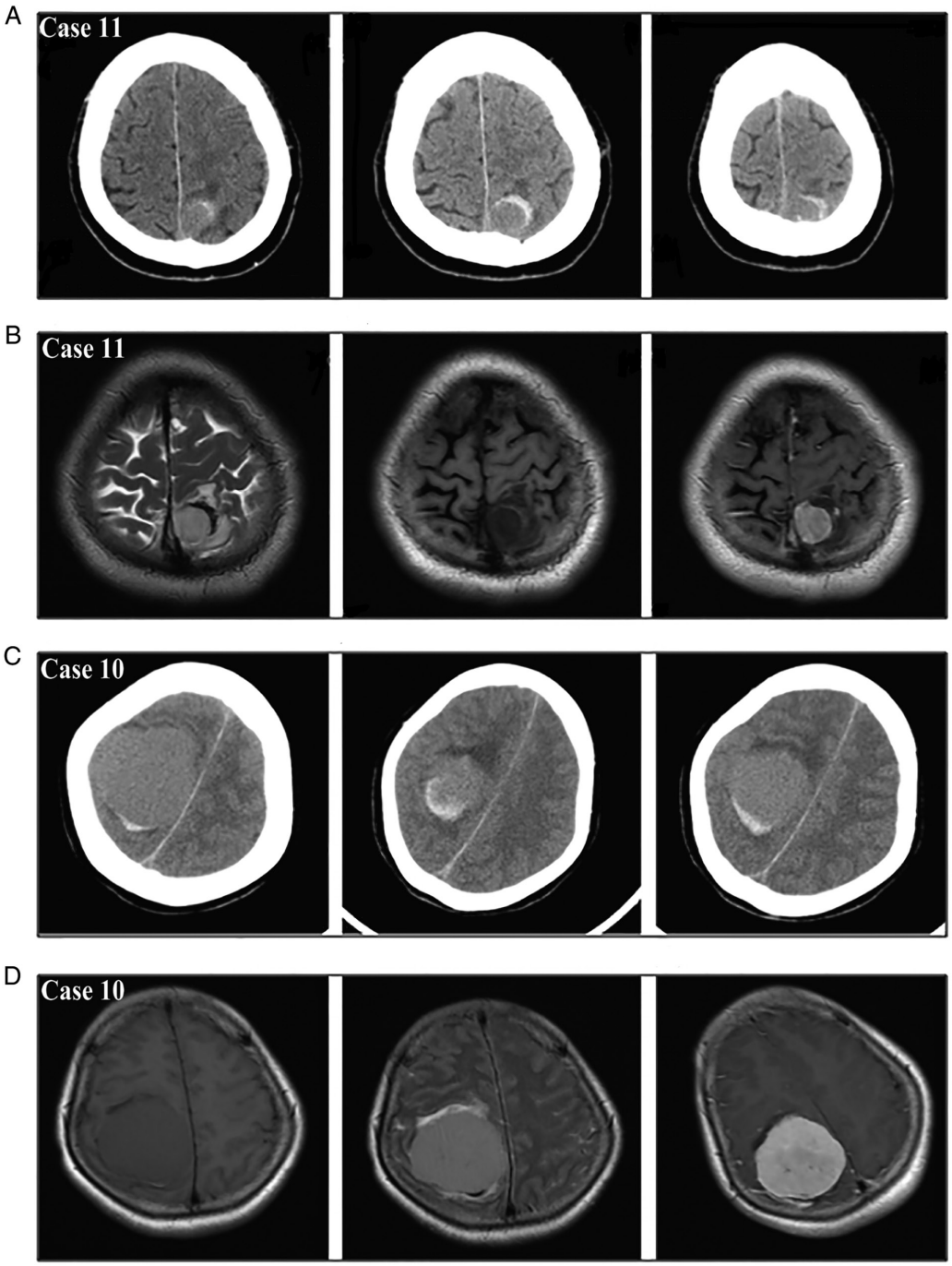

Figure 5. Neuroimaging findings for (A and B) representative case 11 and (C and D) case 10 with purely extratumoral hemorrhage. Preoperative brain computed tomography showing (A) a round iso-dense extra-brain mass with peritumoral hemorrhage in the left parasagittal region of case 11 and (C) a round iso-dense extra-brain mass with peritumoral hemorrhage in the right parietal area of case 10. Magnetic resonance imaging further showing (B) an extra-brain mass in the left parasagittal region of case 11 and (D) an extra-brain mass in the right parietal area of case 10 respectively, which were homogeneously enhanced and had acute peritumoral hematoma.

Pathological and surgical outcomes. The diagnosis of meningioma was established according to standard histopathological criteria following the WHO system. The identified tumors were subtyped as fibrous (n=4), meningothelial (n=3), atypical (n=3), angiomatous (n=2), malignant (n=2), microcystic (n=2), transitional (n=1), psammomatous (n=1) and secretory (n=1). Correspondingly, 14 cases (73.7%) were WHO Grade I tumors, 3 cases (15.8%) were WHO Grade II tumors and 2 cases (10.5%) were WHO Grade III tumors. In group 4, 16 cases (80.0%) were WHO Grade I tumors, 2 cases (10.0%) were WHO Grade II tumors and 2 cases (10.0%) were WHO Grade III tumors. There was no significant difference in the proportion of WHO Grade I tumors between the hemorrhagic group and the control group ($P>0.05$; Table II). Although a statistical analysis was not performed among the four groups in this study due to the limited numbers of cases in the subgroups, the aforementioned different pathological subtypes and WHO Grade tumors were almost evenly distributed in each group. Endothelial hyperplasia, thin-walled dilated vessels, venous obstruction and tumor infarction were observed more frequently on microscopic

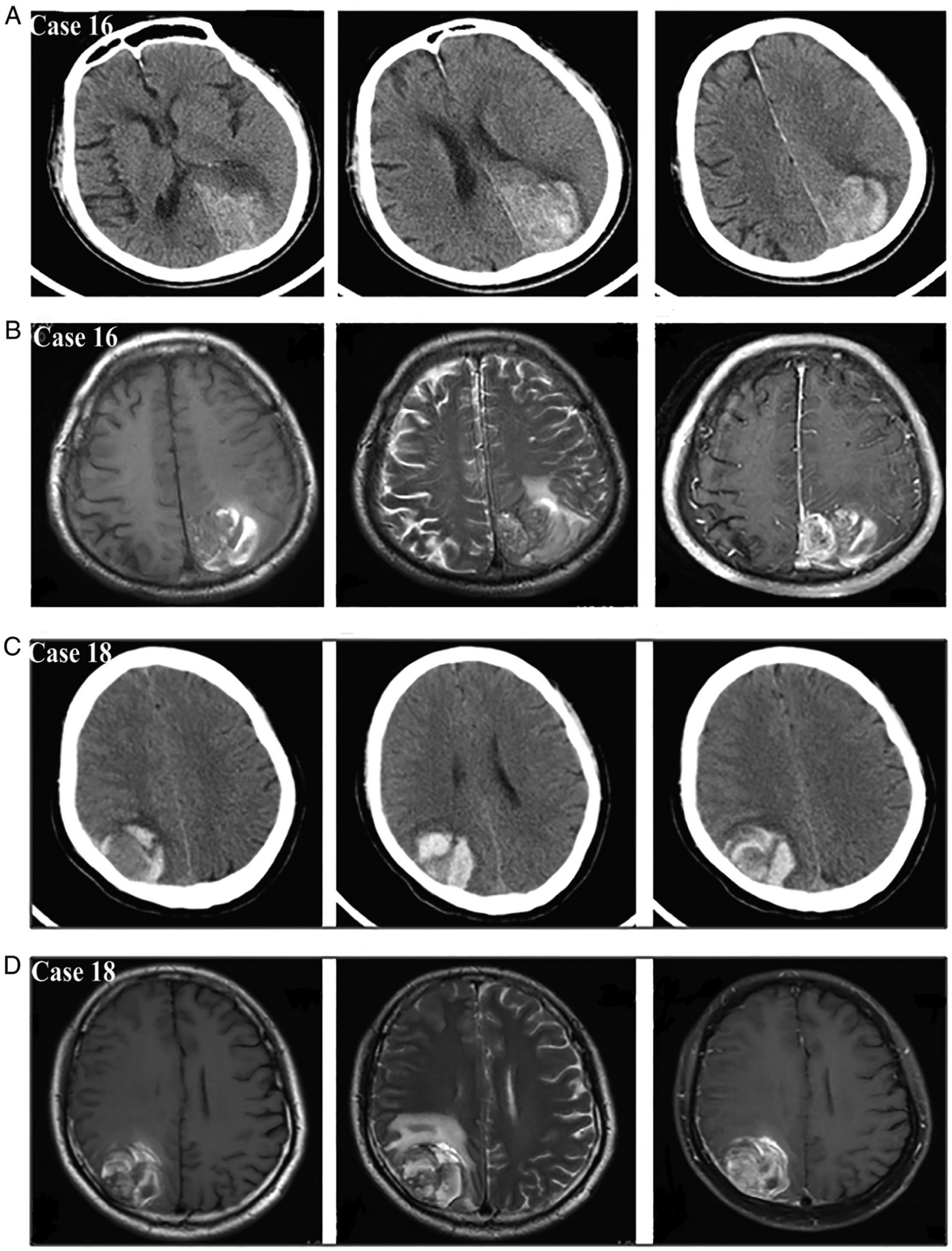

Figure 6. Neuroimaging outcomes of (A and B) representative case 18 and (C and D) case 16 with combined intra/extratumoral hemorrhage. Brain computed tomography displaying (A) an extra-brain mass lesion in the left parasagital region of case 16 and (C) an extra-brain mass lesion in the right parietal-occipital area of case 18, which displaced the adjacent brain and had acute bleeding involving intratumoral hemorrhage, peritumoral hematoma, subarachnoid hemorrhage and subdural hemorrhage. Magnetic resonance imaging further showing (B) an extra-brain mass lesion in the left parasagital region of case 16 and (D) an extra-brain mass lesion the right parietal-occipital area of case 18, which were heterogeneously enhanced, and significant brain edema was visible in the adjacent brain parenchyma.

examination in patients in groups 1 and 3. Radiotherapy was administered as an adjuvant treatment in 3 patients (15.8%) after initial surgery for 2 malignant cases and 1 case of grade IV resection. The postoperative recoveries of these patients were all uneventful; 1 patient died from a cardiovascular event 7 years after surgery and the other patients are currently alive. However, the tumors in 2 patients recurred within a follow-up period of 2 and 5 years respectively, and these individuals underwent a second surgery.

Discussion

Malignant brain tumors, including glioblastoma, metastatic brain tumors and melanoma, may occasionally lead to

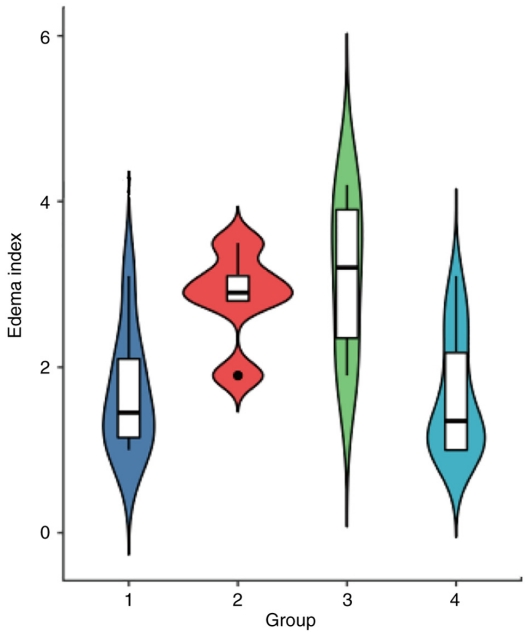

Figure 7. Difference in EI among the four groups. The EI was 1.68±0.97 in group 1, 2.84±0.59 in group 2, 3.12±0.97 in group 3 and 1.65±0.71 in group 4. The EI values in groups 3 and 2 were significantly higher than those in groups 1 and 4 (P<0.05). The EI values between groups 3 and 2 exhibited no significant difference (P>0.05) and there was also no statistically significant difference between groups 1 and 4 (P>0.05). EI, edema index.

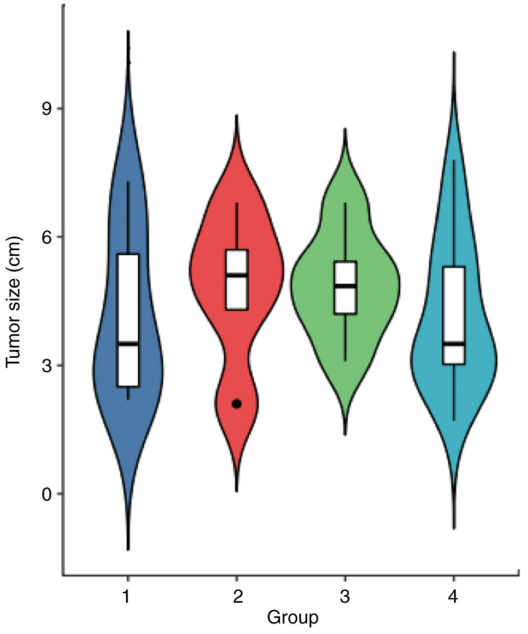

Figure 8. Difference in tumor size among the four groups. The tumor size was 4.2±1.97 in group 1, 4.8±1.76 in group 2, 4.9±1.27 in group 3, and 4.2±1.71 in group 4. No statistically significant difference was detected with respect to the tumor size among the four groups (P>0.05).

intracranial hemorrhage (14). However, spontaneous hemorrhage as an initial presentation for meningioma, even though reported, is less frequent, although they are usually vascular tumors (11). As this condition is rare, the determination of causative factors for the hemorrhage is difficult, and it is not as easy to understand the mechanisms of spontaneous hemorrhage (11,15,16). Cases of spontaneous hemorrhage in meningioma have been sporadically reported, however, and a number of clinical features of the condition have been characterized (4-7,10,11,16-18).

Although CT is the reference standard for the detection of hemorrhage, meningioma with intracranial hemorrhage is not always easy to distinguish on CT, and multi-model radiological examinations are needed (11). Brain CT and MRI usually display dense, well-defined, contoured extra-axial masses that displace the adjacent brain along with acute or subacute hemorrhage (3,6). The site of the hematoma does not typically exhibit hypertensive intracerebral bleeding, and it is usually away from the center of the cerebral parenchyma (3). Masses with a dural base show moderate to strong enhancement on MRI with gadolinium enhancement, with the exception of the region representing the hemorrhage. Previous reports have provided some information on the signal intensity on MRI and have indicated hyperintensity on T2-weighted MRI as a risk factor of meningioma bleeding (16,18); Specifically, Niiro *et al* (16) found that all hemorrhagic meningiomas were remarkably hyperintense on T2-weighted MRI in their study and Lin and Chen (18) reported 1 case with the same above radiological feature. Comparing type II bleeding, this finding of hyperintensity on T2-weighted MRI was found more frequently in the patients with type I and type III bleeding in the present study. While the implication of this hyperintensity has not been fully established, some cases with intratumoral hemorrhage may be attributed to the soft consistency of the tumor (10,16,19). In type III bleeding cases, it is hypothesized that the hemorrhage may have begun within the tumor and then progressed, resulting in blood in the peritumoral areas and even encroachment of the blood in the brain parenchyma (10).

A previous study found that an increased tendency for bleeding was associated with two age groups (<30 years and >70 years), convexity and intraventricular locations, and fibrous meningiomas (2); however, the most frequent localizations were the convexity and parasagittal areas in the present study, and the pathological outcomes of these tumors were in line with the histopathological distribution of meningiomas in general (1). Although the patients with type II and type III bleeding had significant PTBE comparing with the control group in the present study, and PTBE might be an indicator for certain bleeding types, PTBE could be as a result of the tumor hemorrhage. The exact mechanism of the hemorrhage from meningiomas is not fully understood; however, several pathological mechanisms have been considered in the explanation of this rare condition. The proposed mechanisms include weakened blood vessel rupture, endothelial proliferation and resultant vascular occlusion, direct tumor cell invasion of the vasculature, bioactive substance accumulation in the tumor, concomitant vascular malformation or aneurysm, stretching and rupture of subdural bridging veins, venous compression induced by tumor growth and associated with peritumoral edema, and infarction due to rapid tumor growth (2-6,8-11,16-18). In addition, two specific types of blood vessels, differentiated and undifferentiated vessels, were found in our prior study; undifferentiated blood vessels contribute to a fragile tumor vasculature, which a precipitating event may disrupt, thus resulting in a spontaneous hemorrhage (11).

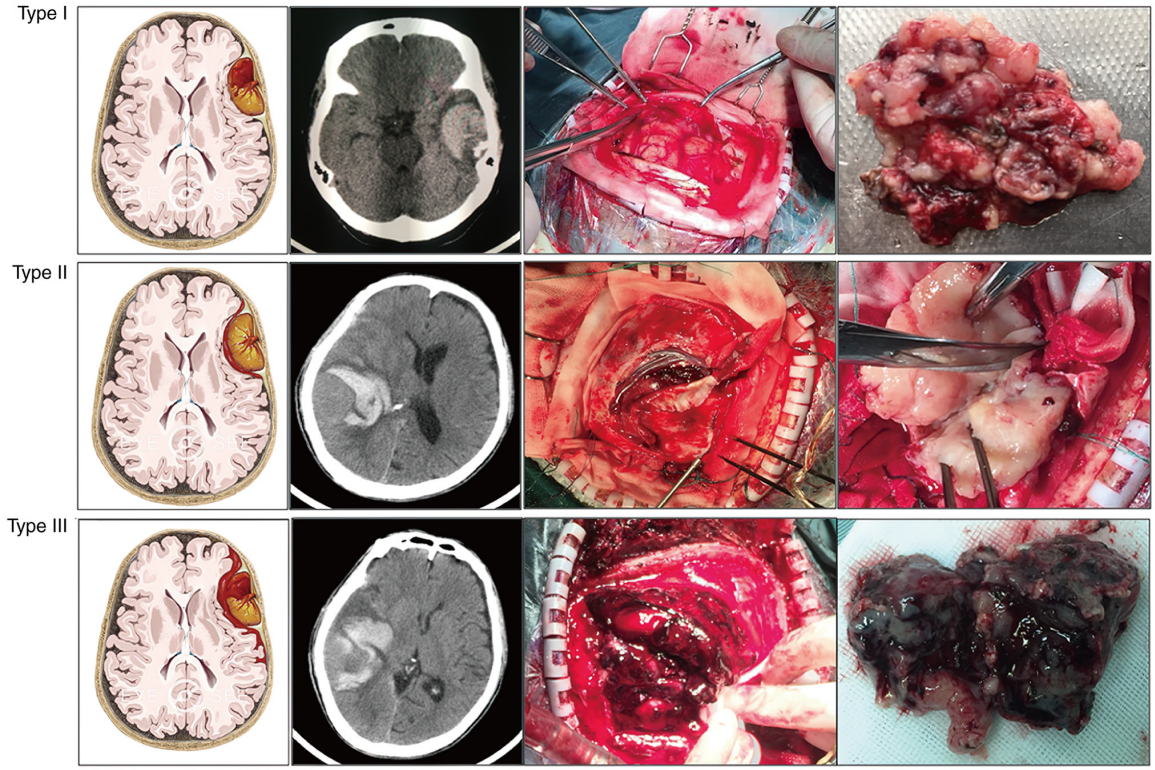

Figure 9. Operative findings associated with corresponding radiological results in different bleeding types. For type I bleeding, the hemorrhage was purely found in the tumor according to the preoperative CT and intraoperatively resected tumor; for type II bleeding, the hemorrhage was purely located in the extra-tumoral region according to the preoperative CT and intraoperatively resected tumor; for type III bleeding, the hemorrhage could be found both in intra- and extra-tumoral regions according to the preoperative CT and intraoperatively resected tumor.

The aforementioned proposed mechanisms were mainly based on reported cases. The majority of these were recorded according to the site of hemorrhage, such as the cases of subarachnoid hemorrhage, intracerebral hematoma, intra-tumoral hemorrhage or subdural hematoma (7-12,18-20). This description cannot reflect the association between meningioma and hemorrhage; moreover, it contributes little to guiding the clinical diagnosis and treatment. Correlating prior reports of such cases with the present cases, a new bleeding classification of meningiomas was proposed in the present study on the basis of the anatomical relationship between meningioma and hematoma. This distinct type of hemorrhage from meningioma was separated into three bleeding patterns: Purely intratumoral hemorrhage, purely extratumoral hemorrhage, and combined intratumoral and extratumoral hemorrhage. According to the intraoperative findings of tumor fragmentation and intratumoral hemorrhage continuous with extratumoral hemorrhage in group 3 tumors, it could be inferred that this type of combined hemorrhage arose from intratumoral bleeding with extension into the surrounding intracranial spaces.

Apart from showing the direct relationship between meningioma and hemorrhage, this new bleeding classification makes it easier to understand the possible mechanism of meningioma hemorrhage. For example, subdural bridging veins may stretch and rupture, which may explain the purely extratumoral hemorrhage involved in subdural hematoma and subarachnoid hemorrhage cases (20). The rupture of weakened or undifferentiated blood vessels is typically associated with a purely intratumoral hemorrhage (11,18). The extratumoral hemorrhage should be secondary to intratumoral bleeding in the third type of hemorrhage (10,11). Infarction and necrosis owing to rapid growth of the tumor could explain the third type of hemorrhage (10,21). Traumatic head injury is unlikely to be a causative factor in cases with purely intratumoral hemorrhage (11,22). In syncytial meningiomas, the bleeding is likely associated with the release of intratumoral vasoactive substances, such as histamine, which could induce vasodilatation and result in the purely intratumoral hemorrhage (23,24). Venous hypertension due to tumor compression of the surrounding veins may also lead to the purely extratumoral hemorrhage (13,25). In addition, cerebral edema and venous obstruction could cause infarction, eventual rupture of the peritumoral vessel and then induce the purely extratumoral hemorrhage (13). Nevertheless, any one of the aforementioned mechanisms alone cannot explain the various bleeding patterns and the mechanism might vary in these different bleeding patterns.

Emergency or early one-stage total removal of the hemorrhagic meningioma and hematoma is the main treatment of choice (2-4,11). In general, the risks of meningioma hemorrhage usually vary with the amount of bleeding, the location of bleeding, the size of tumor or the location of tumor. There is no difference in the therapeutic method for the different bleeding patterns; however, this bleeding classification system could offer some implications for the treatment strategy. According to the review of prior cases reported in the literature (4-8,11,17-21,25,26) and the cases in the present study,

the symptoms in most patients with the first bleeding type were usually mild and their clinical statuses were generally stable, and early or selective surgery could be performed following adequate preoperative evaluations. The symptoms in patients with the second bleeding type were at times mild and in other cases moderate to severe, so emergency or early surgery should be chosen according to the clinical status of the patient and their corresponding radiological results. Almost all patients with the third bleeding type had moderate to severe symptoms, and these patients usually need emergency surgery after necessary examinations. Therefore, the impact on patients of meningioma hemorrhage is closely correlated with hemorrhagic type. Recognizing these facts and consequent treatment changes may result in an improvement of patient outcome.

The main limitation of this study, especially regarding the bleeding subgroups, is the small sample size and lack of integrative data analysis among subgroups. Although the data were preliminary and the bleeding mechanisms were also not proven in the present study, the study highlighted the new bleeding classification of meningiomas based on the anatomical relationship between meningioma and hematoma. Moreover, sharing our opinion and typical radiographic images may help improve awareness of this specific condition. Future research will focus on the issue of collecting more cases to explore the findings in this study.

In summary, although hemorrhagic meningiomas are fairly uncommon, they represent a distinct clinical entity. The following three bleeding patterns were proposed in the present study: Purely intratumoral hemorrhage, purely extratumoral hemorrhage, and combined intratumoral and extratumoral hemorrhage. Patients with different bleeding patterns may exhibit different clinical features and radiological outcomes. This bleeding classification makes it easier to understand the possible hemorrhagic mechanisms and aid in the early diagnosis of this condition and in the selection of a treatment strategy.

Acknowledgements

Not applicable.

Funding

The clinical data collection in this study was supported by a grant from the Natural Science Foundation of Ningbo (grant no. 2019A610283) and NINGBO Medical and Health Leading Academic Discipline Project (grant no. 2022-F04). The figure design and case follow-up in this study were supported by grants from the Ningbo Municipal Bureau of Science and Technology (grant nos. 2021S172 and 2014C50089).

Availability of data and materials

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

Authors' contributions

ZRX, HCW and YLT, interpreted the data prepared the images and wrote the manuscript. HCW contributed to the conception and drafted the manuscript. SWL and BDW contributed to the acquisition and analysis of the data and figure design. MSC and HCW designed the work, revised and edited the manuscript for important intellectual content. HCW, BDW and MSC confirm the authenticity of all raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

Approval of the retrospective study was obtained from the Research Ethics Committee of the Li Hui Li Hospital of Ningbo University (Ningbo, China). Written informed consent was obtained from all the participants.

Patient consent for publication

All patients provided the consent for publication of images.

Competing interests

The authors declare that they have no competing interests.

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