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Characteristic image on cerebral angiography in ruptured blood blister-like aneurysms

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ABSTRACT

Objective: To evaluate the static and dynamic features of blood blister-like aneurysms (BBAs) using cerebral angiography to identify characteristic features to improve the diagnosis of these uncommon aneurysms.
Methods: Digital subtraction angiography (DSA) images were compared between patients with BBAs (n = 12, group A) and patients with unruptured paraclinoid aneurysms ≤ 5 mm in size treated by endovascular procedures (n = 12, group B). DSA images were assessed for irregularities in the diameter of the parent artery and delayed inflow and outflow of contrast medium in the aneurysm. Enlargement of the aneurysm and morphological changes from the first assessment were also evaluated in patients with BBAs.
Results: Compared to the group B, group A had a higher proportion of irregular vessel diameter ($p = 0.013$) and the delayed contrast medium outflow ($p = 0.014$). As well, stagnation of contrast medium along the aneurysm wall was a characteristic finding of BBAs, even for small aneurysms.
Conclusion: Irregular morphological features of the parent artery and delayed contrast medium outflow as characteristic findings of ruptured BBAs may improve the diagnosis of these uncommon aneurysms, which remains challenging in practice.

1. Introduction

Blood blister-like aneurysms (BBAs) are relatively uncommon occurrences, accounting for 0.9–6.5 % of all internal carotid artery (ICA) aneurysms [1,2]. Pathologically, BBAs are considered dissecting aneurysms and are characterized by a hemispherical shape, small size, and broad neck [3–5]. BBAs are difficult to diagnosis and treat in clinical practice. On the diagnostic side, imaging changes of BBAs are subtle at onset, making diagnosis difficult, often resulting in delayed diagnosis, which can lead to significant poor patient outcomes. In terms of treatment, it has been reported that the vessel wall of BBAs is fragile and, thus, conventional neck clipping carries a high risk of intraoperative rupture [3,4]. Previous studies have reported static features of BBAs on computed tomography angiography (CTA) and digital subtraction angiography (DSA) images [2]. However, dynamic features of these aneurysms have not previously been described. Yet, dynamic features could improve diagnostic ability for BBAs when morphological changes are difficult to discern on static images. Accordingly, our aim in this retrospective study was to describe and compare static and dynamic characteristics of cerebral angiography images between patients diagnosed and treated for a BBA, based on the clinical course and imaging findings, and patients with unruptured paraclinoid aneurysms ≤5 mm in size treated by endovascular procedures.

2. Material and methods

2.1. Study design and patient selection

This was a retrospective analysis of patients with an aneurysm diagnosed as a BBA treated at our hospital or its affiliated institutions between 2008 and 2020. BBAs were comprehensively diagnosed by an expert neuro-interventionalist based on the following characteristics: ruptured and small aneurysm, non-bifurcated site of the ICA, aneurysm enlargement over time, irregular vessel wall, and young age. Basic information such as age, sex, and grading of SAH (Hunt and Hess grading system) was obtained from medical records, and 3D-CTA at onset and DSA at endovascular treatment were obtained from imaging databases at our institutions. Cases with insufficient DSA imaging data were

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excluded. Following screening, of the 18 eligible patients (18 BBAs) identified, 12 were included in the final analysis (group A). The comparison group (group B) consisted of 12 patients with unruptured paraclinoid aneurysms ≤5 mm treated by endovascular procedure at our institution between September 2015 and April 2020. All patients included had undergone CTA and DSA. For patients in group A, CTA was performed at the time of initial treatment and DSA on the same day or at a later date based on the suspicion of a BBA. We collected 2D-DSA and 3D-rotational angiography (3D-RA) data for all cases when DSA was performed.

In group A, aneurysms diagnosed as BBAs were located in non-branching sites and were not limited to the anterior and posterior walls of the ICA. In group B, unruptured paraclinoid aneurysms were located in the C2-C3 portion of Fischer classification [6], not including the posterior communicating artery, or non-branching aneurysms. In both groups, the maximum diameter of the aneurysm at the time of treatment was entered as the size of the aneurysm for analysis.

2.2. Imaging analysis

Fusiform dilation and the pearl-and-string sign are common vascular features of dissecting cerebral aneurysms [7]. As BBAs are considered dissecting aneurysms, these morphologic features were selected for evaluation. We classified the morphology of irregular vessel in the ICA into three types, based on CTA, 2D-DSA, and 3D-RA imaging, as follows (Fig. 1): type A, local narrowing of the vessel diameter near the aneurysm; type B, fusiform-like dilation; and type C, no change in the vessel diameter. Among these, types A and B were considered to have vascular irregularities. The flow irregularities were evaluated from the dynamics of contrast medium flow, using 2D-DSA of the ICA at the time of endovascular treatment. Delayed inflow was defined by an apparent difference in time-to-peak contrast medium staining. Delayed outflow was defined by an apparent difference in time between the washout of contrast medium in the aneurysm and in the parent artery. The presence or absence of a delay in inflow and/or outflow was subjectively evaluated. Dynamic flow was evaluated in both groups A and B. Morphological changes and findings of aneurysm enlargement from the initial examination were evaluated in group A only, using CTA, 2D-DSA, and 3D-RA.

Images were evaluated by 3 neurosurgeons. One of these, an author, also extracted patients' information for analysis. The other 2 neurosurgeons, who were blinded to patient data, evaluated the images. All 3 assessors described the presence/absence of the three types of vascular irregularities and delays in the inflow/outflow of contrast medium.

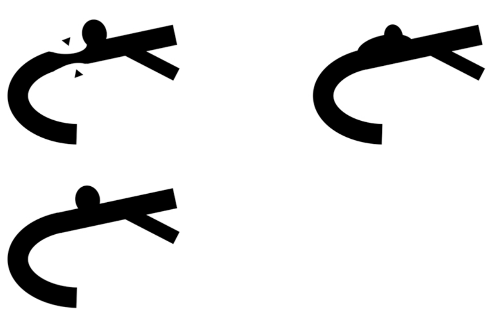

Fig. 1. The site of the aneurysm was not restricted to the anterior and posterior walls of the internal carotid artery. Three types of aneurysms were evaluated, as follows: (A) type A, showing irregularity in the diameter of the parent artery and focal narrowing before and after the aneurysm. (black arrow heads); (B) type B, also showing irregularities in the diameter of the parent artery, with findings of fusiform dilatation of the parent artery; and (C) type C, for which there were no obvious findings of vessel diameter irregularities in the parent artery.

2.3. Statistical analysis

For between-group comparisons, the Mann–Whitney *U* test was used to compare the median (inter-quartile range, IQR) for continuous variables and the chi-squared test or Fisher's exact test to compare proportions for categorical variables. Statistical significance was set at a p-value <0.05. The agreement rate for image assessment was evaluated using Fleiss's kappa. All statistical analyses were conducted using IBM SPSS version 27.0 (IBM Corp., Armonk, NY, USA).

2.4. Ethics statement

This study was approved by the Ethics Committee of our institution (No. 2020–0230) and affiliated participating institutions. Informed consent was obtained using an opt-out approach, with the information on institutions' web site.

3. Result

The inter-rater agreement in images was substantial ($\kappa = 0.795$ for the vascular irregularity types and $\kappa = 0.846$ for the presence/absence of delay in the inflow/outflow of contrast medium). The baseline characteristics and angiographic features of all patients are presented in Table 1. There were no differences in the distribution of age and sex between the two groups. However, the proportion of irregular vessel diameter (P = 0.013) and delayed outflow of contrast medium (P = 0.014) was higher in group A than in group B.

3.1. Image analysis of BBAs

The summary of findings for group A is presented in Table 2. Of the 12 BBAs included, findings of short-term aneurysm growth and/or shape change were identified in 10 (83.3 %), over a median period of 3.0 (IQR, 1–5) days. The 2 cases without a change in aneurysm shape or enlargement were treated on the day of assessment or the next.

Of the 10 patients with identified changes, 9 (75 %) presented two or more of the following findings: short-term aneurysm enlargement and/or morphological change, vascular irregularities of parent artery, and delayed contrast media inflow and outflow. We note that for one case (Case 11), none of these findings were observed.

3.2. Illustrative case

This was 60-year-old man (Case 10) who was diagnosed with a Hunt and Hess grade IV-SAH (subarachnoid hemorrhage). The CTA imaging performed on the day of onset revealed a fusiform enlargement of the

Table 1
Comparison between blood blister-like aneurysm (BBAs) and unruptured paraclinoid aneurysms.

	BBA (n = 12)	UPA (n = 12)	P value
Sex, female (%)	9 (75)	12 (100)	0.11
Age, median (IQR)	46.0 (41.3–57.3)	58.5 (46.8–62.0)	0.11
Aneurysm size, median (IQR)(mm)	3.8 (2.6–4.4)	4.6 (4.0–5.0)	0.046
Aneurysm enlargement and/or morphological change from initial examination, (%)	10 (83.3)	NA	NA
Category			
type A, (%)	2 (16.7)	0	
type B, (%)	6 (50)	2 (16.7)	
type C, (%)	4 (33.3)	10 (83.3)	0.013
Delay of contrast medium inflow, (%)	2 (16.7)	0	0.24
Delay of contrast medium outflow, (%)	7 (58.3)	1 (9)	0.014

NA; not applicable, IQR; inter-quartile range, BBA; blood blister-like aneurysms, UPA; unruptured paraclinoid aneurysms

Table 2
Summary of clinical and image findings for the 12 patients with blood blister-like aneurysms (BBAs, group A).

case number	age	sex	location of ICA	delay from onset to treatment	aneurysm enlargement and/or morphological change from initial examination	category of parent artery	delay of contrast medium inflow	delay of contrast medium outflow
1	39	F	AW	3	+	A	–	+
2	58	F	AW	5	+	B	–	+
3	48	F	PW	3	+	B	–	–
4	38	F	AW	5	+	C	–	+
5	38	F	PW	19	+	B	+	–
6	45	F	AW	1	+	C	–	–
7	74	F	AW	2	+	B	–	+
8	42	M	AW	3	+	C	–	+
9	47	F	PW	1	+	A	–	+
10	60	M	AW	8	+	B	+	+
11	57	F	AW	0	–	C	–	–
12	44	M	AW	1	–	B	–	–

F; female, M; Male, AW; anterior wall, PW; posterior wall, A; type A in Fig. 1, B; type B in Fig. 1, C; type C in Fig. 1, +; positive, -; negative, ICA; internal carotid artery

anterior wall of the right C2-segment of the ICA (Fig. 2A). The DSA imaging at the time of treatment performed eight days later showed obvious morphological changes and a bleb-like formation at the site of fusiform dilation (Fig. 2B, C). In the inflow of contrast medium, there was a clear contrast difference between the parent artery and the aneurysm (Fig. 2D). In the outflow of contrast medium, there was stagnation within the aneurysm, with the contrast medium principally accumulating at the margin of the aneurysm wall (Fig. 2E).

4. Discussion

Previous studies have largely focused on the treatment strategies for BBAs, with little emphasis on the characteristic imaging of BBAs. In this study, we investigated the morphological and contrast medium dynamic characteristics of ruptured BBAs diagnosed from the clinical course and initial imaging, based on DSA. Our findings indicate that irregularity of the parent artery and delayed outflow of contrast medium in the aneurysm were significant imaging findings for BBAs.

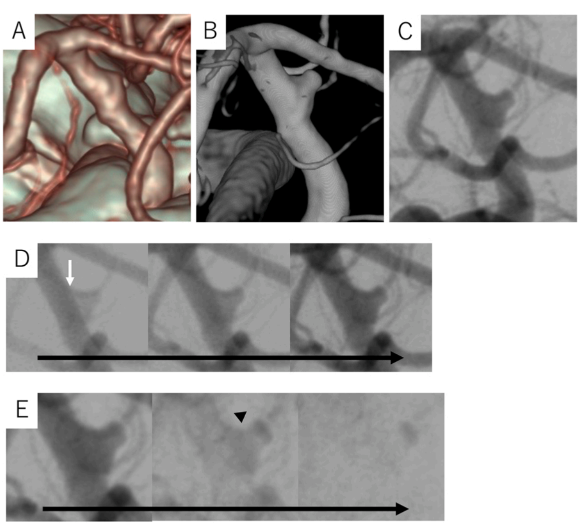

Fig. 2. Findings for case 10 as a representative case. (A) 3D-CT angiography acquired at the first visit, demonstrating a fusiform dilation of the ICA. (B,C) ICA angiogram at the time of treatment, 8 days after initial presentation, showing obvious morphological changes and a bleb-like formation at the fusiform dilatation. B was 3D-RA imaging and C was 2D-DSA imaging. (D) ICA angiogram showing delayed contrast medium inflow, with a clear contrast difference between the parent artery and the aneurysm (white arrow). (E) ICA angiogram showing delayed contrast medium outflow in the aneurysm, especially stagnation at the margin of the aneurysm wall (black arrow head). CT, computed tomography; ICA, internal carotid artery; RA, rotational angiography; DSA, digital subtraction angiography.

We discuss here DSA findings in terms of the histopathology of BBAs. Saccular type aneurysms are covered by intima but with a loss of the inner elastic lamina [8]. The intimal covering of the wall of the saccular aneurysm wall maintains the three-layered structure of the vascular structure. However, the lack of the internal elastic lamina, which is rich in elastic fibers, creates a fragile wall that results in the formation of an aneurysm [9,10]. Unlike the saccular type aneurysms, BBAs are considered dissecting aneurysms. However, this perspective is based on only a few pathological reports of BBAs and on valuable autopsy case. On autopsy, Ishikawa et al. [11] described a localized laceration of the intima and intimal elastic lamina at the site of BBA, with the site comprised only of normal adventitia and fibrous tissue. The BBA presented as an aneurysm-like shape in the dissection cavity.

Irregularity in the diameter of the parent artery is often described as a pearl-and-string sign in cerebral artery dissection. As such, observation of this vascular irregularity in our study was also accepted as a positive finding of arterial dissection. It has been reported that the majority of vascular irregularities in intracranial artery dissection are dilations at SAH onset [12]. In our study, dilations were observed in more than half of our cases, indicating that cases of SAH were likely included in our sample.

On contrast medium flow assessment, the BBAs in our study showed stagnation of contrast medium, even in small size and broad neck aneurysms. Contrast medium stagnation is rarely observed in small aneurysms in practice and was observed in only one case of an unruptured small aneurysm of <5 mm in our study. By comparison, contrast medium stagnation was observed in 58.3 % of patients with BBA in our study and, thus, may be considered a characteristic finding of BBAs. Narrowing of the entry point of the contrast medium into the aneurysm is thought to be the cause of delayed contrast medium outflow. In saccular type aneurysms, the neck length and entry diameter of the aneurysms are generally equal. As arterial dissections, BBAs have a flap structure comprising intima and intimal elastic lamina. Although the DSA image shows a broad neck, which is a characteristic of BBA, the actual entry diameter of blood is thought to be smaller because of obstruction by the flap structure, resulting in the neck length and entry diameter being inconsistent. We note, however, that the vessel wall of the normal ICA is 1.01 ± 0.11 mm in thickness [13] and, therefore, the flap structure, consisting of the thinnest layer, the intima and the internal elastic lamina, is considered undetectable by DSA as a direct finding. The finding of delayed outflow observed in both broad neck and small aneurysm is considered an indirect finding of the flap structure narrowing the entry into the aneurysm and, thus, a useful finding for BBA diagnosis.

Regarding the short-term aneurysmal enlargement and shape changes observed in our study, previous reports on the course of BBAs have reported that close imaging follow-up is necessary because of the likelihood for change over a short period of time [14–16]. In our study, short-term enlargement or shape change was identified in 83.3 % of cases of BBA, indicative of the fragile vascular structure associated with dissection.

The findings of our study are relevant to practice. Recently, 3D high-resolution vessel wall magnetic resonance imaging (MRI) has been shown to be useful for the diagnosis of BBA [15,17]. However, in the acute stage of rupture, when a patient's medical condition is poor, MRI is difficult to perform. DSA provides an easy-to-perform alternative, if the institution has angiography capacity, which can be used even in the acute phase of rupture. DSA also has the benefit of allowing for detailed observation of the dynamics of contrast medium flow. DSA images can also be magnified to observe physical findings of the vascular system, as presented in our study.

The limitations of our study should also be acknowledged. First, the retrospective design prohibits determination of causation. Second, there were technical differences in DSA acquisition between the different institutions, owing to differences in angiography systems used, injection rates, contrast bolus volumes, and catheter tip position in the ICA. Third, the diagnosis of BBA was made by the neuro-interventionalist based on the clinical course and initial CTA imaging, not based on direct view of the aneurysm wall during surgery. Fourth, DSA was performed at the time of onset in a few cases; however, only DSA performed at the time of treatment was used in our study. It would be clinically meaningful if the characteristics of DSA findings were also investigated at the time of onset. Fifth, comparing ruptured and unruptured aneurysms may introduce bias. However, ruptured aneurysms of < 5 mm that occur at the same site as the BBA are clinically extremely rare and, therefore, it was difficult to accumulate cases for comparison. Consequently, unruptured aneurysms were included in our analysis. In future studies, we would like to analyze images of small ruptured aneurysms at the same site. Lastly, the number of cases studied was small and, therefore, our findings will need to be corroborated by future studies, including a sufficiently large sample size and using standard DSA acquisition for cases suspected of BBA based on initial imaging and the clinical course. Data will need to be prospectively collected at multiple institutions.

5. Conclusion

In this retrospective study, we identified irregular morphological features of the parent artery and delayed contrast medium outflow as characteristic findings of ruptured BBAs. Our findings may improve the diagnosis of BBAs which, to date, remain difficult to diagnosis in practice.

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CRediT authorship contribution statement

Naoki KATO: Methodology, Investigation, Data Curation, Writing-Original draft, Takashi IZUMI: Conceptualization, Project administration, Masahiro NISHIHORI: Writing-review & Editing, Resources, Shunsaku GOTO: Resources, Formal analysis, Yoshio ARAKI: Writing-review & Editing, Kinya YOKOYAMA: Writing-review & Editing, Ryuta SAITO: Supervision.

Declaration of Competing Interest

None.

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