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Simultaneous intracerebral and subarachnoid hemorrhages caused by multiple infectious intracranial aneurysms treated endovascularly and by microsurgical clipping: illustrative case

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BACKGROUND Infected intracranial aneurysms are relatively rare but tend to occur in multiple locations. Establishing an optimal treatment strategy for multiple ruptured aneurysms is often challenging, especially when simultaneous ruptures occur in different locations. We report a case of simultaneous intracerebral and subarachnoid hemorrhages caused by the rupture of multiple infected intracranial aneurysms.

OBSERVATIONS A 23-year-old male with a 2-week history of chronic fever presented with sudden onset of severe headache and visual disturbance. Computed tomography showed intracerebral hemorrhage in the right occipital lobe and subarachnoid hemorrhage in the area of the left Sylvian fissure. Further investigation documented *Staphylococcus* bacteremia, verrucae on the mitral valve, and aneurysms arising from the right posterior cerebral artery (PCA) and the left middle cerebral artery (MCA). A larger aneurysm arising from the PCA was successfully occluded endovascularly, but subsequent endovascular occlusion of the MCA aneurysm was unsuccessful because some important branches were observed extending from the aneurysm. The left MCA aneurysm was then obliterated by angioplastic clipping via left pterional craniotomy. The patient showed a favorable neurological recovery after treatment.

LESSONS In such complex cases of infectious aneurysms, the method and timing of treatment need to be carefully determined based on the medical condition.

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KEYWORDS clipping; coiling; craniotomy; endovascular; infectious aneurysm; rupture

Infectious intracranial aneurysms (IIAs) are a relatively rare manifestation that account for between 0.7% and 6.5% of all cerebral aneurysms[1] and are mainly caused by bacterial, fungal, or viral infections. Bacterial infection accounts for the largest proportion (72.8%), with *Streptococcus* spp. or *Staphylococcus* spp. being the most common and tightly related to infective endocarditis.[2–4] Infection of the arterial wall leads to disruption of the inner elastic lamina and weakening of the arterial wall, resulting in lower tolerance to blood pressure and subsequent aneurysm formation.[1,3,5] IIAs are often small in size and multiple occurrences are reported in approximately 20% of cases.[2] As the average mortality rate reaches up to 24.1%, reported as 10%–30% for unruptured aneurysms and 80% for ruptured aneurysms,[2,6–9] the priority is to administer antibiotics to treat the infection.

Treatment strategies for IIAs, such as craniotomy or endovascular treatment, depend on whether the aneurysm is ruptured or unruptured as well as location, shape, and size.[3,8,10,11] Establishing a treatment strategy for a single ruptured aneurysm may be relatively straightforward, however, it is difficult to develop an optimal treatment strategy, especially when multiple aneurysms simultaneously rupture at different locations. There are few reports of such cases. Here, we report a case

ABBREVIATIONS 3D = three-dimensional; CTA = computed tomography angiography; IIA = infectious intracranial aneurysm; MCA = middle cerebral artery; PCA = posterior cerebral artery.

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with simultaneous intracerebral and subarachnoid hemorrhages caused by the rupture of multiple IIAs that were successfully resolved with a combination of endovascular treatment and open surgery.

Illustrative Case

A 23-year-old male with a 2-week history of chronic fever and a tooth extraction 4 months prior presented with sudden onset of severe headache and visual disturbances. Two days before admission, he noticed a visual disturbance while driving in the afternoon, followed by an intolerable headache that night. Upon admission, he was alert and had no neck stiffness, but slight left visual field impairment was observed, and body temperature was elevated to 37.8°C. During physical examination, a systolic murmur was heard in the mitral valve area. A blood sample showed inflammatory findings with a white blood cell count of 8,220/μL, C-reactive protein of 4.97 mg/dL, and erythrocyte sedimentation rate of 61 mm/hr. The electrocardiogram and chest radiograph were pathologically unremarkable. Other vital signs, including blood pressure, were normal and there were no signs of heart failure.

Computed tomography showed intracerebral hemorrhaging in the right occipital lobe and subarachnoid hemorrhaging in the area of the left Sylvian fissure (Fig. 1A and B). Magnetic resonance imaging also supported the evidence of subarachnoid hemorrhage (Fig. 1C and D). Magnetic resonance angiography and three-dimensional computed tomography angiography (3D-CTA) showed aneurysms arising from the right posterior cerebral artery (PCA) and the left middle cerebral artery (MCA) (Fig. 2A–C). Infective endocarditis was suspected based on chronic fever, heart murmur, and inflammatory findings at such a young age, and transthoracic echocardiography showed verrucae on the mitral valve. These aneurysms were diagnosed as IIAs due to infective endocarditis, three sets of blood cultures were taken, and antimicrobial treatment with meropenem 3 g/day and ceftriaxone 2 g/day was started.

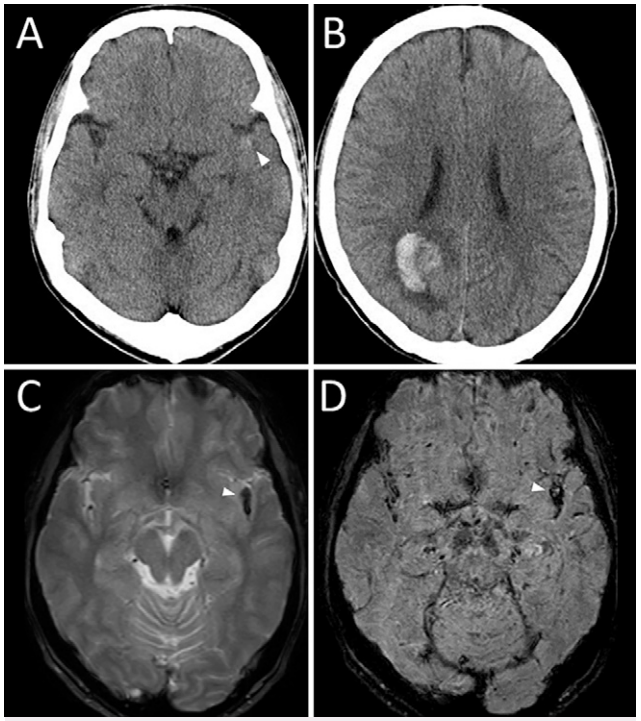

FIG. 1. Computed tomograms on admission showing subarachnoid hemorrhaging (*arrowhead*) in the left Sylvain fissure (**A**) and intracerebral hematoma in the right occipital lobe (**B**). T2-weighted fast field echo magnetic resonance image showing a low signal intensity area, suggesting hemorrhage in the left Sylvian fissure (*arrowhead*) (**C**). Susceptibility-weighted (SWI) magnetic resonance image showing a high signal intensity area within a low signal intensity area, suggesting an ruptured aneurysm with subarachnoid hemorrhage (*arrowhead*) (**D**).

These two aneurysms were thought to have ruptured at about the same time and both required timely treatment to prevent rerupture. Endovascular treatment was considered first because it seemed possible to simultaneously treat both aneurysms. In particular, the right distal PCA aneurysm, which appeared to be larger and at increased risk of rerupture, appeared amenable to endovascular treatment based on 3D-CTA findings. Under general anesthesia, selective angiography of the right vertebral artery was performed (Fig. 2D and E). Next, a guiding catheter was introduced into the right V2 segment, and 3D digital subtraction angiography was performed. The aneurysm, 12 × 16 × 12 mm in diameter with a broad neck, was located at the peripheral right calcarine artery. A microcatheter was introduced into the aneurysm and coil embolization was conducted for flow control of the liquid embolic substance before 33% n-butyl-2-cyanoacrylate was slowly injected to trap the aneurysm. The right PCA aneurysm disappeared after trapping and the calcarine artery distal to the aneurysm was angiographically visualized in retrograde.

Subsequent endovascular treatment of the left MCA aneurysm was unsuccessful because some important branches originating from the aneurysm were observed (Fig. 2F). Therefore, a craniotomy was performed the next day to treat the left MCA aneurysm. A left pterional craniotomy was performed and the frontal and parietal branches of the superficial temporal artery were dissected from the skin flap in preparation for bypass and trapping. There was a blood clot, indicating rupture, around the aneurysm (which itself was partially thrombosed) but the parent artery was not highly inflamed. The aneurysm underwent angioplastic clipping while maintaining blood flow to the distal portion of the aneurysm. Intraoperative indocyanine green angiography showed good blood flow to the distal vessels while monitoring of motor-evoked potentials showed no significant changes throughout the surgery. Bypass and trapping were not required.

The postoperative course was uneventful, and the patient showed good neurological recovery. Postoperative 3D-CTA confirmed the disappearance of the aneurysms (Fig. 3). Six days after the craniotomy, streptococci were detected in blood cultures, therefore, the antibiotic was changed to ampicillin and therapy was continued for another 5 weeks. After weekly postoperative magnetic resonance angiography showed no de novo aneurysms, the patient was transferred to the cardiac surgery department for a mitral valve replacement with favorable neurological status.

Discussion

IIA is a well-recognized but relatively rare intracranial vascular lesion and mortality remains high.[2,6–9] Because no standard treatment for IIAs exists due to a lack of randomized, controlled trials, individualized treatment must be considered, which is challenging. First and foremost, causative infections must be managed. Then, conservative treatment is considered for unruptured aneurysms while craniotomy and/or endovascular treatment are generally

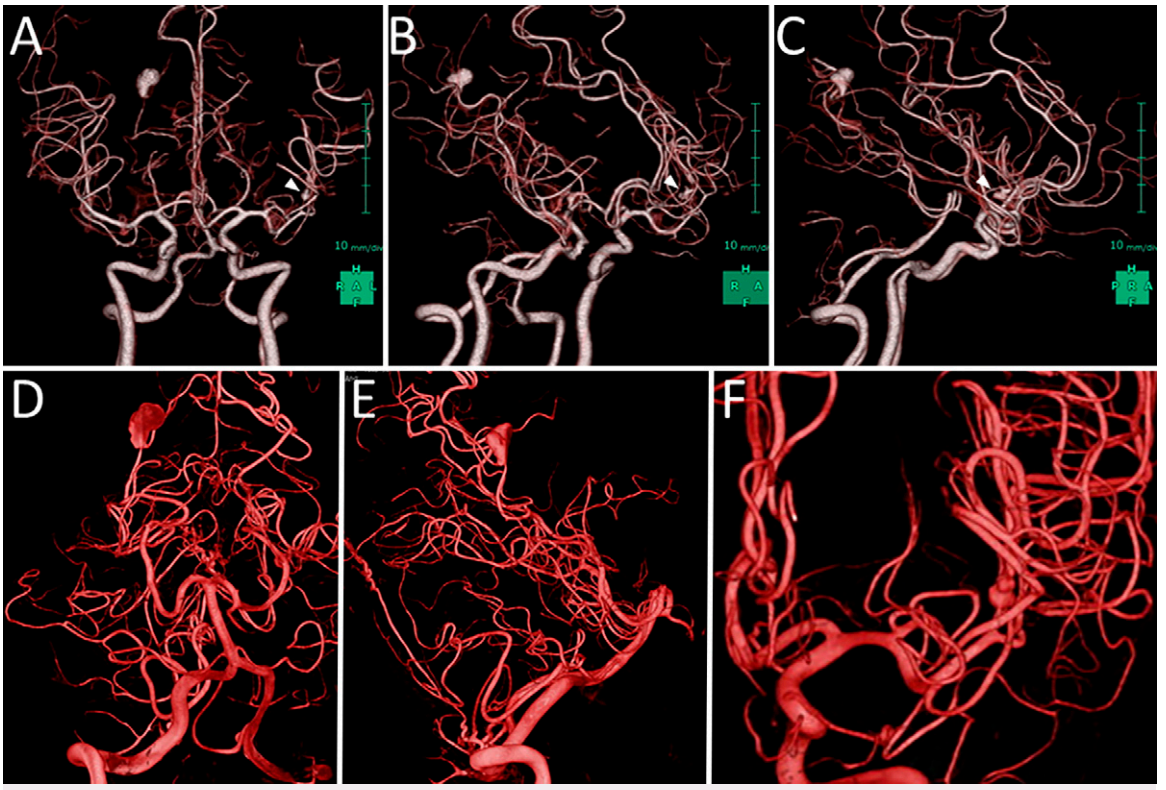

FIG. 2. 3D-CTAs showing an aneurysm arising from the right posterior cerebral artery and an aneurysm arising from the left middle cerebral artery (*arrowhead*) (**A**, A-P view; **B**, oblique view; **C**, lateral view) 3D digital subtraction view of selective angiographies of the right vertebral artery (**D**, A-P view; **E**, lateral view) and left internal cerebral artery (**F**, A-P view). A-P = anteroposterior.

reserved for ruptured aneurysms. All patients should receive antimicrobial therapy until blood cultures become negative, or for 4–6 weeks, regardless of whether surgery or endovascular treatment is performed.[1–3,8] After initial treatment with antimicrobial agents, IIAs may resolve, shrink, enlarge, rupture, or emerge anew,[12,13] therefore, regular follow-up imaging is essential during the clinical course.

If the IIAs enlarge or rupture during conservative treatment, craniotomy or endovascular treatment is indicated, with craniotomy preferred if there is a mass effect or increased intracranial pressure.[1–3] In addition, if branches from a ruptured aneurysm perfuse an eloquent area, the risk of endovascular treatment is considered high and bypass and trapping via a craniotomy are preferable.[1–3] On the other hand, clipping via craniotomy may be difficult due to the irregularity of the aneurysm neck and the fragility of the parent arterial wall due to infection.[1,3,10] Also, if there is vasospasm in the cerebral arteries, craniotomy timing should be reconsidered.

Endovascular treatment has the advantages of better distal access, the ability to treat multiple aneurysms at once, and less risk of bleeding from anticoagulants.[3,5,8] It is preferred to craniotomy in patients requiring prompt cardiac surgery because of the need for anticoagulation.[2,10,13] Theoretically, the purpose of endovascular treatment is to occlude the lumen of the aneurysm and the parent artery together. Thus, if intrasaccular coiling is not possible due to the fragility of the aneurysm wall, only parent artery occlusion

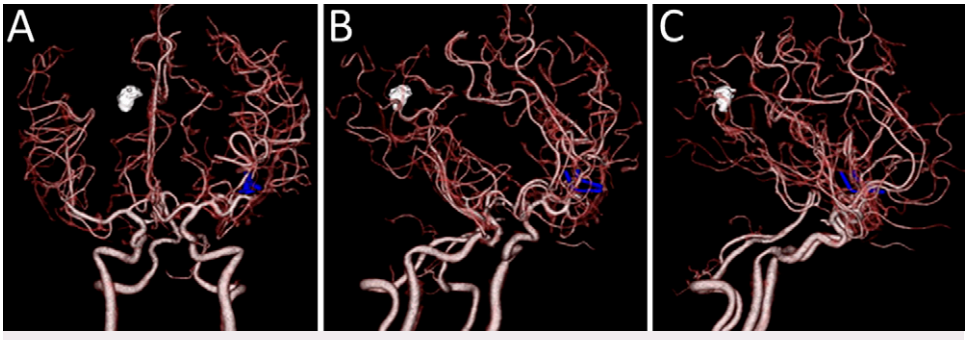

FIG. 3. Postoperative 3D-CTAs showing complete disappearance of the aneurysms (**A**, A-P view; **B**, oblique view; **C**, lateral view). A-P = anteroposterior.

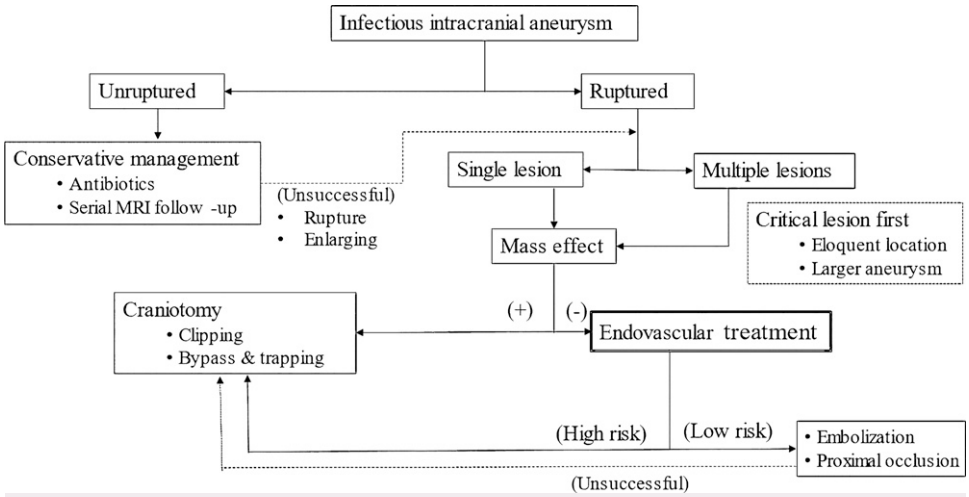

FIG. 4. Management algorithm for multiple infectious intracranial aneurysms.

should be considered. As we observed, in case of parental artery occlusion in a peripheral aneurysm, ischemic complications are minimal because the distal segment is usually filled from the distance of the pial lateral branch.[6] Also, external foreign bodies (such as coils) may aggravate the infection but this has rarely been observed in recent reports of endovascular treatment for IIAs.[1,11,14–17] Considering these factors, the most appropriate treatment method must be defined for each unique case.

IIAs tend to occur in multiples and, therefore,[2] establishing a treatment strategy for multiple, ruptured aneurysms becomes technically challenging. Furthermore, layers of complication occur when multiple aneurysms are located in different cerebral arteries, such as the right PCA and the left MCA, as seen in our case. Because it is not possible to treat multiple aneurysms at once in the same craniotomy field, the craniotomy option is less likely to be chosen. There are several case reports of multiple ruptured aneurysms,[6,14,17–23] in which most ruptures occurred in the distal MCA, that were mainly dealt with by endovascular treatment.[6,14,17,22,23] Some were treated microsurgically with clipping, wrapping, and bypass, but the outcome for most cases was unfavorable.[20,21] With the recent development of endovascular techniques, endovascular treatment appears more frequently used than craniotomy.

In our case, the two aneurysms appeared to have ruptured at about the same time, based on clinical course, radiological, and intraoperative findings. In this regard, most previous reports showed aneurysmal rupture at different times[14,18,19,21] or did not clearly explain the intervals between ruptures. To the best of our knowledge, there is only one report of a case with multiple aneurysms showing multiple ruptures at about the same time.[20] Although their case had an unfortunate outcome, the treatment itself could be performed simultaneously in the same craniotomy field on the day of onset. If individual aneurysms cannot be treated at the same time for some reason, urgent prioritization is necessary; it is better to prioritize aneurysms that are at high risk of rerupture and those that have a significant impact when ruptured. Also, larger aneurysms, aneurysms with blebs, and aneurysms in the eloquent region are generally considered more critical. Although surgical intervention is still indispensable, endovascular treatment, which has better distal access and can treat multiple lesions at once, will play a leading role in the treatment of these pathological conditions. Our treatment strategy, with these factors in mind, to guide the choice of conservative, endovascular, or surgical management options is shown in Fig. 4. A multimodality approach is required to treat complex critical conditions such as simultaneous multiple ruptured aneurysms. Therefore, while the method shown in Fig. 4 may help guide therapeutic decisions, each case must be individualized, and treatment must be tailored to each case. Accumulation of further case knowledge is essential for establishing an optimal treatment strategy for such complex pathological conditions.

Observations

We report a rare case in which multiple IIAs ruptured simultaneously but a combination of endovascular treatment and craniotomy resulted in favorable neurological status.

Lessons

Factors that may determine the management of patients with IIA include the presence of a ruptured aneurysm, the presence of a hematoma with mass effect, the presence of eloquent brain tissue supplied by the parent artery, and the high risk of rerupture of the individual aneurysm. In such complex cases of multiple infectious intracranial aneurysms, the method and timing of treatment need to be carefully determined based on the medical condition.

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Disclosures

Dr. Matsumaru reported personal fees from Medtronic, Stryker, Terumo, Cerenovas, Kaneka, and Medicos Hirata outside the submitted work. No other disclosures were reported.

Author Contributions

Conception and design: Akimoto, Yanaka, Nakamura, Takada, Hosoo, Matsumaru. Acquisition of data: Akimoto, Takeda, Hosoo. Analysis and interpretation of data: Akimoto, Yanaka, Hosoo, Matsumaru. Drafting the article: Akimoto, Yanaka, Hosoo. Critically revising the article: Ishikawa, Yanaka, Hosoo, Matsumaru. Reviewed submitted version of manuscript: Ishikawa, Nakamura, Hosoo, Matsumaru. Approved the final version of the manuscript on behalf of all authors: Ishikawa. Administrative/technical/material support: Nakamura, Hosoo. Study supervision: Ishikawa, Nakamura, Matsumaru. Participated in critical discussion: Saura.

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