

Intracranial infectious aneurysm caused by infective endocarditis resulting in intracerebral rebleeding following previous surgery for intracerebral hemorrhage: A case report and literature review

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Abstract. Intracranial infectious aneurysm (IIA) is one of the most severe complications of infective endocarditis (IE). Approximately 2-9% of patients with IE have IIA, which possibly results in severe neurological deficits. Currently, the most common treatment for IIA is endovascular treatment, while excision surgery is less common. The present study describes the case of a 33-year-old male patient who underwent a primary evacuation of an intracerebral hemorrhage (ICH) in the right temporal lobe. The patient was diagnosed with IE and IIA by examinations with an enhanced computed tomography scan, echocardiography and blood culture. In the recovery period after surgery, the patient suffered intracerebral rebleeding and underwent a surgery of IIA excision. The patient finally achieved a good prognosis without severe neurological dysfunction. In summary, IIAs are extremely rare entities, and a rare cause of spontaneous ICH. Previous research has demonstrated that the majority of ruptured IIAs receive endovascular treatment rather than conventional surgery. In the case presented herein, IIA surgical excision was successfully performed and complete pathological results were obtained, which has rarely been reported in the literature. The present case report reinforces the validity of traditional craniotomy according to the characteristics of IIAs.

Introduction

It is known that 20-40% of patients with infective endocarditis (IE) present with cerebrovascular complications (1,2), of which the most severe are spontaneous intracranial hemorrhage (SICH) and intracranial infectious aneurysm (IIA) (3). IIA is a cerebrovascular lesion caused by the microbial infection of the cerebral arterial vessel wall, accounting for 0.7-5.4% of all intracranial aneurysms (4). Of note, ~2-9% of patients with IE have IIAs. In fact, the actual incidence may be higher, considering that many IIAs are asymptomatic and resolve with anti-infective therapy (5,6).

Therefore, IIA, as an easily misdiagnosed complication of IE, possibly results in severe neurological deficits and even in mortality. Currently, the most common treatment for ruptured IIAs is endovascular treatment, while excision surgery is less commonly reported. The present study describes the case of patient with IIA caused by IE, who sequentially developed SICH twice, and underwent IIA excision surgery.

Case report

Primary intracerebral hemorrhage (ICH). A 33-year-old male, who had experienced fever and knee joint pain for 1 week, presented with a sudden headache. The patient was transported by ambulance to the Emergency Department of The First People's Hospital of Huzhou (Huzhou, China) in May 2021. The Glasgow Coma Scale (GCS) score decreased rapidly from E4V5M6 to E3V2M5 within 2 h. A computed tomography (CT) scan revealed an acute hematoma at the temporal and occipital lobe (Fig. 1). At the same time, CT angiography (CTA) did not reveal any identify aneurysm or arteriovenous malformation (Fig. 2). The patient underwent surgery involving external ventricular drainage and craniotomy for hematoma removal.

A persistent fever occurred after the surgery. An echocardiography demonstrated aortic valve vegetations (Fig. 3). Blood culture suggested that the pathogen was coagulase-negative *Staphylococcus* (CoNS). Combined with the abnormal serological results, the patient was diagnosed with IE. Based on the drug susceptibility results, linezolid was selected for anti-infective therapy for 4 weeks. The dose was 0.6 g administered every 12 h. The patient had a good

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Abbreviations: IIA, intracranial infectious aneurysm; IE, infective endocarditis; ICH, intracerebral hemorrhage; SICH, spontaneous intracranial hemorrhage; GCS, Glasgow Coma Scale; CT, computed tomography; CTA, computed tomographic angiography; CoNS, coagulase-negative *Staphylococcus*

Key words: intracranial infectious aneurysm, intracerebral hemorrhage, intracerebral rebleeding, aneurysm excision

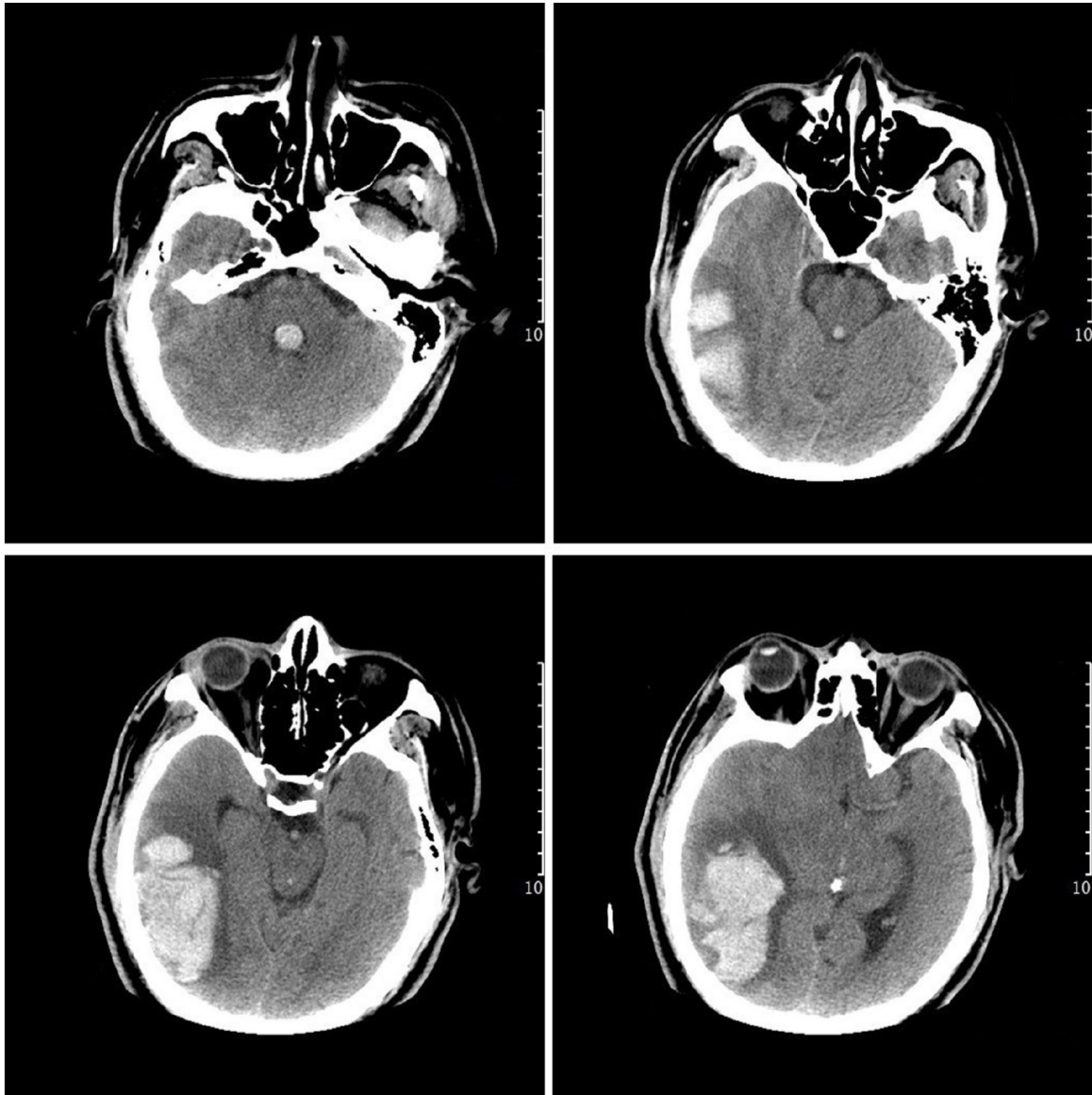


Figure 1. Computed tomography scan illustrating an acute hematoma in the right temporal and occipital lobes at four different scanning levels as presented in the figure (6.8x4.6 cm in maximal dimensions), which broke into the ventricular system and filled the right lateral ventricle, third ventricle and fourth ventricle. There was a midline shift of 0.9 cm towards the left due to the mass effect of the hematoma.

post-operative recovery without any neurological dysfunction and underwent a follow-up CT scan on post-operative day 11 (Fig. 4). At 26 days after the first presentation, the patient underwent a heart valve operation at The Second Hospital of Zhejiang University Medical College (Hangzhou, China). During the surgery, a bicuspid aortic valve was found with a number of vegetations, the largest of which was ~2.0 cm in diameter. Another vegetation of 2.0 cm in diameter was also found in the anterior mitral leaflet near the tendon cord. The aortic and mitral valves were each removed and replaced with mechanical valves.

Intracerebral rebleeding. On the 36th day, an enhanced CT scan revealed an 11 mm equal density of the nodule in the right temporal lobe with surrounding calcification (Fig. 5). These graphic features suggested that the lesion was an IIA rather than an abscess. On the 66th day, the patient had a severe headache and fell into a coma with left limb hemiplegia. A CT



Figure 2. Computed tomography angiography did not reveal any intracranial aneurysms or arteriovenous malformation. The 'A' in the image indicates 'anterior'.

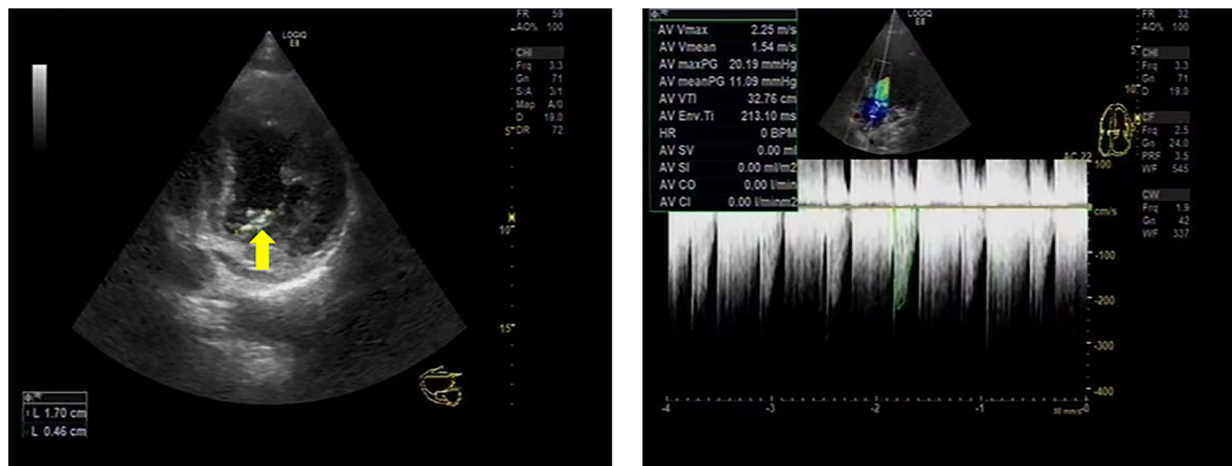


Figure 3. (Left panel) Echocardiography illustrating a bicuspid aortic valve with severe insufficiency and hyperechoic plaques, which was considered to be vegetations (yellow arrow). (Right panel) Echocardiogram suggested significant reverse blood flow, indicating that the patient had severe aortic valve insufficiency.

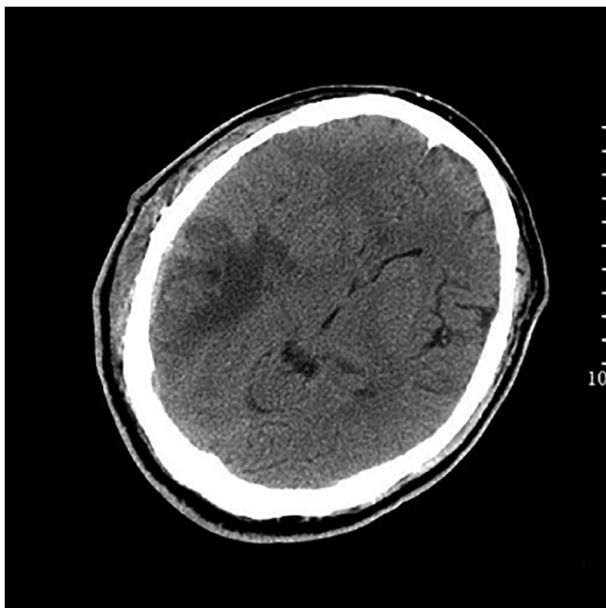


Figure 4. Follow-up computed tomography scan on post-operative day 11 revealing that the hematoma was significantly reduced compared to pre-operative period.

scan revealed an acute hematoma in the area of the original hemorrhage, which was mainly located around the previously identified IIA.

The patient underwent another emergency craniotomy. The scalp incision approach was selected from the previous surgery. During the surgery, a blind end enlargement of a small artery was found in the hematoma cavity (Fig. 6). The IIA was completely excised from the supplying artery (Fig. 6) and pathological analysis with H&E staining was performed as follows: The IIA was immersed in 4% paraformaldehyde for 4 h and transferred to 70% ethanol. Individual lobes of IIA biopsy material were placed in processing cassettes, dehydrated through a serial alcohol gradient and embedded in paraffin wax blocks. Tissue sections (5- μ m) were prepared and dewaxed in xylene, rehydrated through decreasing

concentrations of ethanol and washed in PBS. Subsequently, the slides were stained with H&E and then dehydrated through increasing concentrations of ethanol and xylene (all steps performed at room temperature). Histopathology revealed typical features of IIA (Fig. 7). The remaining hematoma was evacuated and the bone flap was removed after surgery. A CT scan and CTA reexamination revealed the absorption of the hematoma and no recurrence of the removed IIA (Fig. 8). The left limb strength of the patient returned to grade 5 after 4 weeks. The latest outpatient review at ~1 year after the first presentation revealed that the patient had returned to work.

Discussion

An analysis of the pooled cohort of patients from the literature revealed that 65% of patients with IIAs presented with bacterial IE (5). In the pre-antibiotic era, this ratio commonly arises in patients with prosthetic valves, nosocomial-acquired blood stream infections, or a history of intravenous drug use (6,7). Less commonly, IIA can also result from the direct extension of intracranial bacterial infections, such as meningitis, cavernous sinus thrombophlebitis and orbital cellulitis, often in patients who are immunosuppressed (8). The most common site of IIAs is the middle cerebral artery, which can account for almost 50% of all cases (5). In order to diagnose IE, two findings are necessary: A positive blood culture and positive imaging test results (9). In the case presented herein, the blood culture of CoNS and the echocardiography led to the definitive diagnosis of IE. The pre-operative diagnosis for IIA usually relies on angiography or CTA (10,11), which were replaced by an enhanced CT scan in the case described herein. Digital subtraction angiography (DSA) or pathological results of IIA are considered to be the gold standard for pre- or post-operative diagnoses (5,11). However, in the present study, the patient was unable to complete the DSA as the first ICH was of acute onset. After a proposed diagnosis of IIA by an enhanced CT scan, the patient had been scheduled for a DSA. However, a secondary intracerebral rebleeding occurred prior to the DSA. Fortunately, however, pathological graphics were obtained, which directly verified the diagnosis for IIA.

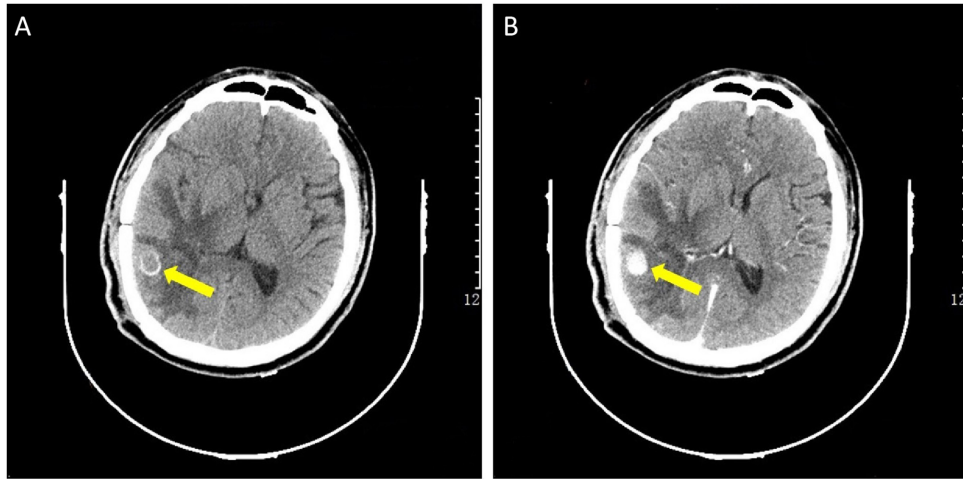


Figure 5. Computed tomography illustrating (A) an 11-mm equal density of nodule in the right temporal lobe with surrounding calcification (yellow arrow), and (B) the nodule was significantly and uniformly enhanced after contrast injection (yellow arrow).

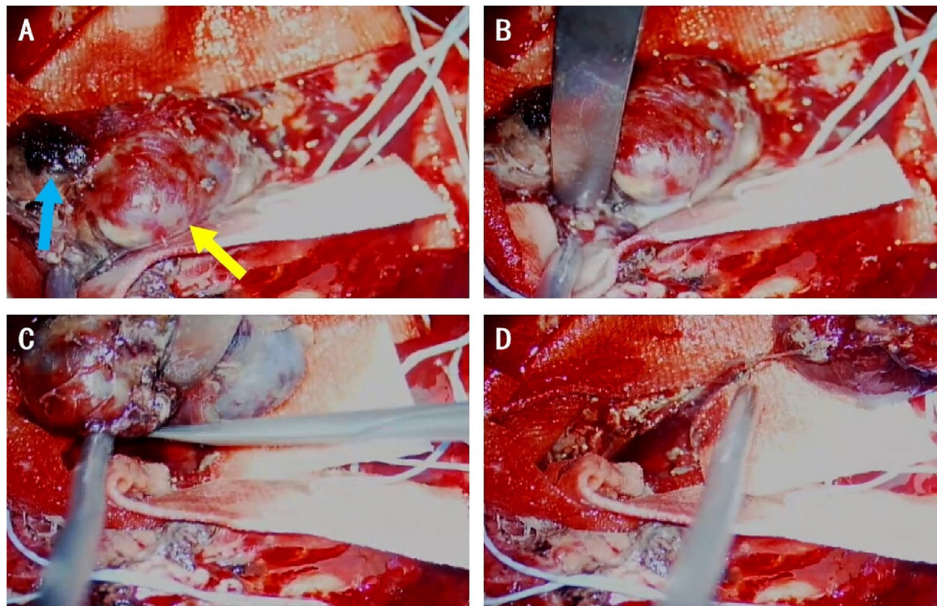


Figure 6. Intraoperative images. (A) The yellow arrow indicates the body of the pseudoaneurysm and the blue arrow indicates the rupture hole. (B) The adhesion between the top of aneurysm and arachnoid was separated. (C) The adhesion between aneurysm and arachnoid was further loosened. (D) The aneurysm was completely removed.



Figure 7. Pathological image of IIA (H&E staining; magnification, x200). The part of the nucleus that aggregated (the left part of the figure) was the wall of the IIA. The fraction lacking cellular components was the intraluminal hematoma. The anatomy of the wall of IIA was different from that of the typical aneurysm. H&E, hematoxylin and eosin

Although the pathogenesis of IIA remains uncertain, arteritis is generally considered the pathological basis of IIA (12). The possible underlying mechanism is that bacteria-containing neoplasms adhere and cause inflammatory damage to the artery wall. The infectious process leads to an acute infiltration of both the media and adventitia of the vessel wall by inflammatory cells, as well as the marked proliferation of the intima and destruction of the internal elastic lamina. Hydrostatic pulsation and thrust against the infected arterial wall then promote aneurysmal development and subsequent growth (5). The aforementioned pathophysiological process finally leads to arteritis. Due to the different pathological structures form other types of aneurysms, IIAs are generally considered a type of pseudoaneurysm (13). In the case in the present study, the causes of the twice-occurring intracranial hemorrhages were presumed not to be the same, since no suspicious aneurysms

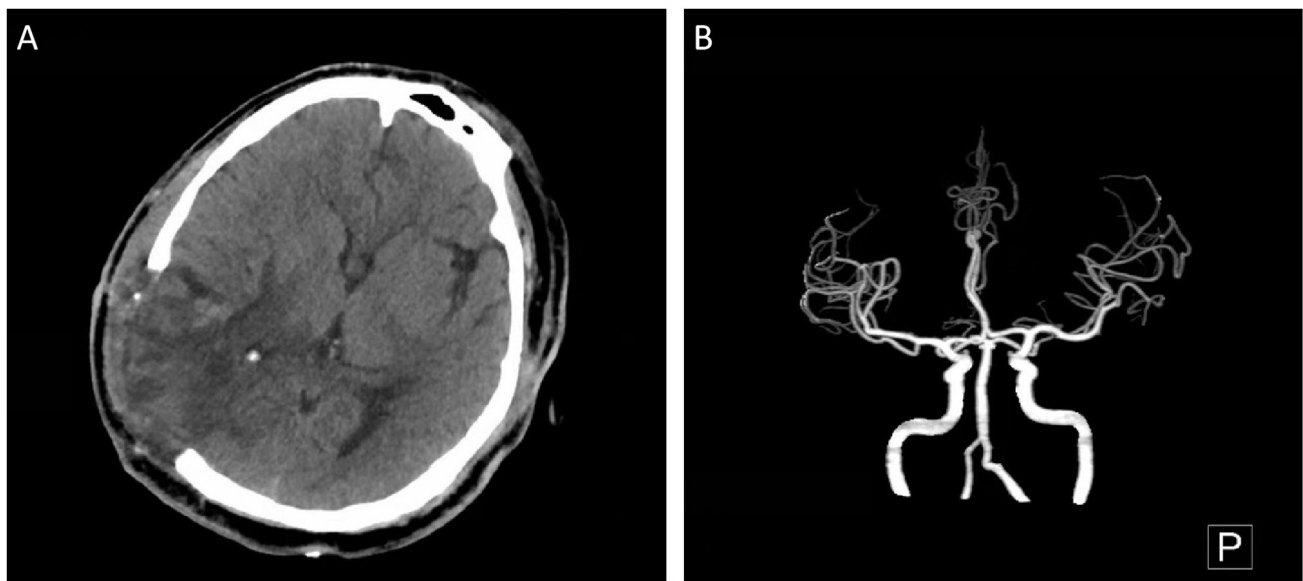


Figure 8. Computed tomography and computed tomography angiography reexamination in 2 weeks after the second surgery. (A) The original hematoma was completely absorbed. (B) No recurrence of the removed IIA was observed. The 'P' in the figure indicates 'posterior'.

were identified through the CTA or during the first surgery. The second of intracranial hemorrhage with severe clinical symptoms was confirmed to be caused by an IIA rupturing, while the first one with milder clinical symptoms, may have been caused by arteritis. According to the aforementioned analysis, it was found that the intracranial hemorrhages with IIA may be more severe than those without IIA caused by IE.

The treatment of unruptured IIAs, according to a previous study on 16 cases, mainly involves a prolonged course of antibiotics (14). However, according to a clinical study published in 2016, IIA has a higher risk of rupture compared with other aneurysms, of which the proportion is even as high as 48% (15). Therefore, surgical treatment should be actively adopted for IIAs that have ruptured or have a higher risk of rupture. Previous research has indicated that the majority of ruptured IIAs have received endovascular treatment, such as coiling and parent artery occlusion (16). The majority of the studies on the outcomes of surgery have focused on unruptured IIAs (15,16), while only a limited number of studies have reported on the surgical prognosis for ruptured IIAs (14). From sporadic case reports, it was found that both endovascular treatment and surgical clipping have resulted in equivalent outcomes for ruptured IIAs (5,14,17).

In the case in the present study, treatment with sensitive antibiotics was continued when the IIAs were found unruptured following clinical standard treatment (14,15). However, the aneurysm suddenly ruptured during anti-infective treatment. In order to remove the intracranial hematoma while treating the aneurysm, craniotomy surgery was selected as opposed to endovascular embolization. The patient finally achieved a good prognosis without severe neurological dysfunction. In a nationwide database sampled by Singla *et al* (15), it was found that patients with ruptured IIAs undergoing neurosurgical treatment had better outcomes than those who underwent conservative treatment. Regrettably, the absence of intraoperative and pathological images is a limitation of the present study, as the heart surgery was performed at another medical center.

In conclusion, although ICH caused by IIA is rare, secondary ICH following a previous surgery caused by IIA is more rare. It can result in severe consequences and requires prompt surgical treatment. In the case described herein, it was found that traditional craniotomy may be more appropriate than endovascular embolization for such specific ruptured IIAs.

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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

HG was involved in the writing of the original draft, in the writing, reviewing and editing of the manuscript, and in the collection of clinical data of the patient. ZZ was involved in the writing, reviewing and editing of the manuscript, in the surgical treatment of the patient, and in the collection of clinical data of the patient. Both authors have read and approved the final manuscript. ZZ and HG confirm the authenticity of all the raw data.

Ethics approval and consent to participate

The patient provided signed informed consent for the inclusion of his data in the present case report.

Patient consent for publication

The patient provided signed informed consent for publication.

Competing interests

The authors declare that they have no competing interests.

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