

# Treatment Strategies for Infectious Intracranial Aneurysms: Report of Three Cases and Review of the Literature

Kazuhiro ANDO,<sup>1</sup> Hitoshi HASEGAWA,<sup>1</sup> Bumpei KIKUCHI,<sup>1</sup> Shoji SAITO,<sup>1</sup> Jotaro ON,<sup>1</sup> Kohei SHIBUYA,<sup>1</sup> and Yukihiro FUJII<sup>1</sup>

<sup>1</sup>Department of Neurosurgery, Brain Research Institute, Niigata University, Niigata, Niigata, Japan

## Abstract

We retrospectively reviewed the cases of three patients with infectious intracranial aneurysms (IIAs), and discuss the indications for surgical and endovascular treatments. We treated two men and one woman with a total of six aneurysms. The mean age was 43.3 years, ranging from 36 to 51 years. One patient presented initially with an intraparenchymal hemorrhage, one with mass effect, and the other one had four aneurysms (one causing subarachnoid hemorrhages and the other causing delayed intraparenchymal hemorrhages). The average size of all aneurysms was 12.2 mm (range, 2–50 mm). They were preferentially located in the distal posterior cerebral artery, and then, in the middle cerebral artery. All cases were caused by infective endocarditis. We selected endovascular treatments for five aneurysms and treated all but one within 24 h from detection. One aneurysm was treated by combined therapy with endovascular intervention and surgery. After treatment, none of the IIAs presented angiographical recurrence or re-bleeding. If feasible, endovascular treatment is probably the first choice, but a combined surgical and endovascular approach should be considered if surgery or endovascular treatment alone are not feasible. The method of treatment should be individualized. For cases with high risk of aneurysm rupture, treatment should be performed as soon as possible.

Key words: infectious intracranial aneurysm, treatment strategy, surgical treatment, endovascular treatment, combined therapy

## Introduction

Infectious intracranial aneurysms (IIAs) account for 0.7–5.4% of all cerebral aneurysms<sup>1–5)</sup> and are identified after or concomitantly with systematic bacterial infections, especially infective endocarditis (IE), and sometimes systemic fungal or mycobacterial infections.<sup>6)</sup> These aneurysms are found in 3–10% of patients with IE and develop as a result of septic embolisms commonly found in the distal cerebral arteries.<sup>7)</sup> If unruptured, they are known to resolve or decrease in size with antimicrobial therapy.<sup>8,9)</sup> Conversely, ruptured, symptomatic, or growing aneurysms should be considered for surgical or endovascular treatment. Endovascular treatment has become more popular and has been adopted as an

alternative to surgical treatment.<sup>7,10)</sup> Guidelines for the management of IIAs are based on select reviews or retrospective studies and are still controversial.

We retrospectively reviewed cases of IIAs treated at the Department of Neurosurgery, Niigata University and discuss the indications for treatments, including surgical and endovascular approaches.

## Materials and Methods

We retrospectively reviewed the hospital and treatment records of the patients with IIAs treated at our institute from 2002 to 2018 focusing on clinical features, aneurysm locations, procedure types, and clinical outcomes.

## Results

We treated three patients, including two men and one woman with a total of six aneurysms. Table 1 represents a summary of the characteristics of IIAs

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Table 1 Summary of three patients with infectious intracranial aneurysms

Case number	Age/Gender	Initial presentation	Aneurysm number	Location	Size (mm)	Shape	Primary disease	Pathogen	Procedure	Time from detection to procedure	Recurrence/ Re-bleeding	Clinical outcome (mRS)	Follow up (months)
1	36/F	ICH	1	Distal PCA	10	Saccular	IE	NA	Proximal occlusion with coil	<24 h	No	2	204
2	43/M	Mass effect	2	Proximal MCA	50	Fusiform	IE	<i>Enterococcus faecalis</i>	Proximal occlusion with coil and revascularization	17 days	No	3	240
3	51/M	SAH	3	Distal MCA	3.5	Fusiform			Internal trapping with coil	<24 h	No		3
		Infarction → ICH	4	Distal PCA	5	Saccular			Endosaccular coiling	<24 h	No		2
		ICH	5	Distal PCA	3.5	Saccular	IE	<i>Streptococcus salivarius</i>	Internal trapping with coil	<24 h	No	2	2
		ICH	6	Distal PCA	2	Fusiform			Internal trapping with coil and NBCA	<24 h	No		2

F: female, ICH: intracerebral hemorrhage, IE: infective endocarditis, M: male, MCA: middle cerebral artery, mRS: modified Rankin Scale, NA: not achieved, NBCA: N-butyl-2-cyanoacrylate, PCA: posterior cerebral artery, SAH: subarachnoid hemorrhage.

and the procedural and clinical results. The mean age was 43.3 years, ranging from 36 to 51 years.

One patient initially presented with an intraparenchymal hemorrhage, one with mass effect, and the other one had four IIAs (one causing subarachnoid hemorrhage (SAH) and three causing delayed intraparenchymal hemorrhage). Cases 1 and 3 were screened for aneurysms by magnetic resonance imaging (MRI) or three-dimensional computed tomography angiography (3DCTA) after the IE diagnosis, but no aneurysms were detected.

The average size of all aneurysms was 12.2 mm, ranging from 2 to 50 mm. IIAs were preferentially located at the distal posterior cerebral artery (PCA), and then at the middle cerebral artery (MCA). In Case 2, the IIA was located at the proximal MCA. Three aneurysms were fusiform and three were saccular in shape.

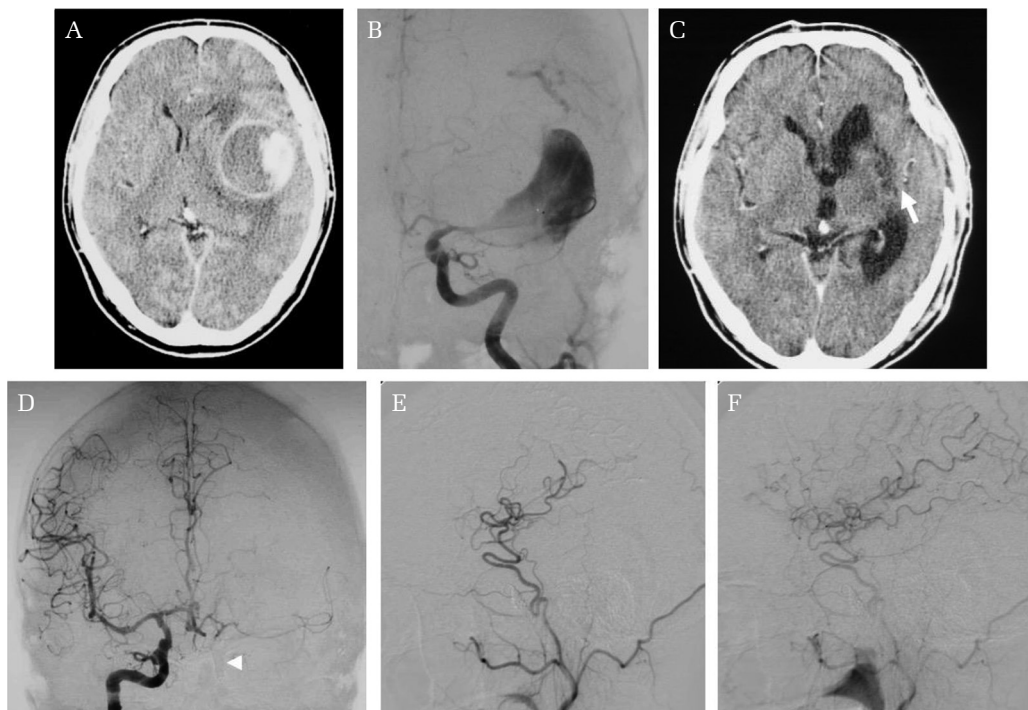
All cases were secondary to IE. The causative pathogens were revealed in two cases (*Enterococcus faecalis* in one and *Streptococcus salivarius* in the other); the pathogen in third case remained undetected.

We chose endovascular treatments with detachable coils or combination of coil and N-butyl-2-cyanoacrylate (NBCA) for five IIAs. The other aneurysm was treated using a combined therapy with endovascular intervention and surgery (Case 2). In the endovascularly treated group, we performed proximal occlusion with detachable coils in one case, internal trappings in two cases, and endosaccular coil embolization for one saccular aneurysm. For the last case, we used internal trapping with coils and NBCA. We encountered no complications during the endovascular procedures.

Except for Case 2, all IIAs were treated within 24 h from detection. All patients had favorable clinical outcomes, and none presented angiographical recurrence or re-bleeding after the treatments.

### Representative case

Case 2 was a 43-year-old man without previous medical history presented with sudden headache and sensory aphasia. Neurological examination revealed mild consciousness disturbance as defined by Japan Coma Scale 3. Initial enhanced computed tomography (CT) showed a 50 mm partially thrombosed aneurysm accompanied with mass effect in the left temporal lobe (Fig. 1A). Digital subtraction angiography (DSA) revealed a partially thrombosed giant aneurysm at the proximal portion of MCA and the branches of MCA were not clearly visible (Fig. 1B). By the balloon occlusion test, the aneurysm was observed by crossflow through the anterior communicating artery. As he was asymptomatic

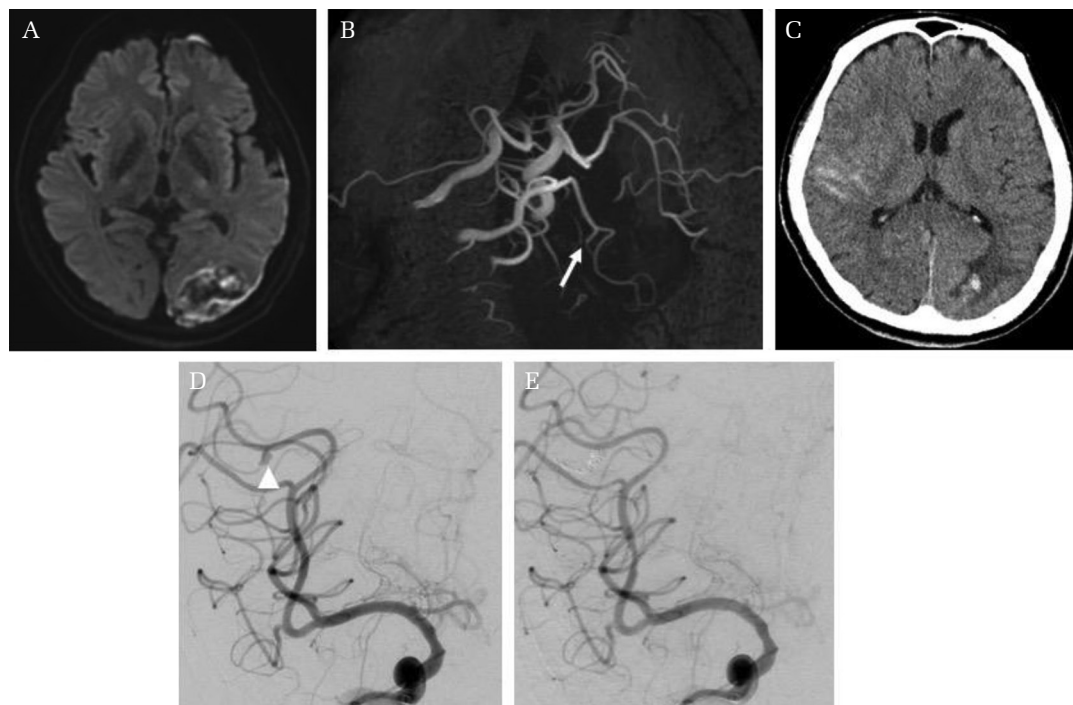


**Fig. 1** (A) Initial enhanced computed tomography (CT) showing 50 mm partial thrombosed aneurysm accompanied with mass effect in left temporal lobe. (B) Left internal carotid angiogram showing partially thrombosed giant aneurysm at the proximal portion of middle cerebral artery (MCA). Each branches of MCA were not clearly visible. (C) Post procedural CT showing disappearance of the aneurysm (*arrow*). (D) Right internal carotid angiogram post procedure. Proximal MCA was found by cross flow through the anterior communicating artery, but the aneurysm was not observed. Left internal carotid artery was occluded with platinum coils (*arrow head*). (E and F) Post procedural left external carotid angiogram of early phase (E) and late phase (F). Left distal MCA was found through the superficial temporal artery and MCA anastomoses.

during 30 min of IC occlusion, he was clinically decided to be tolerant. Although parent artery occlusion after revascularization was considered the best option, it was judged difficult to secure the proximal MCA during direct surgery. Thus, we decided that revascularization should be performed at first, then endovascular internal carotid artery (ICA) occlusion was to be performed by detachable coils. However, after craniotomy, due to a severely elevated intracranial pressure, we were unable to open the dura matter because of severe tension, forcing a change in plans. We decided to first perform endovascular ICA occlusion to decrease blood flow to the hemispheric parenchyma as well as the aneurysm, resulting in decreased intracranial pressure. Then it became to be possible to open the dura and perform revascularization (Figs. 1C–F). After the procedure, intracranial pressure management was performed in the intensive care unit and the patient's general condition slowly improved. In this case, the patient developed a fever of unknown origin after admission. Blood cultures were positive for *E. faecalis* and echocardiography

revealed a mobile vegetation on the aortic valve. He was diagnosed with IE and performed aortic valve replacement after treatment of intracranial aneurysm.

Case 3 was a 51-year-old man with severe mitral regurgitation admitted to our hospital with a low-grade fever. Echocardiography revealed a mobile vegetation on the mitral valve, and the blood culture was positive for *S. salivarius*. He was diagnosed as having IE and intravenous antibiotic medication was started. On day 4 of hospitalization, the patient presented a sudden onset of headache and right hemianopia. MRI revealed a left occipital hemorrhagic infarction and left PCA third segment occlusion (Figs. 2A and 2B), but no aneurysms were detected on either magnetic resonance angiography (MRA) or 3DCTA. However, on day 6 of hospitalization, a follow-up CT showed a small SAH in the right sylvian fissure and CTA and DSA revealed a 3.5 mm sized fusiform aneurysm at the distal MCA (Figs. 2C and 2D). This SAH was suspected of being associated with an infectious aneurysm secondary to the IE. We immediately performed



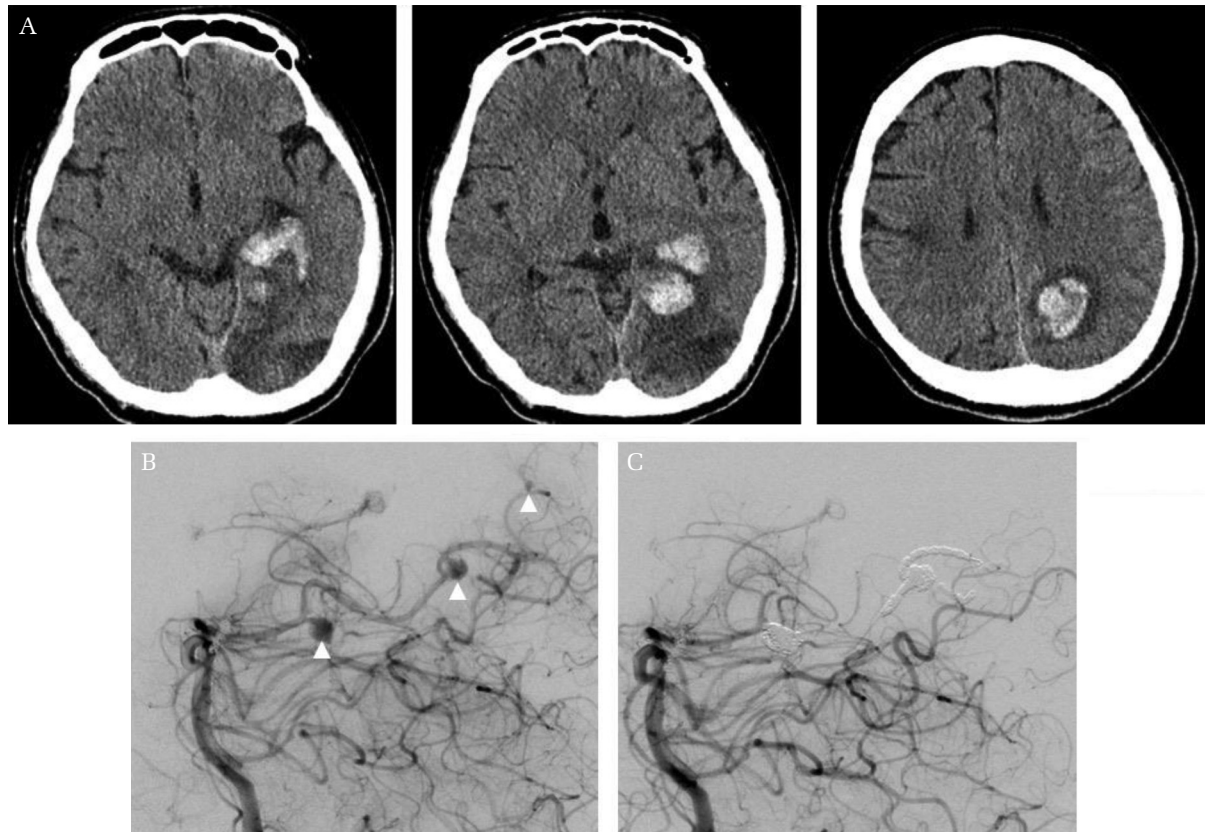
**Fig. 2** (A) Diffusion-weighted magnetic resonance imaging showing mixed-intense changes in the left occipital cortex. (B) Magnetic resonance angiography showing the third segment of the left posterior cerebral artery (*arrow*). (C) Follow-up CT, on day 6 of hospitalization revealing a small subarachnoid hemorrhage in the right sylvian fissure. (D and E) Digital subtraction angiography (DSA) revealing a 3.5 mm sized fusiform aneurysm at the distal MCA (*arrowhead*) showing internal endovascular trapping of the aneurysm with detachable coils.

internal trapping of the IIA endovascularly with detachable coils (Fig. 2E). The immediate postoperative course was uneventful and no neurological deficits, except a right hemianopia caused by left occipital infarction, remained. However, in spite of a 1-month antibiotic infusion, the low-grade fever continued, and echocardiography showed an increased mitral valve vegetation, suggesting the IE was not controlled. On day 35, the patient complained of a sudden headache with transient consciousness disturbance. A CT showed multiple left occipital intraparenchymal hemorrhages (Fig. 3A), and DSA revealed multiple aneurysms of the left distal PCA (aneurysms 4–6, Fig. 3B). We performed an immediate endovascular treatment after the examination using internal trapping with detachable coils and NBCA for one lesion, detachable coils alone for another one, and endosaccular coil embolization for the other one, achieving complete obliteration of the aneurysms without procedure-related complications (Fig. 3C). After the procedure, intravenous antibiotic medication was continued for a total of 2 months, and the patient was discharged to go home with a modified Rankin Scale score of 2. No angiographical recurrences had occurred at the time of the follow-up DSA.

## Discussion

Infectious intracranial aneurysms are rare, representing between 0.7% and 5.4% of all intracranial aneurysms.<sup>1–5)</sup> The main angiographic features of IIAs are their distal location involving secondary and tertiary arterial branches, irregular or fusiform morphology, and the presence of multiple aneurysms in the same patient. IIAs are typically small in diameter, but they can rapidly enlarge and reach up to several centimeters.<sup>7)</sup> Alawieh et al.<sup>7)</sup> reported 44.2% of IIAs being small in size (<5 mm), 56.9% being located in the MCA and 13.1% in the PCA. In this series, a majority of the aneurysms were small in size, but in Case 2, the IIA formed a partial thrombus and its size was as large as 50 mm. Although a giant intracranial aneurysm resulting from IE has not been previously published, and thus should be considered atypical, we consider the aneurysm was IIA because of his clinical course. We speculate that an asymptomatic aneurysm may have preexisted, and an abscess developed in its wall, causing inflammation and development of a purulent pouch, leading to formation a giant aneurysm causing mass effect.

Infectious intracranial aneurysms occur in 2–10% of patients with IE, a likely underestimation because



**Fig. 3 (A–C) CT showing multiple left occipital intraparenchymal hemorrhages and DSA revealing multiple aneurysms of the left distal posterior cerebral artery (arrowheads). Aneurysm treated endovascularly with multi-modal embolization materials.**

IAs may not be detected and often recede with antibiotic treatment.<sup>7)</sup> The time between IE onset and IIA rupture may range from 2 to 5 weeks.<sup>7)</sup> In Cases 1 and 3, although the aneurysms were not detected during the MRI or 3DCTA screenings for IE patients, the IIAs grew rapidly and ruptured, causing intraparenchymal hemorrhage and SAH. Patients with IE must be closely monitored by serial neuroimaging, including MRA, CTA, and DSA, especially within 2–5 weeks from the onset of IE. Despite advances in noninvasive neuroimaging technology, DSA remains the gold standard for the detection of IIAs and is recommended even if noninvasive tests are negative.<sup>11)</sup>

The treatment strategies for IIAs are controversial; options include conservative medical management using antibiotics and close radiographical monitoring, surgical treatment, or endovascular treatment.<sup>2,7,8,10,12)</sup> Antibiotic treatment of the infectious etiology, most commonly bacteria and sometimes, fungi, viruses, and parasites, is the standard medical therapy for IIAs.<sup>8,9)</sup> Unless large, symptomatic, or enlarging unruptured aneurysms can be managed with antibiotics and monitored by serial neuroimaging.<sup>10)</sup>

Matsubara et al.<sup>10)</sup> reported the treatment of seven IIAs by medical treatment alone, with all of them disappearing without recurrence or re-bleeding afterward. However, in cases of ruptured, symptomatic, or enlarging aneurysms, surgical or endovascular intervention should be considered because of the high risk of rupture and subsequent significant mortality ranging from 30% to 80%.<sup>1,2,5,9,10)</sup>

The treatment of IIAs is specially challenging due to increased fragilities of the affected parent artery and aneurysm wall in contrast to those of classical saccular intracranial aneurysms.<sup>1)</sup> Endovascular intervention is becoming popular as an alternative treatment option due to the advances in endovascular techniques.<sup>7,10)</sup> Indeed, endovascular intervention is the first-line treatment in patients with ruptured IIAs or in those who fail conservative treatment since it is associated with significantly lower mortality, easier access to distal aneurysms, higher success in treatment of multiple aneurysms, shorter delay to subsequent cardiac surgery, and lower risk of hemorrhage from anticoagulation compared with microsurgical craniotomies.<sup>7)</sup> Especially in patients with IE requiring heart valve replacement,

endovascular intervention is recommended because perioperative anticoagulation may also be necessary.<sup>8)</sup> Furthermore, patients with IE often suffer from heart failure. Endovascular intervention is a minimally invasive procedure and can reduce anesthetic time as compared with surgical treatment. In addition, it is potentially performed under local anesthesia, which decreases the risk of general anesthesia for patients with cardiovascular instability.<sup>10)</sup> In this series, all IIAs were treated endovascularly, and all patients had favorable clinical outcomes without angiographical recurrence or re-bleeding. Treatment of aneurysms should be performed as soon as possible in cases of high risk of bleeding. The risk of rupture is higher during the acute phase, and fatal bleeding may occur during this period.<sup>5)</sup> Except for Case 2, we treated all IIA within 24 h of detection. In Cases 1 and 3, in spite of antibiotic infusion, IIAs ruptured, suggesting that growth of aneurysms were not controlled by antibiotics administration alone.

Regarding the embolization material for endovascular treatment, detachable coils or liquid embolization agents (NBCA, onyx, or others) are used for IIA treatment.<sup>1,3,4,7,10,13)</sup> Ding et al.<sup>8)</sup> reported a case with IIAs treated with stent assisted coil embolization. The induction of foreign materials into an infected vessel may cause prolongation of infection or abscess formation.<sup>10,13,14)</sup> However, no deteriorating or new infectious complications resulting from endovascular treatment have been reported. In this series, we experienced no local infections after coiling or casting of NBCA during the perioperative period. The application of antibiotics before and after endovascular intervention may prevent infectious complications.<sup>10,14)</sup>

The fragilities of the affected parent artery and aneurysm wall contribute to the increased difficulty of certain surgical techniques such as clipping,<sup>12)</sup> and aneurysms are often unclippable in shape and

fragile.<sup>2,10,12)</sup> However, when an aneurysm is associated with large intraparenchymal hematomas or mass effect, it needs to be treated surgically.<sup>10)</sup> In addition, IIAs are sometimes located at the proximal cerebral arteries as a result of the contiguous spread from sinusitis or meningitis.<sup>9,10)</sup> Because of their anatomical location, aneurysmal neck clipping may be impractical, so the aneurysm needs to be treated with proximal parent artery occlusion or parent artery trapping with revascularization to cover the distal blood flow.<sup>2,7)</sup> Ota et al.<sup>2)</sup> reported two cases with ruptured IIAs of the distal MCA treated successfully by trapping and revascularization. For treatment of a proximal MCA giant IIA in the present series, we had to use parent artery occlusion and revascularization. Our combined approach with endovascular and surgical intervention performed in Case 2 may not be a standard strategy for IIAs, but it can be a useful strategy in complicated cases.

Regarding the treatment strategy of ruptured, symptomatic or enlarging IIAs, we recommend multimodal management (Fig. 4). If feasible, endovascular treatment is probably the first choice. Surgical treatment should be considered if the aneurysm is associated with large intraparenchymal hematomas or edema, or if revascularization is necessary. Combined surgical and endovascular treatments should be considered if IIAs cannot be treated by surgery or endovascular treatment alone because of their size, shape, or location. In all, the method of treatment considered is case dependent, but for cases with high risk of aneurysm rupture, the treatment should be performed as soon as possible.

In conclusion, our case series suggests that endovascular treatment should probably be considered a first treatment option for ruptured, symptomatic or enlarging IIAs. In select cases, surgical treatment with/without endovascular treatment is advised.

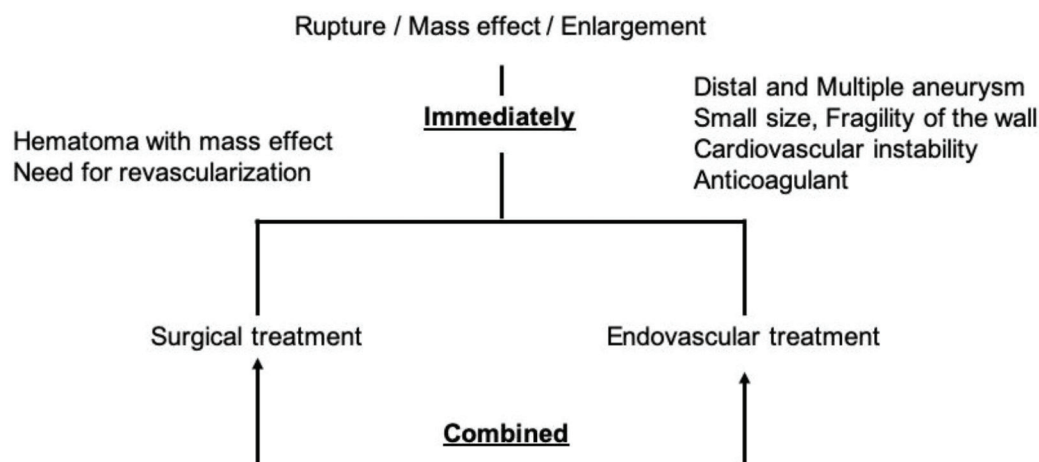


Fig. 4 Clinical management algorithm for multimodal management of infectious intracranial aneurysms.

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## Conflicts of Interest Disclosure

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this manuscript.

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*Address reprint requests to:* Kazuhiro Ando, MD, Department of Neurosurgery, Brain Research Institute, Niigata University, 1-757 Asahimachidori, Niigata, Niigata 951-8585, Japan.  
*e-mail:* upper-swing@hotmail.co.jp