Successful endovascular coiling of infectious cerebral aneurysm following Staphylococcus haemolyticus endocarditis

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Abstract
Recent reports suggest that Staphylococcus haemolyticus can cause infective endocarditis (IE). However, no data are available regarding infectious intracranial aneurysm (IIA) following S. haemolyticus endocarditis. Endovascular coiling is a challenging approach for the treatment of IIA. We describe the case of a 63-year-old woman who suddenly developed aphasia and dysarthria following an acute cerebral infarction in her left insular and temporal cortex. After a total hysterectomy at the age of 39, the patient had suffered from recurrent bacterial pyomyositis in her legs. At admission, there was no evidence of cerebral aneurysm, as assessed by magnetic resonance angiography, and no vegetation, as assessed by transesophageal echocardiography (TEE), resulting in an incorrect diagnosis. However, subarachnoid hemorrhage and development of cerebral aneurysm in the left middle cerebral artery occurred within 1 week of hospitalization.
Continuous positive blood culture results and a second TEE finally revealed that IE was caused by *S. haemolyticus*. Coil embolization of the IIA was successful on day 26 after symptom onset; after this procedure, the patient began to recover. This case demonstrates that *S. haemolyticus*-induced endocarditis can cause IIA. Endovascular coiling is a potentially effective approach to treat IIA.

**Keywords**

*Staphylococcus haemolyticus*, infectious cerebral aneurysm, infectious endocarditis, endovascular therapy, endovascular coiling, infectious intracranial cerebral aneurysm

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**Introduction**

Infectious intracranial aneurysm (IIA) is an important complication of infective endocarditis (IE). In most cases, subarachnoid hemorrhage (SAH) occurs following rupture of the IIA with extremely unfavorable prognosis. Although *Staphylococcus haemolyticus*, a coagulase-negative staphylococcus, was previously considered to be weakly virulent, recent reports indicated that *S. haemolyticus* can cause IE. Recent data have demonstrated that coagulase negative staphylococci are responsible for 8% of all cases of native valve endocarditis, resulting in a 25% mortality rate, and that methicillin-resistant isolates cause 60% of prosthetic valve endocarditis cases. However, data on IIA following *S. haemolyticus* IE are still lacking. The current standard treatments for IIA are clipping (assessed by craniotomy under general anesthesia) or conservative treatment with antibiotics, while endovascular coiling remains a challenging approach.

Here, we report the first case of a patient with IIA and subsequent SAH followed by *S. haemolyticus* IE who was successfully treated by endovascular coiling. The reporting of this study conformed to CARE guidelines. The requirement for ethical approval was waived by the Ethical Committee of Jichi Medical University based on the study design (case report). Written informed consent was obtained from the patient for publication of this case report.

**Case report**

A 63-year-old woman suddenly developed aphasia and dysarthria. She was admitted to our hospital 9 hours after symptom onset. Her past medical history included endometrial cancer surgery and a total hysterectomy at age 39 years. After surgery, she suffered from recurrent bacterial pyomyositis in her legs. Physical examinations showed pitting edema in the lower legs and neurological examinations showed Wernicke’s aphasia. Her initial National Institutes of Health Stroke Scale (NIHSS) score was 5. Upon admission, she had a fever (37.8°C). Laboratory examinations showed normal white blood cell counts but an elevated erythrocyte sedimentation rate of 37 mm/h and positive anticardiolipin IgG antibody. A cerebrospinal fluid (CSF) examination revealed an elevated cell count (152/μL) and elevated protein content (90 mg/dL) with slight xanthochromia. Diffusion weighted images from cranial magnetic resonance imaging (MRI) showed high-intensity lesions in the left
insular and temporal cortex, indicating acute cerebral infarction (Figure 1a). At that time, the area of hyper-intensity was limited, as assessed by fluid-attenuated inversion recovery (FLAIR) (Figure 1b) and no cerebral aneurysm or stenosis was observed by magnetic resonance angiography (MRA) (Figure 1c). No SAH findings

Figure 1. (a) Axial DW, (b) FLAIR, and (c) MRA images on day 0 of hospitalization. Arrows show an acute infarction in the left middle cerebral artery lesion, but no aneurysm. (d) Axial DW, (e) FLAIR, and (f) MRA images on day 7 of hospitalization. The lesion was expanded (yellow arrows). In addition, SAH (arrowheads) and a novel aneurysm (red arrow) appeared. (g) Axial DW, (h) FLAIR, and (i) MRA images on day 17 of hospitalization. The lesion diminished in the DW image but expanded in the FLAIR image (yellow arrows). An aneurysm developed (red arrow in yellow circle).

DW, diffusion-weighted; FLAIR, fluid-attenuated inversion recovery; MRA, magnetic resonance angiography; SAH, subarachnoid hemorrhage.
were detected in either FLAIR or T2-star weighted images from MRI at admission. We suspected IE upon admission but a transesophageal echocardiography (TEE) on day 1 showed no vegetation or valvular diseases. Thus, we suspected that her cerebral infarction was caused by central nervous system vasculitis based on the positive detection of anticardiolipin IgG antibody and CSF results. We initiated antithrombotic treatment for cerebral infarction (aspirin 100 mg/day and unfractionated heparin 10,000 international units/day) and steroid pulse therapy for vasculitis (methylprednisolone 1000 mg/day) for 3 days. On day 2 after onset, her aphasia disappeared and her NIHSS score improved to 0. Although blood culture results for two samples taken upon admission were both positive for *S. haemolyticus*, we believed that these results might have been caused by contamination because her symptoms had improved and her fever improved to 36.5°C. However, novel high-intensity lesions along the parietooccipital sulcus appeared and the hyper-intense lesion in the temporal lobe expanded by FLAIR on day 7 (Figure 1e). In addition, a novel cerebral aneurysm in the left middle cerebral artery M2/M3 bifurcation was detected by MRA (Figure 1f). Based on MRI results, we suspected SAH and performed another lumber puncture. The CSF results revealed continuous and more evident xanthochromia, and we diagnosed the patient with SAH following rupture of the aneurysm.

Antithrombotic therapy was stopped on day 7. Three-dimensional computed tomography angiography (3D-CTA) on day 8 showed a cerebral aneurysm 2 mm in diameter, in agreement with the MRA findings. The cranial MRI on day 17 (Figure 1g–i) and the 3D-CTA on day 23 (Figure 3a) showed an enlargement of the lesion and cerebral aneurysm. At this stage, we strongly suspected IIA with IE. The second TEE on day 19 revealed vegetation on the mitral valve (Figure 2a) and worsened severe mitral regurgitation (Figure 2b). *S. haemolyticus* was again identified in a second set of blood cultures. The patient was finally diagnosed with IE caused by *S. haemolyticus*, with subsequent cerebral infarction and IIA. We initiated treatment with vancomycin (2 g/day) and ceftriaxone (4 g/day) for 6 weeks starting on day 17. On day 26 after onset, coil embolization was performed without any complications (Figure 3b, pre-treatment;

![Figure 2.](image)

(a) TEE on day 19 showing mitral valve vegetation (arrow) and (b) severe mitral valve retardation (arrowhead).

TEE, transesophageal echocardiography.
Coil embolization was performed under general anesthesia. A 5-French guide catheter (Medikit; Tokyo, Japan) was placed in the left distal cervical internal carotid artery and an Echelon 10 microcatheter (Medtronic; Dublin, Ireland) was navigated into the M2/3 bifurcation aneurysm using a Tenrou S 10 microguidewire (Kaneka; Osaka, Japan). The aneurysm was then occluded using Target 360 Ultra (Stryker; Kalamazoo, MI, USA) and HyperSoft 3D coils (Terumo; Tokyo, Japan). After endovascular treatment, no infarction, infection, or hemorrhage occurred. Moreover, there were no changes in the patient’s mitral valve state and no mitral valve retardation. She returned home without further antibiotic therapy on day 63 after onset. After discharge, her activities of daily living were preserved without stroke recurrence for more than 3 years. The patient’s clinical course is shown in Figure 4.

**Discussion**

We treated a patient whose ischemic stroke and delayed cerebral aneurysm formation following *S. haemolyticus* endocarditis was initially difficult to diagnose. Because of difficulties in the initial diagnosis and the rapid development of her IIA, the patient finally recovered without sequelae following combination treatment with antibiotics and endovascular coiling. We initially suspected IE; however, neither mitral vegetation nor severe mitral valve retardation were evident. Consequently, the initial diagnosis was mistaken. TEE is an important method for the diagnosis of IE, but in some cases shows negative findings during the initial phases of IE.8 Previous reports have demonstrated the importance of repeat TEE examinations when IE is strongly suspected, as it was in our patient.

As demonstrated by the case described here, *S. haemolyticus* infection can induce subacute mitral changes and IIA formation. The vast majority of causes of IIA are caused by *Staphylococcus aureus* and *Streptococcus* species.9 Gram-negative pathogens including *Salmonella* and *Pseudomonas aeruginosa* have also been reported as causative agents of IIA.10 *S. haemolyticus* was recently reported to be an important hospital pathogen;11 it is the second most frequently isolated pathogen from human blood cultures12 and has

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**Figure 3.** (a) 3D-CTA on day 23 showing an aneurysm at the M2/M3 bifurcation (arrow). (b) Cerebral angiography on day 26 showing the developed aneurysm (arrow). (c) Coil embolization was completed and there was no arterial flow into the aneurysm (arrow). 3D-CTA, three-dimensional computed tomography angiography.
the highest levels of antimicrobial resistance.\textsuperscript{13} \textit{S. haemolyticus} is the most common pathogen responsible for pyomyositis.\textsuperscript{14} Our patient also suffered from recurrent bacterial pyomyositis in her legs after total hysterectomy and intermittent use of antibiotics, which we believe may have been the primary focus of infection. Although recent reports have shown that \textit{S. haemolyticus} can cause endocarditis,\textsuperscript{2,3} they did not reveal short-term IIA or SAH. The case presented here suggests that \textit{S. haemolyticus} endocarditis might induce the development of IIA and SAH.

We decided to use endovascular coiling instead of clipping for the treatment of IIA in this patient because we had planned cardiac valve replacement surgery and a short-term approach was needed at that time. Ultimately, cardiac valve replacement surgery was not required. Recently, a few successful cases of endovascular coiling for treatment of IIA have been reported.\textsuperscript{15} Endovascular therapy has several advantages, including reduced risk of anesthetic complications and short time lag, among others. However, endovascular coiling in IIA carries a risk of aneurysm rupture because of the thin, friable, and fragile arterial wall that is susceptible to microbial infection.\textsuperscript{9} Infection and inflammatory responses lead to infiltration of neutrophils and destruction of the arterial wall. Consequently, IIAs tend to be thin-walled and friable, and achieving endovascular coiling without complications is difficult. A previous case report demonstrated successful treatment of IAA following infection by viridans streptococci by endovascular coiling, suggesting the importance of treatment interval from SAH.\textsuperscript{15} In that study, SAH occurred 3 days after ischemic stroke and endovascular coiling was performed within 24 hours of SAH in a 25-year-old male patient. Although endovascular coiling occurred over 13 days after the occurrence of SAH in our patient, the combination of antibiotic therapy and endovascular coiling without cardiac surgery was effective and the patient had no sequelae. Although the treatment intervals after SAH occurrence were different, the IIAs were in the distal M2 portion in both the previous case\textsuperscript{15} and in our patient.
The position of the IIA and technique may be important parameters for a successful endovascular coiling approach. Coil embolization of the IIA is also challenging in terms of treatment of the infection. Releasing foreign material into the infectious focus is not desired. We speculate that the success of endovascular treatment in our patient was aided by effective initiation of dual antibiotic therapy 9 days before endovascular treatment. Antibiotic therapy was continued for a long period.

In conclusion, this case showed that \textit{S. haemolyticus} endocarditis can cause IIAs, although diagnosis can sometimes be challenging. Endovascular coiling of IIAs, taking into consideration the timing of events, is a potentially effective treatment approach.

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