Online October 16, 2020
Journal of Neuroendovascular Therapy 2021; 15: 175–180 DOI: 10.5797/jnet.cr.2020-0106

Case Report

Mechanical Thrombectomy for Acute Ischemic Stroke Complicated by Bacterial Meningitis and Infective Endocarditis

Masaaki Kubota,[1,2] Eiichi Kobayashi,[1,2] Yoichi Yoshida,[1,2] Ryousuke Orimoto,[1,2] Yousuke Watanabe,[1] Akihiko Adachi,[1,2] and Yasuo Iwadate[1]

Objective: We report a case of cerebral embolism from a bacterial embolus due to infective endocarditis (IE) during treatment of bacterial meningitis.

Case Presentation: During treatment of bacterial meningitis, an 82-year-old woman developed left middle cerebral artery embolism. Mechanical thrombectomy was performed, and the yellowish-white emboli were retrieved. From the culture and pathological findings of the embolus, the same bacteria as the meningitis, *Streptococcus gordonii*, was identified and was considered to originate from IE. She was treated by postoperative antibiotics, but was transferred to the rehabilitation hospital on the 37th postoperative day due to slight right hemiparesis.

Conclusion: We should always consider bacterial embolism in acute ischemic stroke combined with bacterial meningitis.

Keywords cerebral embolism, infective endocarditis, bacterial meningitis, mechanical thrombectomy, *Streptococcus gordonii*

Introduction

Several previous studies reported thrombolysis or mechanical thrombectomy (MT) for cerebral embolism due to a bacterial embolus related to infective endocarditis (IE), but such cases are relatively rare, and neither the safety/efficacy nor the treatment methods have been established. We report a patient with cerebral embolism due to bacterial emboli related to IE during the treatment of bacterial meningitis in whom MT led to a favorable course and review the literature.

[1]*Comprehensive Stroke Center, Chiba University Hospital, Chiba, Chiba, Japan*
[2]*Department of Neurological Surgery, Graduate School of Medicine, Chiba University, Chiba, Chiba, Japan*

Received: May 27, 2020; Accepted: August 4, 2020
Corresponding author. Masaaki Kubota. Department of Neurological Surgery, Graduate School of Medicine, Chiba University, 1-8-1 Inohana, Chuo-ku, Chiba, Chiba 260-8677, Japan
Email: kubota_masaaki@hotmail.com

Case Presentation

Patient: The patient was an 82-year-old woman.
Medical history: The patient's medical history consisted of hypertension and peripheral vertigo.
Family history/lifestyle: The patient's family history/lifestyle was not contributory.
Present illness: The patient consulted the emergency outpatient unit of a local hospital for fever, headache, and disturbance of consciousness. Detailed examination led to a diagnosis of bacterial meningitis, and she was admitted on the same day. Treatment with meropenem and vancomycin was started. Pyretolysis was achieved on Day 2. Consciousness became clear on Day 3, and rehabilitation was conducted. On Day 4, *Streptococcus gordonii* was identified on blood culture, and the above antimicrobial drugs were switched to Penicillin G (PCG) at 4000000 units/day. She was found fallen beside her bed early in the morning on Day 6. MRI revealed occlusion of the left middle cerebral artery. She was brought to our hospital by ambulance.

Neurological findings

On arrival, the Glasgow Coma Scale score was E2V1M5. Right incomplete hemiplegia involving the face and aphasia was noted. The National Institutes of Health Stroke Scale (NIHSS) score was 20 (2-1-0-2-0-2-0-3-0-3-0-2-1-2-2).

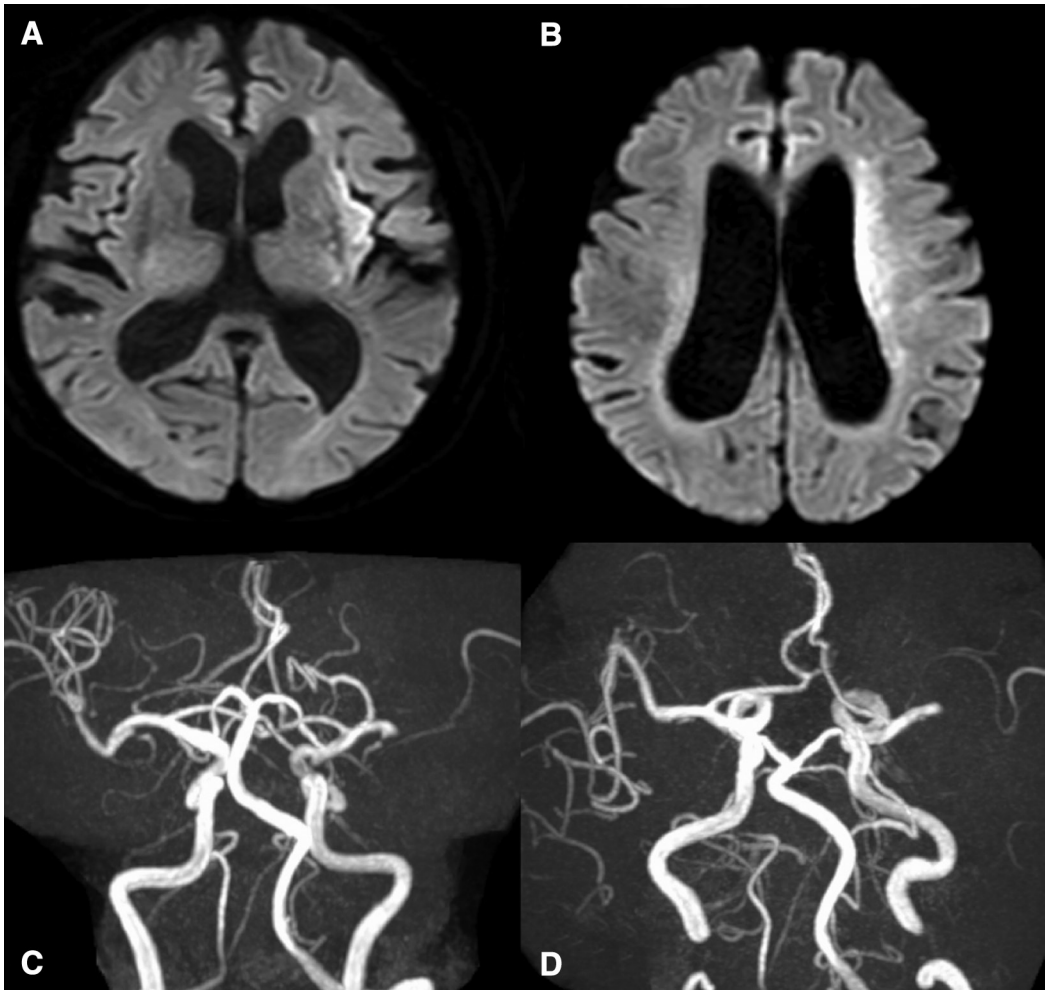

Fig. 1 (**A** and **B**) Initial DWI after arrival to our hospital shows acute ischemic change in the left insula and corona radiata. (**C** and **D**) MRA shows left M1 occlusion. DWI: Diffusion-weighted image

Imaging findings

Diffusion-weighted image (DWI) of MRI revealed diffusion-restricted areas in the left insular cortex and corona radiata. The DWI-Alberta Stroke Program Early Computed Tomography Score was 9. MRA demonstrated occlusion of the M1 proximal left middle cerebral artery (**Fig. 1**).

Laboratory data

Hematology

The total protein, albumin, aspartate aminotransferase, alanine aminotransferase, lactic acid dehydrogenase, total bilirubin, urea nitrogen, creatinine, sodium (Na), potassium (K), chlorine (Cl), creatine kinase, and C-reactive protein levels were 6.3 g/dL, 3.3 g/dL, 23 U/L, 24 U/L, 263 U/L, 0.5 mg/dL, 18.0 mg/dL, 0.62 mg/dL, 130 mEq/L, 4.1 mEq/L, 96 mEq/L, 99 U/L, and 3.1 mg/dL, respectively. The white blood cell (WBC) count, red blood cell (RBC) count, hemoglobin level, and hematocrit value were 9.03×10^3/mL, 354×10^4/mL, 10.9 g/dL, and 33.0%, respectively. The mean corpuscular volume was 93.2 fL. The mean corpuscular hemoglobin (MCH) level was 30.8 pg. The MCH concentration was 16.6 g/dL.

Cerebrospinal fluid test

The cell count was 1194/mL. The mononuclear cell count was 237/mL. The polynuclear cell count was 952/mL. The protein, glucose, and Cl levels were 68 mg/dL, 54 mg/dL, and 116 mEq/L, respectively.

Cerebrospinal fluid culture

There was no significant bacterial growth.

Electrocardiography

Both 12-lead electrocardiography and continuous electrocardiographic monitoring during admission demonstrated sinus rhythm. There was no arrhythmia.

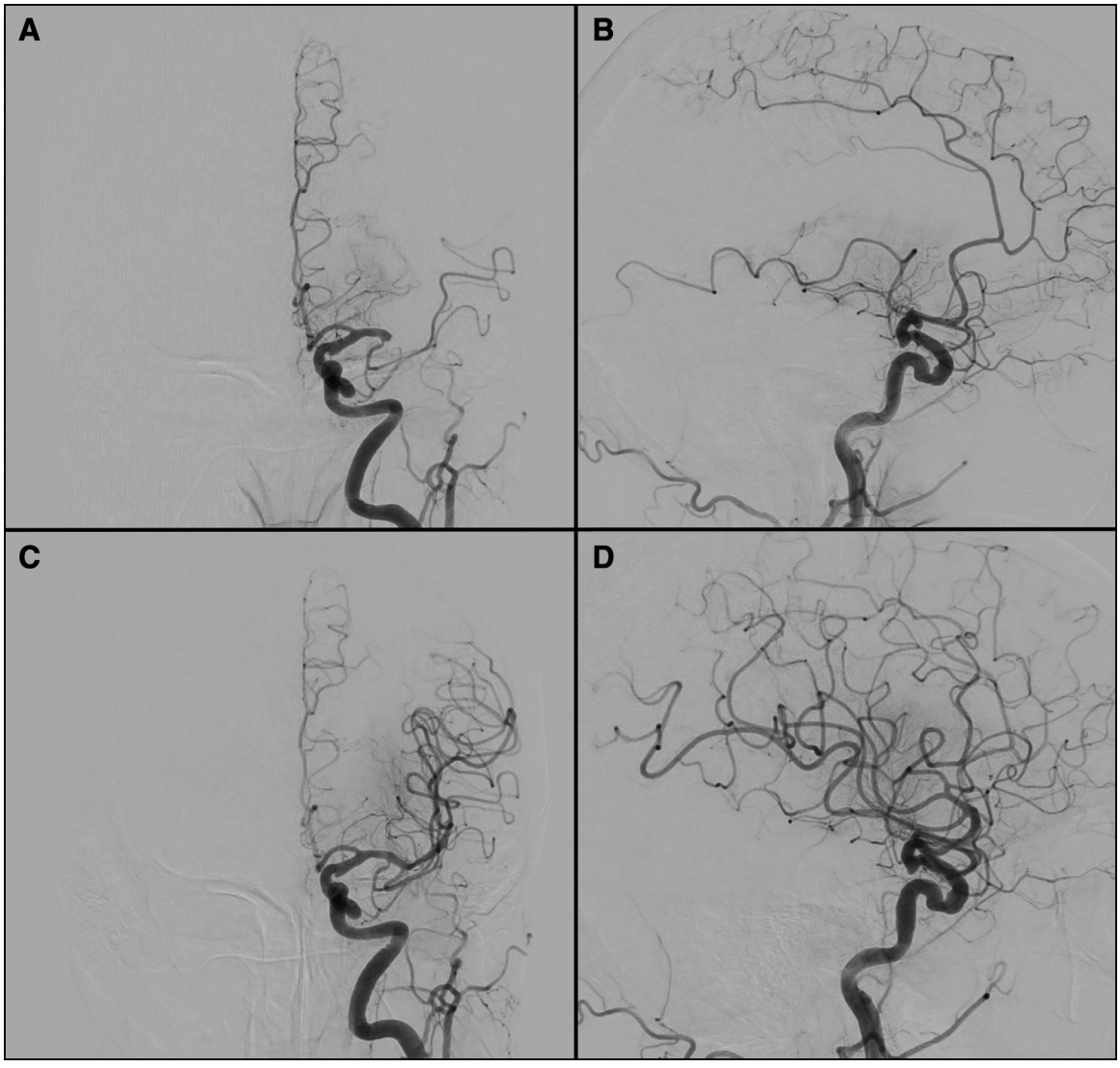

Fig. 2 (**A** and **B**) Preoperative cerebral angiography shows left M1 occlusion. (**C** and **D**) Postoperative cerebral angiography after MT shows complete recanalization (TICI 3). TICI: thrombolysis in cerebral infarction

Echocardiography

There was no sclerosis of the aortic valve, valvular disease, or verrucous endocarditis.

Treatment

The interval from the final confirmation of a healthy state until arrival to our hospital was 4.5 hours. Intravenous thrombolysis was not performed in accordance with the guidelines for optimal treatment by intravenous thrombolysis with recombinant tissue plasminogen activator (rt-PA) (alteplase). To treat embolism of the left middle cerebral artery, MT was conducted under local anesthesia. The activated coagulation time (ACT) at the start of treatment was 130 seconds, and heparin at 2800 units was intravenously injected. On additional examination after 1 hour, the ACT was 290 seconds. Right femoral artery puncture was performed, and a 9 Fr Sheath introducer (Medikit, Tokyo, Japan) was inserted. A 9 Fr Optimo balloon catheter (Tokai Medical Products, Aichi, Japan) was inserted into the left common carotid artery. A Penumbra 5MAX ACE60 (Penumbra, Alameda, CA, USA) was inserted into the M1 proximal left middle cerebral artery, and lesion crossing with a Marksman catheter (Medtronic, Minneapolis, MN, USA) was conducted. The catheters were placed in the M2 segment. While aspirating thrombi using the Penumbra 5MAX ACE60, a Solitaire 3 Platinum 4 mm × 20 mm (Medtronic) was deployed (continuous aspiration prior to intracranial vascular embolectomy [CAPTIVE] technique). Two passes led to thrombolysis in cerebral infarction grade 3 recanalization (**Fig. 2**) (onset-to-door time:

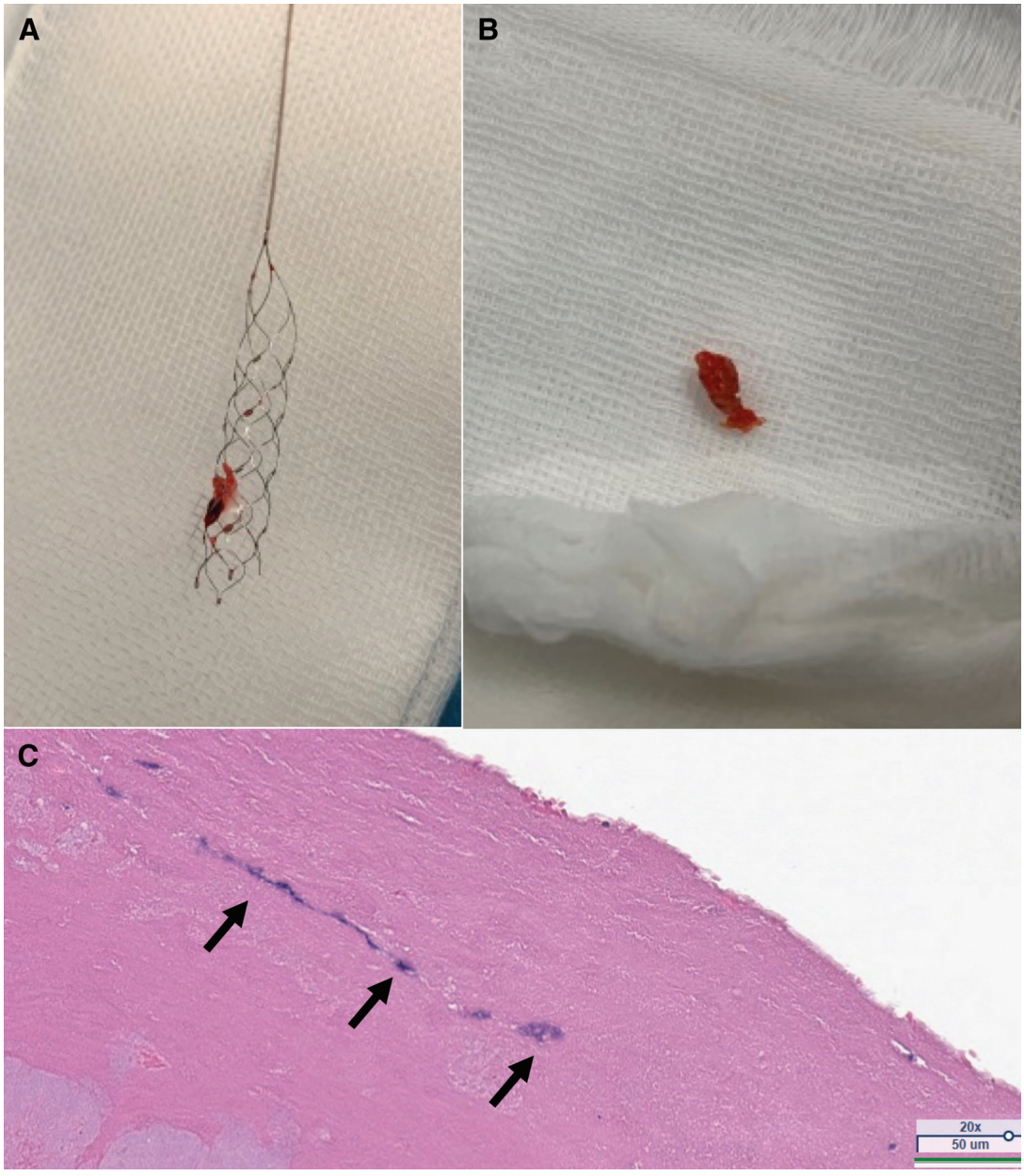

Fig. 3 (**A** and **B**) A gross image of retrieved clots. Clots were yellowish-white and elastic hard. (**C**) Hematoxylin and eosin staining (20×) shows a fibrin clot with Gram-positive cocci infection (arrows).

270 minutes, door-to-puncture time: 53 minutes, puncture-to-reperfusion time: 56 minutes, and onset-to-reperfusion time: 369 minutes). A total of 2 emboli were collected through the 2 passes. They were yellowish-white and elastic hard (**Fig. 3A** and **3B**). The emboli were submitted for pathological examination and bacterial culture.

Postoperative anticoagulant therapy was not performed for the following reasons: There had been no arrhythmia since admission to the previous hospital, bacterial meningitis and a positive reaction on blood culture were present on arrival to our hospital, and the characteristics of the collected emboli suggested IE. During admission, continuous electrocardiographic monitoring was performed for arrhythmia surveillance. On the 1st postoperative day, mild right incomplete hemiplegia remained, but aphasia reduced. Marked improvement was achieved (NIHSS score: 5). The pathological examination suggested fibrin clots contained in bacterial masses (**Fig. 3C**). Furthermore, *S. gordonii* was cultured from the emboli, leading to a diagnosis of IE according to the pathological diagnostic criteria of the modified Duke's classification. During the course, transthoracic echocardiography was performed twice, but there was no significant

finding. To treat meningitis and IE, PCG was continued for 26 days. No prophylactic antithrombotic drug for cerebral infarction was used. On the 37th postoperative day, the patient was referred to a recovery-phase rehabilitation hospital. The modified Rankin Scale score after 90 days was 3.

Discussion

Bacterial meningitis complicated by IE accounts for 1.1% to 2% of cases of bacterial meningitis, being rare. However, the incidence of ischemic stroke is 38%, and the mortality rate is 29%; the prognosis is markedly poor. As causative bacteria, *Streptococcus pneumoniae* (54%) and *Staphylococcus aureus* (33%) have been reported.[1,2] On the other hand, primary causative bacteria for IE include *Streptococcus viridans*, *Streptococcus bovis* (*Streptococcus gallolyticus*), HACEK group, and *S. aureus*.[3] In a previous study, T2-weighted MRI demonstrated microhemorrhage involving the cortex in 57% of patients with IE, suggesting that IE should be suspected based on this imaging finding and clinical symptoms such as cardiac murmurs, repeated fever, and a history of valvular disease.[4] Another study hypothesized a mechanism: the oral flora, such as *S. gordonii*, which was a type of causative bacteria in the present case, has a specific platelet-binding protein that specifically adheres to platelets and invades the vascular lumen.[5] In the future, further clarification may aid in IE prevention.

IE-related central nervous complications are observed in 10% to 35% of patients with IE. The most frequent complications are cerebral infarction and transient ischemic attacks. Complex factors, such as disseminated infection with causative bacteria and inflammation, are involved.[2,6–8] It was previously reported that the incidence of intracranial hemorrhage after intravenous thrombolysis for acute ischemic stroke complicated by IE is 20%, and the mortality rate in the presence of bacterial meningitis was 65%. In the guidelines for the prevention and treatment of IE in Japan, and guidelines for optimal treatment by intravenous thrombolysis (rt-PA) revised in March 2019, intravenous thrombolysis is not recommended.[3,9–11] Regarding prophylactic antiplatelet therapy for cerebral infarction related to IE, a randomized controlled trial with aspirin and placebo suggested that this therapy increases the risk of hemorrhagic complications without reducing the risk of embolism; this therapy is not recommended.[12] Furthermore, there is little evidence regarding anticoagulant therapy, but it may also increase the risk of hemorrhagic complications; therefore, the new initiation of this therapy is not recommended. In patients with thrombi suggestive of IE, whether anticoagulant therapy should be performed early after surgery may be evaluated by confirming the presence of bacteria using rapid smear microscopy, in addition to bacterial culture and pathological diagnosis.

On the other hand, concerning MT for acute vegetation-related major artery occlusion, only 13 case reports have been published. However, there was no hemorrhagic complication in any patient, and favorable results were obtained in 9 (69%), suggesting the safety and efficacy of MT.[13] Factors for the high risk of intravenous thrombolysis in comparison with MT include latent peripheral intracranial microhemorrhage, which is often observed in patients with IE, and cerebral infarction. Direct infiltration of the vascular intima or basement membrane by bacteria or inflammatory cells contained in emboli induces injury or bleeding tendency.[14] Intravenous thrombolysis in which more distal areas may be diffusely reached by such a mechanism may increase the risk of hemorrhagic complications in comparison with MT involving topical endovascular passage.

According to a recent case series and systematic review of the results of treatment between IE patients who underwent intravenous thrombolysis with rt-PA and those who underwent MT, the incidence of postoperative cerebral hemorrhage was higher in the former, although the neurological prognosis and mortality rate were similar between the two groups, suggesting that MT should be selected if either method is available.[15] However, the number of patients in whom a diagnosis of IE can be made before treatment is limited. In patients in whom IE is clinically suspected, MT should be prioritized even if intravenous thrombolysis is possible.

MT for infective emboli was reported to induce inflammation or serious vasospasm at the site of occlusion in some patients; for MT, devices that are minimally invasive for the vascular endothelium should be selected.[16] Teng et al. conducted *in vitro* and *in vivo* studies to investigate the degree of vascular endothelial cell injury related to different devices for MT and reported that each stent retriever more markedly damaged the endothelial cells compared with a Penumbra 5MAX ACE, being more invasive.[17] In the present case, the CAPTIVE technique with a combination of the two devices was adopted, and 2 passes led to recanalization. Treatment was accomplished in the absence of vasospasm. To our knowledge, no study has reported treatment results with respect to devices or procedures. However, treatment in consideration of the balance between prompt recanalization and a minimally invasive procedure may be important.

Rapid, minimally invasive MT should always be considered through the introduction of new devices, improvements of procedures, and case accumulation.

Conclusion

We report a patient in whom cerebral embolism related to bacterial emboli was complicated by bacterial meningitis and IE. In ischemic stroke patients with bacterial meningitis, IE-related bacterial embolism must always be considered for treatment. Furthermore, MT should be prioritized in patients with cerebral embolism complicated by IE; the indication of antithrombotic therapy must be carefully evaluated.

Disclosure Statement

The authors declare no conflict of interest.

References

1) Lucas MJ, Brouwer MC, van der Ende A, et al: Endocarditis in adults with bacterial meningitis. *Circulation* 2013; 127: 2056–2062.
2) Eishi K, Kawazoe K, Kuriyama Y, et al: Surgical management of infective endocarditis associated with cerebral complications. Multi-center retrospective study in Japan. *J Thorac Cardiovasc Surg* 1995; 110: 1745–1755.
3) Nakatani S, Ohara T, Ashihara K, et al: JCS 2017 guideline on prevention and treatment of infective endocarditis. *Circ J* 2019; 83: 1767–1809.
4) Hess A, Klein I, Iung B, et al: Brain MRI findings in neurologically asymptomatic patients with infective endocarditis. *AJNR Am J Neuroradiol* 2013; 34: 1579–1584.
5) Takamatsu D, Bensing BA, Sullam PM: Two additional components of the accessory sec system mediating export of the *Streptococcus gordonii* platelet-binding protein GspB. *J Bacteriol* 2005; 187: 3878–3883.
6) García-Cabrera E, Fernández-Hidalgo N, Almirante B, et al: Neurological complications of infective endocarditis: risk factors, outcome, and impact of cardiac surgery: a multicenter observational study. *Circulation* 2013; 127: 2272–2284.
7) Heiro M, Nikoskelainen J, Engblom E, et al: Neurologic manifestations of infective endocarditis: a 17-year experience in a teaching hospital in Finland. *Arch Intern Med* 2000; 160: 2781–2787.
8) Snygg-Martin U, Gustafsson L, Rosengren L, et al: Cerebrovascular complications in patients with left-sided infective endocarditis are common: a prospective study using magnetic resonance imaging and neurochemical brain damage markers. *Clin Infect Dis* 2008; 47: 23–30.
9) Mook-Kanamori BB, Fritz D, Brouwer MC, et al: Intracerebral hemorrhages in adults with community associated bacterial meningitis in adults: should we reconsider anticoagulant therapy? *PLoS ONE* 2012; 7: e45271.
10) Asaithambi G, Adil MM, Qureshi AI: Thrombolysis for ischemic stroke associated with infective endocarditis: results from the nationwide inpatient sample. *Stroke* 2013; 44: 2917–2919.
11) Toyoda K, Koga M, Iguchi Y, et al: Guidelines for intravenous thrombolysis (recombinant tissue-type plasminogen activator), the third edition, March 2019: a guideline from the Japan Stroke Society. *Neurol Med Chir (Tokyo)* 2019; 59: 449–491.
12) Chan KL, Dumesnil JG, Cujec B, et al: A randomized trial of aspirin on the risk of embolic events in patients with infective endocarditis. *J Am Coll Cardiol* 2003; 42: 775–780.
13) Bolognese M, von Hessling A, Müller M: Successful thrombectomy in endocarditis-related stroke: case report and review of the literature. *Interv Neuroradiol* 2018; 24: 529–532.
14) Omoto T, Saito K, Kashima T, et al: Mycotic aneurysm of the right coronary artery. *Asian Cardiovasc Thoracic Ann* 2006; 14: 331–332
15) Marquardt RJ, Cho SM, Thatikunta P, et al: Acute ischemic stroke therapy in infective endocarditis: case series and systematic review. *J Stroke Cerebrovasc Dis* 2019; 28: 2207–2212.
16) Nishino W, Tajima Y, Inoue T, et al: Severe vasospasm of the middle cerebral artery after mechanical thrombectomy due to infective endocarditis: an autopsy case. *J Stroke Cerebrovasc Dis* 2017; 26: e186–e188.
17) Teng D, Pannell JS, Rennert RC, et al: Endothelial trauma from mechanical thrombectomy in acute stroke: in vitro live-cell platform with animal validation. *Stroke* 2015; 46: 1099–1106.