Case Report

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Successful Medical Treatment of Bivalvular Infective Endocarditis Complicated with Young Stroke

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Abstract

Background: The aim of his study was to evaluate the frequency of two most Staphylococcus aureus bacteremia (SAB) associated with infective endocarditis (IE) is common. Ischemic infarction is a frequent neurological complication of IE; however, young stroke resulting from IE is rare. We herein report a case of acute mitral valve and aortic valve infective endocarditis complicated with young stroke 8 days after left foot debridement due to methicillin-sensitive Staphylococcus Aureus (MSSA)-related cellulitis. The patient was discharged successfully after 6 weeks of antibiotics with oxacillin in spite of valve replacement surgery due to hemorrhagic transformation of right frontoparietal lobes.

Keywords: Infective endocarditis; Young stroke; Staphylococcus aureus bacteremia

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Introduction

Young stroke is uncommon in all strokes. The etiology of cardio-embolism for young adults under 45 years of age accounts for 15-35% [1]. The frequency of cardio-embolism related to endocarditis is approximate 3% [2]. We herein report a case of *MSSA*-related bivalvular infective endocarditis with young stroke resulting from left foot cellulitis. Blood cultures grew *MSSA*. Meanwhile, Janeway lesion of the right thumb, splinter hemorrhage of the right 4th finger, and hemorrhagic transformation of frontoparietal lobes were found. The association of young stroke and other diseases such as antiphospholipid syndrome, systemic lupus erythematosus, protein C deficiency, protein S deficiency, and antithrombin III deficiency were excluded [2-4]. There is no specific treatment strategy for IE in young stroke patients. In accordance with most reviews, valve replacement surgery was postponed at least for 4 weeks because of the possibility of adverse neurological complications such as cerebral hemorrhage or progressive brain ischemia occurring during surgery [5-7]. Antibiotics with oxacillin 12 g per day effective controlled the infection of *MSSA*. Blood culture revealed negative findings finally.

Case Report

A 41-year-old male with a history of alcoholism, gouty arthritis, and intravenous drug abuse with unkown entity 10 years ago presented to the emergent department with a 2-day history of fever, malaise, consciousness disturbance and right-sided hemiparesis. He was diagnosed with *methicillin-sensitive Staphylococcus Aureus (MSSA)* cellulitis of the left foot and underwent debridement at our plastic surgery department 8 days before admission. Physical examination showed high-grade fever of 39.3°C, blood pressure of 137/76 mmHg, heart rate of 93 beats/min, respiratory rate of 18 breaths/min, grade III of systolic murmur at left lower sternal border and apex. Neurological condition showed Glasgow Coma Scale (GCS: E4VAM5), dysphagia, aphasia, right-sided hemispatial neglect, conjugate deviation to left without nystagmus of eyes, right facial palsy and right-sided hemiparesis. The National Institutes of Health Stroke Scale (NIHHS) score was estimated as about 29. Laboratory examination showed white blood cell count of 18900/μL, C- reactive protein level of 20.54 mg/dL, creatine phosphokinases of 46 U/L, creatine phosphokinases-MB of 10 U/L, and troponin I of <0.01 ng/mL. Electrocardiography (EKG) revealed sinus tachycardia and left ventricular hypertrophy. Chest radiography (CXR) revealed no active lung lesion. Brain computed tomography scan (CT) revealed large hypodensity lesions in left frontotemporoparietal lobes, and right parietal lobe with hemorrhagic transformation (**Figure 1**). He was admitted to our intensive care unit and antibiotic treatment with ceftriaxone 2.0 g per day was initiated. On the next day of admission, transthoracic echocardiography (TTE) revealed mild tricuspid regurgitation (TR), mild aortic regurgitation (AR), and unremarkable finding of valvular vegetation. Two days after admission, he was transferred to the general ward due to improvement of his consciousness level gradually (GCS: E4V1M6). He was still aphasic and had

right-sided hemiparesis. On the fifth day of admission, two sets of blood cultures grew MSSA. We switched antibiotic to oxacillin 2.0 g every 4 hours. Brain magnetic resonance imaging (MRI) with diffusion-weighted imaging (DWI) revealed acute large-scale infarction in left frontotemporoparietal lobes, middle cerebral artery territory with small hemorrhagic transformation in right frontoparietal lobes (**Figure 2A and 2B**). Magnetic resonance angiography (MRA) and sagittal T2-weighted imaging revealed occlusion of left M2 segment of middle cerebral artery (MCA) (**Figure 2C**). The survey of young stroke was carried out and showed protein C levels of 119.8% (normal 70 to 140), protein S levels of 117.9% (normal 58.6 to 126), anti-thrombin III levels of 131.6% (normal 75 to 125), homocysteine levels of 10.57 umol/L (normal 5.46 to 16.20), anti-phospholipid IgG of 1.48 RU/ml (normal <12), anti-streptolysin O titer of 40 IU/mL (normal <145), rheumatoid factor of <11.5 IU/mL (normal 0 to 15.9), normal antinuclear antibody titer of <1:20, erythrocyte sedimentation rate of 105 mm/hr (normal 0 to 15), and C-reactive protein level of 11.73 mg/dL. One week after admission, two sets of blood culture still grew *MSSA*. Transesophageal echocardiography (TEE) revealed one vegetation of left coronary cusp (LCC) of aortic valve, and another one of anterior leaflet (AL) of mitral valve (**Figure 3**). Moreover, severe mitral regurgitation (MR) and AR were found. The cardiac surgeon suggested conservative antibiotic treatment for at least four weeks. The ophthalmologist examined his eyes and no Roth's spot existed; however, he had developed splinter hemorrhage of right 4th finger and non-tender Janeway lesion of the right thumb (**Figure 4**). After 4 weeks of antibiotic treatment, his blood culture turned negative finally; however, the patient developed hospital-acquired pneumonia with sputum culture of *penicillin-resistant streptococcus pneumoniae (PRSP).* Thus, we combined intravenous moxifloxacin 400 mg per day, gentamycin 80 mg every 8 hours per day with oxacillin 2.0 g every 4 hours. On the 36th day, follow-up TTE revealed severe AR, moderate MR, mild TR and unremarkable vegetation. Carotid phonoangiography revealed no measure plaque or stenosis of left carotid artery. On the 37th day, coronary and cerebral angiography revealed one fistula of left circumflex branch of left coronary artery, and total occlusion of left MCA. His infective endocarditis improved after antibiotic use. Although the sequelae of impairment of verbal skill and right-sided hemiparesis remained, his muscle power of limbs recovered and gradually contributed to the rehabilitative program. He was discharged successfully on the 50th day after admission. After six months of follow-up, his splinter hemorrhage and Janeway lesion disappeared. However, TTE still revealed severe MR.

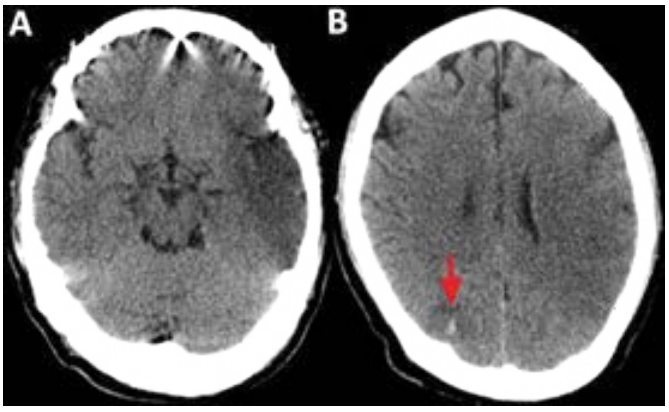

Figure 1 Brain computed tomography scan without contrast enhancement on admission revealed (A) Large hypodensity lesions in left frontotemporoparietal lobes; (B) Hypodensity lesion in the right parietal lobe with hemorrhagic transformation (Red arrow).

Discussion

Staphylococcus aureus has a leading high mortality rate in patients with healthcare–associated infection [8]. In IE patients, staphylococcus aureus infection accounts for 31%, and *MSSA* is a predominant pathogen in healthcare-associated patients [9]. The pathogenesis of IE with SAB infection is assumed to arise from adhesion of pathogen colonized on the damaged native valve, caused by turbulent blood flow [5]. The frequency of IE in SAB patients accounts for 10 to 46% [10]. The present case

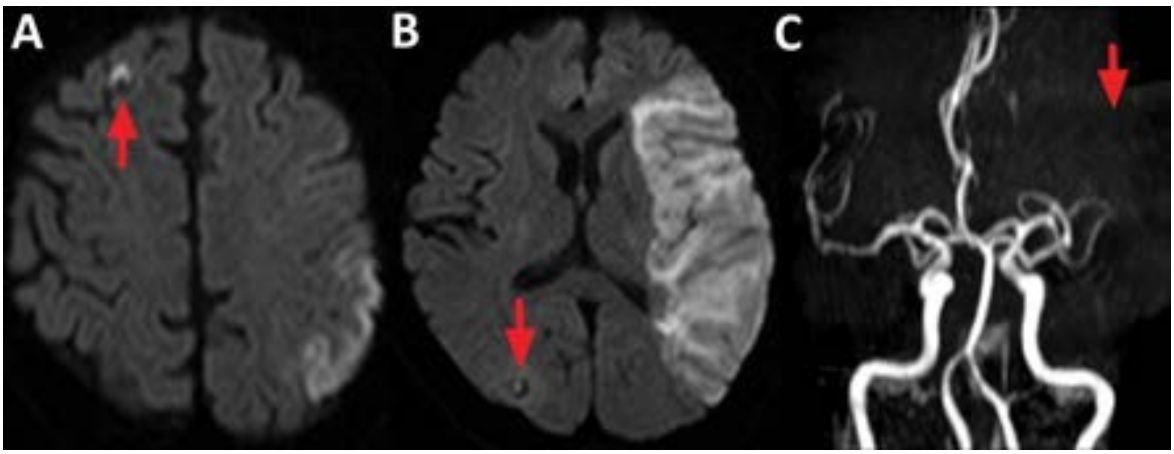

Figure 2 Brain magnetic resonance imaging on the fifth day of admission (A+B) DWI revealed hyperintensity lesions in left frontotemporoparietal lobes, middle cerebral artery territory with small hemorrhagic transformation in right frontal and parietal lobes (Red arrows). (C) MRA revealed occlusion of left M2 segment of middle cerebral artery (Red arrow).

fulfilled the criteria of non-nosocomial healthcare-associated infection [8] because the patient underwent surgery, wound care and medical treatment of *MSSA* cellulites of the left foot 8 days before admission. Mitral valve and aortic valve IE with left MCA infarction was as a result from the emboli of SAB. Choon et al. [11] stated that the emboli from left-sided valvular vegetation could become dislodged or fragmented into the brain via systemic circulation, resulting in neurological complications. In most reviews, the undetermined etiology is the most common subtype in young stroke patients [3,4]. The determined etiology of cardio-embolism accounts for up to 30% in young adults [1,3]. The incidence rates of young stroke are more predominant for men than women in Asian [1,3,4]. However, cardioembolic stroke is more common in women in Taiwan.

The other determined etiologies of antiphospholipid syndrome, systemic lupus erythematosus, protein C deficiency, protein S deficiency, and antithrombin III deficiency were excluded in this article. Brain CT and MRI demonstrated the lesions of infarction. Furthermore, carotid and cerebral angiography showed total occlusion of left MCA without stenosis but no occlusion of the left internal carotid artery.

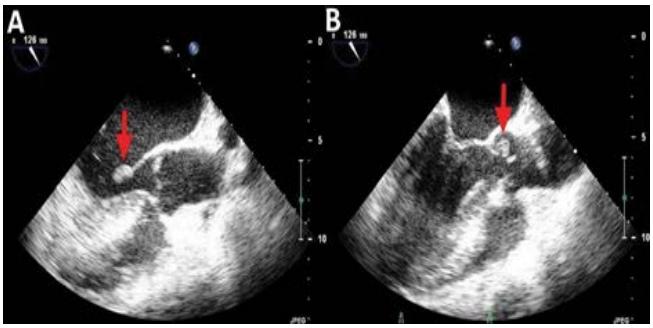

Figure 3 Transesophageal echocardiography (Long-axis view) three weeks after admission revealed two oscillating vegetations. (A) Anterior leaflet of mitral valve (Red arrow). (B) Left coronary cusp of aortic valve (Red arrow).

Our case fulfilled the modified Duke criteria for the Diagnosis of Infective Endocarditis [12] including the two major criteria with four sets of blood culture, which yielded *Staphylococcus aureus*, and vegetations confirmed by TEE. The minor criteria are fever of 39.3°C, Janeway lesion, splinter hemorrhage, new murmur and cerebral infarction. In a previous study, the less common signs accounted for 5% in Janeway lesions, and 8% in splinter hemorrhages [5]. Right-sided IE is usually associated with intravenous drug users, whereas aortic or mitral valve (left-sided) IE are common in non-intravenous drug users [11]. SAB with IE and cerebral infarction contribute to high risk of outcome and mortality. In-hospital mortality of IE is from 15 to 35% [5,9]. The strategy of treatment in young stroke patients caused by IE is not specific. As the pathogen was found in two or more sets of blood culture, earlier appropriate antibiotic treatment is suggested to minimize neurological complications [5,7]. Moreover, the research by Vincent Le Moinget et al. in 2015 [10] suggested the duration of treatment for SAB with IE patients should be 4 to 6 weeks. Oxacillin 2.0 g every 4 hours for this case controlled *MSSA* infection effectively.

The indications of surgery for IE patients are heart failure, severe valvular regurgitation, paravalvular complication, vegetation size, uncontrolled infection, abscess, or prevention of embolic events [5,7,13]. In the present case, aortic and mitral valve IE with severe AR, fever with persistent bacteremia for more than 1 week, and infarction event were emergencies indicating surgery; nonetheless, hemorrhagic transformation of right frontoparietal lobe accompanied with ischemic stroke was contraindicated for surgery. The accompanying complications of intracerebral hemorrhage caused by hemorrhagic transformation or neurologic deterioration during surgery were rather concerning. Hemorrhagic transformation accounts for 50% in IE with embolic stroke patients [6]. Valve replacement repair surgery should be postponed for at least for 4 weeks from the timing of the stroke due to the higher mortality rate during surgery [6,7].

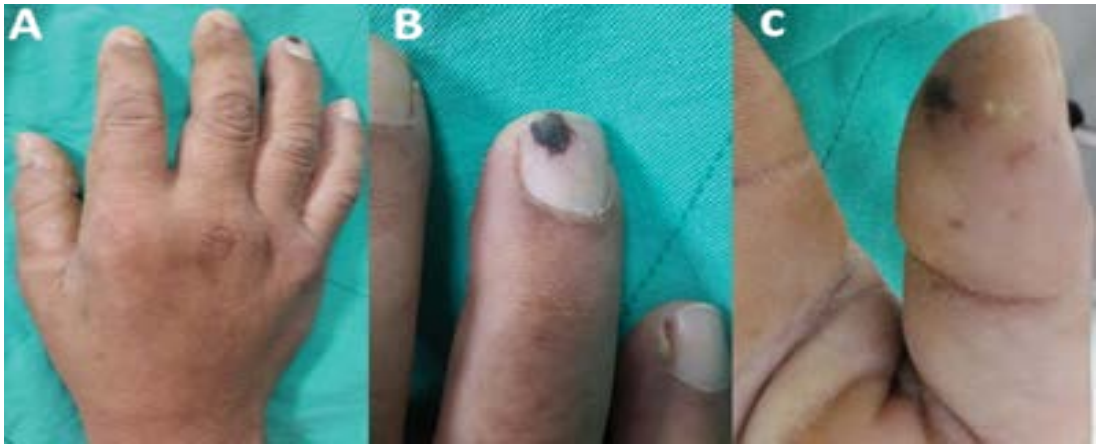

Figure 4 (A+B) Splinter hemorrhage of right 4th finger. (C) Janeway lesion of right thumb.

After discussion with the cardiologist, cardiac surgeon, neurologist, and infection specialist, medical therapy was our first choice. We did not use aspirin due to the increased risk of cerebral bleeding and no significantly decreased incidence of stroke events in IE patients [5,14]. In addition, we combined rehabilitative therapy for this case. His neurological complications recovered gradually, and there was no progression of ischemia or hemorrhage shown by follow-up brain CT. The research by Elfriede Ruttmann et al. in 2006 [15] described a favorable prognosis of cardioembolic stroke and a highly successful rate of rehabilitation among young patients. The disappearance of Janeway lesion and splinter hemorrhage in this case may imply the effective control of infection after six months of follow-up. However, persistent severe MR indicated irreversible damage due to SAB IE.

Conclusion

Stroke results in disability and is the second/third leading cause of death in the world [3,15]. The survey of etiology in young stroke is crucial to the strategy of treatment, which leads to different prognoses. In patients with young stroke and fever, we should not neglect the clinical diagnosis of infective endocarditis, especially in patients with recent surgery involving *Staphylococcus aureus* infection. The detection of vegetative growth by transesophageal echocardiography dependent on the practitioner's technique is important. In this group, carotid and cerebral angiography are practical methods to exclude the possibility of vertebral artery insufficiency or atherosclerotic plaques related to stroke. The performance of cardiac catherization should be careful because the risk of embolization with dislodged aortic valve vegetations may increase during the procedure [15]. Due to high mortality rate, we highlight that earlier appropriate antibiotic use is warranted as soon as infective endocarditis is suspected. Furthermore, the duration of medical treatment for young stroke patients should be adequate and timely.

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