Infective endocarditis due to methicillin-sensitive Staphylococcus aureus in a patient with untreated atopic dermatitis who was successfully treated without surgery

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Abstract
Atopic dermatitis (AD) is one of the most common chronic inflammatory skin diseases and Staphylococcus aureus has been frequently isolated from patients with AD. Infective endocarditis (IE) caused by S. aureus is one of the most serious complications of AD. A 46-year-old Japanese woman was admitted to the hospital due to persistent fever. She had untreated AD, and methicillin-sensitive S. aureus was isolated from blood and skin smear cultures. Echocardiography revealed a large mobile vegetation adhered near the annulus of the posterior mitral leaflet; it was diagnosed as AD-associated IE. Although surgical intervention was considered, the patient refused surgery. She was successfully treated with antibiotic therapy only, and resolution of the vegetation was confirmed on follow-up transesophageal echocardiography on Day 42. AD should be considered a predisposing factor of IE and appropriate skin treatment is essential to prevent IE in patients with AD.

INTRODUCTION
Infective endocarditis (IE) is a life-threatening infection, even in the post-antibiotic era. Currently, Staphylococcus aureus has become the most common cause of IE worldwide [1], with a significantly higher in-hospital mortality rate than streptococcal/enterococcal IE (17.5 vs. 8.9%) [2]. Atopic dermatitis (AD) is one of the most common pruritic and chronic inflammatory skin diseases [3]. Changes in the skin microbial flora in addition to chronic skin inflammation in patients with AD could be risk factors for infections caused by S. aureus [4].

IE is one of the most serious complications in patients with AD. However, only a limited number of cases showing the association between IE and AD have been reported [5]. In addition to antibiotic therapy, cardiovascular surgery is usually required to treat left-sided IE caused by S. aureus in most cases; cases treated with antibiotic therapy alone were rare.

CASE REPORT
A 46-year-old woman was referred to our hospital because of persistent fever. Fever started 3 weeks before admission. Her medical history was unremarkable except for untreated AD since childhood. She denied recreational drug use and any recent medical and dental procedures. At initial presentation,
she looked distressed. Her vital signs included body temperature, 38.1°C; blood pressure, 96/49 mmHg; heart rate, 85 beats/min; respiratory rate, 20 breaths/min; and oxygen saturation, 99% (room air). Her skin was generally dry; scales and scratch scars were observed on the upper extremities. Heart murmur was not heard on auscultations. No physical finding indicating IE was observed. Blood examination revealed elevated white blood cell counts (10,600/μL, normal range: 3800–9100/μL) and C-reactive protein levels of 11.20 mg/dL (<0.3 mg/dL). Her serum creatinine level was within the normal range and urinalysis showed absence of proteinuria, hematuria and bacteriuria. Chest X-ray and electrocardiography showed no abnormalities. Methicillin-sensitive S. aureus (MSSA) was isolated from all three sets of blood cultures and a smear culture of the skin on Day 2, which were obtained during admission. Transthoracic echocardiography (TTE) was performed on the same day as the screening test for IE; it revealed a large mobile vegetation adhered near the annulus of the posterior mitral leaflet (Fig. 1A). Mitral regurgitations (MR) and left-to-right shunts were not observed and the ejection fraction was preserved (72%). Although intravenous ceftriaxone (2 g every 8 h) and vancomycin (1 g every 12 h) were continued from the time of admission, medication was switched to intravenous cefazolin (2 g every 8 h) on Day 2 based on the causative organism. The patient became afibrile on Day 3. Transesophageal echocardiography (TEE) was performed on Day 7 and a large vegetation was still observed without MR (Fig. 1B). Although the patient did not have any neurological abnormalities, magnetic resonance imaging (MRI) of the head performed on Day 5 revealed two small lesions indicating septic emboli (Fig. 2). Abscess formation and other embolic lesions were not detected on contrast-enhanced computed tomography (CT) on the same day. Although the risk of further septic embolization was considered, the patient refused surgical intervention. The vegetation was followed-up by TTE; the size of the vegetation gradually decreased without any new abnormal findings on repeated MRI and contrast-enhanced CT performed on Days 18 and 21, respectively. TEE performed on Day 42 showed resolution of the vegetation (Fig. 3). The skin condition also improved with the use of betamethasone dipropionate and heparinoid creams during hospitalization. Antibiotic therapy (total 6 weeks after confluence of negative blood cultures on Day 3) was completed; the patient was discharged without any complications. Although mild-to-moderate MR remained on follow-up TTE, the patient did not show any signs of heart failure or infection recurrence 2 years after discharge without requiring any oral medications.

DISCUSSIONS

In patients with AD, reduction in antimicrobial peptides, diminished recruitment of innate immune cells to the skin, epithelial barrier disruption, and toll-like receptor 2 defects have been observed; these changes have been associated with susceptibility to S. aureus infection [6]. S. aureus enterotoxin contributes to corticosteroid resistance in T cells and alters regulatory T-cell activity [3]. S. aureus colonized the skin of >90% of patients with AD, compared with 10% of healthy individuals [7]. This fact could explain why S. aureus is the most common causative organism in patients with AD-associated IE Prompt diagnosis and immediate treatment, including antibiotic treatment and surgery, are critical because IE caused by S. aureus is associated with more severe clinical manifestations than IE caused by other organisms, with higher rates of preoperative embolic events and preoperative strokes [8].

Fukunaga et al. [9] reviewed cases of cardiovascular surgery performed at their faculty and reported that the incidence of AD among patients with IE was 6.7% and the mean age was significantly lesser in patients with IE with AD than in those without AD (28.4 vs. 53.7 years). Yamamoto et al. [5] reviewed nine previously reported cases of AD-associated IE in addition to their own case and reported S. aureus as the causative organisms in all cases; almost all cases (90%) required surgery. Yamamoto et al. [5] reported on a patient with AD-associated IE who had a total of five recurrences of prosthetic valve endocarditis. Improvement of skin conditions could be a key to lowering...
the risk of IE in patients with AD and preventing recurrent infections. Considering the increased prevalence of AD in industrialized countries (15–30% in children and 2–10% in adults) [3], attention always should be paid to the risk of IE in patients with AD, particularly those with untreated and uncontrolled disease.

Our case was unique in that the patient exhibited a good clinical course with antibiotic therapy alone, even though she had a large left-sided vegetation and intracranial complications due to MSSA, for which a surgical intervention may usually be considered [10]. We considered the location of the vegetation (near the annulus of posterior mitral leaflet) might contribute to a good clinical course in the present case. Attention should be paid to skin conditions of patients with IE if the causative organism is S. aureus, particularly in young patients.

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CONFLICT OF INTEREST STATEMENT
No conflicts of interest.

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ETHICAL APPROVAL
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CONSENT
Written informed consent was obtained from the patient.

GUARANTOR
Dr Hibi Arata.

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Figure 3: Follow-up transthoracic echocardiography (TTE) images taken on Days 14, 21 and 35 and transesophageal echocardiography (TEE) images taken on Day 42. (A) On TTE, the size of the vegetation is confirmed to be reduced on Day 14 (major axis, 11 mm), the vegetation is barely visible on Day 21 (encircled by dotted line) and became undetectable on Day 35. (B) Resolution of the vegetation is confirmed on TEE performed on Day 42. On color Doppler mode, mild-to-moderate mitral regurgitation was detected. LV, left ventricle; LA, left atrium.
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