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CASE REPORT



A case of infective endocarditis associated with atopic dermatitis perioperatively treated with dupilumab

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ABSTRACT

Background: Several case reports and reviews support a relationship between atopic dermatitis (AD) and infective endocarditis (IE). Here, we present a case of severe AD suspected of causing IE.

Case presentation: A 21-year-old man with severe AD was admitted to our hospital due to unidentified fever, syncope, and headache. He was diagnosed with IE with cerebral embolism and mitral regurgitation. Before elective cardiac surgery, he was subcutaneously administered dupilumab for 2 months to control AD. Dupilumab improved AD, and cardiac surgery was performed without complications.

Conclusions: Dupilumab may be effective in AD cases as preparation for cardiac surgery.

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KEYWORDS

Infective endocarditis;
atopic derma-
titis; dupilumab

Background

Only about 25% of patients with infective endocarditis (IE) have a definite cause, such as invasive dental treatment or surgery (1). Atopic dermatitis (AD) is a common skin disease and affects 20% of children and 1–3% of adults in most countries (2). A few case reports and reviews have shown the relationship between AD and IE (2–7). Colonization by *Staphylococcus aureus* is observed in skin lesion in more than 90% of patients with AD due to the abnormality of the skin barrier (3,4,8). Scratching pruritic skin lesions can lead to invasive *S. aureus* infections, such as bacteremia and endocarditis. We treated a patient with severe AD, which was suspected to cause IE. The patient was treated with dupilumab perioperatively through cardiac surgery.

Case presentation

A 21-year-old man with AD was admitted to our hospital 8 days after the onset of fever. He had suffered from AD since his childhood and had been treated by his dermatologist. His AD, which worsened due to psychological stress, was not sufficiently controlled for 3 years despite topical administration of very strong corticosteroids and tacrolimus ointment. The patient had never been pointed out about the cardiac abnormalities. He did not have any episodes such as recent dental treatment, surgery, tooth decay, or injection. A sudden fever, which increased to 39.7°C, caused headache and syncope 4 days after its onset. Before the patient's admission to our hospital, his unidentified fever had been treated with intravenous administration of fosfomycin for 5 days and oral levofloxacin for 4 days by a practitioner. On admission, the patient was alert, his body temperature was 38.5°C, and he had arthralgia in his left wrist. No paralysis, paresthesia, or meningeal signs were detected. His skin was dry, with longstanding skin eruptions, multiple eczematous lesions, chronic papules, and lichenification on the neck, trunk, and extremities. A skin survey did not find Osler's nodes or Janeway lesions. Laboratory

examinations showed a white cell count (WCC) of 8600/mm³, C-reactive protein (CRP) level of 12.45 mg/dl, and IgE level of 62057.8 IU/ml. Transesophageal echocardiography revealed the anterior leaflet flail of mitral valve (A3) with severe mitral regurgitation (MR), whose jet with a decent proximal isovelocity surface area was blowing while shifting to the posterior wall of left atrium. The Left ventricular end-systolic diameter (LVESD) was 43 mm. No significant vegetation was detected. Brain magnetic resonance imaging (MRI) showed multiple high-signal-intensity lesions on T2-weighted images (Figure 1). Computed tomography revealed a low amount of left pleural effusion and ascites as well as hepatosplenomegaly. No bacteria were detected by two sets of blood cultures taken on admission. The syncope, headache, and multiple abnormal lesions on brain MRI suggested the diagnosis of cerebral infarction caused by IE. After drug therapy with antibiotics for 27 days (intravenous administration of sulbactam (SBT)/ampicillin (ABPC) 12 g and gentamicin sulfate (GM) 120 mg per day for 9 days, SBT/ABPC 9 g and GM 120 mg for 4 more days, and SBT/ABPC 9 g and ABPC 6 g for 14 more days), the patient was discharged.

Owing to the MR, the mitral valve plasty under general anesthesia was scheduled. However, the patient's skin condition remained unchanged since the onset of IE. His neck, trunk, face, and extremities were covered with erythema, fissures, and lichen planus (Figure 2). His Eczema Area and Severity Index (EASI) was 36.5 (maximum 72) 47 days after admission. The body surface area of abnormal skin lesions was 50%. His AD was classified as the middle or severe level. Fearing that *S. aureus* in abnormal skin lesions might cause postoperative infection and that insertion and taping of catheters would be difficult, dupilumab was administered to treat AD for 11 weeks before cardiac surgery. Dupilumab (600 mg) was subcutaneously administered once, and a half dose was administered every 2 weeks. Fifty-two days after starting dupilumab, the IgE level improved to 13498.6 IU/ml. On the same day, the laboratory tests also showed a normal level of thymus

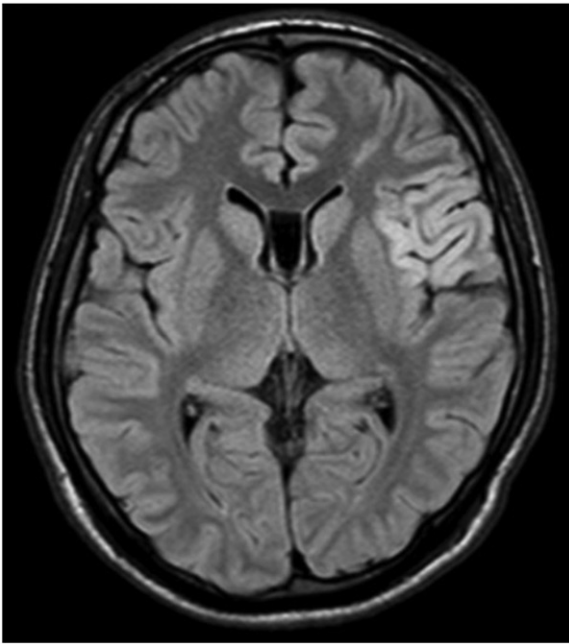


Figure 1. Brain magnetic resonance imaging (MRI) showed multiple high-signal-intensity lesions on T2-weighted images.



Figure 2. Atopic dermatitis in the present case.

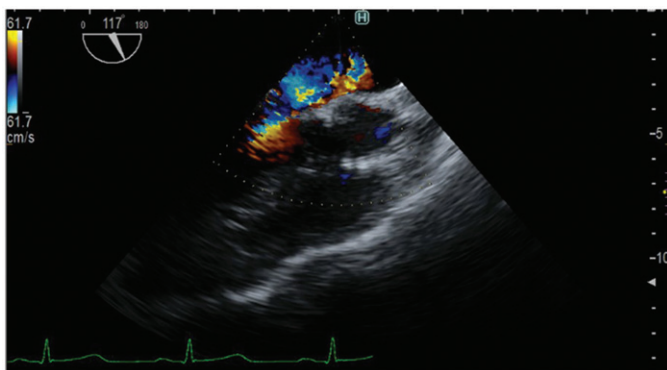


Figure 3. Mitral regurgitation prior to surgery.

and activation-regulated chemokine (TARC) at 251 pg/ml. Although trivial erythematous lesions remained, itching and fissures on the trunk and face disappeared. Seventy days after starting

dupilumab, EASI improved to 10. Cardiac surgery under general anesthesia was performed approximately 5 months after the onset of IE. Figure 3 was visualized under general anesthesia prior to the surgery, which revealed that the strut chorda and the primary chordae of A3 had been broken. The mitral valve plasty was performed without any complications or transfusion. No skin troubles were observed perioperatively. Postoperative transthoracic echocardiography performed 9 days after the surgery showed no MR and the smaller LVESD, which was measured at 38 mm. Treatment with dupilumab continued for 12 weeks after the surgery until the sternum belt was put off.

Discussion

A case report referred to 24 cases of IE related to AD (3). According to it, blood cultures in 23 of 24 cases demonstrated infection with *S. aureus*. According to Kondo et al. (2), the age distribution of patients with AD showed a bimodal pattern, with peak incidences in the age ranges of 0–5 and 21–25 years. The incidences of very severe and severe AD are significantly higher in adolescent/adult-type AD group than in the infantile and childhood groups (2). Furthermore, patients with IE and AD are much younger those without AD. According to two surveys in Japan, the percentages of IE with AD among total IE were 0.6% and 1.2% respectively (2). Fukunaga et al. (5) reported that 6.7% of IE also had AD.

This case was not able to demonstrate bacterial infection because the patient had been administered antibiotics for 5 days before admission to our hospital. However, the findings of MR, fever exceeding 38°C, cerebral embolisms, and the active inflammatory findings in laboratory tests such as elevated WCC and CRP supported the diagnosis of this case as IE (1). The present case had no other episodes that may have caused IE, such as surgery, tooth decay, drug injection, dental treatment or injuries, except for AD.

As no vegetation was detected with echocardiography, the patient was first treated with drug therapy. The mitral valve plasty was scheduled to repair the severe MR after the patient's AD improved. Dupilumab is an IL-4R α monoclonal antibody inhibiting signaling of IL-4/IL-13, key drivers of type-2-driven inflammation, as demonstrated by its efficacy in AD (9). In Japan, dupilumab was approved for manufacture and sale in January 2018. The present case is the first report of a patient administered dupilumab to prepare for elective cardiac surgery. The present case's EASI, which is one way to evaluate the level of AD, improved after the administration of dupilumab (10). The patient's IgE level and TARC examination results after administration of dupilumab also supported the efficacy of this drug.

Although AD is a common disease and affects 1–3% of adults, few case reports describe how to control the skin conditions perioperatively. In fact, difficulty with taping and inserting catheters are common in AD patients. The colonization of *S. aureus* in AD might cause bacteremia when the insertion or incision is performed on abnormal skin lesions (8). Fukunaga et al. (6) reported that 3 of 25 AD patients who underwent cardiac surgery at their institution over a 13-year period suffered from postoperative mediastinitis due to methicillin-resistant *S. aureus*. They proposed that thoracotomy might be a better surgical approach than median sternotomy in patients with AD who require thoracic surgery. Besides a surgical approach, administration of dupilumab may be effective for controlling AD perioperatively.

Conclusion

Administration of dupilumab might be one of the effective choices to control AD perioperatively.

Consent for publication

The patient's consent to publish this case report was obtained and documented.

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Disclosure statement

The authors declare that they have no competing interests.

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