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Case report

Infective endocarditis and Sjögren's syndrome diagnosed simultaneously

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ABSTRACT

Poor dentition and/or dental infection due to insufficient oral care are presumed to be risk factors for infective endocarditis (IE). We present a case of endocarditis caused by *Granulicatella adiacens* and Sjögren's syndrome (SS) with oral complications diagnosed simultaneously.

A 67-year-old woman was admitted to our hospital with fever, general fatigue, arthralgia, and back pain. She was diagnosed with primary SS according to the criteria of the American-European Consensus Group. Transthoracic echocardiography carried out to examine her persistent fever revealed vegetation formation (14 × 5 mm) on the aortic valve and her blood cultures were positive for *G. adiacens*. According to modified Duke's criteria, she was also diagnosed with IE. She underwent aortic valve replacement and was administered ampicillin with gentamicin for 6 weeks following surgery.

G. adiacens, which is formerly known as one of the nutritionally variant streptococci, is found as part of the normal microbiota of the oral cavity. The patient had chronic periodontitis associated with SS that likely predisposed to *G. adiacens* bacteremia and subsequent seeding of the aortic valve. Patients with SS may be at risk of IE because of the increased risk of bacteremia from oral complications such as dental caries or periodontal disease.

An association between SS and IE has not yet been reported. Our case indicates that SS may be the underlying pathology in patients with IE due to an oral bacterium.

Introduction

Infective endocarditis (IE) is relatively uncommon, but its in-hospital mortality rate ranges 19%–22.8% [1,2]. A plethora of microorganisms has been implicated in IE, but streptococci and staphylococci account for 80%–90% of the cases in which an identification is made [3]. The most predominant pathogens of IE are bacterial species found in the oral cavity or the skin, and poor dentition and/or dental infection, presumably due to insufficient oral care, are risk factors for IE [4,5]. *Granulicatella adiacens*, formerly classified as nutritionally variant streptococci (NVS), is found as part of the normal microbiota of the oral cavity. We present a case of endocarditis due to *G. adiacens* and Sjögren's syndrome (SS) with oral complications diagnosed simultaneously.

Case report

A 67-year-old woman was admitted to a hospital with fever, general fatigue, arthralgia, and back pain. She had been well until 4 months before admission, when she began to have back pain, bilateral shoulder pain, and left wrist pain. Seven days earlier, she began to have intermittent fever culminating in admission.

On admission, the patient reported no respiratory symptoms, no painful urination, and no weight loss, and she looked well. Physical examination revealed a body temperature of 36.9 °C, pulse rate of 100 beats/min, respiratory rate of 16/min, and blood pressure of 120/40 mmHg. Tenderness was found on her left fourth finger, left foot joint, and upper dental ridge. There was no tenderness of the spinous processes on tapping. Her lungs were clear on auscultation and no heart murmur was audible. There was

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no rash, palpable lymph nodes, or hepatosplenomegaly. The patient had no previous medical history. She drank alcohol socially and did not smoke. She lived in Japan and had no travel history for 1 year and no known contact with sick individuals or animals. There were no collagen diseases in her family history.

Laboratory data showed a markedly elevated erythrocyte sedimentation rate (107 mm/h); her white blood cell count was 4500 cells/μL, hemoglobin level was 12.6 g/dL, and C-reactive protein level was 6.1 mg/dL. Antinuclear antibodies were detected at a dilution of 1:640. Test results were positive for anti-La/SSB antibody, but there was no decrease in the C3 and C4 or CH50 complement levels, and negative anti-dsDNA and anti-Sm antibodies. Schirmer's test showed tear production of <5 mm/5 min in both eyes, and salivary scintigraphy showed delayed uptake and reduced concentration. According to the criteria of the American-European Consensus Group, the patient was diagnosed with primary SS [6]. An oral cavity examination by a dentist revealed chronic periodontitis.

The patient required further examination because of her persistent fever. Lumbar spine MRI showed no evidence of vertebral osteomyelitis or discitis. Whole-body CT scanning revealed no evidence of malignancy or deep abscesses. Transthoracic echocardiography revealed vegetation measuring 14 × 5 mm on the aortic valve associated with severe aortic regurgitation. Three sets of blood cultures were obtained, and ampicillin/oxacillin (24 g/day) with gentamicin (150 mg/day) were initially administered owing to suspected native valve endocarditis. After 1 day of incubation, the three sets of blood cultures were positive for gram-positive cocci, which were identified as *G. adiacens* 4 days later. Thus, ampicillin (12 g/day) with gentamicin was administered based on the antimicrobial susceptibility findings.

According to modified Duke's criteria, the patient was diagnosed with IE due to *G. adiacens* with SS. On day 14 after admission, she underwent aortic valve replacement because of the presence of movable vegetation >10 mm. The valve culture and following blood cultures were negative. Therefore, she was treated with ampicillin with gentamicin for 6 weeks following surgery (Fig. 1). She was discharged home in good condition and resumed her usual lifestyle. She received no medications for SS and was subsequently followed up as an outpatient.

Discussion

G. adiacens was formerly classified as an NVS that requires pyridoxal or cysteine for growth and produce leucine aminopeptidase and arylamidase. *G. adiacens* as these organisms are no longer streptococci are found as part of the normal microbiota of the upper respiratory, urogenital, and gastrointestinal tracts of humans and cause approximately 5% of bacterial endocarditis cases, may be classified as culture-negative IE because of their slow growth and requirement of specific media for growth [3] although most modern blood culture media will support the growth of the organism. NVS are less susceptible in vitro to penicillin than other streptococci. Approximately 67% of strains are resistant (minimum inhibitory concentration [MIC], ≥0.5 μg/mL), and 14% of isolates are highly resistant to penicillin (MIC, ≥4 μg/mL). High-level aminoglycoside resistance has not been reported in NVS [7]. According to American Heart Association guidelines, it is reasonable to treat patients with IE due to NVS with a combination of ampicillin or penicillin plus gentamicin as is done for enterococcal IE [5].

In this case, the *G. adiacens* bacteremia that caused the IE presumably resulted from the chronic periodontitis because the patient had no sites of focal infection and no recent history of dental treatment before admission. Considering the inflammation of the finger and foot joint improved spontaneously before administration of antimicrobials, these symptoms were regarded as symptoms associated with SS. A relationship between

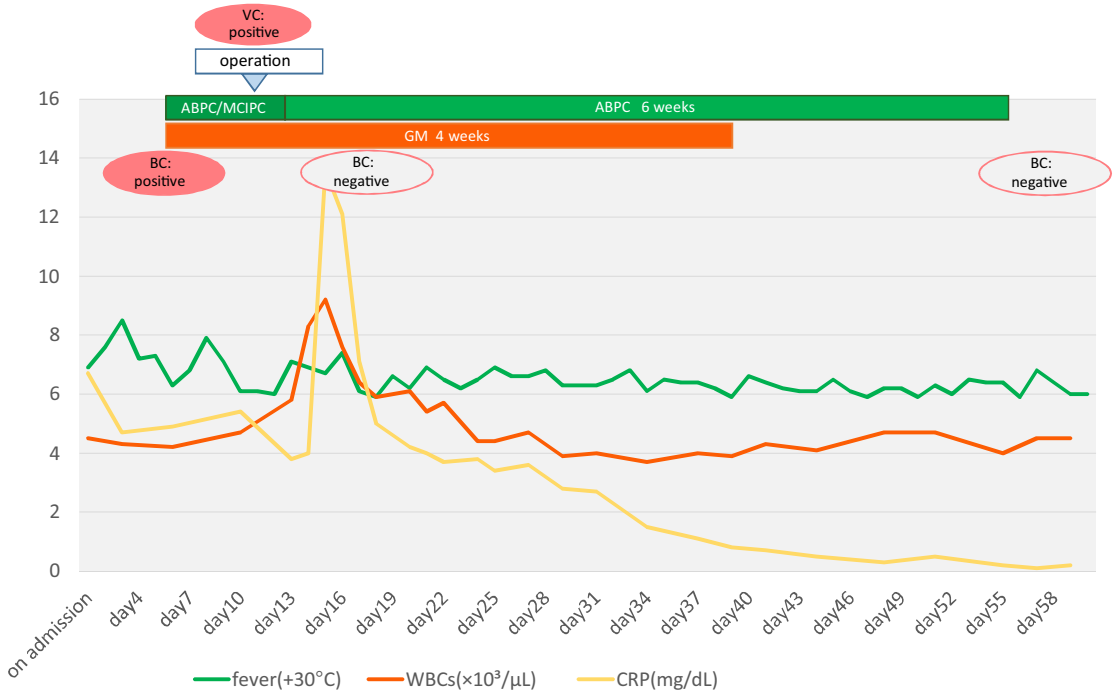

Fig. 1. Clinical course. BC = blood culture; VC = valve culture; ABPC/MCIPC = ampicillin/oxacillin; ABPC = ampicillin; GM = gentamicin; WBC = white blood cell; CRP = C-reactive protein.

periodontal inflammation and bacteremia has been reported in an observational study showing that patients with gingivitis/periodontitis more often developed bacteremia owing to coagulase-negative staphylococci and oral viridans streptococci during neutropenia than did those with a healthy periodontium ($p = 0.047$) [8]. A retrospective study showed that 61.5% of cancer patients with NVS bacteremia had mucositis or gingivitis [9]. In non-neutropenic patients, a previous report showed that the generalized presence of gingival bleeding after tooth brushing (which is a sign of gingivitis or periodontitis) was associated with an almost eightfold increase in the risk of bacteremia [10].

In our patient, who was first diagnosed with SS, it was inferred that her saliva secretory capacity had decreased before her admission and that SS could have been the cause of her periodontal disease. SS is a chronic inflammatory disorder characterized by diminished lacrimal and salivary gland function. The principal oral symptom of SS is xerostomia, which causes increased dental caries and may also lead to periodontal disease [11]. Valvular heart disease, such as mitral-valve prolapse, poor dental hygiene, long-term hemodialysis, diabetes mellitus, and human immunodeficiency virus infection are known as factors predicting development of IE [12]. Therefore, it is presumed that a patient with SS may have IE because of the increased risk of bacteremia from oral complications, such as dental caries or periodontal disease.

There have been only three case reports of IE caused by an oral bacterium in a patient with SS with oral complications. Sugimoto et al. reported IE suspected to be caused by *Staphylococcus saccharolyticus* in a patient with SS who had severe tooth decay [13]. Nomura et al. also reported repeated bacteremia and possible IE caused by *Streptococcus mutans* in a patient with SS who had dental caries [14]. De Chiara et al. also reported IE due to *Streptococcus agalactiae* in a patient with SS [15]. However, an increased risk of IE among patients with SS has not been reported. Further investigation of the association between IE and SS is necessary. Our case findings indicate that SS may be the underlying pathology of IE due to an oral bacterium.

Conflict of interest statement

The authors declare that they have no conflicts of interest.

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