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Infective Endocarditis Caused by Brevibacterium sanguinis and a **Review of Literature**

Brevibacterium sanguinis'in Neden Olduğu Enfektif Endokardit Olgusu ve Literatürün Gözden Geçirilmesi

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Abstract

The Brevibacterium spp. are opportunistic Gram-positive bacilli found in human skin flora and dairy products. Although not generally accepted as human pathogens, the Brevibacterium species are rare causes of infections such as bacteremia, endocarditis, peritonitis, and osteomyelitis, especially in immunosuppressive patients, in recent years. Herein, we aimed to report the first case of infective endocarditis caused by Brevibacterium sanguinis in a patient undergoing hemodialysis for chronic renal failure via an indwelling hemodialysis catheter.

Keywords: Brevibacterium sanguinis, infective endocarditis

Öz

Brevibacterium spp. insan derisi florasında ve süt ürünlerinde bulunan fırsatçı Gram-pozitif basillerdir. Brevibacterium türleri genel olarak insan patojeni olarak kabul edilmese de son yıllarda özellikle immünsüpresif hastalarda bakteriyemi, endokardit, peritonit ve osteomiyelit gibi enfeksiyonların nadir nedenleri olarak gösterilmektedir. Bu çalışmada, kronik böbrek yetmezliği nedeniyle kalıcı hemodiyaliz kateteri ile hemodiyaliz tedavisi alan bir hastada Brevibacterium sanquinis alt türünün neden olduğu, literatürde bildirilen ilk enfektif endokardit olgusunun sunulması amaclandı. Anahtar Kelimeler: Brevibacterium sanguinis, enfektif endokardit

Introduction

The Brevibacterium spp. are catalase-positive, non-motile, obligate aerobic, and diphtheroid-form bacteria. It is found in raw milk and imparts aroma and coloring properties to ripened cheese products. It can also be found as normal flora on the skin of some animals and humans^[1]. It is also thought to cause foot odor in humans^[2]. Until the number of cases reported in literature had increased, it was not considered a pathogenic bacterium; it was considered apathogenic for several years^[3].

The Brevibacterium species are rarely isolated as infectious agents. They usually cause opportunistic infections in

immunocompromised patients such as those with human immunodeficiency virus (HIV) infection or malignancies. There have been rare cases of infections such as peritonitis, brain abscess, endophthalmitis, pericarditis, and osteomyelitis caused by the Brevibacterium species. They are most commonly isolated from blood cultures^[4-8], and a majority of these are catheterrelated blood stream infections^[9].

The most common Brevibacterium species detected in clinical specimens is Brevibacterium casei. Other species, such as B. otitidis, B. paucivorans, B. epidermidis, B. mcbrellneri, B. luteolum, and B. iodinum have also isolated. B. sanguinis is a new Brevibacterium species that has been recently identified^[10].

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One of the reasons for the increase in the number of cases caused by the *Brevibacterium* species is the increasing number of immunocompromised patients who are susceptible to opportunistic infections and are hospitalized in intensive care units. Another reason for this is the use of mass spectrometry for bacterial identification in microbiological laboratories in recent years^[11]. With the use of mass spectrometry, microorganisms that could not be distinguished by conventional methods have become identifiable^[12].

Herein, we aimed to present the first case of infective endocarditis (IE) caused by *B. sanguinis* in a patient with a history of chronic renal failure for 5 years who was receiving hemodialysis via an indwelling catheter in the right subclavian region.

Case Report

A 54-year-old female presented to the cardiology outpatient clinic with complaints of shortness of breath and fatigue. The patient's vital signs were stable and she had a history of hypertension and chronic renal failure. She had been undergoing hemodialysis three days a week for five years due to end-stage renal failure. The hemodialysis was being performed via a permanent indwelling catheter at the right subclavian region, since the existing arteriovenous fistula was not functional. The cardiovascular examination revealed an early diastolic murmur. Examination of the other systems were not significant. The patient's body temperature was within the normal limits. There was no discharge or redness at the catheter site. Transthoracic echocardiography revealed a normal left ventricular ejection fraction, severe aortic regurgitation, and a mass consistent with vegetation in the right coronary cusp of the aortic valve. Thus, the patient was admitted to the cardiology department. The laboratory test results were as follows: white blood cell count, 7600 K/µl; PCT, 0.92 ng/ml; C-reactive protein, 66 mg/L; and erythrocyte sedimentation rate, 38 mm/30 min and 95 mm/ hour. A transesophageal echocardiography confirmed advanced aortic regurgitation and a 14x5 mm mass at the right and left coronary cusps, which was consistent with highly mobilized vegetation (Figure 1). The patient was preliminary diagnosis with acute/subacute bacterial endocarditis and the treatment was adjusted accordingly.

The patient's blood was drawn simultaneously from the catheter and a peripheral vein and was sent for blood culture. Three hours later, a blood sample was obtained for culture from a peripheral vein. The blood culture samples were placed in an automated blood culture device (VITEK 2°; Biomerieux, Marcy l'Etoile, France). As empirical therapy the following antibiotics were administered: ceftriaxone 1 gm (twice daily) and vancomycin 1 gm (once daily). All three blood samples yielded a positive result, and the signaling time for the catheter blood, 1st peripheral vein blood sample, and 2nd peripheral vein

blood sample was 23 hours, 38 hours, and 18 hours, respectively. Gram-staining of all of three samples revealed Gram-positive bacilli and coccobacilli, some of which were curved. Samples from the blood culture bottles were inoculated on sheep blood agar and eosin methylene blue agar and incubated at 37 °C for 24 hours. The bacterial colonies that grew on the sheep blood agar were gray-white in color, slightly sticky, and had a cheese-like odor (Figure 2). The growing bacteria was identified using a mass spectrometry device (VITEK MS[®]; Biomerieux, Marcy l'Etoile, France) as *B. sanguinis* in all three sets of blood cultures. The bacteria were pure. The diagnosis of acute/subacute natural valve endocarditis was confirmed.

There is no international standard treatment protocol for *B. sanguinis*. The antibiotics to be used in the antibiotic



Figure 1. A) A mass of 14x5 mm, which is attached to the right coronary and left coronary cusp, compatible with highly mobilized vegetation. B) Advanced aortic regurgitation



Figure 2. Grey-white, slightly sticky bacterial colonies growing on sheep blood agar

susceptibility test were based on the 2021 EUCAST 11.0 quideline for Corynebacterium spp. Antibiotic susceptibility testing revealed that the bacteria was sensitive to ciprofloxacin, moxifloxacin, rifampicin and vancomycin and was resistant to clindamycin. Thus, the empirical antibiotic therapy that was initiated was not changed. The patient was followed up without removal of the indwelling catheter. The patient was evaluated by the Cardiovascular Surgery Clinical Council for aortic valve replacement and a very high risk operation was planned. After 14 days of vancomycin administration the patient underwent surgery. No growth was detected in the tissue sample obtained intraoperatively. B. sanguinis growth was not detected in the blood cultures sent postoperatively. The patient was followed up in the intensive care unit for approximately two months after the operation. During the follow-ups, her general condition was moderate to poor. She died at the end of the two-month follow-up period.

Discussion

Apart from virulent bacteria *Corynebacterium diphtheriae*, other Coryneform bacteria generally have low virulence. However, they can sometimes cause severe and fatal infections. Additionally, its clinical importance is increasing^[5,13,14].

The *Brevibacterium* species cause recurrent opportunistic infections^[2,10,15]. Patients who develop infections with these species should be carefully followed up due to the high recurrence rate and to prevent worsening of the prognosis. The *Brevibacterium* species can cause serious infections such as brain abscess, catheter-related septicemia, and osteomyelitis in immunocompetent individuals as well as in immunocompromised patients^[5,9,8].

There are 45 different species in the genus *Brevibacterium*. However, only 10 species have been isolated from clinical specimens. *B. sanguinis* is a newly described species^[10].

In a study conducted by Wauters et al.^[10], six strains phenotypically resembling *B. casei* that were isolated from blood cultures and dialysate fluid samples were analyzed by molecular method. They determined that the growing bacteria was *B. sanguinis*. This study was the first to identify *B. sanguinis* and identified it as the causative microorganism. Wauters et al.^[10] also stated that the thallium acetate susceptibility test can be used to differentiate between *B. casei* and *B. sanguinis*. Similar to the disc diffusion test, this test involves placing 50-µg thallium acetate discs on the surface of blood agar medium after preparing a standard concentration (0.5 McFarland turbidity) of bacterial inoculum. The test results indicate that *B. casei* was resistant to thallium acetate, while *B. sanguinis* was susceptible to it. However, there is not enough data regarding this test and its standardization. In the study by Wauters et al.^[10], one patient had an HIV infection, one patients had acute myeloid leukemia, one patient had a neurological disease, and one pediatric patient had no underlying disease. In another patient, they could not determine the underlying medical history. The study did not provide any information regarding the patient from whom the dialysate fluid sample was evaluated. However, the fact that it was obtained from a dialysate fluid sample suggests that the patient was undergoing hemodialysis.

In recent years, the number of IE cases caused by the Brevibacterium species is increasing. A case of mitral valve IE caused by B. otitidis was first described in 2002 in a patient with a prosthetic heart valve^[16]. Cases such as native aortic valve endocarditis caused by *B. epidermidis*, recurrent native aortic valve endocarditis caused by B. casei, and native tricuspid valve endocarditis caused by a Brevibacterium spp. (species not specified) have also been reported^[17-19]. Herein, we have presented the first case of IE caused by *B. sanguinis*, IE is difficult to diagnose and has high morbidity and mortality rates. Among all the IE types, the most frequently identified agents are S. aureus (32%), viridans group streptococci (19%), coagulasenegative Staphylococcus (CNS) (11%), and Enterococcus spp. (11%). In our country, the frequency of S. aureus, Streptococcus spp., CNS, Enterococcus spp., and Brucella spp. was 20%, 19%, 10%, 9%, and 7%, respectively.

The viridans group streptococci (e.g., *S. anginosus*, *S. mitis*, *S. mutans*, and *S. sanguinis*) are the most common causative agents of community-acquired natural valve endocarditis. The *Staphylococcus* spp. are the most common causative agents of healthcare-associated IE and *S. epidermidis* is the most common causative agent of artificial valve IE^[20]. Apart from these, the HACEK group bacteria (*Haemophilus parainfluenzae*, *Aggregatibacter* spp., *Cardiobacterium* spp., *Eikenella corrodens*, and *Kingella* spp.) and non-HACEK Gram-negative bacteria (e.g., *Escherichia coli* and *Klebsiella pneumoniae*) can also cause IE. *B. sanguinis* is a rare causative agent^[15].

Patients undergoing hemodialysis are at a high risk for developing IE due to impaired immunity, frequent intravenous interventions, and intravascular calcifications. In patients with predisposing factors, rare bacteria should be considered as the causative agent and diagnostic tests should be performed accordingly. Because, as can be seen in this case we present, it causes serious infections that can be fatal. Although this is the first case of IE caused by bacteria, our identification with the mass spectrophotometry system contributed positively to our detection of bacteria. Since mass spectrometry devices with highly advanced technology have come into routine use, rare microorganisms that were previously unidentified and not encountered as causative agents have begun to be easily identified. *Brevibacterium sanguinis* identification may be difficult for laboratories that do not use automated systems such as VITEK MS[®] (Biomerieux, France). If suspected, advanced identification methods (such as mass spectrophotometry, sequence analysis) should be applied. Awareness should be created among clinical physicians on this issue. Timely treatment with appropriate antibiotics could prevent severe sepsis and multiple organ failure and reduce the risk of embolism and mortality and morbidity rates^[21].

Conclusion

Although the *Brevibacterium* species is rarely isolated, it should be considered in immunocompromised individuals. Our literature review did not reveal any prior case of *B. sanguinis*-induced IE. Thus, this was the first case of IE caused by *B. sanguinis*.

Ethics

Informed Consent: Consent form was filled out by all participants.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: İ.K., M.Ş.Y., Concept: Ö.A., M.K., Design: Ö.A., M.K., Analysis or Interpretation: M.K., Literature Search: G.O., Writing: Ö.A., G.O.

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