

Paravalvular Abscess as a Complication of Streptococcus Salivarius Infective Endocarditis of a Bioprosthetic Aortic Valve

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Abstract Rates of implantation of prosthetic valves and cardiac devices have increased significantly in the last thirty years, accounting, at least in-part, for the growing incidence of infective endocarditis cases. Prosthetic valve endocarditis (PVE) is an endovascular, microbial infection occurring on parts of a valve prosthesis or on reconstructed native heart valves. We present a case of a 63-year-old man with multiple comorbidities including extensive cardiovascular disease, who recently underwent bioprosthetic aortic valve replacement. Patient presented to the emergency department with exertional chest pain, dyspnea, fever, melena and lethargy. Blood cultures grew Streptococcus salivarius and transesophageal echocardiography confirmed PVE with an aortic paravalvular abscess. The patient was treated with appropriate antimicrobial therapy based on culture sensitivity and subsequently referred to cardiothoracic surgery for urgent evaluation. This case highlights several important points which include but are not limited to: investigation into the pathogen Streptococcus salivarius and its relationship to other known pathogens, understanding of the complications associated with PVE, and the importance of early identification of PVE and initiation of medical and surgical therapy with respect to prognosis.

Keywords: prosthetic valve endocarditis, paravalvular abscess, bioprosthetic aortic valve streptococcus salivarius

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1. Introduction

Infective endocarditis (IE) is a rare infectious disease with an annual incidence ranging from 3 to 7 per 100,000 person-years according to recent population surveys. Although relatively uncommon, IE continues to be characterized by increased morbidity and mortality and is currently the third or fourth most common deadly infection syndrome, after sepsis, pneumonia, and intra-abdominal abscess. Cardiac risk factors predisposing patients to IE have shifted from rheumatic heart disease, primarily seen in young adults, to degenerative valvular disease, which is mainly seen in the elderly [1]. Also, due to medical advancements and preventative prophylaxis, the age of the population diagnosed with IE has steadily increased. The relatively new entity of healthcare-associated IE, which disproportionately affects older adults, has emerged secondary to the introduction of therapeutic modalities such as cardiac devices, dialysis shunts, intravascular catheters, parenteral lines, and other external devices [1,2]. Left untreated, death from IE is inevitable and with the best available therapy, contemporary mortality rates from this condition are approximately 25% [2].

As aforementioned, prosthetic valves and cardiac devices are well established risk factors for IE. Rates of implantation of these devices have increased significantly in the last thirty years, accounting for the growing rates of infectious endocarditis cases. For example, in a recent cohort of 2,781 adults in 25 countries with an established diagnosis of IE, one-fifth had a prosthetic valve and 7% had a cardiac device (5). Moreover, the emergence of healthcare-associated IE has been accompanied by an increase in the prevalence of Staphylococcus aureus and coagulase-negative staphylococci, whereas the proportion of IE due to viridans-group streptococci (VGS) has declined. Enterococci are the third leading cause of IE and are increasingly linked to healthcare contact [2].

We present a case of prosthetic valve endocarditis (PVE) in a patient who underwent bioprosthetic aortic valve replacement (AVR). Brennan et al., investigated patients from the Society of Thoracic Surgeons Adult Cardiac Surgery Database who underwent AVR from 1991 to 1999. They reported a higher risk of prosthetic valve endocarditis in patients with biological compared with mechanical valves (HR, 1.60; 95% CI, 1.31-1.94). Bioprostheses are expected to undergo structural valve deterioration during a patient's life. It is possible that the gradual degeneration of bioprostheses makes them

susceptible to bacterial implantation and provide a nidus for infection [3].

2. Report of the Case

Our patient is a 63-year-old undomiciled man with an extensive medical history including chronic kidney disease stage 3, deep vein thrombosis, cerebrovascular accident, methadone dependence and chronic gingivitis. His cardiovascular history includes hypertension, persistent rate-controlled atrial fibrillation, extensive coronary artery disease (CAD) requiring percutaneous coronary intervention (PCI) in 2010, followed by two-vessel coronary artery bypass surgery (CABG) with concomitant AVR using an EDWARDS INTUITY Elite trileaflet bioprosthetic valve, 8 months prior to presentation. In the emergency department, the patient reported non-specific symptoms including a one-week history of dizziness, lightheadedness, non-productive cough, progressive dyspnea, subjective fevers, and left-sided exertional chest pain. He also complained of chronic constipation and melena. On admission he was hemodynamically stable and afebrile. An electrocardiogram (EKG) showed an irregularly irregular rhythm consistent with atrial fibrillation. Chest radiography was not specific for cardiopulmonary disease. Blood tests revealed a hemoglobin (Hgb) of 6.2 (baseline Hgb approximately 7.0) and mean corpuscular volume (MCV) of 73. In the context of symptomatic anemia and multiple episodes of melena, gastrointestinal bleeding was suspected.

In the emergency department, the patient received 2 units of packed red blood cells and was scheduled to undergo upper and lower endoscopy. On the night prior to his scheduled procedures, the patient became febrile to a temperature of 102.3F (39C), and blood cultures were drawn. Endoscopy was postponed and the patient was started on empiric broad spectrum antibiotic therapy. In spite of antimicrobial treatment, the patient continued to spike fevers over the next few days. Further history was obtained and the patient revealed that 2 months ago he had lost and swallowed multiple teeth while masticating, likely secondary to chronic gingivitis. At that time, he presented to the ED however no intervention was performed. Since this episode of dental avulsion, the patient had experienced constitutional symptoms similar to his current presentation. Overall due to poor socioeconomic status the patient has had poor dentition since childhood.

Transesophageal echocardiography (TEE) was performed and revealed a 4 mm mobile echodensity, determined most likely to be a vegetation along the ventricular side of the aortic valve associated with paravalvular regurgitation along the left coronary cusp. The regurgitant jet was moderate in severity and there was also an area of thickening around the aortic valve, which contained an echo free space, suspicious for fluid, and concerning for abscess (Figure 1 A and Figure 1B). The patient's antimicrobial therapy was adjusted to intravenous ceftriaxone 2g (every 24 hours), with the intention of at least 6 weeks of treatment. Cardiology was consulted and recommended the patient be transferred to another facility for urgent evaluation by cardiothoracic surgery. One day into his hospitalization at the new facility, the patient left against medical advice and was lost to follow up. To the

best of our knowledge the patient has been contacted and the risks and benefits of further postponing surgery have been discussed.

3. Imaging

Figure 1, A and B Paravalvular abscess at the aortic valve seen with standard 2D and Color Doppler echocardiography.

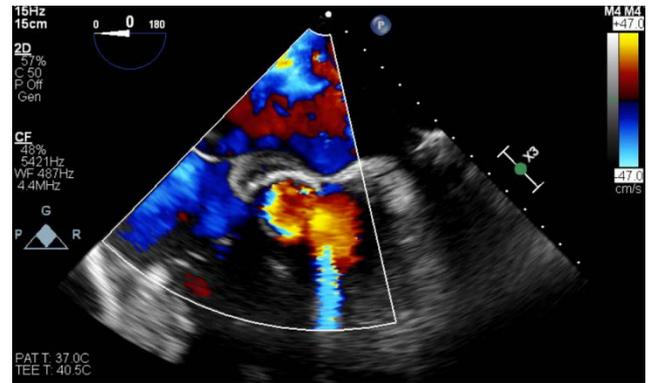


Figure 1A.

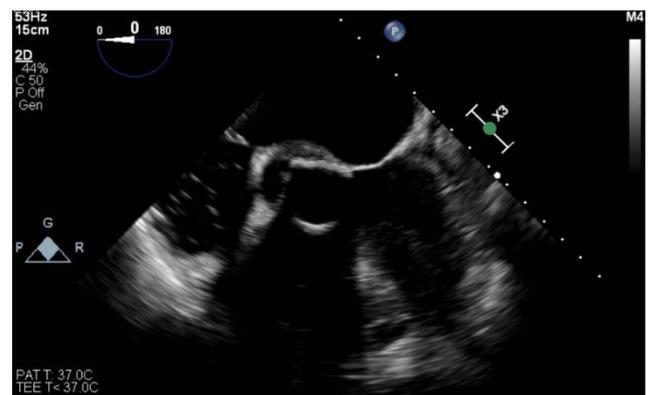


Figure 1B.

4. Discussion

Streptococcus salivarius is found in the oral flora of humans, where it may exert an antagonistic effect against group A streptococci and other microorganisms. Information about *S. salivarius* bacteremia is scarce, likely because *S. salivarius* is rarely isolated from blood: only 5-15% of blood culture isolates of viridans streptococci are *S. salivarius*. In addition, *S. salivarius* is usually considered a contaminant or an unclear cause of infections [4]. Given this information, it is not farfetched to assume that had our patient not suffered from an extensive cardiac history with recent aortic valve replacement, his positive blood cultures may have been determined to be contaminated. A study by Calderwood et al. showed that out of seven patients with clinically significant bacteremia caused by *S. salivarius*, three had bacterial endocarditis and one had an associated colonic neoplasm [5].

As aforementioned, our patient experienced melanic stools with a resultant chronic anemia. Although workup of a possible gastrointestinal bleed was deferred in favor

of management of PVE, his gastrointestinal symptoms may be connected to *S. salivarius* as this bacterium was shown to have a connection to streptococcus bovis, a gram positive bacteria well known to be associated with endocarditis and malignant gastrointestinal disease. In fact, according to 16S rRNA gene analysis, *S. salivarius* is closely related to *Streptococcus bovis* and exhibits similar genotypic characteristics, so that the two organisms may be easily mistaken for one another in clinical labs if sufficient tests are not done [6]. A prospective study done by Corredoira et al. showed that most of their patients with *S. salivarius* bacteremia had predisposing local factors such as mucosal disruption and/or serious underlying disease [4]. In addition to having serious underlying heart disease, chronic anemia due to gastrointestinal blood loss, and other comorbidities, our patient also suffered recent mucosal oral disruption secondary to dental avulsion. With this slew of active issues, this places him at a relatively high risk for *S. salivarius* bacteremia and endocarditis.

PVE is a rare but serious complication of valve replacement, with a high morbidity and mortality, accounting for 10-30% of all cases of IE [7]. Its diagnosis and treatment can be challenging, often requiring serial imaging and microbiological tests. Management involves identifying an effective antimicrobial regimen, understanding cardiac anatomy and pathology, and integrating medical and surgical therapies when indicated. TEE is the most valuable and widely used diagnostic imaging technique with a sensitivity of over 80% and a specificity of about 95%. Other imaging modalities such as computed tomography (CT) are useful when echocardiography is insufficient. There are several complications associated with PVE that require surgical intervention in order to avoid lethal outcomes. [8]

In general, the decision about whether to perform surgery in PVE is made based on complications related to valvular pathology and inability to eradicate infection. According to the 2015 AHA Statement on IE in Adults, indications for early surgery in PVE include: symptoms or signs of heart failure resulting from valve dehiscence, intracardiac fistula, or severe prosthetic valve dysfunction; persistent bacteremia despite appropriate antibiotic therapy for 5 to 7 days in whom other sites of infection have been excluded; IE that is complicated by heart block, annular or aortic abscess, or destructive penetrating lesions; or PVE caused by fungi or highly resistant organisms. It is also reasonable in cases of recurrent emboli despite appropriate antibiotic treatment or for patients with relapsing PVE. It may be considered in patients with mobile vegetations >10 mm [9]. Although lost to follow up, our patient met the criteria for early emergent surgery as he had symptoms and signs of heart failure (shortness of breath, lower extremity swelling, jugular venous distension) and a suspected cardiac abscess on TEE.

Nearly 40 to 50 percent of patients with PVE are treated surgically. In another 15 to 20 percent surgery does not take place due to patient refusal or comorbid conditions/complications that contraindicate surgical intervention. [10] The presence of paravalvular extension often determines whether surgery is advised in addition to medical therapy. Early diagnosis of PVE without

paravalvular extension can be treated medically. In our case surgery was warranted for our patient due to PVE complicated by a paravalvular abscess. Cardiac abscesses are observed in 20 to 30% of cases of IE and in at least 60% of PVE. The aortic valve ring is more frequently affected than the mitral valve ring. The abscess can lead to complications like conduction defects, communication between the cardiac chambers, pericardial disease, aortic disease, and myocardial ischemia. The presence of a cardiac abscess is a poor prognostic factor in IE. The diagnosis must be made at an early stage when surgical treatment is optimal. [11]

Varela Barca et al. reported on the prognostic pre-operative risk factors that have an impact over postoperative mortality and represent poor long term surgical outcomes in patients undergoing surgery for IE. These prognostic factors include increased age, female gender, urgent or emergency surgery, previous cardiac surgery, NYHA \geq III, cardiogenic shock, prosthetic valve, multivalvular affection, renal failure, paravalvular abscess, *S. aureus* infection. [12] In our case, our patient met 6 of these 11 criteria. Another meta-analysis by Tao et al. of 10,754 patients with IE of native valves undergoing valve replacement (6776 biological valves and 3978 mechanical valves) concluded that the all-cause mortality risk of the biological valve group was higher than that of the mechanical valve group [HR = 1.22, p = 0.023]. Recurrence of IE, as well as risk of reoperation was also significantly higher in patients with biological valves. When assessing the survival rates of patients with PVE, they determined there was no significant difference between both groups [13].

Overall, IE is almost fatal without adequate treatment, and even at experienced centers, operations for IE are associated with the highest mortality of any valve disease. Studies report an in-hospital mortality of 15-20% and 1-year mortality approaching 40%. [14]

5. Conclusion

In summary, infective endocarditis, defined by infection of a native or prosthetic heart valve, the endocardial surface, or an indwelling cardiac device, is a leading cause of mortality worldwide. The causes and epidemiology of the disease have evolved in recent decades with a doubling of the average patient age and an increased prevalence in patients with cardiac surgery and intracardiac devices. Given a history of aortic valve replacement, chronic gingivitis and recent oral mucosal disruption, our patient had a clear source of infection for developing infective endocarditis. However, the fact that his blood cultures grew *Streptococcus salivarius*, a relatively rare cause of the disease, and that his condition was further complicated by an aortic abscess raises more questions regarding the disease's pathophysiology. Although the isolation of *streptococcus salivarius* could potentially be interpreted as a contaminant, the patient's comorbidities, risk factors and clinical presentation favor its isolation as the true etiology of his condition. Although rare, the identification of *S. salivarius* is crucial for therapeutic guidance, association of complications, and epidemiological studies. Moreover, as previously reported

in literature, a relationship exists between streptococcus salivarius and different serotypes of streptococcus bovis. Both share similar genetic characteristics and are associated with endocarditis, colon cancer and other malignancies. Therefore, *S. salivarius* in blood should not be systematically considered a contamination, but rather addressed in the appropriate clinical context.

This case emphasizes the need for further investigation into the pathogen *S. salivarius* and its relationship to other known pathogens, as well as better understanding the complications associated with prosthetic valve endocarditis. The early recognition of disease symptoms, identification of complications and adequate treatment are cornerstones to improve survival and decrease long-term sequela.

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