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Case Report

Streptococcus Pluranimalium Infective Endocarditis Complicated by New Onset Heart Failure

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Abstract

Bacterial or infectious endocarditis (IE) is a relatively rare infection, but is associated with significant incidence of mortality. While IE most often results from infection of one or more heart valves by *Staphylococcus* or *Streptococcus spp*., other less virulent bacteria can be the etiologic agent and generally produce more indolent disease. Here we report the occurrence of native valve endocarditis due to infection with the emerging bacterium *Streptococcus pluranimalium*. Review of available literature indicates this is the fifth reported case globally of endocarditis following *S. pluranimalium* bacteremia and the first case associated with the complication of new onset heart failure.

Keywords: *Streptococcus pluranimalium*, Endocarditis, Heart failure, Native heart valve, Dental caries, Computed tomography, Computed tomography angiography, Vitek2

Abbreviations: IE: Infectious Endocarditis; CIED: Cardiac Implantable Electronic Devices; ED: Emergency Department; CT: Computed Tomography

Introduction

Infectious endocarditis (IE) is an infection of the interior lining of the heart, most often on one or more heart valves, and presents most commonly with fever and a new or worsened heart murmur. However, IE is associated with many other symptoms such as anorexia, weight loss, malaise, myalgias, arthralgias, dyspnea, splenomegaly, petechiae, Janeway lesions, Osler nodes, and splinter hemorrhages [1]. Complications that may occur with IE include valvular insufficiency which can lead to heart failure, septic emboli which can lead to organ infarction and pulmonary embolism, intracerebral hemorrhage, metastatic infection, and systemic immune reactions such as glomerulonephritis. Notably, heart failure is a relatively common complication of infective endocarditis [2] and is associated with increased morbidity and mortality [2,3]. Diagnosis of endocarditis is usually straightforward. However, the modified Duke criteria can be used as a guideline for diagnostic assessment if the presentation is unusual or complicated by confounding signs or symptoms [4].

IE is a diagnosis that needs to be made rather quickly due to the severity of the disease and its associated mortality, especially when heart failure develops. Heart failure is the most common cause of death in native valve infective endocarditis [3]. As such, its rapid diagnosis and treatment are essential for patient care. The incidence of endocarditis has begun to increase over the past two decades, and this is attributed in large part to increased use of intracardiac procedures and cardiac implantable electronic devices or CIED [1]. In contrast, the prevalence of infective endocarditis associated heart failure seems to be declining in recent years [2]. Treatment includes antibiotic therapy and addressing any valvular damage and resulting complications. This can include medical treatment for congestive heart failure and valvular replacement surgery. Early surgery in this context is clinically important since it reduces mortality and improves patient outcomes [1,3-5].

Species of *Staphylococcus* and *Streptococcus* are the etiologic agents in approximately 80% of IE cases, with *S. aureus* being the most common cause [6]. Among streptococcal-associated cases,

viridians *Streptococcus* causes 76% of these infections, while pyogenic streptococci account for 17% of the cases with *S. agalactiae* associated with 78% of the pyogenic streptococcal infections [7]. Other bacteria involved in IE include *S. epidermidis*, *Enterococci*spp, *S. gallolyticus* group members, and the HACEK group (comprised of *Haemophilus* spp.,*Aggregatibacter*spp.,*Cardiobacteriumhominis*, *Eikenellacorrodens*, and *Kingella*spp. [6]. Several risk factors have been clearly associated with the development of IE and, in some cases, with specific etiologic agents [6]. Intravenous injection drug use is a major risk factor for developing endocarditis and is most associated with *S. aureus* infections. Another risk factor traditionally associated with endocarditis is poor dentition, allowing a pathway for oral flora such as viridans streptococci to invade the bloodstream. Additional conditions that may predispose for development of IE include underlying rheumatic heart disease or congenital heart disease, intravascular cardiac procedures, use of CIED, prosthetic valve replacement, hemodialysis, intravenous catheters, and immune suppression [6].

In the past five years, a new bacterium has been implicated in at least four cases of IE [8-11]. This bacterium, *Streptococcus pluranimalium*, was first isolated in 1999 from a case of bovine mastitis, but has been isolated from a number of other agricultural and domesticated animals including chickens, goats, cats, canaries, sheep, Nile tilapia, a pheasant, and an alpaca [12-14]. *S. pluranimalium* can be isolated from various mucosal surfaces (e.g. cervix, vagina, lung, tonsils), avian crop, and from milk of infected dairy animals [12,15]. In addition to IE, *S. pluranimalium* has been reported as the causal agent in three cases of a brain abscess including one patient whose primary presentation was IE [11,16,17], one case of subdural empyema [18], and five cases of sepsis [19-23] with one case including septic arthritis [21], one case developing sepsis following a dental procedure [22], and a third case initially presenting as pneumonia with *S. pluranimalium* isolated from blood cultures [23]. This report now describes a fifth case of IE with *S. pluranimalium* associated bacteremia and is the first report of new onset heart failure as a complication of this infection.

Case Presentation

A thirty-one year old female with a past medical history of gastroesophageal reflux disease, morbid obesity, and Graves' disease post-status thyroid ablation presented to the emergency department (ED) with dyspnea and bilateral ankle swelling that began four days prior. The patient stated her symptoms were constant, but worsened with activity or when lying supine, and were alleviated with an upright posture. She also reported a nonproductive cough that was associated with a 'stretch' pain in her upper abdominal areas which was worse in the morning and when lying supine. The patient denied both drug use and contact with any farm animals, but reported having a pet dog.

Review of the patient's medical records showed she had presented to the ED one month earlier with right upper quadrant pain radiating to the left with constipation, fever, vomiting associated with a cough, dizziness, and shortness of breath, leading to hospital admission. Four blood cultures performed during this initial presentation grew *Streptococcus pluranimalium* with identification of the isolated bacterial colonies determined using the Vitek-2 system (bioMérieux, Durham, NC). Computed tomography (CT) imaging of the head revealed no abnormalities (inflammatory or structural) in the paranasal sinuses, eye orbits, or cranial structures (not shown). However, the imaging showed dental caries with apical lucency surrounding the root of the most posterior molar in the right maxilla (Figure 1), indicating dental decay and suggesting poor dental hygiene as a possible source for the bacteremia. Transthoracic echocardiogram showed large vegetations on the aortic and mitral valves with an ejection fraction of 60 – 85%, confirming the diagnosis of bacterial endocarditis. Based upon culture sensitivity testing of the isolated *S. pluranimalium*, a course of penicillin was started. Post-treatment follow-up blood cultures showed no growth, so an additional twenty-eight day course of penicillin G, was started in preparation for mechanical valve replacement. The patient was then discharged with a peripherally inserted central catheter.

At the second ED presentation, the patient's vital signs consisted of a blood pressure of 151/77 mm Hg, a temperature of 36.7 °C, a heart rate of 135 beats/min, a respiratory rate of 26 breaths/min, and pulse oximetry at 94% on room air. Physical examination of the patient was significant for a pansystolic 3/6 murmur and 1+ pitting edema in bilateral ankles. Trace crackles were auscultator in the postero inferior lung fields. Laboratory results included a white blood cell count of 8,800cells/μL, hemoglobin of 11.4g/dL, tropon in levels of 0.01ng/mL, and brain natriuretic peptide levels of 238ng/L. Blood cultures were performed and were negative. A two-view chest x-ray showed marked cardiomegaly and possible mild congestive changes. Computed tomography angiography of the chest was unremarkable for pulmonary embolism or aneurysm, but was notable for cardiomegaly and a small pericardial effusion. A transthoracic echocardiogram showed a moderately dilated left ventricle with an ejection fraction of 55 – 66%. The aortic valve had mildly thickened leaflets with mild regurgitation, and the mitral valve had mildly thickened leaflets with a small mobile vegetation with moderate regurgitation. There was no evidence of deep venous thromboses with venous Doppler.

The patient was admitted and subsequently underwent surgical replacement of the aortic and mitral valves with mechanical valves. The patient was placed on indefinite anticoagulant therapy with warfarin. The patient's recovery progressed well with no recurrence of symptoms related to *S. pluranimalium* infection reported in the eight months following initial antibiotic therapy and six months following valve replacement.

Discussion

The epidemiology and management of infective endocarditis has been changing in the past 1-2 decades with the advent of new vascular and cardiac medical interventions, with the expanded use of immunosuppressive therapies, and with the emergence of new bacteria, particularly those with antibiotic resistance. One of these changes is the identification of *Streptococcus pluranimalium*as a causative agent of IE and other human infections. *S. pluranimalium* is a newly identified and unusual member of the *Streptococcus* genus and has been isolated in multiple agricultural and domesticated animal species [12]. Of particular interest in relation to this case report, *S. pluranimalium* has been associated with endocarditis and septicemia in adult broiler chickens [24], suggesting that there may be a conservation of bacterial pathogenic mechanisms in both animal and human infections. *S. pluranimalium* presents challenges in diagnosis, treatment, and potentially in understanding the epidemiology of this emerging pathogen. This bacterial species is capable of alpha hemolysis, but varying biochemical profiles are seen in isolates from cattle and other agricultural animals [12]. Thus, with the presence of alpha hemolytic Gram-positive cocci in pairs and short chains, limited biochemical testing has led to the classification of *S. pluranimalium* as a member of either the viridans or *S. gallolyticus* groups of streptococci in some reports. However, full biochemical testing strategies have been established that can generally distinguish these bacteria [15]. Full protein analyses can conclusively identify *S. pluranimalium*, but this level of testing cannot be routinely performed in a clinical diagnostic laboratory. In case descriptions reporting the identification method for *S. pluranimalium*, most relied solely upon bacterial identification by Vitek instrumentation with a single report confirming Vitek identification with 16SrRNA sequencing [19]. Primary use of Vitek-based assays for identification has been called into question by a report from Pongratz, et. al. that showed an inability of molecular techniques such as MALDI-TOF or 16S rRNA sequencing to confirm *S. pluranimalium* as the identity of clinical bacterial isolates identified as such by Vitek [25]. Thus, given the apparent high degree of variability among clinical isolates, it may be necessary to re-evaluate the validity or standardization of *S. pluranimalium* identification techniques if conclusive identification is deemed necessary for effective treatment.

A second potential challenge is effective treatment of *S. pluranimalium*. Resistance to multiple antibiotics has been reported in some isolates of *S. pluranimalium*, and it is likely that the different strains of *S. pluranimalium* have differing levels of antibiotic resistance. Antimicrobial susceptibility testing of *S. pluranimalium* seems to indicate that at least one strain has developed resistance to erythromycin and lincomycin [26]. Currently, first-line antimicrobial agents are reported to include aminoglycosides, cephalosporins, linezolid, and vancomycin [19]. However, as evidenced in this case report, some *S. pluranimalium* strains are still susceptible to more commonly used antibiotics such as penicillin. Thus, it may be advisable to urge antibiotic sensitivity testing with a diagnosis of *S. pluranimalium* infection in order to appropriately treat the patient while avoiding unwarranted use of antibiotics such as vancomycin to minimize acquisition of drug resistance against our "last line" antibiotics.

The third challenge in considering *S. pluranimalium* associated disease is fully understanding the epidemiology of this organism. As it was initially isolated from cattle with bovine mastitis and shown to be present in a number of agricultural animals including chickens, goats, sheep, pigs, tilapia, and alpaca, the potential for human infection was first considered to be zoonotic in people having regular contact with these animals. Additional studies then identified *S. pluranimalium* infection in domesticated animals, particularly cats and canaries, expanding the epidemiologic considerations of disease transmission. This diversity of host species is unusual as most streptococci are pathogenic to only one or a few hosts that are phylogenetically related [12]. While more diverse than normal, these established host associations may be useful in identifying at risk populations. However, if the list of host species significantly expands, there may come a point where a history of contact with defined animal species may no longer be clinically useful. This lack of association may already be suggested. To date and including this case, thirteen human *S. pluranimalium* infections with subsequent disease have been reported, but only ~30% have documented interactions with farm animals, chickens, or cats. An alternative association may be colonization of the human oral cavity with *S. pluranimalium* that then results in bacteremia and disseminated disease when the physical or immunologic defenses become compromised. This hypothesis may be supported by the isolation of *S. pluranimalium* from gingival plaque following tooth extraction in healthy people [27] and the onset of *S. pluranimalium*-associated disease following dental procedures [22] and in patients with evidence of poor dental hygiene in this report and others [11,22,18]. With a high incidence of viridans streptococci causing endocarditis and a degree of morphological and biochemical similarity between viridans streptococci and *S. pluranimalium*, it is intriguing to consider whether some cases of endocarditis attributed to viridans streptococci may in fact be due to *S. pluranimalium*. Furthermore, with the occurrence of five cases of *S. pluranimalium* associated endocarditis and eight additional cases of septicemia, brain abscess or subdural empyema, septic arthritis, or pneumonia caused by *S. pluranimalium* in the past six years, one might speculate whether this may be related to the policy change of antibiotic prophylaxis prior to dental procedures in some previously designated at-risk populations.

This paper describes the development of endocarditis following *S. pluranimalium* bacteremia with the first description

of the complication of new onset heart failure. The report adds to the growing body of literature that demonstrates *S. pluranimalium* is an emerging pathogen associated with endocarditis, septicemia, and brain infections. With consideration of the additional twelve cases globally, questions regarding the accurate identification of *S. pluranimalium*, its treatment, and understanding of the epidemiology and transmission for human infection have been raised.

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Conflicts

None to report.

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