Bivalvular endocarditis due to *Granulicatella adiacens*

**Patient:** Male, 50

**Final Diagnosis:** Bivalvular endocarditis due to *Granulicatella adiacens*

**Symptoms:** Fever • fatigue

**Medication:** —

**Clinical Procedure:** Echocardiogram • valve replacement surgery

**Specialty:** Infectious Diseases

**Objective:** Rare disease

**Background:** Infective endocarditis remains a prominent cause of morbidity and mortality worldwide. It has been estimated that 50% of cases are caused by streptococcal organisms. *Abiotrophia* and *Granulicatella*, often grouped as nutritionally variant streptococci (NVS), have become recognized as the cause of nearly 5% of infective endocarditis cases. NVS endocarditis historically has a higher rate of morbidity and mortality, partially due to difficulties in adequately culturing and treating the causative organisms.

**Case Report:** In this report, we review the complicated hospital course and successful treatment of a middle aged Hispanic gentleman who presented with systemic symptoms of fevers, chills and weight loss over 3 months. He was found to have *Granulicatella* infective endocarditis of the mitral and aortic valves, presumably from a dental source. Despite severe valvular insufficiency noted on echocardiogram, the patient did not initially present with any symptoms of decompensated heart failure. With adequate antibiotic therapy followed by replacement of both valves, the patient had a successful recovery.

**Conclusions:** This case report highlights the growing role that nutritionally variant streptococcus plays in endocarditis and how crucial early identification of the organism is to proper treatment. A brief literature review is also included about the diagnosis and recommended management of nutritionally variant streptococcal endocarditis.

**Key words:** bacterial endocarditis • *Granulicatella* • nutritionally variant *Streptococcus*

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**Background**

Infective endocarditis remains a prominent cause of morbidity and mortality worldwide. It has been estimated that 50% of cases are caused by streptococcal organisms [1]. *Abiotrophia* and *Granulicatella*, often grouped as nutritionally variant streptococci (NVS), have become recognized as the cause of nearly 5% of infective endocarditis cases [2–4]. NVS endocarditis historically has a higher rate of morbidity and mortality, partially due to difficulties in adequately culturing and treating the causative organisms [2]. In this report, we review the hospital course and successful treatment of a middle-aged gentleman with *Granulicatella* infective endocarditis.

**Case Report**

A middle aged Hispanic male presented to a hospital in San Diego with complaints of fevers and chills for two weeks, as well as a 20 pound weight loss and night sweats during the last 3 months. The patient lives in Tijuana, Mexico and travels across the United States-Mexico border for work. He was initially evaluated for his symptoms several weeks ago in Mexico, but was unable to provide an accurate history about the results. He believed he was diagnosed with kidney stones, colitis, and diverticulitis. He recalled being treated with a variety of medications including antibiotics, but did not recall specific drug names. He also underwent a barium enema. Further questioning revealed that he may have had a history of rheumatic heart disease as a child and underwent an unspecified dental procedure one month ago during which he received antibiotics.

Physical exam on arrival revealed a fever of 38.5 degrees Celsius and heart rate of 100, but overall patient did not appear ill or short of breath. Auscultatory exam revealed a 3/6 holosystolic murmur at the apex with radiation to the axilla, a 2/6 diastolic murmur at the left lower sternal border, and pulmonary crackles on inspiration. There was mild anterior cervical lymphadenopathy and palpable splenomegaly. There was no digital clubbing, Osler’s nodes, Janeway lesions, or Roth’s spots. Jugular venous pressure was normal, and there was no peripheral edema.

Laboratory exam showed hemoglobin of 10.7 g/dL, hematocrit of 33.1%, mean corpuscular volume of 72 fl. There was no leukocytosis. C-reactive protein, estimated sedentation rate and ferritin were all elevated. Electrocardiogram was normal. Echocardiogram revealed vegetations on both the mitral and aortic valves, evidence of a flail mitral leaflet, and bilateral pleural effusions. Ejection fraction was estimated at 57%, and there was severe mitral regurgitation, severe aortic insufficiency, and severe pulmonary hypertension. A CT scan of the abdomen showed a 6.7 cm thick-walled splenic cyst. Blood cultures grew gram-positive cocci in chains and clusters, which were eventually identified as *Granulicatella adiacens*. The patient was initially treated with vancomycin, which was later narrowed to penicillin and gentamicin based on antibiotic susceptibility.

During a 6 week hospitalization, the patient had continuous antibiotic therapy and a CT-guided catheter placement for drainage of the splenic cyst. The fluid from the cyst proved to be sterile, and by hospital day 4, blood cultures were negative. All other infectious disease workup proved to be negative. The patient’s hospital course was unfortunately complicated by intermittent heart failure symptoms secondary to his severe valvular insufficiency. Furthermore, he required video-assisted decortication of a left-sided loculated pleural effusion which developed secondary to the splenic cyst. He eventually underwent mitral and aortic valve replacement and was prescribed an additional two week post-operative course of intravenous penicillin. He was discharged home in excellent condition and returned to performing all activities with no limitations two months after hospitalization.

**Discussion**

Nutritionally variant streptococci (NVS) were initially discovered in 1961 and are known to be a potential cause of sepsis and endocarditis [5–7]. NVS require a medium supplemented with cysteine and pyridoxine or the presence of a helper bacteria such as staphylococcus for proper growth [1,6–8]. Furthermore, the organisms exhibit unique growth characteristics such as satellite colonies around other bacteria, prolonged incubation periods, and variable gram-stain characteristics [2–5]. By 2005, nutritionally variant streptococci were divided into the genera *Abiotrophia* and *Granulicatella* on the basis of 16S rRNA sequencing [9,10].

NVS are a normal part of the oral, intestinal and genitourinary flora. The bacterial entry point for most cases of endocarditis is believed to be the oral cavity [2,3]. In 2007, it was estimated that NVS were responsible for 3% to 5% of streptococcal infective endocarditis cases [3,4]. However, given the unique requirements for culturing NVS and that nearly one third of endocarditis cases have negative blood cultures, this figure is likely an underestimation of the true number of NVS endocarditis cases [2–4,11]. Beyond endocarditis, it is also common for these organisms to cause infections such as pancreatic abscesses, endophthalmitis, conjunctivitis, and post-partum sepsis [12,13].

Amongst the NVS species, the more virulent strains are believed to be *A. defective* and *G. adiacens*, due to their ability to bind more readily to extracellular matrix proteins such as fibronectin [2,12,13]. Though underlying valve injury is a risk factor for endocarditis, there have been several noted cases...
of normal valves being affected by NVS [3,12]. Typically, NVS endocarditis has a slower, more indolent course but one with much higher rates of complications such as heart failure symptoms, septic embolization, and death [2–4,12–14]. Classic peripheral endocarditis findings such as Osler’s nodes, Janeway lesions, and Roth’s spots are infrequently seen despite higher rates of septic embolization [2]. It has previously been reported that nearly 30% of NVS strains show resistance to penicillin and that nearly 41% of cases fail medical therapy with antibiotics [2]. In 2001, 27% of patients required valve replacement surgery and almost 20% of patients died of uncontrolled heart failure or complications from systemic emboli [2]. More recent studies show a trend towards lower mortality, higher antibiotic susceptibility, and higher rates of valve replacement surgery [1,3,4,12–14]. One retrospective case study by Lin et al. reviewed the number of cases of NVS endocarditis at a large, tertiary-care hospital in Taiwan across a ten year period from 1996 to 2006 [3]. In this study, 8 out of 428 cases of infective endocarditis were caused by NVS: 4 cases by A. defectiva and 4 cases by G. adiacens. Amongst these cases, 7 out of 8 patients eventually underwent valve replacement surgery for complications due to valvular insufficiency. There was no reported morbidity or mortality after surgery.

In our patient, the most likely entry point for the bacteria was his poor dental hygiene and recent dental procedure. The possible history of childhood rheumatic heart disease likely increased his risk for endocarditis. Given the high frequency of embolization seen with NVS septicemia, it was initially believed that the patient’s splenic fluid collection could have been an abscess. Though the splenic fluid collection proved to be sterile, it did lead to significant complications in the form of a loculated pleural effusion. Furthermore, despite the severity of his valvular insufficiency, the patient did not initially present with any symptoms of decompensated heart failure. He did eventually develop symptoms of decompensated heart failure, including shortness of breath and orthopnea, in the process of managing his complicated disease. Ultimately, the definitive treatment involved a regimen of prolonged antibiotic therapy and valve replacement surgery.

Conclusions

Nutritionally variant streptococcus is becoming a more frequently recognized cause of endocarditis in both normal and previously damaged heart valves. Though past data suggests a growing antibiotic resistance amongst NVS, penicillin and gentamicin remain viable treatment options in many cases. Early recognition of the causative organism combined with valve replacement surgery in symptomatic patients may contribute to decreased morbidity and mortality in NVS endocarditis.

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