Abiotrophia endocarditis: a case report and review of literature

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Abstract

Nutritionally Variant Streptococci (NVS) were first grouped under viridans streptococci, although they differed from the latter by variant growth characteristics. NVS cause approximately 5% of cases of bacterial endocarditis. Infective endocarditis caused by NVS has a higher rate of complications than endocarditis caused by other viridans streptococci. Recently NVS were separated from other viridans streptococci to form a new genus Abiotrophia. Since then, only four case reports have described the clinical course of Abiotrophia endocarditis. Therefore, current knowledge on this disease derives from previous data on NVS endocarditis. We present the case of Abiotrophia endocarditis, followed by discussion of relevant literature.

Introduction

Nutritionally variant streptococci (NVS) were recently separated from other viridans streptococci to form a new genus *Abiotrophia*.[1] Since this taxonomic revision, only four case reports have described the clinical course Abiotrophia endocarditis.[2-4] Therefore, current knowledge on this disease derives from previous data on NVS endocarditis. We present the case of Abiotrophia endocarditis, followed by discussion of relevant literature.

Case Report

A 31-year old male was admitted for a one-month history of malaise, night sweats, low-grade fever and palpitations. The patient denied previous rheumatic heart disease, IV drug use, recent dental, gastrointestinal or urogenital surgery. He recalled a heart murmur in his childhood. On physical examination he had painful nodules over the tips of his fingers, mild conjunctival pallor and a diastolic murmur at the left upper sternal border. Erythrocyte sedimentation rate was elevated at 55 mm/Hr. Echocardiography showed concentric left ventricular hypertrophy, moderate aortic insufficiency, left ventricular ejection fraction of 60% and a thickened aortic valve with a 2mm verrucous lesion on the right coronary cusp. Native valve endocarditis was suspected and the patient was started on intravenous ampicillin 2gm IV Q6hrs and gentamicin 70mg IV Q8hrs. Blood cultures drawn on the day of admission did not reveal an initial growth. The patient was discharged home on day 4 of hospitalization. Upon discharge, the antibiotic regimen was changed to ceftriaxone 2gm IV Q24hrs and gentamicin 210mg IV Q24hrs. Ten days after his discharge, blood cultures showed fastidious growth of *Abiotrophia adiacens*, susceptible to ampicillin, ceftriaxone, chloramphenicol, clindamycin, erythromycin, penicillin and vancomycin. The patient completed a 4-week course of outpatient, intravenous antibiotic therapy with ceftriaxone and gentamicin.

The patient remained clinically stable during the next two months, until he developed symptoms of an upper respiratory tract infection. He was seen as an outpatient and was started on clarythromycin. During the ensuing week he noted progressive shortness of breath, orthopnea and paroxysmal nocturnal dyspnea. A chest roentgenogram documented bilateral diffuse lower lobe infiltrates. He was readmitted to the hospital.

The admission physical examination showed a well-developed man in mild respiratory distress at rest. His vital signs were: blood pressure130/70, heart rate 127, respiratory rate 24 and temperature of 98.4. Jugular venous pressure was 7cm with hyperdynamic waveforms. His heart examination showed normal S1 and S2, a loud S4 and II/VI early decresendo diastolic murmur over aortic region. Lung examination was significant for rales over lower 1/3 of lung fields. Hyperdynamic distal pulses were present. His extremities were without peripheral edema. An echocardiogram showed evidence of dilated cardiomyopathy, global impairment of left ventricular systolic function with an ejection fraction of 20-30% and aortic regurgitation. It was difficult to assess the extent of the valvular lesion. The patient underwent urgent cardiac catheterization, which documented 4+ aortic insufficiency, enlarged left ventricle with global hypokinesis and an estimated ejection fraction 20-30%.

Urgent aortic valve replacement surgery was performed with placement of St. Jude mechanical prosthesis. At the time of surgery, the patient was noted to have a congenital bicuspid aortic valve with partial fusion of commissures. The valve had areas of damage with approximately 1 cm perforations in both leaflets. There were areas of valvular thickening, but no vegetations were observed. The annulus was normal except for an area around the right coronary sinus where a localized pocket suggested a healed abscess.

Gram stain of valve tissue did not reveal white cells or organisms. Pathologic evaluation of the aortic valve documented fibrous valvulitis with focal granulation tissue consistent with acute and chronic inflammation. Aerobic and anerobic cultures of the aortic valve and blood cultures obtained at the time of presentation were sterile. The

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patient was placed on intravenous levofloxacin and cefazolin. He had an uneventful recovery and was discharged on the day 8 of hospitalization.

Discussion

Nutritionally variant (deficient) streptococci (NVS) were originally described in 1961 by Frenkel and Hirsch as fastidious gram-positive bacteria that grew as satellite colonies around other bacterial species.[5] NVS were first grouped under viridans streptococci, although they differed from the latter by variant growth characteristics. These organisms did not grow on blood or chocolate agar, but were shown to grow in complex media supplemented with L-cysteine or pyridoxine. Streaking blood agar with a gram positive organism such as S. aureus, or with gram negative organism or yeast were shown to provide NVS with the necessary nutrients that would allow the organism to grow as a halo of satellite colonies a phenomenon called microbial commensalism.[6,7] Subsequently NVS were referred by a variety of names including "nutritionally deficient", "cell wall deficient", "thiol-requiring", "L-form", "satelliting" or "pyridoxine dependent streptococci".[6]

The taxonomic position of NVS remained unclear until 1989 when Bouvet et al. performed DNA-DNA hybridization studies and reclassified the NVS into *Streptococcus adjacens* and *Streptococcus defectives*.[8] In 1995 Kawamura et al. determined the 16S rRNA sequences of these strains and transferred them to a new genus *Abiotrophia* as *A. adiacens* and *A. defectiva*.[1] This was followed by the description of other potential human pathogens with in the same genus, *A. elegans* and *A. para-adiacens*.[9,10] The term *Abiotrophia* indicated the innate nutritional deficiency of these organisms and their dependence on supplemental media for growth. Recently, another taxonomic revision has been proposed by Collins et.al., as the genus *Abiotrophia* appear to have two distinct phyletic lineages. The reclassified genus has been named *Granulicatella*.[11]

NVS are found in the normal flora of the oral cavity, upper respiratory, urogenital and gastrointestinal mucosa of humans.[6] They have been recovered from blood, brain and pancreatic abscesses, oral ulcers, dental plaques, wound infections and urethral samples.[6,12-17] NVS have also been isolated from patients with otitis externa, otitis media, conjunctivitis, endophthalmitis, infectious keratopathy, vertebral osteomyelitis, discitis, iatrogenic meningitis, post-partum sepsis and endocarditis.[2,4-6,18-25]. Given their fastidious growth rate and requirement of special microbiologic media, it is likely that the true incidence of NVS infections is underreported.

It is estimated that NVS cause approximately 5% of cases of bacterial endocarditis.[6] Historically, NVS also accounted for cases of culture-negative endocarditis.[26] Most reported cases of NVS involve native valves while only a few cases involve prosthetic valves.[2,6] Often, endocarditis occurs in the setting of previous valvular disease and is characterized by a slow, indolent course.[25,27,28]

Present data suggest that infective endocarditis caused by NVS leads to a higher rate of complications than infections caused by other viridans streptococci. Comparison studies have shown a higher mortality rate (14% vs 5%), greater risk of embolization (33% vs. 11%), more congestive heart failure due to valvular insufficiency (33% vs. 18%) and increased rate of surgical intervention (33% vs.18%) when NVS is compared with other viridans streptococci.[29] Treatment failure and relapse have been observed in 41% cases, as compared with 17% in other viridans streptococci.[30]

A recent study showed that *A. adiacens* strains have a markedly high fibronectin binding capacity to extracellular matrix proteins, which may contribute to the high virulence of these organisms.[31] They overproduce exopolysaccharide, which may play an additional protective role in the survival of the organism.[28] Moreover, *Abiotrophia* isolates have been shown to involve conjugative transposons in the dissemination of antibiotic resistance.[3]

In vitro studies have shown that when compared to most other viridans streptococci, NVS strains have moderate susceptibility and can develop tolerance to penicillin.[7,30,32-34] Although high dose therapy has been recommended in certain circumstances, patients with NVS endocarditis may relapse after a full course of treatment despite in vitro high susceptibility to penicillin.[6,35] NVS are generally susceptible to aminoglycosides and vancomycin.[7,30,32,34] The synergistic combination of penicillin or vancomycin with an aminoglycoside has been shown to be more effective than penicillin alone.[6,12,36] It is generally recommended that all patients with NVS endocarditis be treated with combination therapy for 4-6 weeks.[37]

In a recent study of 39 isolates of *A. adiacens* and *A. defectiva*, the proportion of strains susceptible to penicillin were 55% and 8% respectively. In the same study, the susceptibilities for other antimicrobials were; amoxicillin 81% and 92%, ceftriaxone 63% and 83%, meropenem 96% and 100% respectively for the two strains. Both species showed 100% susceptibility to clindamycin, rifampin, levofloxacin, ofloxacin, quinupristin/dalfopristin and vancomycin [34]. Another recent study of 20 Abiotrophia isolates reported susceptibility to cefotaxime 65%, cefepime 47%, erythromycin 70%, clindamycin 95% and meropenem 90%.[7] However, it should be noted that while NVS are susceptible to clindamycin, chloramphenicol and erythromycin, these antibiotics are not recommended for the treatment of NVS endocarditis.

Upon his second admission to the hospital, our patient did not show any evidence of on-going endocardial infection. The histopathology revealed sterile valves and repeated serum microbiology studies remained negative for infection. Hence, acute aortic regurgitation on his second admission was likely a non-infectious, delayed complication of abiotrophia endocarditis.

Abiotrophia endocarditis frequently has a high rate of complications. Long- term combination antibiotic therapy guided by susceptibility studies as well as clinical correlation, is necessary. High morbidity and mortality despite extended antibiotic therapy, is common. Abiotrophia endocarditis warrants regular follow up, despite apparent clinical recovery of the patient. Any change in clinical status, calls for close attention for early identification of complications or relapse.

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