Endocarditis caused by *Abiotrophia defectiva*

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Abstract: A 35-year–old man with pre-existing rheumatic heart disease and aortic regurgitation (AR) presented with intermittent fever, ankle swelling and clinical evidence of endocarditis. Transoesophageal echocardiogram (TEE) revealed vegetations and destruction of the aortic valve (AV). Blood cultures grew a gram positive coccobacillus which was phenotypically identified as Abiotrophia defectvia (A.defectiva). A diagnosis of infective endocarditis (IE) due to A.defectiva was made. Treatment, with penicillin and gentamicin, was administered for 4 weeks. Mechanical valve replacement was required few days after starting the antibiotic therapy. The patient had a favorable outcome on follow up. Although A.defectiva is an uncommon cause of endocarditis, early and correct identification of this pathogen is important to improve the outcome and the prognosis of patients with IE due to this organism.

Key Words: *A.defectiva, Abiotrophia defectiva, IE, infective endocarditis, valve, AR: aortic regurgitation*

Introduction

A.defectiva was originally known as a member of the nutritionally variant streptococci (NVS)[1]. The NVS were first described by Frenkle and Hirsch as new types of viridans streptococci based on certain phenotypic characteristics [2]. Two genera have been proposed based on 16S rRNA which are: Abiotrophia and Granulicatella [3]. A.defectiva is the only species belonging to the Abiotrophia generus [4].

A.defectiva is part of the normal flora of the oral cavity, the urogenital and the intestinal tracts [5]. This bacterium has been associated with various serious infections including bacteremia, endocarditis, brain abscess, septic arthritis and total knee arthroplasty infections [6-9].

In this report, we describe a patient with IE caused by A. defectiva in an attempt to increase awareness about this organism and to highlight the difficulties encountered in the diagnosis and in the treatment.

Case Report

A 35 years old Saudi male was diagnosed to have rheumatic heart disease in the year 1991. Few years later, the patient developed severe aortic regurgitation (AR). In late February 2005, he was admitted to Prince Sultan cardiac center through the emergency department as he presented with intermittent fever for six months, left ankle joint pain and swelling for 5 days, significant weight loss and fatigue. He underwent dental extraction seven months prior to presentation with no appropriate endocarditis prophylaxis. The patient had been non-compliant with the monthly penicillin prophylaxis for the last seven years and he repeatedly refused AV replacement.

Physical examination on admission revealed: a pulse rate of 105/minute, temperature of 36.9oC and blood pressure of 133/48 mmHg. He had finger clubbing, left ankle swelling, splenomegaly, displacement of apex beat and a high pitched early diastolic murmur heard maximally over the third and fourth left intercostals spaces. Fundoscopic examination was normal. Laboratory investigations were as follows: WBC 8 x 109/L, Haemoglobin: 8.1 g/dl, platelets: 305x109/L, ESR: 73 and CRP: 101mg/L. TEE revealed highly mobile vegetation (2.9 x 0.6 mm) attached to the ventricular surface of the non-coronary cusp of the rheumatic AV with no aortic root abscess. The left ventricle (LV) was severely dilated with abnormal systolic function and the LV ejection fraction was 40%.

Four sets of blood cultures were obtained. Blood cultures were processed in the Bactec 9240 blood culture system (Beckton Dickinson). All the blood culture sets showed pleomorphic gram positive coccobacilli microscopically. The organism grew well on chocolate agar but poorly on 5% blood agar after 48 hour incubation. Gram stain revealed gram positive cocci in chains. Satellitism was found after a single cross-streak of Staphylococcus aureus was placed on the blood agar plate. The bacterium was identified as A. defectiva with >95% confidence by API 20 Strep system after 24 hour incubation. Antimicrobial susceptibility was determined by the E-test for penicillin and the disc diffusion method on Mueller-Hinton agar with 5% sheep blood for the other antibiotics. Results were interpreted according to the Clinical Laboratory Standard Institute (CLSI) criteria for a-hemolytic streptococci other than Streptococcus pneumoniae. The organism was found to be susceptible to penicillin, cefuroxime, ceftriaxone, erythromycin, imipenem, vancomycin, chloramphenicol and rifampicin but resistant to gentamicin. The minimal inhibitory concentration (MIC) for penicillin was 0.02 µg/ml. High level resistance to gentamicin was not seen in this isolate (gentamicin MIC was < 500 µg/ml). Vancomycin MIC was <1 µg/ml.

The patient was initially treated with vancomycin and gentamicin until the blood culture isolate was identified after which vancomycin was replaced by

intravenous penicillin G 24 million units per day and gentamicin was continued intravenously at a dose of 1 mg/kg every eight hour. Few days later, surgery was performed as the clinical condition of the patient deteriorated and as the repeated echocardiogram showed persistently large vegetations and progressive AV desrtuction. At surgery a large vegetation was seen on the ventricular side of the AV leaflet, the AV annulus was enlarged and the aortic non-coronary cusp was found to be perforated. The damaged AV was excised and a Carbomedics size 2.7 mm mechanical valve was implanted. The histologic examination demonstrated large vegetations with dense fibrin and platelet aggregates in addition to few leucocytes and bacterial colonies i.e. the infiltrate was suggestive of IE.

Cultures of the AV and follow up blood cultures were all negative. The antibiotics were continued for one month and the patient was discharged home in March 2005. Thereafter, he remained well on the out-patient follow up.

Discussion

A.defectiva is a rare cause of endocarditis [10]. However, some studies have estimated that this organism is responsible for 5-6% of all cases of IE [1,11]. Endocarditis caused by A.defectiva carries greater morbidity and mortality than endocarditis caused by other streptococci [13]. It is characterized by the occurrence of certain complications such as congestive heart failure, embolization and an increased rate of surgical interventions [13,16]. These infections usually respond poorly to antibiotics and several studies have reported bacteriologic failure rates of up to 40% with relapse rates of up to 17% despite the treatment with antibiotics that were effective in vitro [14]. Multiple factors contribute to the increased virulence of Abiotrophia species such as the production of an exopolysaccharide, the long generation time which can have an impact on the in vivo tolerance; and the persistence as a result of the development of cell-wall deficient bacteria promoted by the treatment with □-lactam antibiotics [2,17,18].

A.defectiva is a fastidious organism with unique nutritional requirements that are essential for growth. It grows more slowly than other streptococci, thus cultivation and identification are often difficult [1,2]. Identification based on phenotypic methods can result in misidentification of the pathogen. Many different enzyme profiles have been found in conventional biochemical tests [19]. Molecular techniques were used to improve the detection and facilitate the identification of A.defectiva. The use of 16S rRNA gene polymerase chain reaction amplification followed by restriction fragment length polymorphism (PCR-RFLP) was shown to be a rapid and a more accurate method for the identification of A.defectiva [6]. Abiotrophia is less susceptible in-vitro to penicillin than other streptococci and several studies have shown that the prevalence of beta-lactam and macrolide resistance is high. Also, resistance to the extended–spectrum cephalosporins and the new fluoroquinolones have been reported [20,21]. However, high level of resistance to the aminoglycosides, as encountered with enterococci, has not been reported with A.defectiva. The in-vitro antimicrobial susceptibility testing of Abiotrophia has not been standardized yet and the results of in-vitro susceptibility testing do not correlate well with the clinical outcome in patients treated for endocarditis [14]. Therefore it is recommended that patients with endocarditis should be treated with a long-term combination therapy e.g. penicillin and gentamicin for 4-6 weeks [22]. Even with this regimen, the rates of bacteriologic failure and relapse are still high therefore careful follow up of these cases is mandatory [14,16].

The portal of entry in most reported cases of endocarditis is via the oral cavity. The dental extraction in our patient served as a risk factor for the development of IE in the previously damaged AV leading to progressive valvular destruction and perforation. The lack of prophylactic antibiotic prior to the procedure had contributed significantly to the disease process. Heart failure is the most serious complication of endocarditis and often requires valve replacement [16]. Endocarditis caused by A.defectiva has been reported to result in heart failure by destroying heart valves [13].

In our patient, replacement of the AV was carried out due to the extensive valvular damage and the large vegetation size with the potential of embolization. The isolated A.defectiva was found to be susceptible to penicillin. He was treated with a combination regimen of penicillin and gentamicin for 4 weeks. A multi-disciplinary approach from cardiology, cardiac surgery, intensive care, microbiology and infectious diseases departments contributed to the favorable outcome.

Conclusion

A.defectiva is a recognized cause of endocarditis. Clinicians and microbiologist should be aware of this organism and its pathogenic potential. Proper identification of this pathogen is important to achieve a better outcome.

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