

Infective Endocarditis due to *Abiotrophia defectiva*: A Report of Two Cases

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Background and aim of the study: Endocarditis due to *Abiotrophia* sp. is rare and often associated with negative blood cultures. The rates of treatment failure, infection relapse and mortality are higher than in endocarditis caused by other viridans streptococci.

Methods: A retrospective review of *A. defectiva* endocarditis in a patient with prosthetic aortic valve and in a patient with Marfan syndrome was performed.

Results: *A. defectiva*, susceptible to penicillin (MIC 0.064 mg/l and 0.016 mg/l, respectively) was isolated from blood cultures of both patients. Treatment with penicillin and gentamicin was started in both patients. Since the first patient developed a macular

rash and leukopenia, penicillin was substituted with ceftriaxone. Both patients responded well to antibiotic treatment, did not need prosthetic valve insertion or reinsertion, and were without any sequelae at one year follow up.

Conclusion: Standard treatment of bacterial endocarditis with penicillin and gentamicin was effective in both patients. In contrast to previous reports, the present patients had a favorable outcome on completion of treatment and at one-year follow up.

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Nutritionally variant streptococci colonize the oral cavity and the intestinal and genitourinary tracts as normal flora (1). They were first described by Frenkel and Hirsch in 1961 (2), but in 1995 were transferred by Kawamura et al. from other viridans streptococci to form a new genus, *Abiotrophia* (3).

Endocarditis due to *Abiotrophia* sp. is rare, and accounts for less than 4.3% of all cases of streptococcal endocarditis (4). It is often associated with negative blood cultures. Rates of treatment failure, infection relapse and mortality are higher than in endocarditis caused by other viridans streptococci (5). Despite several reports of *Abiotrophia* sp. endocarditis, a treatment scheme has not been universally accepted. To the best of the present authors' knowledge, only five cases of *Abiotrophia defectiva* endocarditis have been reported since the introduction of the new taxonomy, including three case reports in adults (6-8) and two in children (9,10).

Herein are reported two cases of *A. defectiva* endo-

carditis: the first in a patient with a prosthetic aortic valve, and a second in a patient with Marfan syndrome, the latter being the first such reported case.

Case reports

Case 1

A 62-year-old man was hospitalized for suspected prosthetic valve endocarditis. At the age of 15 he was diagnosed with aortic valve endocarditis, probably due to rheumatic fever. At the age of 41 he underwent aortic valve replacement, and seven years ago he had a pacemaker implanted. Four months prior to the present admission, the patient underwent a dental procedure (for which he received antibiotic prophylaxis with amoxicillin) and subsequently contracted pneumonia. One month later he became febrile, experienced palpitations, back pain, and noticed swelling of the small joints of the hands. On the present admission a precordial systolic murmur was noted. Laboratory analysis showed a normal leukocyte count ($8.8 \times 10^9/l$; normal level $4.0-10 \times 10^9/l$) and an elevated C-reactive protein (CRP) level (40 mg/dl; normal level <5 mg/dl). Blood cultures were drawn on admission and several times during hospitalization. *A. defectiva* was isolated from the first blood cultures (penicillin MIC of 0.064 mg/l), while all subsequent blood cultures

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Figure 1: Vegetation on the ventricular side of the bicuspid aortic valve in the patient with Marfan syndrome (at admission).

remained sterile. Echocardiography showed a probable vegetation on the ventricular side of the prosthetic aortic valve and a mild mitral regurgitation. Parenteral antibiotic treatment with penicillin (5×10^6 IE q.i.d.) and gentamicin (120 mg b.i.d.) was started. The patient received gentamicin for a period of two weeks. After 25 days of therapy with penicillin, he developed macular rash and leukopenia. Penicillin was substituted by ceftriaxone (2 g o.d.), but after 15 days the leukopenia was noted again. The patient completed six weeks of treatment, and the white blood cell count returned to normal after discontinuation of ceftriaxone. Dental extraction of the avital teeth under antibiotic prophylaxis was indicated and performed. Echocardiography performed prior to discharge showed a reduction in the size of the aortic valve vegetation. At one year fol-

low up the patient's clinical condition was unremarkable.

Case 2

A 26-year-old patient was admitted to hospital with chest pain and fever. He recalled frequent episodes of sore throat, and two weeks prior to the present admission had suffered inflammation of a toe on his left foot, which resolved spontaneously. Four days prior to the present admission the patient had a 24-h episode of fever, abdominal pain, headache and malaise, but denied any episodes of fatigue. On admission he was febrile (39.4°C) and had tonsillitis with exudate. His appearance was marfanoid, with acromegaly, pectus excavatum, a highly arched palate and thoracic scoliosis. The patient also had clubbed fingers, Osler's node on the right thenar, splenomegaly, tachycardia, a systolic murmur over the whole precordium, and a soft diastolic murmur in the aortic position. Endocarditis was suspected and a series of blood cultures was drawn. Laboratory tests suggested bacterial infection (leukocyte count 12×10^9 /l and a CRP level 126 mg/dl). Echocardiography demonstrated dilatation of the sinus of Valsalva (4.2 cm), bicuspid aortic valve, vegetations on the ventricular side of the aortic (Fig. 1) and atrial side of the mitral valve, massive aortic regurgitation, systolic anterior movement of the mitral valve, and massive mitral regurgitation. Empirical treatment of endocarditis with penicillin (6×10^6 IE q.i.d.) and gentamicin (240 mg o.d.) was started. *A. defectiva*, which was susceptible to penicillin (MIC 0.016 mg/l), was isolated from the blood cultures. The patient received gentamicin for two weeks and penicillin for six weeks. All subsequent blood cultures remained sterile. Echocardiography during hospitalization and prior to discharge showed that the vegetations on both

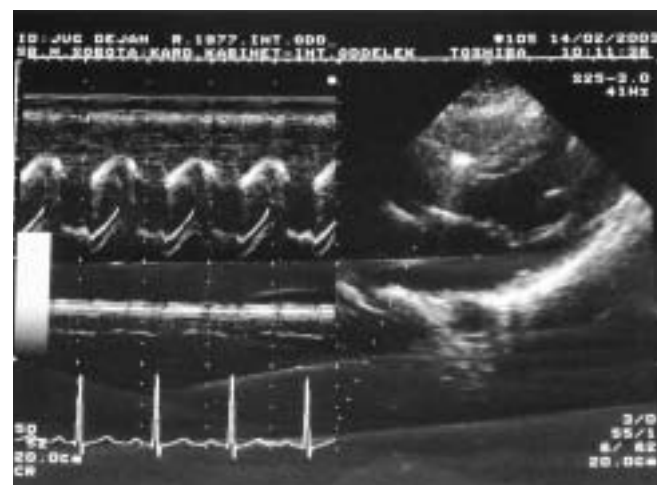


Figure 2: Diminishing of vegetations on the bicuspid aortic valve in the patient with Marfan syndrome during hospitalization (a) and prior to discharge (b).

valves had diminished (Fig. 2a and b), as had the regurgitation jets. The patient was referred to a cardiovascular surgeon for further evaluation. Marfan syndrome was confirmed by genetic testing. At one-year follow up the patient was free of any complaints.

Discussion

Abiotrophia sp. is a part of the normal flora of the oral cavity (1). In an experimental comparison of *A. defectiva*, oral isolates of healthy humans with the reference strains from an endocarditis patient, Okada et al. (11) showed high infectivity and moderate levels of binding to fibronectin and other extracellular proteins in endocarditic strains. With respect to a previous dental procedure in the first patient and tonsillitis in the second patient, it is presumed that the oral cavity was the source of the *A. defectiva* causing endocarditis. The oral origin, triggered by a dental procedure, has already been suggested in a five-year-old child (9). Thus, the oral cavity might be the source of *A. defectiva* in patients with infective endocarditis more often than previously reported (5,12,13).

Abiotrophia sp. endocarditis is usually characterized by an indolent and slow course (5). Peripheral manifestations such as Osler nodes, finger clubbing or petechiae are not frequent, while peripheral embolizations can occur in one-third of cases (1,4). The first of the present patients matched this description well, while the exact course in the second patient remains unclear. The history of an inflamed toe would suggest a slow indolent course, whilst the rapid onset with fever, elevated body temperature and tonsillitis favors an acute course. The latter is also supported by the sudden onset of an Osler node, finger clubbing, and no previous complaints of reduced physical ability.

In both patients, the aortic valve was morphologically abnormal. It is known that *Abiotrophia* sp. predominantly affects morphologically or functionally abnormal valves. In two previous reports, pre-existing valve disease was found in 90% and 62% of cases, respectively (4,9). Here, the first patient had a prosthetic valve, which is less often associated with endocarditis caused by this microorganism (4). The second patient had a bicuspid valve and is, to the present authors' knowledge, the first reported case of *A. defectiva* endocarditis in a patient with Marfan syndrome.

Previous reports have shown excessive morbidity and mortality of patients with *Abiotrophia* sp. endocarditis when compared to those with endocarditis caused by other viridans streptococci and enterococci (5). In spite of in-vitro bactericidal effects, bacteriological failure occurs in 41% of cases (4). Penicillin was shown to be ineffective in up to 30% of *Abiotrophia adjacens* and *A. defectiva* strains, with a penicillin MIC of

0.12 mg/l (5). The reported mortality rates are between 17 and 20%, while 27% of patients receive a prosthetic valve (5). In contrast to these data, the present patients had a favorable outcome at one-year follow up. Furthermore, both isolates had penicillin MIC values less than 0.12 mg/l and responded well to treatment with penicillin. The low MIC was most likely the reason for a good response to antimicrobial treatment. Although the phenomenon of tolerance to penicillin in nutritionally variant streptococci is well known, the clinical implications are not clear and the response to treatment is usually satisfactory (5). In addition, an absence of hemodynamic compromise in the first patient, and young age in the second patient, presumably contributed to a favorable outcome.

A combination of penicillin and aminoglycoside is the recommended treatment regimen (1), and this proved to be both successful and safe in the second patient, although it was necessary to adapt the treatment in the first patient. The alternatives usually consist of vancomycin, amoxicillin and rifampin (9,10).

Side effects of penicillin have already been described in this form of endocarditis (6). Here, the first patient developed rash and leukopenia after 25 days of treatment. Penicillin was substituted with ceftriaxone but after 15 days the leukopenia re-emerged.

In conclusion, this report adds to the body of literature relating to *A. defectiva* endocarditis, and also presents the first patient with Marfan syndrome as an underlying disease. In contrast to previous reports, both patients responded to a standard treatment of endocarditis and had a favorable outcome at one-year follow up.

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