

# Infective endocarditis – A word of caution on non-typical bacteria

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**Abstract.** – A previously healthy 52-year-old man presented to our department with remitting and relapsing fever for more than 6 weeks. During complex staged work-up, we revealed that he suffered from an *Abiotrophia defectiva* endocarditis of the mitral valve with mitral regurgitation and vegetation requiring mitral valve replacement. He recovered well postoperatively and is currently being followed at our Outpatient Cardiology Clinic.

Key Words:

Endocarditis, *Abiotrophia defectiva*, Valve replacement, Antibiotics.

## Introduction

Infective endocarditis is still a leading problem in Western population despite modern antibiotic treatment and prophylaxis. Ahead of typical bacteria being susceptible for classic clinical presentation, diagnostic work-up as well as antibiotic treatment there are several non-typical bacteria with non-typical clinical presentation and diagnostic gaps resulting in severe clinical courses being associated with poor prognosis.

## Case Presentation

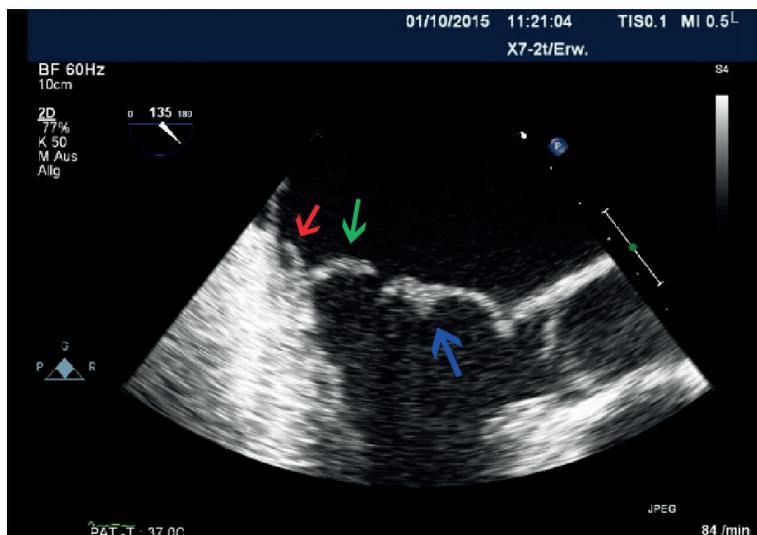
A 52-year-old man, with no prior history of illness, presented to his general practitioner with a 2 weeks history of intermittent fever until 38.2°C and night sweating. He had no dyspnea, palpitations, coughing, dysuria symptoms, cough or thoracic pain. There was no prior history of sore throat, dental or urogenital procedures, skin rash, injection drug use and smoking. He was participating on sports activities without having any symptoms. On his medical history was remarkable the presence of mitral valve prolapse and arterial hypertension. He had no history of travel.

He had been prescribed levofloxacin for 10 days by his general practitioner but after the discontinuation and a short period of 3 days of remission, his symptoms relapsed. He was subsequently referred to our department for further work-up. By the admission remarkable was a systolic murmur at left 4. Intercostal space and fever up to 38.2°C. No signs of neurological defects or other embolization signs on the skin were detected. After his admission blood cultures had been taken, and an empirical regiment with antibiotics (ampicillin, gentamycin and flucloxacillin) was started. The transesophageal echocardiography showed a myxomatous degenerated mitral valve with prolapse of the A2 scallop indicating an existing Barlow's disease, as well as a posterior flail leaflet as a consequence of ruptured chordae regarding to a severe mitral regurgitation. Vegetations were seen on both the posterior and anterior leaflets as well as on the mitral annulus posteriorly under the inserting point of P2. The results of blood cultures were positive for *Abiotrophia* specimen. The patient was admitted to our intensive care unit for monitoring. A diagnostic coronary angiography ruled out a coronary arterial disease. A cerebral computed tomography was performed without signs of embolisation. Due to these results a surgical procedure was discussed in our Heart Team and was carried out at the following day. The results from blood cultures and tissue cultures from the extracted valve confirmed the diagnosis of *Abiotrophia defectiva*, with susceptibility to ampicillin, penicillin G, vancomycin, meropenem and cefotaxime. The patient did not have any signs of congestive heart failure; his clinical status was unremarkable and we were able to oralise his antibiotics for the rest 4 weeks after his discharge from hospital and to start the warfarin therapy. We arranged a rehabilitation program and follow-up clinical control after the discharge.

## Discussion

*Abiotrophia defectiva* is primarily isolated in the oral cavity but can also be found in the intestinal and genitourinary tract and through this areas, it can enter the bloodstream. In healthy individuals, the rates of oral colonization are estimated at about 11.8%<sup>1-3</sup>. Apart from endocarditis, it is also implicated as a cause of endomyelitis, brain abscess, meningitis and septic arthritis<sup>1-5</sup>. Endocarditis due to *Abiotrophia defectiva* is quite rare, but accounts for up to 5% of streptococcal endocarditis and some cases of culture negative endocarditis<sup>6-8</sup>. The majority of patients with *Abiotrophia defectiva* infective endocarditis have a pre-existing heart disease and in approximately 10% of cases prosthetic heart valves are involved<sup>7,8</sup>. As described in literature, the clinical course is slow. The frequency of congestive heart failure and surgical intervention is higher as compared to streptococci induced endocarditis. Although few cases of *Abiotrophia defectiva* infective endocarditis have been reported, the majority have resulted in valve replacement despite adequate antibiotic therapy, as in our patient<sup>9-11</sup>. Of note, despite *in vitro* sensitivity to several antibiotics, this organism still causes a significant structural destruction of valves, raising concerns regarding the *in vivo* sensitivity to these antibiotics<sup>12</sup>. This may be due to the ability of the organism to produce L-forms that partially or completely lack a cell wall when exposed to suboptimal conditions, thus rendering antibiotics that target cell wall synthesis ineffective<sup>9,13-15</sup>. When exposed to suboptimal conditions the Gram stain for

these organisms also varies widely, with some appearing as Gram-negative bacilli, Gram-negative cocci or even resembling fungal elements<sup>8,10,16</sup>. The ability to produce an exopolysaccharide and bind moderately to fibronectin, and the exhibition of high levels of infectivity, all contribute to the virulence of *Abiotrophia defectiva* isolated from endocarditis patients<sup>8,14</sup>. Stein and Nelson<sup>9</sup> were the first to note that patients with nutritionally variant streptococci endocarditis had higher mortality rates, higher rates of relapse and higher rates of treatment failure despite the use of antibiotics that were effective *in vitro*. Lin et al<sup>17</sup>, in their retrospective study of eight cases of nutritionally variant streptococci endocarditis, showed that seven of the cases were associated with large vegetation size, that is, greater than 10 mm. It was also noted that seven of the eight cases went on to have a valve replacement, performed either because of vegetation size or severe heart failure. Thus, it is important to be aware of this aetiological agent, as prompt and aggressive treatment is necessary to improve outcomes. Prompt diagnosis is not always possible for two main reasons. First, the organism does not grow well on standard blood agar without supplementation. Second, once colonies grow, they are still difficult to identify in laboratory with limited microbiological technology. Porte et al<sup>18</sup> noted a similar problem where the API 20 Strep system initially identified the organism as *A. adjacens* with 80% certainty. Owing to the discrepancy, 16S rRNA sequencing eventually had to be performed to confirm that the isolate was *A. defectiva*. Matrix-assisted laser desorption ionisation time of flight mass spectro-



**Figure 1.** Notice the myxomatous degeneration of the mitral valve (in this image better seen at A2, blue arrow), the P2 flail leaflet (green arrow) as well as the vegetation on the annulus (red arrow).



**Figure 2.** Severe mitral insufficiency due to flail leaflet.

metry (MALDI-TOF-MS) is another technique that can greatly reduce time to identification. On our case PCR was used to confirm the diagnosis. Historically, *Abiotrophia defectiva* has declared itself more difficult to treat than *Streptococcus*<sup>20</sup>. As such, the American Heart Association recommends that the treatment regime used is the same as that used for *Enterococcus endocarditis*<sup>20</sup>. Typically, this consists of ampicillin or penicillin G in addition to gentamicin for a 4-6 week period. Alternatively, vancomycin plus gentamicin for a 6-week period can be used. In the retrospective study performed by Lin et al<sup>17</sup>, only 30% of patients were successfully treated with penicillin and gentamicin. One case required treatment with rifampicin and ceftriaxone after the failure of combination therapy with vancomycin and gentamicin. Perhaps this is an organism that may warrant triple antibiotic therapy and this can be explored in future studies. It is noteworthy that the Early Surgery versus Conventional Treatment for Infective Endocarditis (EASE) trial<sup>11</sup> found that patients with severe valve disease and large vegetation had had a more favourable outcome with an early surgery approach. Our patient had severe mitral valve regurgitation due to endocarditis; therefore, the early mitral valve replacement was the appropriate choice. It is becoming more recognised that infective endocarditis caused by *Abiotrophia defectiva* has a poor prognosis, frequently resulting in large vegetation with valve destruction and heart failure. *Abiotrophia defectiva* has also been implicated as one of the organisms associated with the highest rates of systemic embolisation. Therefore, it is prudent that this organism is suspected in cases of cul-

ture negative endocarditis and additional testing with supplemented media should be performed to encourage the growth of colonies<sup>12,19,20</sup>. Subsequently, MALDI-TOFMS or 16S rRNA may provide the fastest means of identification. Once this organism is identified, in conjunction with appropriate antibiotics, early surgical treatment should be considered.

## Conclusions

Infective endocarditis is a common cause for acute destruction of a cardiac valve. The clinic as well as clinical course is somewhat difficult to identify in case of non-typical bacteria and have to be taken in mind in patients presenting with undetermined symptoms like fever, discomfort or neurological events.

## Conflicts of interest

The authors declare no conflicts of interest.

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