CASE REPORT

Abiotrophia defectiva endocarditis

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SUMMARY

A previously healthy 27-year-old Jamaican man presented to the University Hospital of the West Indies with recurrent joint pain, remitting and relapsing fever, and shortness of breath. He was subsequently found to have *Abiotrophia defectiva* endocarditis. This was the first time this organism had been isolated at our institution. Despite culture directed antibiotics, his clinical course was quite severe with mitral regurgitation and congestive cardiac failure requiring mitral valve replacement. He recovered well postoperatively and is currently being followed at our outpatient cardiology clinic. This report highlights the severe presentation and often poor outcome associated with *A. defectiva* endocarditis and stresses that the outcome may be improved by early and appropriate surgical intervention.

BACKGROUND

Endocarditis due to *Abiotrophia defectiva* is quite rare, but accounts for up to 6% of streptococcal endocarditis and some cases of culture negative endocarditis.^{1–5} Previously, *A. defectiva* fell under the ‘umbrella’ group of nutritionally variant streptococci (NVS), which were initially described in 1961 by Freckle and Hirsch.^{6,7} In 1989, Bouvet *et al* used DNA–DNA hybridisation to divide NVS into *Streptococcus defectivus* and *Streptococcus adjacens* based on DNA homology.¹ These were later transferred to a new genus, *Abiotrophia*, using 16S rRNA sequencing.⁸ Collins and Lawson⁹ have reclassified the genus *Abiotrophia* with *A. defectiva* as the only species in this genus. Classically, *A. defectiva* has been described as non-motile, Gram-positive cocci in chains that are catalase negative, pyridoxine dependent and exhibit satellitism.^{10,11}

A. defectiva has been identified as part of the normal flora of the human oral cavity, gastrointestinal tract and urogenital tract.^{7,12} There is a propensity for these organisms to cause bacteraemia and infective endocarditis, but they have also been implicated in other infections such as sinusitis, osteomyelitis, corneal ulcers and scrotal abscesses.¹⁰ Although an uncommon cause of endocarditis, the clinical outcome can be severe, with need for early surgical intervention.¹³

This report describes the first case of *A. defectiva* infection identified in Jamaica, and highlights its propensity to cause endocarditis, the delays in identification and the fact that isolation may require more advanced microbiological diagnostic methods.

CASE PRESENTATION

A 27-year-old man, with no prior history of illness, presented to his general practitioner with a

3-month history of intermittent fever, night sweats, joint pain, central chest pain, palpitations, shortness of breath and paroxysmal nocturnal dyspnoea. Two months prior, he had noticed clubbing of his fingers and toes and had transient ‘black and blue’ discolouration of the tip of the third digit of his left hand.

There was no prior history of sore throat, dental procedures, skin rash, injection drug use or congenital heart disease. He had no history of travel outside of Jamaica. He had been prescribed a non-steroidal anti-inflammatory drug by his general practitioner but this provided no relief.

He was subsequently referred to the accident and emergency department of the University Hospital where a murmur was detected prompting referral to the cardiology clinic.

At the cardiology clinic, physical examination revealed mucosal pallor and a grade three on six (III/VI) apical pansystolic murmur, in keeping with mitral regurgitation. A portable transthoracic echocardiogram was performed, which showed a 2.0 cm oscillating mass attached to the anterior mitral leaflet. The leaflet was flail and prolapsed into the left atrium. There was associated moderate posterior mitral regurgitation. The left ventricular systolic function was normal. Right ventricular systolic pressure (RVSP) was elevated at 50 mm Hg.

The patient was then admitted with a presumptive diagnosis of infective endocarditis (IE). He was empirically started on ceftriaxone and gentamicin. On admission, his vital signs were within normal range. Laboratory findings on admission are found in table 1.

Three sets of blood cultures were taken and all six bottles grew Gram-positive cocci. After 9 days of repeated attempts, *A. defectiva* was identified with low discrimination using the Vitek 2 system (bioMérieux). After identification of the organism, the patient had been switched to vancomycin only for suspected penicillin/cephalosporin resistance. The isolate was subsequently found to be sensitive to penicillin, ampicillin, coamoxiclav, ceftriaxone, gentamicin, erythromycin and vancomycin. The antibiograms of the six isolates were the same. As such, ceftriaxone was restarted with erythromycin, as gentamicin was not available at the time.

Despite culture directed antibiotic therapy the patient’s condition gradually deteriorated, eventually resulting in severe congestive heart failure on day 16 of admission. He was treated with lisinopril 5 mg once daily and furosemide 20 mg once daily. A repeat echocardiogram showed an increase in the size of the oscillating vegetation from the previously seen 2.0–2.4 cm and an increase in

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Table 1 Laboratory findings on admission

	On admission	Normal ranges
ESR	47	<20 mm/h
CRP	0.43	<0.5 ng/dL
Antistreptolysin O	281↑	<200 IU/mL
VDRL	negative	
HIV	negative	
Urinalysis	No abnormality	
Serum Fe	8	6–25 µmol/L
TIBC	51	44–72 µmol/L
Percentage of saturation	16	13–43%

CRP, C reactive protein; ESR, erythrocyte sedimentation rate TIBC, total iron binding capacity VDRL, Venereal Disease Research Laboratory.

the previously recorded pulmonary pressures from a RVSP of 50–76 mm Hg. The cardiothoracic surgical team was contacted and plans were made for urgent mitral valve (MV) replacement.

On Day 29 of admission, MV replacement was performed with a mechanical valve. Intraoperatively, vegetations to the anterior leaflet of the MV were seen and there was rupture of the chordae tendineae. Valve culture was negative.

Five days postoperatively, a transthoracic echocardiogram showed improvement in the patient's pulmonary hypertension with RVSP now 50 mm Hg. Additional treatment included transfusion with three units of packed red blood cells for anaemia and sildenafil 20 mg twice daily for pulmonary hypertension. The patient's congestive cardiac failure resolved and he was discharged home to continue penicillin prophylaxis against recurrent attacks of rheumatic fever, warfarin therapy and follow-up in the cardiology clinic.

INVESTIGATIONS

See [tables 1](#) and [2](#).

DIFFERENTIAL DIAGNOSIS

- ▶ Infective endocarditis.
- ▶ Active rheumatic fever.
- ▶ Congestive cardiac failure.

The differential diagnosis was made based on the patient's presentation and was finally confirmed by investigation.

TREATMENT

Summary of treatment

Empirical treatment was initiated with ceftriaxone 2 g intravenously once daily and gentamicin 5 mg/kg (320 mg) once daily. On day 9 of admission, *A. defectiva* was identified from blood

cultures and the microbiology department recommended that ceftriaxone be switched to vancomycin until sensitivities became available. The patient received vancomycin for 3 days and was switched to culture directed ceftriaxone, with erythromycin 500 mg orally four times daily. The patient received this regime for 2 days. On day 15 of admission the patient developed heart failure, so furosemide 40 mg intravenously once daily and lisinopril 5 mg once daily were started. The patient completed 14 days of gentamicin preoperatively and 21 days of ceftriaxone preoperatively. Post operatively the patient continued to receive ceftriaxone 2 g intravenously once daily to complete a 6-week course. He was started on warfarin 7.5 mg once daily for his mechanical valve. Laboratory findings throughout his hospital stay are summarised in [table 2](#).

OUTCOME AND FOLLOW-UP

After an eventful course requiring mitral valve replacement, the patient's condition resolved and he was sent home, scheduled to return to clinic for follow-up visits. He returned 1 month later and was found to have supraventricular tachycardia for which he is now on carvedilol 12.5 mg twice daily. He continues to get his prophylaxis against recurrent attacks of rheumatic fever with benzathine penicillin G 1.2 million units intramuscularly every month until age 40.

DISCUSSION

Although few cases of *A. defectiva* infective endocarditis have been published in the literature, the majority have resulted in valve replacement despite adequate antibiotic therapy.^{10–14} The outcome in our case was similar. Despite appropriate antibiotic therapy, the patient's clinical condition continued to deteriorate leading to severe pulmonary hypertension and congestive cardiac failure requiring valve replacement.

Of note, despite in vitro sensitivity to several antibiotics, this organism still causes significant structural destruction of valves, raising concerns regarding the in vivo sensitivity to these antibiotics.¹⁵ Previous studies have also demonstrated high levels of penicillin resistance.¹⁶ 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.^{6 7 13 17} 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.^{12 14 18} 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 *A. defectiva* isolates from endocarditis patients.^{7 12}

Table 2 Laboratory findings throughout hospital stay

	On admission	Day 3 postoperation	Day 18 postoperation	Normal range
Haemoglobin	9.8	7.5	12.0	11.5–16.5 g/dL
Haematocrit	0.31	0.25	0.40	0.37–0.53
Platelet	380	198	481	150–400×10 ⁹ /L
WCC	7.8	8.9	7.1	4–11×10 ⁹ /L
PT	18.1/13.9	17.9/12.9	38.4/13.0	
PTT	42.5/32.8	41.1/32.4	42.7/31	
Sodium	133	129	136	135–145 mmol/L
Potassium	4.3	4.5	4.2	3.5–5.0 mmol/L
Chloride	100	96	98	95–105 mmol/L

PT, Prothrombin time; PTT, Partial thromboplastin time; WCC, white cell count.

Stein and Nelson were the first to note that patients with NVS 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.^{11–15 19–21} In their literature review of nine cases of *A. defectiva* endocarditis, Hashimoto *et al*¹² showed that five of nine cases warranted valve replacement despite appropriate antibiotic treatment. Ramos *et al*¹¹ found similar results in developing countries. Lin *et al*, in their retrospective study of eight cases of NVS 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 valve replacement, performed either because of vegetation size or severe heart failure.¹⁹ 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.^{18 22} Second, once colonies grow, they are still difficult to identify with the limited microbiological diagnostic technology available in developing countries such as Jamaica. For instance, in our case the Vitek 2 system (bioMérieux) was only able to identify *A. defectiva* with low discrimination after 9 days of repeated unsuccessful attempts. Porte *et al* noted a similar problem where the API 20 Strep (bioMérieux) 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*.²² Matrix-assisted laser desorption ionisation time of flight mass spectrometry (MALDI-TOF-MS) is another technique that can greatly reduce time to identification.¹⁸

Historically, *A. defectiva* has declared itself more difficult to treat than *Streptococcus*. As such, The American Heart Association recommends that the treatment regime used is the same as that used for *Enterococcus* endocarditis.²³ 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*, only 30% of patients were successfully treated with penicillin and gentamicin. One case required treatment with rifampicin and ceftriaxone after failure of combination therapy with vancomycin and gentamicin.¹⁹ 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 found that patients with severe valve disease and large vegetation had had a more favourable outcome with an early surgery approach.²⁴ Our patient had a vegetation size of greater than 1 cm and congestive cardiac failure suggesting that he might have been a candidate for early mitral valve replacement ideally within the first 48 h of admission.²⁴

It is becoming more recognised that infective endocarditis caused by *A. defectiva* has a poor prognosis, frequently resulting in large vegetations with valve destruction and heart failure. *A. defectiva* has also been implicated as one of the organisms associated with the highest rates of systemic embolisation.^{15 21 23} Therefore, it is prudent that this organism be suspected in cases of culture negative endocarditis and additional testing with supplemented media should be performed to encourage growth of colonies. Subsequently, MALDI-TOF-MS 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.

LIMITATION

The organism was only cultured after repeated and prolonged incubation on blood agar. It was subsequently identified by the VITEK2 automated identification system only after repeated attempts. This is a phenotypic method and not as accurate as 16S rRNA PCR.¹⁹

Gentamicin becoming unavailable at the hospital for 15 days could have impacted the clinical progression of this case and accounted for the deterioration, as opposed to the virulence of the organism itself.

Learning points

- *Abiotrophia defectiva* infective endocarditis may account for a significant number of culture negative endocarditides as the organism requires very specific conditions for optimal growth.
- Given the propensity for poor outcomes, early surgical intervention with valve replacement should be considered.
- Confirmatory testing or early identification by 16S rRNA PCR or matrix-assisted laser desorption ionisation time of flight-mass spectrometry (where cultures are available) is recommended, as early cultures appear sterile; or for rapid identification of cultures.

Competing interests None.

Patient consent Obtained.

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