

# Double-Valve Heart Disease and Glomerulonephritis

Consequent to *Abiotrophia defectiva* Endocarditis

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*Abiotrophia defectiva*, a nutritionally deficient streptococcus, is a rare cause of infective endocarditis. It has been associated with hemophagocytic syndrome. We present the first case of *A. defectiva* infective endocarditis that led to antineutrophil cytoplasmic antibody-associated glomerulonephritis. The patient was a 55-year-old man whose endocarditis affected the mitral and aortic valves. His course was complicated by atrial fibrillation, stroke, and glomerulonephritis. He was successfully treated with antibiotics and dual valve replacement. (*Tex Heart Inst J* 2020;47(1):35-7)

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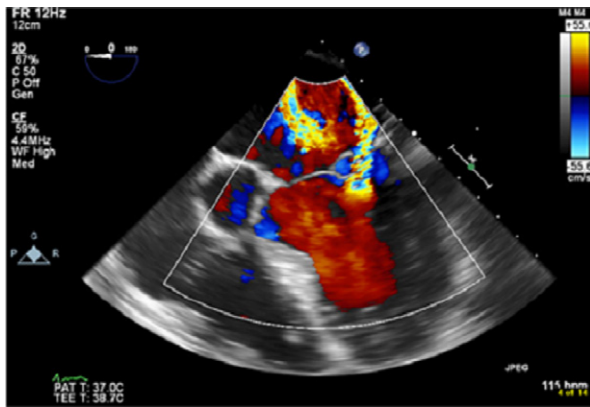
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**A** *biotrophia defectiva*, or nutritionally deficient streptococci, is a rare cause of infective endocarditis (IE). *Abiotrophia defectiva* was first described as a type of streptococcus by Frenkel and Hirsch<sup>1</sup> in 1961 and was reclassified under the new genus of *Abiotrophia* in 1995.<sup>2</sup> Although responsible for only 5% of IE cases, *A. defectiva* is a major cause of culture-negative cases.<sup>3</sup> Known for causing embolic complications, *A. defectiva* has an aggressive disease course, with a 17% relapse rate despite antibiotic use.<sup>4</sup> The American Heart Association guidelines recommend using penicillin G or ceftriaxone plus gentamicin to treat these patients.<sup>5</sup> This infection has been associated with hemophagocytic syndrome,<sup>6</sup> which has, in turn, been associated with antineutrophil cytoplasmic antibody (ANCA)-positive vasculitis. To our knowledge, we are first to report a case of *A. defectiva* endocarditis that led to the development of ANCA-associated glomerulonephritis.

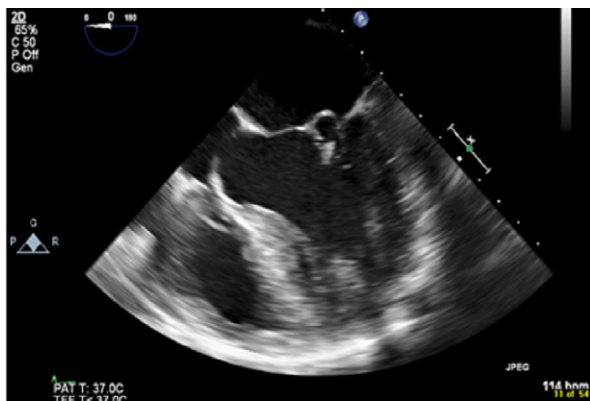
## Case Report

In 2017, a 55-year-old man with no relevant medical history presented at the hospital because of a 6-month history of weight loss (total, 30 lb), progressive malaise, nonproductive cough, and dyspnea on exertion. He was treated for pneumonia as an outpatient with 2 short courses of antibiotics and steroids and was given a new presumed diagnosis of asthma. His cough and malaise improved; however, he later presented at the hospital because of worsening symptoms. Initial evaluation in the hospital revealed tachycardia (heart rate, 104 beats/min), a blood pressure of 149/76 mmHg, and a fever that peaked at 102.8 °F. Blood test results showed levels of blood urea nitrogen at 29 mg/dL, creatinine at 2.7 mg/dL, and a white blood cell count of  $6.6 \times 10^9/L$ . Auscultation revealed a pansystolic murmur that radiated to his axilla and a decrescendo diastolic murmur heard loudest over his apex. When *A. defectiva* was grown from blood cultures, intravenous treatment with vancomycin was started.

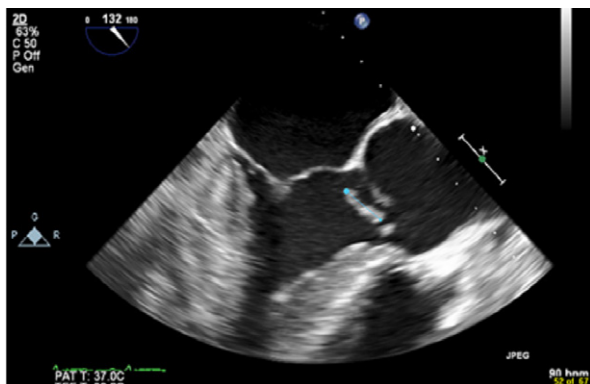
Transthoracic echocardiograms (TTE) and transesophageal echocardiograms (TEE) revealed a 0.5-cm vegetation on the mitral valve that perforated the anterior leaflet, along with severe mitral regurgitation (Figs. 1 and 2). The TEE also showed an aortic vegetation of  $1.4 \times 0.5$  cm on a functional bicuspid aortic valve, as well as severe aortic regurgitation (Fig. 3). Blood cultures taken after vancomycin was started were negative. Further blood tests revealed elevated rheumatoid factor (156 IU/mL) and antineutrophil antibody titer (1:320, homogeneous appearance), normal complement C3 and C4 levels and myeloperoxidase autoantibody concentration, and increased levels of proteinase 3 autoantibodies (1.1 U/mL). The patient was discharged from the hospital with instructions to take ceftriaxone. Aminoglycosides could not be be-



**Fig. 1** Transesophageal echocardiogram (color-flow Doppler mode) shows 2 jets of severe mitral regurgitation, one directed posteriorly and one anteriorly.



**Fig. 2** Transesophageal echocardiogram shows mitral vegetation on the left ventricular side of the mitral valve.



**Fig. 3** Transesophageal echocardiogram shows aortic vegetation.

cause he had renal dysfunction. Aortic and mitral valve replacement surgery was recommended after 6 weeks of antibiotic therapy.

The patient returned to the hospital 2 weeks after discharge with worsening malaise and dyspnea on exertion. Repeat TTE showed that the mitral vegetation

had resolved but that the aortic vegetation remained. Atrial fibrillation was then diagnosed, and he was treated with rate-control agents. He had an acute large left hemorrhagic parieto-occipital stroke, which was managed conservatively. His renal function worsened, and a kidney biopsy specimen showed focal necrotizing and diffuse crescentic glomerulonephritis of the pauci-immune type (ANCA-associated). He was started on prednisone and cyclophosphamide, and his creatinine level decreased from a peak of 3.8 mg/dL to 1.5 mg/dL before he was discharged from the hospital.

Two months after the initial diagnosis of IE, the patient underwent aortic and mitral valve replacements with bioprostheses. All his blood cultures, including those taken intraoperatively, were negative after the first set, and ceftriaxone was discontinued after 6 weeks total. There was no evidence that atrial fibrillation recurred, and anticoagulation was discontinued after 6 months. Follow-up for more than a year showed stabilized kidney function with a new baseline creatinine level of 2.1 mg/dL, and his only medication was aspirin (81 mg).

## Discussion

In this patient, *A. defectiva* IE led to ANCA-associated glomerulonephritis. *Abiotrophia defectiva* is part of the normal flora of the mouth and the urogenital and intestinal tracts.<sup>6</sup> Outcomes in cases of *A. defectiva* IE have ranged from complete cure with antibiotics to multiple complications and the necessity of valve replacement.<sup>7-12</sup> The secretion of exopolysaccharide and the ability to adhere to fibronectin explains the affinity of *A. defectiva* for endovascular tissue,<sup>13</sup> although it can also cause osteomyelitis, cerebral abscess, septic arthritis, and meningitis.<sup>6</sup>

Molecular techniques have been used to improve the detection and identification of *A. defectiva*. One rapid and accurate method is the use of 16S rRNA gene polymerase chain reaction amplification, followed by restriction fragment length polymorphism.<sup>14</sup>

The current guidelines are to treat *A. defectiva* IE with penicillin G or ceftriaxone plus gentamicin.<sup>5</sup> Our patient was first placed on vancomycin because the initial isolate was identified as *Micrococcus luteus*, which was resistant to penicillin. This result appeared to be wrong on the basis of isolate characteristics. Retesting at another laboratory identified the isolate as *A. defectiva*. In general, *A. defectiva* is less susceptible to penicillin and more susceptible to cephalosporin. We gained confidence in the new antibiotic regimen when the minimum inhibitory concentration breakpoints of our isolate were 0.094 µg/mL for penicillin, 1 µg/mL for ceftriaxone, and 1 µg/mL for vancomycin. After confirming the susceptibility results, we switched the patient from vancomycin to ceftriaxone. We continued

to evaluate him at our clinic for more than a year, and he had no symptoms indicating recurrence; all follow-up blood cultures were negative. His successful treatment may be attributed to the susceptibility of the organism to ceftriaxone and to proper surgical management.

Infective endocarditis can lead to renal involvement in different ways; renal infarctions from septic emboli and glomerulonephritis are most typical.<sup>15</sup> Glomerulonephritis is usually associated with IE caused by staphylococci, followed by streptococci. The typical renal biopsy findings are characterized as necrotizing and crescentic glomerulonephritis.<sup>16</sup> Reports of ANCA-positive antibodies in cases of IE have been published.<sup>17,18</sup> Our patient needed cyclophosphamide and prednisone to stabilize his kidney function.

The timing of surgery for IE depends on certain complications.<sup>5,19,20</sup> In our patient, early operation was indicated because he had a vegetation larger than 1 cm on the aortic valve, mitral valve perforation, and aggressive *A. defectiva* infection. In cases of hemorrhagic stroke, the operation may be delayed to avoid further complications. Early surgery may be associated with decreased in-hospital mortality rates for native-valve endocarditis and may reduce the risk of embolic strokes.<sup>21,22</sup>

In conclusion, physicians should recognize that *A. defectiva* IE can be aggressive and lead to double-valve disease and glomerulonephritis. Early surgical intervention may prevent complications and be the preferred approach.

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