A case of endocarditis: When three equals one

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A 32 year-old male smoker presented to the emergency room with increasing breathlessness over two weeks. Past history was unremarkable, including no history of rheumatic fever, heart murmurs, intravenous drug use or recent invasive procedures. Oral hygiene was poor, and an aortic insufficiency murmur was heard on physical examination. Blood work revealed leukocytosis (white blood cells= $18.3 \times 10^9/L$), hyperglycemia (serum blood glucose= 17.8 mmol/L) and ketoacidosis. A chest radiograph displayed cardiomegaly, pulmonary edema and bilateral pneumonia. Serial electrocardiograms showed ST elevation in the precordial leads and troponin I was $4 \mu\text{g/L}$. Two initial blood cultures grew coagulase-negative staphylococci (CNS). The patient was treated with levofloxacin and vancomycin, along with usual therapy for hyperglycemia, congestive heart failure and acute coronary syndrome. A transesophageal echocardiogram (TEE) revealed severe aortic insufficiency, an aortic root abscess and a large cauli-

flower-shaped vegetation extending into the aortic valve. The patient underwent urgent aortic valve replacement and pericardial closure of the abscess. Two preoperative blood cultures each grew *Staphylococcus warneri* and *Staphylococcus haemolyticus*, as speciated by VITEK (bioMerieux, USA). Intraoperative aortic valve and pericardial fluid cultures, as well as two postoperative blood cultures, grew *Staphylococcus epidermidis* and *S. warneri*, which were also speciated by VITEK. The automated antibiograms produced by VITEK for the various isolates differed, which is consistent with a polymicrobial endocarditis. The patient was treated with vancomycin, rifampin and gentamicin (to which all isolates were sensitive), but worsened clinically and demonstrated persistent fever.

What is your diagnosis? What would you recommend?

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Figure 1) Pulsed-field gel electrophoresis demonstrating identical electrophoretic patterning in coagulase-negative staphylococci isolates from pericardial fluid (lane 2), aortic valve vegetation (lanes 3 and 4) and blood (lanes 5-7, 9-13). Lanes 1, 8 and 15 are markers, and lane 14 is a negative control

DIAGNOSIS

Follow-up TEE demonstrated increased vegetation size and new mitral regurgitation. The patient was taken back to the operating room for aortic and mitral valve replacements two-and-a-half weeks after his initial aortic valve replacement. Pulsed-field gel electrophoresis (PFGE) demonstrated identical electrophoretic patterning for all previous bacterial isolates, which was consistent with a monomicrobial CNS native-valve endocarditis (Figure 1). The patient recovered with a six-week course of vancomycin, gentamicin and rifampin. The regional reference laboratory was unable to speciate all of the isolates.

DISCUSSION

This patient presented with a case of native-valve endocarditis with CNS. He had no history of valvular surgery, intravenous drug use or percutaneous vascular access. CNS usually cause prosthetic-valve endocarditis and are uncommon causes of native-valve endocarditis, accounting for less than 5% of such cases.

Native-valve CNS endocarditis is primarily a community-acquired infection. Most case series have demonstrated an underlying cardiac abnormality, either congenital or acquired, in 65% to 75% of patients (1,2). Clinical presentation often involves weight loss, weakness and fever, and up to one-third of patients may exhibit peripheral manifestations, including Osler's nodes, Janeway lesions and splinter hemorrhages (2). Common laboratory abnormalities include anemia and leukocytosis. In approximately one-half of patients, vegetations may be demonstrated via transtho-

racic echocardiography (2). Mortality is between 13% and 20% (1,3,4).

At least 18 CNS species have been isolated from human skin (5). *S. epidermidis* accounts for nearly three-quarters of all isolates (6). However, it has been postulated that *S. epidermidis* possesses virulence factors that are not characteristic of other CNS (7). Other clinically significant species include *Staphylococcus saprophyticus*, *Staphylococcus hominis*, *S. haemolyticus*, *S. warneri* and *Staphylococcus simulans*.

Because polymicrobial endocarditis is uncommon in noninjection drug users or persons without indwelling vascular catheters, PFGE was performed to verify the varying antibiogram results in this case. Discovered in 1984, PFGE is a molecular technique of separating complex mixtures of DNA into different sized fragments by electrophoresis. DNA is isolated intact and is then treated with restriction enzymes to generate pieces small enough to resolve by electrophoresis in agarose or acrylamide. PFGE allows extremely large DNA to be resolved, with the upper size limit of DNA being well over 10 Mb (10,000 kb). During continuous field electrophoresis, DNA that is 30 to 50 kb migrates with the same mobility regardless of size. This is seen in a gel as a single large diffuse band. During PFGE, DNA is forced to change direction during electrophoresis so that different sized fragments begin to separate from each other. Smaller DNA fragments move in the new direction more quickly than larger DNA fragments with each reorientation of the electric field relative to the gel. Thus, larger DNA fragments lag behind smaller ones, providing a visible separation.

PFGE is particularly useful in apparent CNS infections to help differentiate true pathogens from sterile site contaminants (8,9). Repetitive isolation of the same strain from an individual patient increases the probability of clinical significance.

In our case, PFGE demonstrated an identical electrophoretic pattern for all previous bacterial isolates, consistent with a monomicrobial CNS native-valve endocarditis. We recommend that clinicians be skeptical of apparent polymicrobial endocarditis in persons without percutaneous vascular access and that they also recognize the clinical role of molecular techniques to aid diagnosis and therapy in infectious diseases.

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