BARTONELLA INFECTION: A SIGNIFICANT CAUSE OF NATIVE VALVE ENDOCARDITIS NECESSITATING SURGICAL MANAGEMENT

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The early identification of patients with infective endocarditis who do not respond to medical therapy and who require surgery may improve survival.¹ Some organisms causing endocarditis (eg, *Staphylococcus aureus*) respond poorly to medical therapy, and these infections frequently necessitate emergency valvular surgery.² *Bartonella quintana* and *Bartonella henselae* have recently emerged as significant causes of infective endocarditis. These gram-negative bacteria are difficult to culture, and the optimal antibiotic therapy has yet to be determined. Currently, the majority of patients with endocarditis caused by these organisms require heart valve replacement because of progressive hemodynamic decompensation. We report 4 cases of infective endocarditis caused by *Bartonella* species at our hospital between September 1997 and August 1998.

Clinical summaries

PATIENT 1. A 45-year-old man with a history of hostel residency, alcohol abuse, and intravenous drug use was admitted with fatigue, ankle swelling, and fever. A systolic murmur was noted and an echocardiogram demonstrated thickening of the aortic valve without obvious vegetations. No growth was obtained from blood cultures, but serologic testing showed a *B quintana* immunoglobulin G antibody titre of more than 1:256 by indirect immunofluorescence. Antibodies were also detected to *B henselae* and *Chlamydia* species. Doxycycline was added to the treatment regimen of benzylpenicillin and gentamicin. Because of worsening cardiac status he underwent aortic valve replacement and, after initial recovery, died of *Escherichia coli* septicemia, having had a colonic perforation. Histologic examination showed organ-

Fig 1. Warthin-Starry stain of a resected aortic valve from a patient with *Bartonella quintana* endocarditis. This silver stain shows black clumps of bacteria.

isms on Warthin-Starry staining (Fig 1) but not with the Gram stain. Vegetations were not prominent and bands of fibrous tissue were associated with the infiltrate in most areas. *B quintana* was detected by culture and polymerase chain reaction (PCR) for the 16S-23S RNA internal spacer region and the *ftsZ* gene.

PATIENT 2. A 59-year-old man with a history of mixed aortic valve disease had symptoms of left ventricular failure. On examination he was febrile and had splinter hemorrhages. A transthoracic echocardiogram demonstrated vegetations on the aortic valve. No growth was obtained from blood culture, but a serologic response was detected to *Bartonella* species, immunoglobulin G titre 1:256. Treatment was commenced with benzylpenicillin and gentamicin given intravenously. The fever settled and inflammatory markers fell. However, a second echocardiogram revealed worsening aortic regurgitation, and his renal function deteriorated. Aortic valve replacement was performed uneventfully and the patient made a full recovery. *B quintana* was detected from the excised valve by PCR and culture (histologic studies were not available).

PATIENT 3. A 69-year-old man with a history of ischemic

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heart disease was admitted for elective coronary angioplasty. On admission he was febrile, had a purpuric rash on both legs, and had a new pansystolic murmur. He reported weight loss and night sweats of recent onset. Transesophageal echocardiography demonstrated mitral regurgitation and a vegetation on the posterior leaflet of the mitral valve. A coagulase-negative staphylococcus was isolated from 1 of 6 blood culture bottles. Treatment was commenced with benzylpenicillin and gentamicin and later changed to vancomycin and gentamicin. He became afebrile, but a second echocardiogram demonstrated enlargement of vegetations and worsening mitral regurgitation. Renal function also deteriorated. He underwent mitral valve replacement and made a good recovery after an initially stormy postoperative period. Serologic testing for *Bartonella* species, performed postoperatively, revealed immunoglobulin G antibodies in a titre of more than 1:256.

PATIENT 4. A 42-year-old unemployed man with a history of psychiatric illness and alcohol abuse was admitted with cough, weight loss, and chest pain. On examination he was febrile, jaundiced, and had clubbing of the digits. Ascites and a systolic murmur were noted as well. Echocardiography demonstrated a vegetation on the aortic valve and treatment with benzylpenicillin and gentamicin was commenced. No growth was obtained from blood culture. His cardiac status deteriorated, but on the eve of valve replacement surgery he discharged himself from the hospital against medical advice and collapsed in the street with a fatal cardiorespiratory arrest. Antemortem serum contained antibody titers of 1:256 against *Bartonella* species. Postmortem histologic information was not available.

Discussion. *B quintana* causes trench fever, a self-limiting bacteremic illness transmitted by clothing lice, which was prevalent among soldiers during World War I.³ More recently, *B henselae* was identified as the agent of bacillary angiomatosis and cat scratch disease.³ *Bartonella* species were first described to cause endocarditis in reports from Seattle, Washington,⁴ and subsequent cases have been reported from elsewhere in the United States, France, Canada, South Africa, and the United Kingdom.⁵ *Bartonella* species may account for 3% of all cases of endocarditis.⁵ Alcoholism and homelessness are risk factors for endocarditis due to *B quintana*, and native valves with no preceding valvulopathy are predominantly affected.³⁻⁵ *B henselae* more frequently causes endocarditis in patients with pre-existing valvular disease and cat contact.³⁻⁵ Frequent failure of medical therapy is seen for both species, and progression to valve replacement occurred in 30 of 33 published cases.^{4,5} Sera from patients with confirmed *Bartonella* infections (culture or PCR positive) cross reacts in *Chlamydia* antibody assays, but the converse cross reaction

does not occur.^{3,5} Some patients with endocarditis attributed to various *Chlamydia* species were actually infected with *Bartonella* species.^{3,5} The optimal antibiotic therapy for the condition has yet to be determined, but inclusion of an aminoglycoside in the regimen is recommended.³

In 2 of the cases we describe, the species of *Bartonella* causing endocarditis was established by culture and molecular identification methods, and in the 2 other cases *Bartonella* endocarditis was diagnosed on serologic evidence of infection and the failure to recover another pathogen from blood culture. (Current serologic methods are unable to distinguish reliably between infections caused by the different *Bartonella* species). All the patients required surgery because of progressive hemodynamic disturbance while receiving medical therapy, although 1 patient died before he underwent the procedure. Two of the patients were homeless or living in hostels at the time of diagnosis.

Bartonella serologic tests should be performed in all patients with culture-negative endocarditis, especially in those with known risk factors (eg, homelessness, alcoholism, cat contact). Early surgery may be indicated if positive serologic results are obtained. Warthin-Starry staining is indicated for valves removed from patients with culture-negative endocarditis. PCR and specific culture for *Bartonella* should be carried out on resected valves if positive *Bartonella* or *Chlamydia* serologic results were obtained in the preoperative period.

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