Case Report

Bartonella Quintana Endocarditis as a Cause of Severe Aortic Insufficiency and Heart Failure

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We describe the case of a 26-year-old man who developed severe aortic valve insufficiency due to a culture-negative endocarditis, leading to severe heart failure. The diagnosis of *Bartonella quintana* endocarditis was suspected from the clinical presentation and serological immunofluorescence assay, and was confirmed by polymerase chain reaction analysis of excised valve tissue after aortic valve replacement. The aim of this report is to illustrate *B. quintana* endocarditis as an important cause of culture-negative endocarditis that presents challenges in its clinical, diagnostic and therapeutic management.

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Blood culture-negative infective endocarditis remains a challenging clinical, diagnostic and therapeutic problem that accounts for 2-5% of all cases of infective endocarditis.[1] *Bartonella* endocarditis is an important cause of blood culture-negative endocarditis that requires specific serologic tests and molecular biology techniques for its diagnosis. We report the first case from Greece of severe heart failure caused by *Bartonella quintana* endocarditis. The diagnosis was suspected from the clinical presentation and serological immunofluorescence assay and was confirmed by polymerase chain reaction (PCR) analysis of excised valve tissue.

Case presentation

In November 2008, a 26-year-old man was admitted because of continuous fever, malaise, anorexia, weight loss, chest discomfort on exertion and progressive fatigue over the last three weeks. He was born in Pakistan and immigrated to Greece 6 years ago after a long and exhausting journey lasting five months, mainly on foot. He worked in Greece, providing manual labor, and had a low socioeconomic status, living in poor hygienic conditions. No history of contact with cats or lice infestations was noted and there was no history of any cardiac disease.

The patient was hemodynamically stable upon admission (blood pressure 120/60 mmHg, heart rate 90 bpm) with an afternoon fever of up to 38°C. Mucosal examination indicated paleness. A propulsive left ventricular ictus was identified at the 6th intercostal space on the anterior axillary line, while both diastolic and systolic murmurs were present in the aortic valve area. A large-volume collapsing pulse was noted. Lung auscultation was normal and abdominal examination showed mild liver enlargement. The chest X-ray revealed a high cardiothoracic ratio. The electrocardiogram showed sinus rhythm with left ventricular hypertrophy. The patient's skin was unremarkable for lesions.

Transthoracic and transesophageal echocardiography revealed a calcified aor-

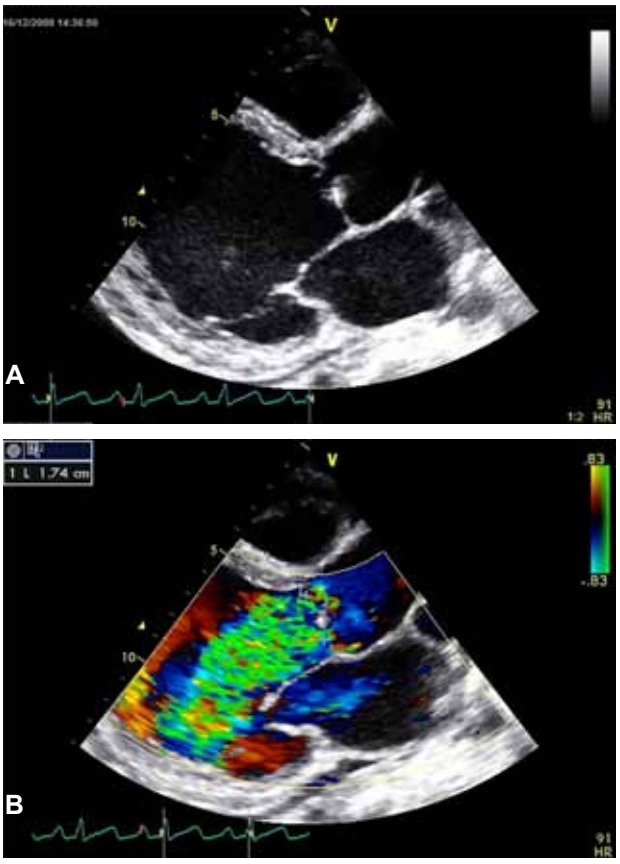

Figure 1. A. 2D-echocardiogram imaging from the parasternal long-axis view, showing left coronary cusp rupture of the aortic valve in the left ventricle during diastole, vegetation on the non-coronary cusp, left ventricular dilatation, and mild pericardial effusion. B. Color-Doppler showing severe aortic regurgitation (green color) with *vena contracta* 1.74 cm.

tic valve with a left coronary cusp rupture, vegetation on the non-coronary cusp, severe aortic valve regurgitation, and significant left ventricular systolic dysfunction (left ventricular ejection fraction ~40% and left ventricular diastolic diameter 75 mm; Figure 1). Hemoglobin was 9.9 g/dl, hematocrit was 30.5% with mean corpuscular volume 70, white cell count was 8900 /μL and platelets 267,000 /μL. Creatinine was 0.7 mg/dL and hepatic biochemistry was within normal limits. Erythrocyte sedimentation rate was 68 mm and C-reactive protein was 8 IU/L. An inverse relation of serum albumin/total proteins was noted and serum electrophoresis showed IgG hypergammaglobulinemia. A bone marrow aspirate was unremarkable. Human immunodeficiency virus serological exam was negative. Three sets of blood cultures within 24 hours of admission were taken before empirical therapy was initiated with gentamycin and vancomycin for possible infective endocarditis. Abdominal and chest CT scan revealed a mild hepato-splenomegaly and a mild bilateral pleural effusion.

Following a week of treatment with standard empirical therapy the patient started to deteriorate rapidly, with daily fever up to 39°C, progressive renal and hepatic impairment, and trilinear myelic aplasia. Repeat echocardiography revealed further deterioration of the preexisting heart failure. All antibiotics were withdrawn and new blood cultures taken. Upon withdrawal the patient stabilized, and a few days later the toxicities were partially reversed.

Positive IgG antibodies were found against *Chlamydia pneumonia/psittaci*, with a titer of >1:800, and against *B. quintana*, with a titer of >1:1024. Serum antibodies against brucellosis and *Coxiella burnetti* were negative. Treatment for possible bartonellosis was initiated with gentamycin and doxycycline. Five days later the patient improved clinically; he was afebrile, while inflammation markers decreased. The patient was then transferred to the cardiac surgery department, where he underwent a successful aortic valve replacement. Tissue was sent for histopathology and PCR analysis, both of which confirmed the diagnosis of *B. quintana* infective endocarditis.

Intraoperatively, the patient had complete atrioventricular block requiring the use of a temporary pacemaker. After clinical stabilization, the patient underwent permanent pacemaker implantation and showed progressive clinical improvement during the first week. However, during his 11th day in the hospital the patient expired as result of irreversible ventricular fibrillation, despite prompt resuscitation. Necropsy did not reveal any specific cause of death.

Discussion

B. quintana endocarditis is an important cause of culture-negative endocarditis,[2] yet its diagnosis remains a challenging problem. The diagnosis is based mainly on clinical suspicion, specific serologic testing,[3] blood/valve tissue culture and immunohistochemical/PCR detection on excised valve tissue.[2]

Bartonella species are Gram-negative bacilli that can cause infective endocarditis. Valve endocarditis caused by bartonellosis has been recognized by recent studies as an increasing cause of culture-negative endocarditis.[4-8] *B. quintana* accounts for the majority of cases of *Bartonella* endocarditis,[9] especially in patients who have predisposing factors for chronic *Bartonella* bacteremia, such as alcoholism, poor hygienic condi-

tions and homelessness.[10] Clinical suspicion should be aroused by symptoms and signs of endocarditis, such as fever, malaise, anorexia, weight loss, anemia, hepatosplenomegaly, clinical manifestations of heart failure, and the presence of calcified valve disease (predominantly of the aortic valve). Further specific serologic testing of blood and valve-tissue cultures, and immunohistochemical/PCR detection on excised valve tissue[11] are needed to establish a certain diagnosis. However, the culture and isolation of *Bartonella* species require specific incubation for several weeks, while subcultures with uncertain results and PCR detection on valve tissue necessitate surgical intervention, making the early diagnosis and therapy of *Bartonella* endocarditis difficult. Although the diagnosis of *Bartonella* endocarditis by PCR with serum has been proposed,[12] the diagnostic accuracy of infective endocarditis by PCR remains generally low.[13]

Recent studies have shown that micro-immunofluorescence of serum can reliably detect *Bartonella* IgG antibodies, and a titer of >1:800 for IgG against *Bartonella* has a high predictive positive value of 0.955 for bartonellosis among patients with endocarditis.[3] In our case, IgG antibodies against *B. Quintana* were detected by immunofluorescence serum testing with a titer of >1:1024, giving the diagnosis of *B. Quintana* endocarditis a high probability. For this reason specific treatment with an aminoglycoside and doxycycline was started, as indicated by previous studies.[14] Confirmation of the diagnosis was made by a PCR-based method applied to excised valve tissue after valve surgery, which was necessitated by our patient's severe aortic insufficiency and progressive heart failure. However, this method requires a specialist laboratory, which is not always available. The positive IgG antibodies against *Chlamydia* found in our patient's serum could be explained by cross reactivity for *Chlamydia* and *Bartonella* species, as reported previously.[8]

Bartonella endocarditis has a subacute evolution, causing severe valve lesions with a potentially fatal outcome if not diagnosed and treated early. Even though we cannot be sure of the presence of a long-standing infection in our patient, it is likely that he had a previous long-standing *B. quintana* infection with late valvular involvement. However, this cannot be deduced from the patient's medical history.

Few data are available regarding the appropriate therapeutic approach to *Bartonella* endocarditis. In a retrospective study[14] that included 101 cases of *Bartonella* endocarditis, it was shown that effective antibiotic therapy should include an aminoglycoside prescribed for a minimum of 2 weeks. Ceftriaxone and doxycycline have also been used as complementary agents for a longer period (6 weeks). In cases of severe valve involvement and/or severe heart failure, surgical therapy should be considered (valve replacement in most cases), and medical treatment (doxycycline) should be continued for 6 weeks postoperatively.

In recent years we have been experiencing within the western world—in our case Europe—challenging cases that are novel to our clinical practice. This first reported case in Greece of *B. quintana* endocarditis provides the impetus for us to reevaluate our medical practice and to take a more global approach to medicine. Recent epidemiological data indicate that a staggering 25% of public health care resources in the European Union are used for the treatment of immigrants. A heightened level of alertness with regard to alternate etiologies that do not necessarily fall within country-specific epidemiology is a prerequisite when treating a patient, while a detailed medical and social history is paramount. Importantly, confounding iatrogenic factors, such as toxicity from the treatment used in this case, may be difficult to discern.

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