CONCISE COMMUNICATION

Clinically and histologically silent Q fever endocarditis accidentally diagnosed by PCR

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A case of Q fever endocarditis was diagnosed in a patient with no sign of active endocarditis by performing PCR targeting eubacterial 16S rDNA on the resected mitral valve. The diagnosis was confirmed by detection of high levels of anti-*Coxiella burnetti* antibodies, positive immunohistologic analysis of the valve tissue with specific antibodies and culture of *C. burnetti* from the valve tissue. As this patient had an unexplained aggravation of valve dysfunction, we recommended routine serologic testing for *C. burnetti* to allow the diagnosis of Q fever endocarditis at a very early stage.

Keywords Q fever, endocarditis, *Coxiella burnetti*

Accepted 16 July 2001

Clin Microbiol Infect 2002; 8: 113–114

A 33-year-old man with a past history of *Streptococcus mitis* mitral valve endocarditis, cured in 1994, was admitted to our hospital in November 1999 for surgical treatment of severe mitral insufficiency. He had no clinical signs of active infective endocarditis (IE), and physical examination revealed only signs of mitral regurgitation. At surgery, fibrous material was seen on the small mitral leaflet, with a perforation, and was considered by the surgeon to be a sequel of the previous episode of endocarditis. Macroscopic and microscopic examination of the excised material showed no evidence of active IE.

A fragment of the small mitral leaflet was included in a prospective study of universal PCR targeting eubacterial 16S rDNA [1] from valve tissue IE. It was used as a negative control for IE, as the patient was considered to be cured of *S. mitis* endocarditis. Surprisingly, PCR yielded a 402-nucleotide fragment whose nucleotide sequence showed significant alignments (>99% homology) with the *C. burnetii* 16S rDNA gene sequence (EMBL, accession number Y10502). The PCR result was confirmed by detection of high levels of anti-*C. burnetii* antibodies by immunofluorescence assay (IgG antibody phase I = 1 : 51 200, phase II = 1 : 102 400), typical of Q fever endocarditis [2]. A second histopathologic examination by H.L., who was aware of the diagnosis, revealed mild inflammation with non-specific inflammatory infiltration mainly composed of macrophages. Immunohistologic analysis using an anti-*C. burnetii* monoclonal antibody demonstrated the presence of *C. burnetii* in macrophages. Culture of valve tissues on human embryonic lung fibroblasts was positive (French National Reference Center for Rickettsia, Marseille).

Q fever endocarditis is the main clinical manifestation of chronic Q fever, and occurs almost exclusively in patients with previous cardiac valve defects (over 90% of Q fever endocarditis patients) [3]. Fever and acute heart failure are observed in 68 and 67% of Q fever endocarditis patients, respectively, but patients may present with non-specific symptoms such as low-grade intermittent fever, fatigue, and weight loss [3]. None of these symptoms was present in our patient. A severe inflammatory syndrome is almost always present, with an increased erythrocyte sedimentation rate in 88% of cases, and polyclonal hypergammaglobulinemia in 94% (up to 60–70 g/L) [3]. Anaemia and thrombocytopenia are present in 55 and 40–56% of

patients, respectively, and hepatic function tests are frequently altered (elevated aspartate aminotransferase (AST) in 83%, alanine aminotransferase (ALT) in 37%, and alkaline phosphatase in 74%) [3,4]. These biological signs were mild in our patient, as a blood sample tested 15 days before surgery revealed only mild anaemia (haemoglobin 101 g/L), mild thrombocytopenia (platelet count 141 G/L), hyperprotinemia (88 g/L, normal range 60–75) caused by hypergammaglobulinemia (30.2 g/L, with an oligoclonal profile), and mild hepatic cytolysis (AST = 47 IU/L, normal range 9–45; ALT = 66 IU/L, normal range 9–65).

Q fever endocarditis differs from endocarditis due to other micro-organisms, in that vegetations are usually absent or small with a smooth nodular appearance. Histologic examination reveals the cusps to be fibrotic with calcified deposits and few infiltrating inflammatory cells (mainly macrophages) [6]. Sometimes the valve can be normal overall [5]. Vegetations are detected by transthoracic echography in only 12.5% of patients [5]. No vegetation were found in our patient, and the inflammatory reaction was so weak that it was initially attributed to degenerative valve damage. This confirms previous reports that routine examination of resected valves for bacterial endocarditis sometimes fails to identify cases of Q fever [6].

Q fever endocarditis is one of the most indolent forms of IE, and the diagnosis is made only several months, or even years, after onset in many cases [3,6]. In our patient, the responsibility of Q fever endocarditis for the mild cardiac congestion is difficult to appreciate. However, the lack of other clinical manifestations, in conjunction with discreet biological signs and pathologic changes, suggests that the Q fever endocarditis in this patient was diagnosed at a very early stage. We cannot determine, however, the precise time of valvular infection with *C. burnetii*, which could have occurred before or after the *S. mitis* endocarditis. As underlying valve damage is an essential risk factor for Q fever endocarditis, we recommend routine serologic testing for *C. burnetii* in patients with an unexplained aggravation of valve dysfunction or even minor biological abnormalities.

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