Case Report

Infective Aortic Valve Endocarditis from Coxiella Burnetii

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We describe the case of a patient with a clinical picture of heart failure, which appeared and worsened rapidly following a reported febrile respiratory infection. The echocardiogram and serological tests established the diagnosis of aortic valve disease from Coxiella Burnetii.

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We describe the case of a patient who was admitted to our clinic with a clinical picture of heart failure. One month before his admission he had experienced a fever lasting three days, which disappeared without treatment. Subsequently, he suffered weakness and fatigue, with rapidly worsening dyspnoea and orthopnoea. The patient was a farmer, engaged in animal husbandry. The echocardiographic examination revealed large vegetations on the aortic valve, whereas all blood cultures were negative. Based on this evidence, a diagnosis was made of probable infective endocarditis with negative blood cultures. Subsequent tests led to the diagnosis of endocarditis from Coxiella Burnetii.

Case presentation

A man aged 55 years had a three-day fever of 38° C, without chills, that was followed by gradual defervescence, leaving malaise and fatigue. After 20 days the patient experienced dyspnoea on effort, which steadily worsened, with the appearance of episodes of paroxysmal nocturnal dyspnoea. Ten days later he was admitted to a provincial hospital with a clinical picture of acute pulmonary oedema. There he was found to have a severe degree of aortic regurgitation and anaemia. After he had been stabilised clinically, the patient was transferred to the cardiology department of our hospital for further investigation.

On admission to our department the patient exhibited dyspnoea, NYHA stage II; he was afebrile, pallid, with a sickly appearance and lower limb oedema. His history included arterial hypertension, which was under treatment and currently satisfactorily controlled. During his clinical examination visible carotid and capillary pulsations were observed. Palpation revealed a strong and displaced cardiac impulse and *pulsus alternans*. The main findings from cardiac auscultation were a third heart sound, a 2/4 diastolic aortic regurgitation murmur (audible over the entire chest with main location right parasternally), and a 2/6 basilar systolic ejection murmur. Femoral artery auscultation revealed the Duroziez and Traube sign.

The ECG showed sinus rhythm with a rate of 85 /minute and negative T-waves in leads V_1-V_4 (Figure 1).

The chest X-ray indicated a moderate degree of increase in the cardiothoracic index and interstitial enhancement.

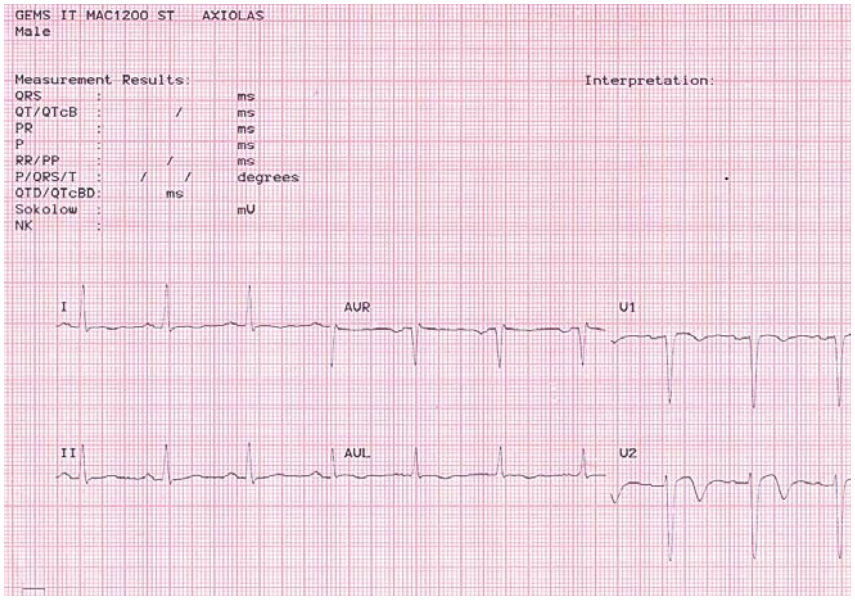

Figure 1. The patient's resting electrocardiogram on admission.

The patient underwent transthoracic and transoesophageal echocardiographic examinations, which revealed two large vegetations on the aortic valve, one elongated (length 2.21 cm) and one cauliflower like, which protruded into the left ventricular outflow tract (Figures 2,3). The aortic valve showed a severe degree of regurgitation and the left ventricle was enlarged (end-diastolic diameter 74 mm) with slightly impaired overall systolic function (ejection fraction 50-55%). The mitral valve showed redundant leaflet tissue, early closure, moderate regurgitation during systole and mild during diastole.

Coronary angiography was negative for coronary artery disease.

Blood tests showed abnormalities in all three series (haematocrit 31%, white blood cells 4×10^9 /L, platelets 120×10^9 /L) and mild renal dysfunction (creatinine 1.6 mg/dl). Six blood cultures were taken, according to the modified Duke criteria, and all were negative. A subsequent serological test detected phase I antibodies for Coxiella Burnetii (Q fever) with a titre of 1:1600.

Initially, the patient had been placed on empirical antimicrobial medication for 'infective endocarditis with negative blood cultures', which included ceftriaxone and gentamycin. Once the serological results were known, the patient was placed on a regimen of oral medication with a combination of hydroxychloroquine 600 mg per day and doxycycline 200 mg per day. He took antimicrobial medication for one month, remained clinically and haemodynamically stable and afebrile, and subsequently underwent surgical aortic valve replacement. One year later, the patient is in good general condition and continues to take the above antimicrobial treatment. The polymerase chain reaction of his native valve was negative for microbial pathogens and Coxiella Burnetii.

Discussion

We present here one of the first cases in Greece of endocarditis from C. Burnetii in a patient with vegetations and acute aortic regurgitation on a substrate of chronic aortic valve insufficiency. This case underlines the importance of checking for Q fever in patients who are involved in animal husbandry and exhibit echocardiographic signs of endocarditis and negative blood cultures, especially when there is a history of pre-existing valvular disease.

The peculiarities of our patient from a cardiological point of view were the large vegetations, the signs of pre-existing chronic aortic valve disease, and the findings of acute aortic regurgitation. The pre-existing aortic valve disease in this patient could be inferred indirectly from the dilated left ventricle and the slight impairment of its systolic function, despite the recent onset of manifestations of the disease. The presence, however, of echocardiographic findings, such as the early closing and diastolic insufficiency of the mitral valve, suggested an acute worsening of the aortic regurgitation. It seems that the deterioration of the aortic valve disease, on a substrate of endocardi-

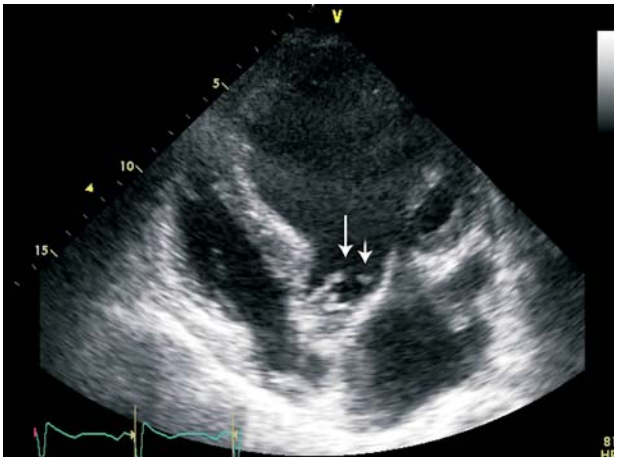

Figure 2. Transthoracic echocardiogram, five-chamber view, showing the aortic valve with vegetations that protrude into the left ventricular outflow tract. One is one elongated (length 2.21 cm, arrow) and the other appears cauliflower shaped (arrowhead).

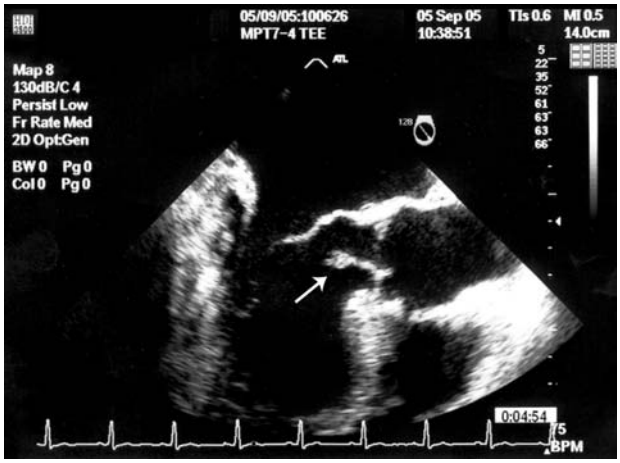

Figure 3. Transoesophageal echocardiogram showing characteristic imaging of the vegetation (arrow).

tis, led to the development of progressively worsening symptoms of heart failure within the space of a few weeks.

C. Burnetii is a gram negative, exclusively intracellular organism that infects humans after the inhalation of dried matter from affected animals, or following contact with such animals (mainly cattle, sheep and goats).[1-3] It is capable of remaining alive for a long time in sporogenic form. In this way, it can survive for up to a month in meat that is kept in a cold environment.[4]

So far, around 400 cases of infective endocarditis from C. Burnetii have been described. Those affected are usually men aged 60-70 years with underlying valvular disease and prosthetic valves.[5] The aortic and mitral valves are affected equally.[6] Patients with underlying immunosuppression (usually lymphoma, neoplasm, or acquired immune deficiency syndrome) are more vulnerable to the disease.[7] Transmission is either airborne or through food.[4]

Q fever occurs in two forms: the less infectious, which involves phase II microorganisms, and the infectious, which is due to phase I microorganisms. Phase II is characterised by a febrile syndrome with accompanying pneumonitis and/or hepatitis that often self resolves. The chronic phase involves the presence of phase I cells that are resistant to phagocytes and affect monocytes, limiting their migration and the production of cytokines such as tumour necrosis factor alpha, and thus preventing their antibacterial action. In this way, the infection persists for a long time and relapses are observed, in spite of the treatment administered.[4,16]

Clinically, endocarditis from Q infection is most usually accompanied by fever (68%) and has a symptomatology of heart failure (67%) together with exhaustion and malaise. An increased erythrocyte sedimentation rate (>90%), anaemia (55%), thrombopenia (56%), and disturbance of liver biology (>80%) are the most common laboratory findings.

On a substrate of infective endocarditis and subsequent dysfunction of the affected valve, heart failure is a common occurrence and usually the only one that leads the patient to the physician.[8]

The diagnosis of the disease is particularly difficult and is often delayed because of the non-specific clinical manifestations, the negative blood cultures, and the difficult to detect echocardiographic lesions.[9,10] It should be noted at this point that the large vegetations on the aortic valve in our case are a rare finding in endocarditis from C. Burnetii. The mean time to diagnosis by experienced personnel has improved in recent years from 18 to about 6 months.[11] Suspicion of the disease should be raised in every case of endocarditis with negative blood cultures where the patient comes into contact with animals. Because of the geographical distribution of rickettsia in Greece, the clinical suspicion in such cases should be high and the indicated serological examination should be carried out by specialised centres.

The contribution of the echocardiographic examination is extremely important in patients with endocarditis from Q fever. The vegetations may be identified with transthoracic echocardiography in 13% of cases, whereas the resolution of transoesophageal echo is

clearly superior.[12,13] The vegetations in endocarditis from C. Burnetii are usually nodular, with a soft surface, and lead to peripheral embolisms (cerebral, upper and lower limbs) in around 20% of cases.[15]

In patients with infective endocarditis and negative blood cultures the diagnosis may be confirmed by the following: a) an immunofluorescence finding of antibodies against phase I antigens in a titre ≥1:800, which belongs to the major diagnostic criteria according to Duke;[17] b) a culture of blood or valvular tissue (extremely difficult); and c) the identification of a pathogen in the replaced valves by immunohistochemical staining or molecular methods.[13,14] It should be noted here that, based on the modified Duke criteria for the diagnosis of infective endocarditis, the major criteria, apart from echocardiographic findings and positive blood cultures, also include a positive serological test for Q fever when the IgG antibody title against phase I is >1:800.[18,19]

In untreated patients, the prognosis of the disease is extremely poor. In older studies, the delay in diagnosis led to the death of around 60% of patients.[1] Better treatment has resulted in an improvement in prognosis, but endocarditis from C. Burnetii remains a particularly serious disease with continual relapses unless it is treated with suitable medication for a strictly observed period of time so that the microbe is completely eradicated. According to the latest data, the suggested combination of hydroxychloroquine and doxycycline over a period of at least 18 months, with simultaneous monitoring of phase I antibodies for C. Burnetii, is the indicated therapeutic approach.[4,14,15] The precise duration of treatment has not been absolutely established, and cessation of antibiotics is recommended when the clinical picture has completely returned to normal and the phase I IgG antibody titre is <1:200.[4] Surgical treatment of the disease, as in all cases of infective endocarditis, is indicated in patients with haemodynamic instability and severe valvular disease.

To conclude, the combination of long-term, targeted antimicrobial medication and surgical intervention when indicated appears to improve the life expectancy of patients with infective endocarditis from C. Burnetii. Equally important, however, is the regular cardiological and pathological monitoring of these patients for the prompt detection of relapses or new episodes.

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