Cardiac Tamponade in Brucella Infection

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Acute pericarditis without any other concurrent cardiac lesion is an extremely rare manifestation of brucellosis. Endocarditis is the main cardiovascular manifestation of brucellosis, predominantly affecting the aortic valve and less frequently the mitral valve. Endocarditis has a subclinical onset and is associated with a poor prognosis. A 55-year-old man with serologically diagnosed brucellosis developed acute pericarditis, without endocarditis, 4 days after the onset of antibiotic therapy. Pericardiocentesis was required because of cardiac tamponade. Pericarditis subsided without any relapse. Six months later, the patient remained completely asymptomatic.

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Pericarditis constitutes a particularly infrequent manifestation of brucella infection, especially when there is no other concurrent cardiac lesion. Thus, despite the wide dissemination of brucellosis worldwide, reports of brucella pericarditis without concurrent or preexisting endocarditis are uncommon in the international bibliography. The majority of these reports originate from Spain, a country with high incidence of brucellosis. We describe the case of a patient who was referred for investigation of pericardial effusion while he was already under treatment for brucellosis during the previous seven days.

Case Report

A 55-year-old man, slaughterhouse worker, was referred by a peripheral hospital for investigation of fever lasting for one month and pericardial effusion diagnosed 3 days earlier. During the last 30 days patient had fever without rigor, (>38.4˚C), that subsided with antipyretics, weakness and smelly perspirations. Ten days earlier, he had been admitted to another hospital because of the symptoms mentioned above, where brucellosis was diagnosed because of a positive Wright reaction. From the third day of his hospitalization the patient was on treatment with doxycycline (100mg × 2) and streptomycin (1g × 1). Fever subsided within 4 days, but on the 5th day patient had an episode of dyspnea and paroxysmal supraventricular tachycardia, and pericardial effusion was diagnosed. Digoxin, diltiazem, furosemide, indomethacin and human albumin were added to the treatment, but the pericardial effusion increased and the patient was referred for further investigation and treatment.

The patient was a heavy smoker (50 cigarettes daily during the last 30 years) and at the same time consumed more than 100g of ethyl alcohol daily. He resided in a rural residence and did not consume any dairy products. He had no history of previous medical illness.

The physical examination revealed: temperature: 36.8ºC, respiratory rate: 24 breaths/min, pulse rate: 100 irregular beats/min, blood pressure:110/70 mmHg, without pulsus paradoxous or postural hypotension. The patient was icteric with extended pitting edema of both tibia and feet. The chest wall movements were normal, but in both lower lung fields no vocal fremitus or breath sounds were present. His jugular veins were dilated but there

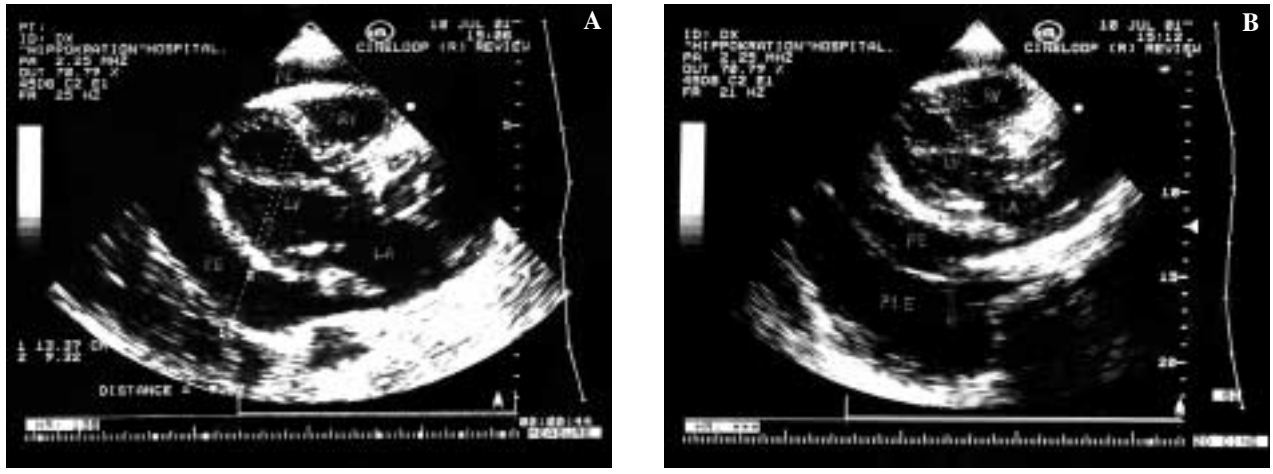

Figure 1. Two-dimensional echocardiogram. Long axis parasternal view. There is a large pericardial **(1A, 1B)** and pleural effusion (1B). The quantity of pericardial effusion was calculated at approximately 1500 ml.
PE=pericardial effusion, Pl.E = pleural effusion, LA= left atrium, LV= left ventricle, RV= right ventricle.

was no Kussmaul sign. The left ventricular impulse was diminished. The heart sounds were weak. Carotid murmurs were present. His liver was soft and painless, palpable 3-4cm below the right costal margin. The spleen was palpable in deep breathing.

Admission laboratory data revealed: Ht: 32.3%, Hb: 10.8 g/dl, basophilic stippling, MCV: 89.8 fl, MCH: 30.5 pg, WBC: 5.200/mm^3 (neutrophils 73%, lymphocytes 16%, monocytes 10%, eosinophils 1%), platelets: 162.000/mm^3, serum iron: 150 μg/dl, ferritin:>1000 ng/ml, ESR: 88 mm, CRP: 4.74 mg/dl, glucose: 344 mg/dl, urea: 67 mg/dl, creatinine: 1.1 mg/dl, sodium: 117 meq/l, potassium: 4.5 meq/l, calcium: 8.5 mg/dl, serum cholesterol: 107 mg/dl, triglycerides: 94 mg/dl, TSP: 8.0 g/dl, albumin: 2.8 g/dl, LDH: 353 U/L, CPK: 125 U/L, serum amylase: 39 U/L, total bilirubin: 6.8 mg/dl, direct bilirubin: 2.8 mg/dl, AST: 87 U/L, ALT: 32 U/L, ALP: 99 U/L, γGT: 62 U/L, uric acid: 4.4 mg/dl, PT: 19.1 s (INR: 1.8), aPTT: 42.2 s, I: 518mg/dl, DD:1mg/dl, FS(+). Arterial blood gas measurements were: pH: 7.47, pCO_2: 32 mmHg, pO_2: 60 mmHg, HCO_3: 24 mmol/l, $satO_2$: 93%, BE: 1 mmol/l. Urine analysis showed: specific gravity: 1020, pH: 6.0, WBC: 6-8/HPF, RBC: 12-14/HPF, protein: (-), glucose: (+). Urine culture was sterile.

Serum agglutination test against brucella was positive at a titer of >1/1280. Serum levels of IgG and IgA were increased (IgG=2410 mg/dl, IgM=176 mg/dl, IgA>700 mg/dl), without the presence of any monoclonal immunoglobulins. Immunological studies including ANA, AMA, ASMA, cANCA, pANCA, ds-DNA and complement were negative or within the normal range. Rheumatoid factor was positive. Tumor markers were also within the normal range while VDRL was negative. Serological studies for Coxsackie, Echo, CMV, Mycoplasma pneumoniae, Coxiella burnetti, Chlamydia psittaci, Toxoplasma gondii, HSV_1, HSV_2, EBV, influenza A and B, HBV and HCV were all negative, as were blood cultures for brucella and other bacteria. Polymerase chain reaction (PCR) results for brucella in the blood as well as bone marrow culture were also negative.

Chest X-ray showed pleural effusion, mainly on the left side, and enlarged cardiac silhouette. On admission echocardiogram, large pericardial and pleural effusions were detected, while the aortic cusps were thickened with relatively good mobility (figures 1A and 1B). Dilatation of the left atrium was also revealed (4.5cm). Left ventricular ejection fraction was estimated at 60-65%. The free wall of the right atrium showed a diastolic motion towards the interatrial septum (Figure 2A). A change in the blood flow through the mitral and the tricuspid valves during inspiration was observed (17% and 29% respectively), indicating a hemodynamic deterioration even though it did not suggest the presence of cardiac tamponade. Electrocardiogram showed atrial fibrillation.

Radionuclide scan of liver and spleen with Tc99 mPHYT (4mCi) revealed localization of the drug in the reticuloendothelial system of the spinal cord, a finding compatible with diffuse injury of the hepatic parenchyma (cirrhosis). Ultrasonography showed small

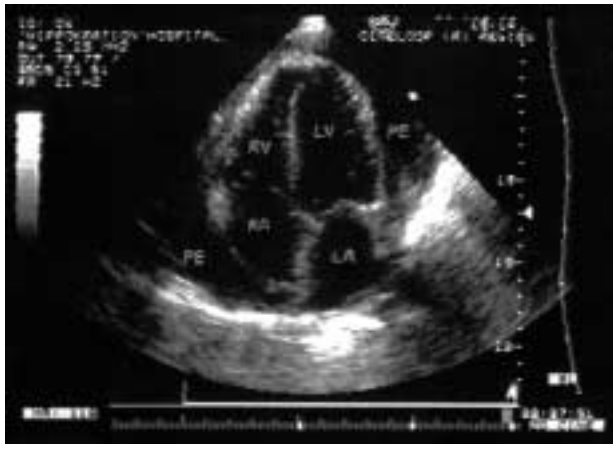

Figure 2A. Two-dimensional echocardiogram. Apical four chamber view. There is a large pericardial effusion and a diastolic motion of the free atrial wall towards the interatrial septum.
RA= right atrium PE=pericardial effusion, Pl.E = pleural effusion, LA= left atrium, LV= left ventricle, RV= right ventricle.

ascitic effusion and splenomegaly (15cm), while thoracic and abdominal CT scan did not detect any lymph node enlargement.

The patient's condition deteriorated during hospitalization with the following symptoms: jugular veins further dilation, tachyarrhythmia, pulsus paradoxous and worsening of dyspnea. Because of cardiac tamponade pericardiocentesis was performed, during which 1l of bloody fluid was obtained. Laboratory tests of pericardial fluid revealed specific gravity: 1017, pH: 7.5, WBC: 300/mm^3 (neutrophils 55%, lymphocytes 35%, monocytes 10%), while cytologic tests were negative for cancer cells. The results of pericardial fluid cultures for bacteria, brucella and mycobacterium tuberculosis were negative, as were the PCR results for brucella and mycobacterium tuberculosis.

The patient was treated with furosemide, spironolactone, human albumin, indometacin, digoxin, doxycycline, and streptomycin while ceftriaxone was also added because of the puncture performed. Fever persisted for three more days as an afternoon fever wave <38.0˚C, without concurrent rigor, and then subsided.

The ultrasound follow-up showed gradual reduction and final disappearance of the pericardial effusion 5 days after the pericardiocentesis. At the same time, pleural fluid and lower extremity edema subsided. The patient was discharged in good condition, under treatment with doxycycline for 6 weeks totally, streptomycin (2 weeks) and indomethacin (2 weeks). Six months later, the patient remained completely asymptomatic and without any pathological echocardiogram findings.

Discussion

The clinical manifestations of brucella infection have a great variety. Most frequent symptoms are fever (95%), anorexia (90%), fatigue (90%), smelly perspiration (80%), arthralgias (25-50%), myalgias (25-50%) and weight loss. Less frequent symptoms are joint involvement (15%), splenomegaly (20%), lymphadenopathy of the bubonic and cervical area (10-15%), bronchitis, pleuritis and empyema, pulmonary abscess (5-10%), orheitis or orchiepididymitis (2-10%)[1].

Cardiac involvement is not frequent during brucellosis. Endocarditis is the main cardiovascular complication, and usually concerns the aortic valve and less frequently the mitral valve. It has a subclinical course and poor prognosis without any surgical treatment[2,3]. The replacement of the affected valve is necessary after 5-7 days of antibiotic therapy[4]. Myocardial involvement, when present, is manifested through T-wave changes and prolongation of atrioventricular conduction. Despite all the above, a case has been reported in the international bibliography of a patient who developed fulminant myocarditis with infiltration of lymphocytes and polymorphonuclear leucocytes[5].

Pericarditis due to brucella has been known for more than 100 years[6]. However, even if brucella can affect any organ, it appears that pericarditis is extremely infrequent. Among 322 cases of brucellosis from Barcelona, no incidents of pericarditis have been recorded[7,8]. In another retrospective study, also originating from Spain (Malaga), it was reported that only 1.5% among 530 cases of brucellosis (8/530) showed cardiac involvement, while only one patient, (percentage 0.2%) was diagnosed with pericarditis without concurrent endocarditis[9].

Cases of pericarditis due to brucella without concurrent endocarditis are exceptionally rare[10], which is why only scattered references exist in the international bibliography[3,10,11]. From these reports it is calculated that the duration of symptoms before the hospitalization of patients lasts approximately 8-30 days. On their admission in the hospital, moderate anemia and hepatosplenomegaly are observed. The titer of the Wright reaction is usually equal to or lower than

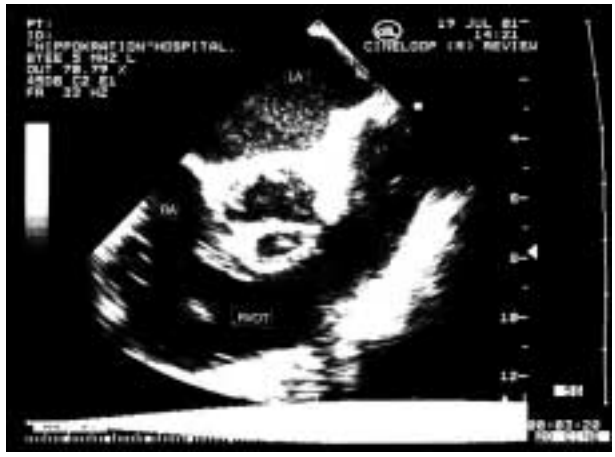

Figure 2B. Transesophageal echocardiogram. Longitudinal view (90^0), short-axis view of aortic valve. The aortic cusps are thickened, without findings indicative of infective endocarditis.
LA= left atrium, RA= right atrium, RVOT= right ventricle outflow tract, Ao= aorta.

1/640. Blood or pericardial fluid cultures are usually positive for brucella. Usual symptoms of these patients are thoracic pain, pericardial friction rub and fever. Cardiac tamponade is rarely observed and consequently pericardiocentesis is only occasionally required. Cardiac tamponade was fatal for 2 out of the 4 patients reported in the international bibliography[3, 10, 11].

Regarding the likely mechanism of pericarditis due to brucella, it is considered that pericardial involvement can take place through either direct affectation by the microorganism, or indirect, aseptic, counteractive, via immunocomplex deposits[12].

The possibility of endocarditis was excluded based on the absence of cardiac murmurs on the clinical examination and on the presence, apart from the thickened aortic cusps, of normal cardiac valves in the transesophageal echocardiogram (Figure 2B). The culture of brucella from the pericardiocentesis fluid was negative. The polymerase chain reaction for brucella DNA in the pericardial fluid was also negative. The analytic sensitivity of this method corresponds to 15-150fg DNA of brucella. However, the presence of high concentrations of leukocyte DNA and heme compounds, as in the bloody pericardial fluid of our patient, inhibits PCR and often leads to false negative results[13]. Finally, the diagnosis of brucella pericarditis was established from Wright's seroagglutination test against brucella (positive at a titer of >1/1280), the history of patient's exposure to the microorganism (as a slaughterhouse worker) and the very good response to treatment.

The presence of polyserositis (large pleural and pericardial effusions and ascites), the persistence of pericardial effusion in spite of the treatment and the deterioration of the patient's condition with cardiac tamponade were factors that made this case especially interesting.

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