Chronic hepatic brucellosis

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Abstract

The hepatic pseudotumoural localization of brucellosis is rare: only 29 cases have been described in the literature.

The authors present a case of chronic hepatic pseudotumoural brucellosis, in a patient who underwent a partial hepatectomy, 14 years earlier, prior to this presentation, for a brucellosis abscess. The diagnosis was established by clinical history and positive serology for Brucellosis. The organism was not isolated microbiologically. After surgery and specific antibiotic therapy the patient became asymptomatic.

Key words: fever, brucellosis, hepatic pseudotumoural granulomatosis.

Introduction

Brucellosis or "Malta fever" is an infectious disease caused by microorganisms belonging to the family Parvobacteriaceae, identified in 1886 by Sir David Bruce.[1]

Humans are secondarily infected through the consumption of unpasteurised milk and its byproducts. Less commonly, the infection is acquired by inhalation, by contamination of abrasive skin lesions, or by contact with the conjunctiva while handling infected material.

Hepatic granulomatous lesions associated with brucellosis, in its pseudotumoral and abscessed form, are rare. However, their diagnosis and treatment, which is almost always surgical and associated with targeted antibiotic therapy, are imperative.[2]

Case report

R.M.M.G., aged 29, male, Caucasian, born and resident in Cascais, occupation bricklayer, an immigrant in France (Grenoble) from 1976 to 1992. In 1981 he was admitted to the Grenoble University Hospital Center, with febrile syndrome, profuse sweating and weight loss, with two months of evolution. Abdominal ultrasound showed a "calcified hepatic mass". Due to the existence of this mass and the patient's apparent septic state, he was submitted to an exploratory laparotomy which showed "...hepatic mass in segments V and IV, apparently inflammatory, 5 cm in diameter, ..., with thick capsule. Thick-walled gallbladder, free of stones. Voluminous adenopathy in the hepatic pedicle. Normal spleen". Due to suspicion of lymphoproliferative disease in the macroscopic examination, he was submitted to partial hepatectomy and splenectomy. Anatomopathological examination of the surgical specimen showed a nonspecific inflammatory reaction. The patient subsequently attended postoperative follow-up consultations and underwent therapy with unknown medications, having been discharged with a diagnosis of "Hepatic tumor granuloma associated with brucellosis" (data obtained from the surgical report and discharge notes of the Grenoble University Hospital Center).

He returned to Portugal in 1992, having apparently felt well until November 1995, time when he went to see his doctor, with a high fever (39-40ºC), mainly at night, anorexia, weight loss (2 kg/month) and general malaise. He was empirically medicated with ciprofloxacin 500 mg (twice daily) and acetylsalicylic acid 1000 mg (at the peaks of the fever). He denied consuming any unpasteurised dairy products or contact with animals.

In February 1996, he went to the emergency room of Hospital Condes de Castro Guimarães (Cascais), due to persistent complaints, having been hospitalized for clarification of the situation. On objective examination he presented poor general state, dehydration, prostration, fever (39.4ºC), radial pulse of 110 ppm and blood pressure of 110/76 mmHg,

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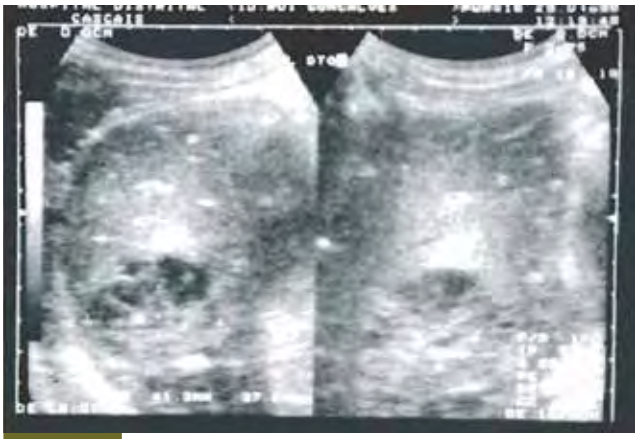

FIG. A

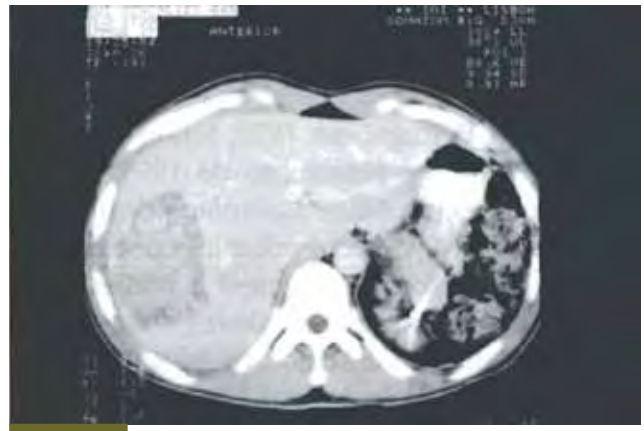

FIG. B

hyperemiated oropharynx, and generalized small, painless adenopathies. Cardiorespiratory semiology showed no alterations, and the abdomen presented a painless hypertrophic median xyphopubic scar, with liver enlargement of 3 cm affecting the left lobe, with smooth surface and edges. Laboratorial tests showed leukocytosis (26,400 mm^3) with neutrophilia (78%), thrombocytosis (754,000 mm^3), elevated ESR and CRP (95mm and 17mg/dL, respectively), ASO of 300 UI, and Mantoux test of 9 mm. All the other values were normal, specifically: erythrogram, PT, PTT, glycemia, kidney and liver function, urinalysis. Huddleston and Widal reactions, the direct and indirect Coombs test, virus serologies (hepatitis A, B, C, HIV1 and 2), amoebiasis and hydatidosis, Mantoux test, KB test in the gastric juice, expectoration culture test, urine culture and blood culture were negative. ECG, chest X-ray and echocardiogram did not present any alterations.

The ultrasound (*Fig. A*) and abdominal CT scan (*Fig. B*) demonstrated the existence of a nodule on the right lobe of the liver, measuring 88 x 60 mm, well defined, hypoechogenic, with a gross central and peripheral calcification, confirming the absence of a spleen.

The patient was started on ampicillin (4 g/day), gentamicin (240 mg/day) and metronidazole (2 g/day) due to suspicion of abscessed hepatic lesion, without significant improvement in the clinical symptoms. In the absence of imaging alterations (in the ultrasound and abdominal CT scan) after 21 days of therapy, the patient was submitted to ultrasound-guided aspiration biopsy of the hepatic nodule, revealing a chronic granulomatous inflammatory process in active phase, with negative culture test. The biopsy of a swollen lymph node in the right groin revealed a reactive inflammatory process.

The serology for brucellosis requested in early February, but only received in early March, was positive (*Table 1*). For this reason the patient was started on rifampicin (600 mg/day) and doxycycline (100 mg/day), appearing apyretic on the 6th day of therapy.

Due to the irreducibility of the hepatic mass, in the 3rd month of antibiotic therapy (with rifampicin and doxycycline) and although apyretic and asymptomatic, the patient was submitted to surgical intervention. The anatomopathological examination of the resected surgical specimen revealed "a nonspecific granuloma with intraparenchymal calcifications". The culture test was once again negative. After the recovery period, which elapsed without any complications, the patient was referred to the Internal Medicine and General Surgery consultation, and medicated with rifampicin and doxycycline, at the doses already indicated. In the 6th month of antibiotic therapy the patient continued to have persistently high ESR values and positive brucella serologies (*Table I*), although clinically asymptomatic. He underwent a bone scan, which did not show any region of increased radionuclide uptake, and the ultrasound and follow-up abdominal CAT scan did not reveal any intra-abdominal mass.

Commentary

Pseudotumoral hepatic granulomas of brucellar origin are rare, having been described in just twenty-nine cases in the literature.[2,3] The vast majority of these were reported in countries of the Mediterranean basin, where brucellosis is particularly frequent.[2]

TABLE I

Progression of Brucella serologies

	9.2	26.6	21.10
Bengal Rose	(+)	(+)	(+)
Wright's reaction	1/40	1/40	1/40
Immunofluorescence r.	1/160	1/20	1/20
Huddleston	(-)	(-)	(-)
2-mercaptoethanol	—	1/20	—
Culture test M.O.	(-)	—	(-)
ESR	95	88	83

TABLE II

Main infections responsible for hepatic granulomas[8]

Bacteria	Mycobacteria
Actinomycosis	Atypical mycobacteria
Botryomycosis	Leprosy
Brucellosis	Tuberculosis
Listeriosis	
Melioidosis	
Nocardiosis	
Streptococcus pyogenes	
Tularemia	

Brucella, upon entering the organism, is phagocytosed by the polymorphonuclear cells, which present the brucella antigen to the mononuclear cells. The activation of these causes an increase in interleukin-1 and stimulation of the T4 lymphocytes, which provokes the agglutination of microphages around the bacteria[4] and the formation of epithelioid granulomas. Hepatic abscesses occur as a result of their slow, progressive fusion, and can acquire a pseudotumoral form.[4,5] Hence the intensity of cell and humoral immunity models the presentation of the chronic forms of these processes.

The clinical condition is characterized by prolonged fever, weight loss, and, in 25% of the cases, hepatomegaly.[6] The laboratory tests almost always show a normal blood test, leukocytosis with neutrophilia, and increased sedimentation rate, C-reactive protein and fibrinogene.[4,7] Liver alterations are inconstant, depending on the volume occupied by the mass in the hepatic parenchyma.[6]

Imaging exams are nonspecific. However, ultrasound and abdominal computerized axial tomography are reliable for visualization of liver abscess, although not very specific.[6] The presence of central calcifications is common, and these may be either multiple or single. Their absence is an indication of recent onset of the infection.[2,4,7]

Ultrasound guided liver biopsy is an important diagnostic element that enables the material to be obtained for culture tests and anatomopathological tests. The existence of granulomatous hepatitis is a diagnostic guidance criterion for a bacterial or parasitic disease (*Table 2*). [6,8] Necrotizing hepatic granulomatous lesions suggest brucellosis, although they are morphologically nonspecific, while if these alterations were to present an epithelial reaction, the differential diagnosis would be made between tuberculosis, Yersinia and Fransciella tularensi.[8]

Although it is known that all species of Brucella can cause abscesses, seldom is the causal agent discovered in hepatic granulomas of brucellar origin.[9] Wright's reaction (preferential method according to the WHO) highlights agglutinant antibodies, where a titer above 1/80 indicates acute brucellosis and a titer equal to 1/40 a past infection, in individuals who have been vaccinated or who live in endemic areas.[10,12] Bengal Rose and Wright's reaction. have good specificity and sensitivity for a diagnosis of brucellosis. However, indirect immunofluorescence is the test with greatest specificity.[2,10,11] Hemoculture is still the best method for isolation of the agent, although it is rarely positive in case of focal brucellosis.[12]

Although infrequent, pseudotumoral hepatic granuloma associated with brucellosis are significant on account of their morbidity. In most cases, treatment involves surgery followed by drawn-out antibiotic therapy,[2] using an association of doxycycline and rifampicin over a period of two to six months. [12,13]

In this clinical case, seroconversion in association with the rise in serologic titers suggested a brucellosis infection with a several months of evolution.[8,10,11,12] These analytical alterations, associated with the presence of calcification of the abscess in the CT scan[4,11,12] and the absence of actual epidemiological data in a patient with a history of brucellic abscess, were strongly suggestive of a chronic process.[11] ■

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