

Portal Hypertension and Fever Secondary to Granulomatous Hepatitis by Tuberculosis

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Abstract

Tuberculosis (TB) is a highly prevalent disease in our country, eventually, most with atypical clinical presentations. We report a case of a young patient with prolonged fever and portal hypertension with clinical and histological diagnosis of granulomatous hepatitis, TB improved after treatment with anti-TB regimen. Then we have a brief literature review on the topic.

Keywords: Granulomatous hepatitis; Hepatic tuberculosis; Tuberculosis

Introduction

Tuberculosis (TB) is a chronic infectious disease caused by bacteria belonging to the *Mycobacterium tuberculosis* complex. It is considered one of the oldest infectious diseases of mankind. In Brazil, 70,047 new cases were reported in 2012 in the Notifiable Diseases Information System (Sinan), which is equivalent to the incidence of 36.1/100,000 population [1].

TB most commonly affects the lungs (pulmonary TB). The main forms of extrapulmonary TB are pleural, peritoneal, pericardial, lymphatic, laryngeal, genitourinary, adrenal, bone, meningeal, intestinal, ophthalmic and skin. The hepatic granuloma TB occurs in about 20% of TB patients and up to 90% of them have a military form. It is common in this context. The isolated presentation of hepatic granulomas without lung disease, however, is less frequent and the presence of portal hypertension syndrome is considered a rare presentation [2-4].

In this paper, we present the case report of a male patient, 38 years old, with nonspecific clinical and laboratory findings, portal hypertension and histopathology analysis of liver

biopsies and spleen showing granulomas with caseous necrosis, suggestive of TB. We also present the literature review of granulomatous hepatitis, its causes and its relationship with portal hypertension.

Case Report

According to Resolution 196/96 of the National Health Council, the research did not present any risk to and assured no conflict of interest between the researcher and the subject of the study. Patient, 38, previously healthy, developed fever (39 °C) and headache in April 2013 associated with appetite loss and postprandial fullness. After a month of onset of symptoms, fever became daily, preserving those traits accompanied by malaise and increased headache.

After a series of referrals, the patient was admitted to our institution with daily fever, about four episodes a day, without specific time of presentation, profuse night sweats and pale skin. He reported weight loss of approximately 7 kg in 3 months. Physical examination revealed significant hepatosplenomegaly with bicytopenia (anemia and leukopenia) to laboratory examination.

After admission, diagnostic investigation was performed (Table 1). An increase of portal and splenic vein caliber was found in abdominal tomography (Fig. 1) and Doppler portal.

We hypothesized lymphoproliferative disease, infectious mononucleosis, typhoid fever, schistosomiasis, Q fever, tuberculosis and leishmaniasis, from the clinical and epidemiological data. However, with the persistence of diagnostic uncertainty, the Medical Clinic Service opted for indication of liver biopsy and splenectomy, given the strong possibility of lymphoma and the therapeutic potential of surgery in these situations. The surgical procedure was performed on August 1, 2013 through swordtail-umbilical midline incision, performing removal of the spleen and liver portion to be sent for biopsy. The spleen biopsy (Fig. 2), liver (Fig. 3) and splenic hilum showed chronic granulomatous inflammation with central caseous necrosis and moderate lymphocytic infiltrate around without evidence of malignancy, with research for AFB and negative fungi. Based on this result, the hypothesis of granulomatous hepatitis of tuberculous etiology was discussed, and therapy with RIPE was started, with good response to treatment, general improvement, greater spacing and subsequent

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Table 1. Tests Performed in the Hospital

Laboratory tests
Tuberculin test: 0 mm
VDRL: no reagent
Viral serology for hepatitis (B and C): negative/anti-HBs +
Serology for toxoplasmosis: IgG + IgM-
Anti-HIV: no blood cultures reagent (three samples): negative
Urine culture: no bacterial growth
Beta-2-microglobulin = 4.47 µg/mL
Reticulocytes 0.93% VIT B12 1,200 pg/mL
Myelogram: slightly hypercellular. Series lymph-mono-plasma cell: lymphocytes around 4%. Plasma cells around 5%. Presence of rare macrophages presenting hemophagocytosis. Suggestive of reactive marrow.
Upper digestive endoscopy: enanthematous gastritis body and erosive den. Bilius gastric stasis
Protein electrophoresis: decreased albumin/globulin
K39: no reaction
Fe saturation index: 7%; ferritin: 432.04 ng/mL; serum iron: 19 g/dL
Antinuclear factor: not reagent
Free T4: 1.00 ng/dL
Serology for EBV IgG: 750 U/mL; IgM: 10 U/mL - no reagent serology for CMV IgG: 245.40 AU/mL; IgM: 0.18 index - not reagent
Bone marrow biopsy: absence of neoplasia. Normocellular marrow bone, myeloid hyperplasia, mild diseritropoiese.
Transesophageal echocardiography: normal, with EF 70%.
Serology for brucellosis IgG and IgM: negative
Liver Doppler: Identifies increase the speedometer of the common hepatic artery and hepatic veins. Increased gate diameter of the vein. Side of absence.
Abdominal ultrasound: hepatomegaly homogeneous and gall bladder collapsed

resolution of febrile episodes, weight gain and return to work activities.

Discussion

The presence of hepatic granulomas can be secondary to many diseases and is often a diagnostic clue to systemic conditions, and therapeutic and prognostic implications [5, 6].

The diagnosis of these pathological conditions requires

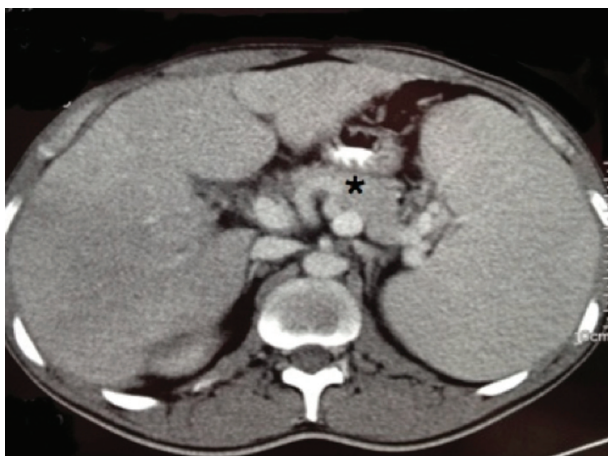


Figure 1. Abdominal tomography showing hepatosplenomegaly with heterogeneity of hepatic parenchyma and increased portal vein caliber and splenic (asterisk).

the location and the type of granuloma which may aid in the differential diagnosis. Four major types can be identified: caseous granuloma (presence of central necrosis), noncaseating (without central necrosis) granuloma, lipogranulomas (core lipid containing vacuoles) and granulomas fibrinoanelares (central vacuoles containing fibrin deposit) [7].

Portal hypertension in this context is uncommon and is caused by the presence of multiple granulomas in portal region, secondary fibrosis inflammatory reaction, portal hypertension due to increased blood flow in cases of splenic involvement and, more rarely, thrombosis secondary to the prothrombotic state of portal vessels.

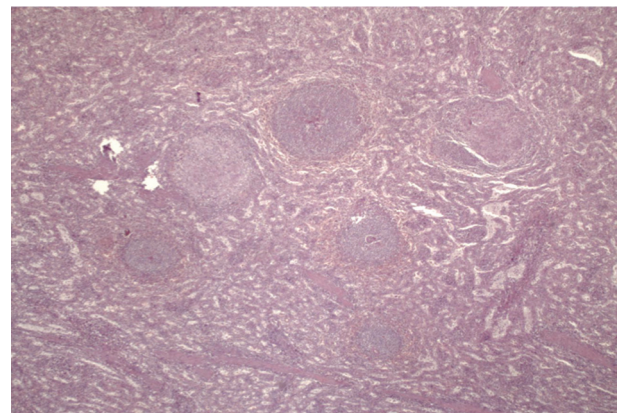


Figure 2. Splenic imaging with granulomas (rounded areas of lighter shade) at 16:19 hours. On average figure line, we observed lymphoid follicles.

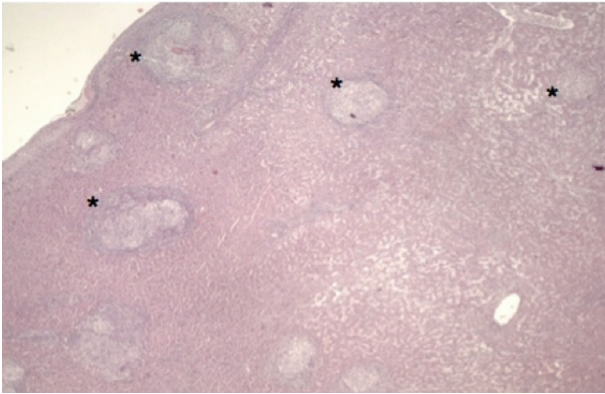


Figure 3. Image with diffuse hepatic granulomas with central necrosis (asterisks).

The main causes of granulomatous hepatitis in the developed world are autoimmune diseases, especially sarcoidosis, vasculitis, and primary biliary cirrhosis [5]. In developing countries, infectious causes dominate, led by TB, Q fever, brucellosis, Yersinia, Lyme disease, leprosy, melioidosis, and deep mycoses. In our case, the presence of granulomas caseating strongly suggests diseases such as TB, brucellosis and, rarely, Hodgkin's lymphoma. Direct analysis of bacilli was negative, but it presents a sensitivity of around 50%. Together with systemic findings and the favorable therapeutic response, the most likely diagnosis is the liver TB.

Conclusion

Portal hypertension in the context of granulomatous hepatitis is rare; however, given the high prevalence of TB in Brazil, it should be considered in the differential diagnosis, especially if there are systemic symptoms compatible with miliary TB,

such as prolonged fever, sweating, weight loss and increased GGT.

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