

Peritoneal tuberculosis, a differential diagnosis for ascites in cirrhosis

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Abstract

This is the case of a patient with a history of chronic alcohol consumption, who consulted for nonspecific abdominal pain, intermittent fever, and weight loss, with subsequent increase in the abdominal perimeter. Ascites and imaging findings suggestive of cirrhosis were found. The study of ascitic fluid was non-hypertensive with a predominance of lymphocytes and elevated adenosine deaminase (ADA) levels. Ultrasound and abdominal tomography showed peritoneal thickening. Laparoscopic peritoneal biopsy was compatible with granulomatous disease, with positive PCR for *Mycobacterium tuberculosis* in a patient with no other causes of immunosuppression. This report shows the importance of keeping a high index of suspicion for TB in patients with abdominal pathology, even in those without evident immunocompromise.

Keywords

Ascites; Hepatic cirrhosis; Peritoneum; Gastrointestinal tuberculosis.

INTRODUCTION

Peritoneal tuberculosis (TB) accounts for 1%-2% of all TB cases and 31%-58% of gastrointestinal TB cases; besides, an association with pulmonary TB has been found in 3.5% of cases (1). Its diagnosis remains a challenge due to its paucibacillary nature and the fact that its clinical findings are nonspecific; peritoneal TB poses important risks such as sepsis, intestinal obstruction and, in women, infertility, so it is considered an almost mandatory diagnosis to be ruled out in the diagnosis of ascites secondary to causes not related to portal hypertension (2).

By 2018, 10 million new TB cases were estimated worldwide, and coinfection with human immunodeficiency virus (HIV) was present in 8.6% of these cases (3). In Colombia,

14 480 cases were recorded in the Public Health Surveillance System (SIVIGILA for its acronym in Spanish), of which 11.1 % had HIV coinfection (4). Although in recent years the number of TB and HIV/AIDS coinfection cases has clearly increased, of the 1.45 million deaths registered by the World Health Organization (WHO), only 251,000 were positive for HIV, which highlights the importance of continuing to consider the presence of this condition in people who are not severely or evidently immunocompromised (3).

CLINICAL CASE

47-year-old man born in a rural area of the department of Boyacá, who lives and works as a driver in Bogotá; the patient had been drinking beer at least once a week

for about 15 years, without any other relevant history of disease, and visited our institution due to the following symptoms and signs: increased abdominal circumference (20 days), diffuse pain (4 months), occasional unquantified increases in body temperature, and a 15 kg weight loss. The patient had attended other health institutions where he was prescribed with symptomatic treatment consisting of antacids. Physical examination on admission findings: normal vital signs, body mass index (BMI) of 22, abdominal distension with signs of moderate ascites and mild diffuse pain on palpation without signs of peritoneal irritation. Admission laboratory tests results: complete blood count: mild normocytic anemia (hemoglobin 11.4 g/dL), normal white blood cell and platelet counts, elevated C-reactive protein levels and elevated erythrocyte sedimentation rate (ESR). Hyponatremia (129 mmol/L) was also evidenced; kidney function was normal, urinalysis results were normal, and no abnormal findings were evidenced on a chest X-ray.

Ascites and a liver of smaller size with lobulated contours were evidenced on an abdominal ultrasound; furthermore, esophageal and splenic varices with mild splenomegaly, and changes suggestive of portal hypertension were identified in a Doppler evaluation of the splenoportal veins and an upper GI endoscopy. Transaminases, alkaline phosphatase and bilirubin (total, direct, and indirect) levels were normal; coagulation times were prolonged (prothrombin time [PT]: 15.8 seconds; international normalized ratio [INR]: 1.44; partial thromboplastin time [PTT]: 41.8, and normal alpha-fetoprotein). Hepatitis B and C serologic tests were negative; antimitochondrial antibodies (AMA) and anti-smooth muscle antibodies tests were also negative.

Ascitic fluid cytochemistry reported a serum-ascites albumin gradient (SAAG) of 0.6, compatible with ascites secondary to causes not related to portal hypertension; leukocytes count of 2400/mm³, lymphocytes count of 100%, glucose level of 82.4 mg/dL and Gram stain negative for germs. Adenosine deaminase (ADA) levels in peritoneal fluid were 102 U/L (reference value < 36 U/L) and cytology showed lymphocytosis and was negative for malignancy. A CT scan of the chest and a CT of the abdomen were performed to rule out the presence of neoplasms as a differential diagnosis. The contrast-enhanced CT scan of the abdomen showed changes in the density of the peritoneum with thickening, multiple small nodules in the upper third part of the abdomen enhanced by the contrast medium (**Figure 1**), a small size liver, and abundant ascites; the CT scan of the chest showed scarce bilateral pleural effusion. So a laparoscopy was performed to obtain samples from the peritoneum and the liver for biopsy purposes; besides, the following findings were reported during the procedure: extensive involvement of the entire peritoneum by yellowish micronodules, presence of some inter-ascitic adhesions, abundant greenish non-purulent fluid in the peritoneal cavity, as well as a cirrhotic liver with some micronodules. The histopathological study of the peritoneum sample was compatible with granulomatous inflammation, with negative Ziehl-Neelsen (ZN) staining (**Figure 2**), but with positive polymerase chain reaction (PCR) for *Mycobacterium tuberculosis*. The enzyme-linked immunosorbent assay (ELISA) was negative for HIV.

The patient was treated for 9 months with a monitored TB treatment regimen, achieving improvement of both

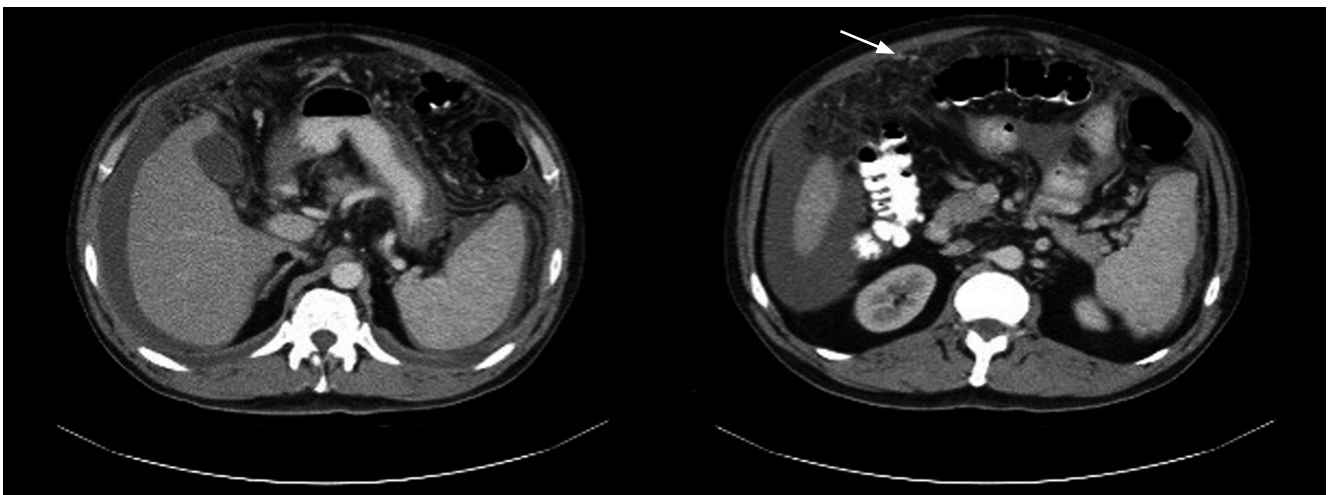


Figure 1. Contrast-enhanced CT scan of the abdomen. Small size liver, thickening and multiple small nodules in the peritoneum enhanced by the contrast medium.

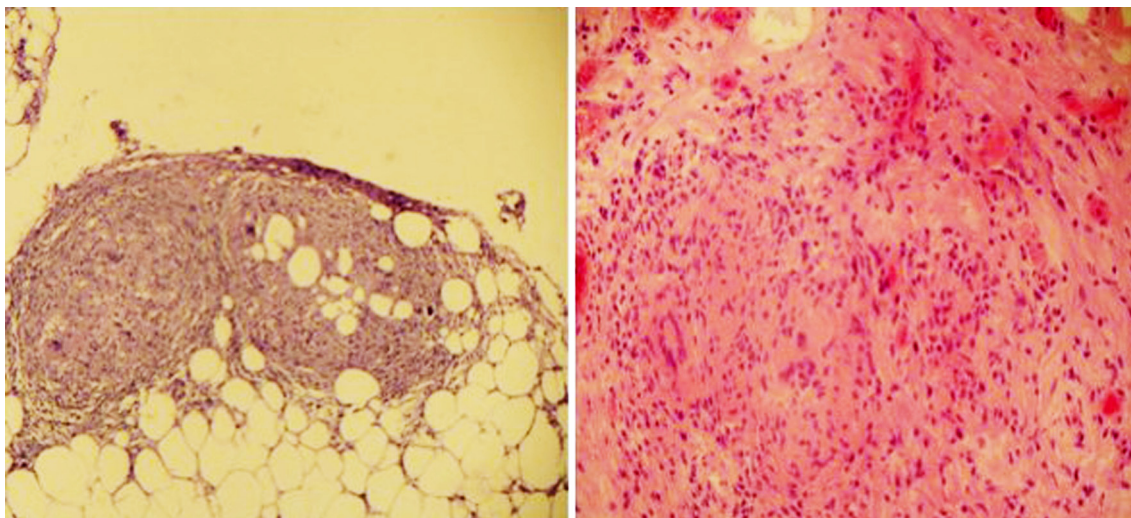


Figure 2. Histopathological study. Hematoxylin-eosin staining showing chronic granulomatous inflammation suggestive of TB. Negative ZN staining for acid-fast bacillus.

clinical signs and laboratory tests values, as evidenced in outpatient follow-up visits; likewise, normalization of body weight and complete resolution of ascites without loss of liver function were achieved after the first phase of treatment was completed. In addition, the patient keeps attending follow-up visits in the hepatology service due to the alcoholic cirrhosis (Child-Pugh score B) diagnosis.

DISCUSSION

It is well known that the clinical presentation of abdominal TB is widely variable and, therefore, it can mimic other frequent and infrequent abdominal diseases. It was first described in 1843 and it can be caused by any of the members of the *Mycobacterium Tuberculosis* complex (*M. tuberculosis*, *M. africanum*, *M. bovis*, *M. caprae*, *M. microti*, among others) known as acid-fast bacilli and is characterized by its paucibacillary nature (1, 2). It is the sixth most frequent cause of extrapulmonary TB, and peritoneal TB accounts for up to 50% of such cases (5). Some associations or possible risk factors for the development of peritoneal TB include HIV infection, peritoneal dialysis, type 2 diabetes, the use of immunosuppressive drugs such as corticosteroids and anti-tumor necrosis factor alpha (anti-TNF- α) agents, and alcoholic cirrhosis, as it happened in the case presented here (5).

The peritoneum can be infected by the bacillus through the following mechanisms: hematogenous or lymphatic route from a pulmonary focus; ingestion of infected material that reaches mesenteric and retroperitoneal lymph nodes that can rupture and disseminate the mycobacterium; direct

extension from neighboring organs or direct contamination of the peritoneum in patients with chronic kidney disease (CKD) on peritoneal dialysis (1, 6). In our case, in a subsequent evaluation, the patient reported having ingested unpasteurized milk, which could be suggested as a possible pathophysiological mechanism of the infection. Clinical findings of peritoneal TB include the presence of ascites, abdominal pain, fever, weight loss, hyporexia and abdominal distension. Given the non-specific nature of its clinical manifestations, together with the subacute nature of the disease, a late diagnosis is made in up to 70% of cases, so a low threshold of clinical suspicion must be always considered (5).

In case of ascites, observing its characteristics such as a yellow-black or even hematic color is fundamental (1); usually, protein concentration is > 30 g/L and cellularity, > 400 cells/mL, of lymphocytic predominance, which constitutes an exudate with SAAG < 1.1 g/dL. However, in patients with peritoneal TB and concomitant cirrhosis, as it happened in the case described here, this index loses sensitivity with values ranging from 29% to 88%; these patients, as well as those on peritoneal dialysis, may present cellularity with neutrophilic predominance, so the possible confusion with spontaneous bacterial peritonitis must be considered (1, 5).

Cytological analysis of peritoneal fluid is necessary in the differential diagnosis of neoplasm. Measurement of lactate dehydrogenase (LDH) in blood or fluid is less sensitive and specific, and is not routinely used. In addition, despite Ca¹²⁵ antigen is elevated in these cases, this test is not recommended either as a routine diagnostic study (1, 2). Imaging studies such as ultrasound and CT scan are fundamental

for reaching a diagnosis, the latter being the most sensitive method for assessing the peritoneum (6).

Regarding the measurement of ADA levels with a cut-off point > 30 IU/mL (1, 3) and 36 IU/mL (7) for others, it can have a high sensitivity and specificity (96% and 98%, respectively) in the absence of immunosuppression or cirrhosis, (1), so that it is a very useful tool, especially in endemic areas with low possibility of taking samples for performing biopsies (1, 8).

ZN staining is positive in only 3% of cases and culture is still the gold standard, for which solid and liquid medium techniques are generally available, including the BD BACTEC automated blood culture method, which reduces the processing time by half (1, 9). In a systematic review, Sanai and Bzeizi reported positivity in 35% of cases (2).

As for immunological tests, tuberculin is not specific for active TB and it has a low sensitivity. Other tests such as interferon gamma (IFN- γ) measurement and specific immunoglobulin G (IgG) against mycobacteria are useful in ascites cases, but their availability is very limited due to their cost. Molecular tests such as PCR and ligase chain reaction (LCR) offer fast results, but their cost is high and sometimes their sensitivity is low (60-80%); in fact, LCR

has a better performance, but is less available (1). In the case presented here, PCR test allowed confirming the diagnosis, which had been highly suspected based on clinical and imaging and laboratory findings.

Finally, peritoneal biopsy by means of laparoscopy is fundamental for histological confirmation and in the differential diagnosis of neoplasm; currently, percutaneous approaches are also being performed in non-fibro-adhesive peritoneal TB cases (1, 2).

Peritoneal TB should be treated with the same treatment regime used for pulmonary TB, being 6 months the usual duration. However, some authors suggest extending treatment time to 9 or 12 months, especially in patients with HIV and who are not receiving antiretroviral therapy (1, 5). Our patient received supervised treatment for 9 months, achieving improvement of both clinical signs and laboratory values at the end of the first phase of treatment.

In conclusion, TB continues to be a highly prevalent disease. Furthermore, peritoneal TB is the most frequent type of gastrointestinal TB, and since it can occur with non-specific manifestations, a low threshold of clinical suspicion must be always maintained, even in patients who are not immunocompromised.

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