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CASE REPORT

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Complicated and delayed diagnosis of tuberculous peritonitis

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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ABCDE Massimo Bolognesi
FG Diletta Bolognesi

Internal General Medicine, Cesena, Italy

Corresponding Author: Massimo Bolognesi, e-mail: massimo.bolognesi@medici.progetto.sole.it

Background: Peritoneal tuberculosis is very rare in European countries. However, its incidence is increasing due to the continued immigration of people from endemic areas affected by tuberculosis.

Case Report: The authors report a case of tuberculous peritonitis in a 46-year-old male patient from North Africa. The presenting symptoms of the disease were hiccups, dyspepsia, anorexia, and weight loss. Physical examination revealed an abdominal distension that suggested the presence of ascites. Subsequent investigations of ultrasound and computed tomography of the abdomen revealed the presence of massive ascites. A diagnostic laparoscopy went on to highlight a macro micronodular degeneration of the peritoneum. Histological examination showed the presence of epithelioid granulomas with typical Langhans cells with areas of caseous necrosis. The diagnosis of tuberculous peritonitis was then made, and the ascites quickly disappeared in response to the anti-mycobacterial therapy. The patient remained free of symptoms after 6 months of clinical follow-up.

Conclusions: In this case the clinical diagnosis was complicated and delayed due to clinicians' suboptimal knowledge of and experience with this disease. This case demonstrates why laparoscopy with peritoneal biopsy should be the gold standard in any clinical suspicion.

Key words: tuberculous peritonitis • hiccup and ascites • ultrasound tomography and computed tomography scan • diagnostic laparoscopy • ascitic fluid cytology

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Background

Tuberculosis causes approximately 3 million deaths per year worldwide and is increasing in incidence in developed and developing countries. Abdominal tuberculosis, which may involve the gastrointestinal tract, peritoneum, lymph nodes or solid viscera, constitutes up to 12% of extrapulmonary TB and about 3% of the total cases [1]. The disease can mimic many conditions, including inflammatory bowel disease, malignancy, and other infectious diseases [2].

Diagnosis is therefore often delayed, even though it is known that the peritoneum is one of the most common extrapulmonary sites of tuberculous infection [3].

The clinical case presented here explains the clinical aspects and diagnostic problems with the management of patients with tuberculous peritonitis.

Case Report

In October 2011, the authors visited a 46-year-old immigrant Moroccan for the first time.

The patient reported having suffered 4–6 months from a relentless hiccup, irregular dyspeptic illness, a lack of appetite, a tense (but not painful) abdomen, and weight loss. He did not report fever or sweating. The examination showed the presence of hard, non-painful, bilaterally enlarged lymph nodes in the inguinal and axillary sites, and abdominal distension that suggested an ascitic fluid collection. No cardiovascular signs or symptoms were present. An abdominal ultrasound examination (Figure 1) confirmed the presence of ascites, but there was no enlargement of the liver or the spleen. In summary, an ascitic fluid collection with no signs of portal hypertension was present. The patient was admitted to the hospital, where further diagnostic procedures were performed including: an esophagogastric-duodenoscopy (OGD-scopy) showing signs of *Helicobacter pylori* and erosive gastritis, and colonoscopy showing a villous adenoma with low-grade dysplasia. A chest and abdomen CT scan (Figure 2) revealed bilateral apical scarring of the lung parenchyma and absence of hilar and mediastinal lymphoadenomegaly, and confirming the presence of abundant ascitic fluid. No significant alterations were seen in the other organs. Blood tests showed normochromic and normocytic anaemia (Hgb 10.6 gr/dl), low iron, and normal ferritin. Transaminases were slightly high, and indexes of inflammation were consistently high, with CRP values between 3.4 and 4.3 mg/dl, D-Dimer 1187 ng/ml, and ESR 42. A Mantoux intradermal reaction was positive (8 mm), but an HIV test, tumor markers, and serologies for hepatitis were negative. The following test results were normal: rheumatoid test

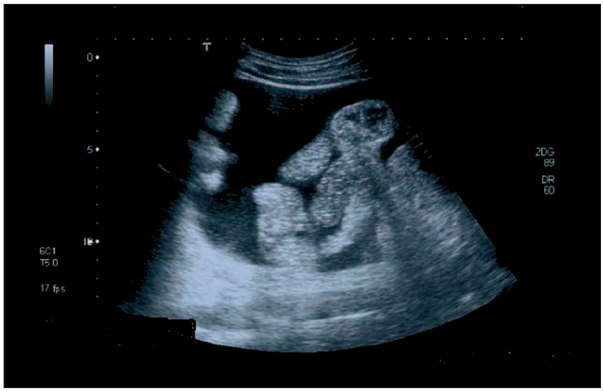

Figure 1. Abdominal US scan showed abundant ascites, with no other significant pathology.

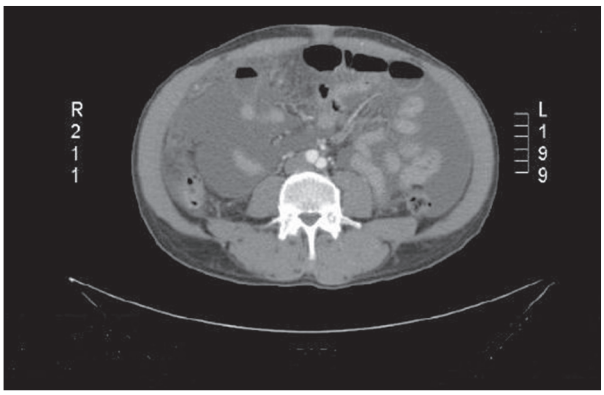

Figure 2. Abdominal TC scan confirming the presence of abundant ascitic fluid and no significant alterations in the remaining organs.

(anti-nuclear antibodies), antimitochondrial antibodies, anti-smooth muscle antibody, liver-kidney-microsome antibodies, and anti-neutrophil cytoplasmatic antibodies), antiphospholipid antibodies, and circulating immunocomplex and complement factors. Examination of the ascitic fluid was positive to alkaline reaction, and the Rivalta test showed a protein content of 65.3 g/l. Microscopic examination of the sediment revealed the presence of erythrocytes, leukocytes with predominantly mature lymphocytes (lymph: 80%), and a total amount of polymorphonuclear leukocytes of 1100 n°/mmc. Direct bacterioscopy and cultures for mycobacteria were consistently negative. Cytological analysis for atypical cells was negative.

The average albumin in the ascitic fluid was 3.2 g/dL, and the average albumin in the serum was 2.8 g/dl; therefore, the serum ascitic albumin gradient (SAAG) was 0.4 g/dl.

M. tuberculosis PCR (Polymerase Chain Reaction), performed in a laboratory at another local hospital, was negative. A biopsy of 2 small lymph nodes in the left inguinal side showed only aspecific reactive inflammation. The patient was discharged from the hospital after 32 days, with a diagnosis of “ascites

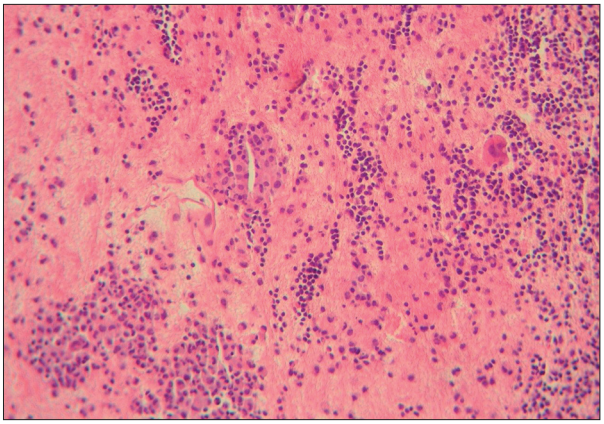

Figure 3. Ascitic fluid cytology: abundant lymphocytes are present, along with Langhans-like polynucleated cells.

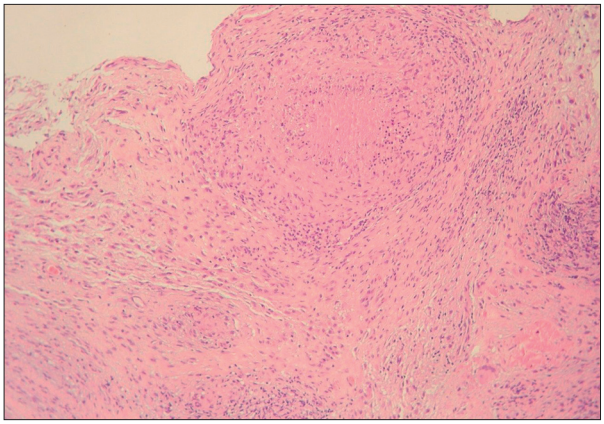

Figure 4. Peritoneal biopsy: cluster of epithelioid lymphocytes, with Langhans-type giant cells and a wide area of caseous Necrosis.

of uncertain nature and signs of inflammation". Radiographic examination of the small intestine was negative. A laparoscopy with directed peritoneal biopsy, which is thought to be the best diagnostic procedure for tuberculosis peritonitis, was subsequently performed at another hospital. Laparoscopy of the abdomen revealed large macro- and micro-nodular degeneration of the visceral and parietal peritoneum, and the presence of plaques and omental thickening, interpreted macroscopically to be similar to a massive peritoneal carcinomatosis.

Histological examination of the peritoneal biopsies showed epithelial granuloma with the presence of Langhans-type giant cells and a wide area of caseous necrosis, but without acid-fast bacilli Figure 3). Cytological examination of the ascitic fluid showed the presence of inflammatory cells, predominantly lymphocytes, monocytes, and a small number of polymorphonuclear cells, similar to Langhans cells (Figure 4). The patient was dismissed with a final diagnosis of massive peritoneal tuberculosis. During the short period (15 days) of hospitalization in the Infectious Disease Department, the patient was started on a 4-drug regimen of isoniazid, rifampicin, pyrazinamide, and streptomycin. During the final stay in the hospital, direct examination and cultures of urine, feces, and sputum for mycobacteria were performed, but all results were negative. After administration of the last treatment with streptomycin, the patient was dismissed in good general condition, with maintenance therapy and a follow-up protocol.

Discussion

Abdominal tuberculosis has diverse and non-specific symptoms. No single test is adequate for the diagnosis of abdominal tuberculosis in all patients. Diagnosis of abdominal TB in non-HIV-positive patients remains an ongoing dilemma requiring a high index of clinical suspicion [4]. Tuberculous peritonitis (TP) constitutes up to 1% of all causes of ascites. TP is an exceptionally rare disease in the Western world, but is still present in Africa and developing countries, where most young females are affected [5]. Abdominal tuberculosis can be diagnosed by culture growth of *Mycobacterium tuberculosis* in the ascitic fluid, or the presence of caseating granuloma, with or without positive smear for acid-fast bacilli, in biopsy specimens obtained by laparotomy. Laparoscopy with directed biopsy is currently the best way to make a rapid, specific diagnosis [6]. A diagnosis of tuberculous peritonitis is highly probable if the patient responds to antituberculous drug treatment with no recurrence. PCR analyses for the *M. tuberculosis* complex in ascitic fluid is a rapid test to obtain a diagnosis, but with low accuracy. Ascitic fluid adenosine deaminase (ADA) activity has been proposed as a useful diagnostic test for abdominal TB with good accuracy [7]. It is known that tuberculous peritonitis often manifests without any evidence of other sites of tuberculous infection [8]. In our patient, the signs and symptoms observed were generally consistent with those of other reports on the presence of ascites. As reported in the literature, a positive result from the Mantoux test is another diagnostic sign [9]. Moreover, the presence of predominantly lymphocytes in the ascitic fluid and polymorphonuclear leukocytes in amounts up to 250 cells/mm^3 are evidence of infection. The majority of cases reported in the literature, like our report, were diagnosed via laparoscopy with directed biopsy of the peritoneum [10]. Even though it is a relatively rare disease, abdominal tuberculosis requires a high index of clinical suspicion, particularly in case of ascites of uncertain nature without signs of portal hypertension [11] and cardiac insufficiency, and in the presence of lymphocytes in the ascitic fluid and a serum ascitic albumin gradient (SAAG) of less than 1.1 g/dl. A delay in diagnosis can be fatal [12]. Abdominal tuberculosis must be suspected if the patient is from countries with a high prevalence of the disease, for example African countries such as Morocco [13]. In accordance with our clinical report, the gold standard for diagnosis of peritoneal tuberculosis infection is laparoscopic surgery with peritoneal biopsy [6].

This technique allows examination and exploration of the peritoneum, and, particularly, the ability to obtain bioptic specimens for the subsequent histological examination (necessary for a definitive diagnosis and specific therapy [14]). The only treatment for peritoneal tuberculosis is pharmacological.

The first-choice regimen is represented by 5 drugs: isoniazid, rifampicin, pyrazinamide, ethambutol, and streptomycin. The efficacy of the therapy is determined by the resolution of symptoms and the disappearance of ascites. A delay in initiating therapy has been associated with higher mortality rates [12]. Although the current recommendations on the duration of therapy suggest a pharmacological treatment of 6 months, other studies suggest continuing therapy for 12 months. The only study that has compared different times of therapy (9 to 12 months) found no difference in the outcome between the 2 groups [15]. After 2 months of treatment for tuberculosis, our patient showed a significant improvement in his general condition; markers of inflammation returned to normal and ascites disappeared almost completely.

We are thus confident that, given the favorable evolution of the disease, the prognosis for our patient is now good. The treatment of our patient with standard antituberculous therapy for 6 months should lead to definitive recovery.

Conclusions

Peritoneal tuberculosis is particularly uncommon in European countries. However, its incidence is growing due to the continuous immigration of people from tuberculosis endemic areas.

As a consequence, the diagnosis of this disease is not immediate or easy in those countries where peritoneal tuberculosis is thought to have been eradicated. In the case report described, the clinical presentation of the disease is fairly original. In the first phase there was incurable hiccupping, which proved to be the main clinical sign of the course of the illness during treatment.

It is clear that the diagnostic gold standard of non-specifically diagnosed ascitic effusion is laparoscopy with a possible biopsy; however, in this case peritoneal tuberculosis might also have been hypothesized on the basis of anamnesis and ascitic effusion, and, above all, on the basis of the presence of lymphocytes in the exudates. Peritoneal biopsy was only performed in a second phase for diagnostic certainty, because during the first hospitalization no diagnosis had been made and the patient had been discharged with generic instructions and with no indications of any specific treatment.

Conclusions

In conclusion, this case study may be an example of the difficulty of diagnosing peritoneal tuberculosis, and explains why it should include laparoscopy with peritoneal biopsy as the gold standard in any cases of clinical suspicion. Furthermore, in the case considered, it is clear that the semiological marker was represented by the ascites and, above all, by the persistency of the hiccuping, which gradually disappeared during antitubercular therapy and with the improvement of the ascites.

Abbreviations

TB – tuberculosis; **TP** – tuberculous peritonitis; **CRP** – C-reactive protein; **OGD-scopy** – esophagogastroduodenoscopy; **ESR** – erythrocyte sedimentation rate; **SAAG** – serum ascitic albumin gradient; **PCR** – polymerase chain reaction; **ADA** – ascitic fluid adenosine deaminase; **HIV** – human immunodeficiency virus.

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