

# Peritoneal tuberculosis: diagnostic challenge for the gynecologist

## Tuberculose peritoneal: desafio diagnóstico para o ginecologista

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### Abstract

Peritoneal tuberculosis is an uncommon form of extra-pulmonary tuberculosis. A 53-year-old female presented with weight loss, fever and abdominal pain with abnormal vaginal discharge. On physical examination rebound lower abdominal tenderness, leucorrhoea and painful cervical motion were noted. Intravenous antibiotics were started, assuming the diagnosis of pelvic inflammatory disease, without clinical improvement and a pelvic MRI was done that showed signs consistent with peritoneal carcinomatosis. Surgical peritoneal biopsies showed multiple granulomas with central necrosis. Tuberculosis treatment was started with clinical improvement.

Among suspicious cases peritoneal biopsies are essential to confirm the diagnosis of peritoneal tuberculosis.

**Keywords:** Peritoneal tuberculosis; Peritoneal carcinomatosis.

### INTRODUCTION

Tuberculosis (TB) is the second leading cause of death from infectious diseases worldwide, accounting for 1,3 million reported deaths<sup>1</sup>. Peritoneal tuberculosis (PT) is an uncommon form of extra-pulmonary tuberculosis (EPTB) accounting for 4-10% of extra-pulmonary tuberculosis cases<sup>2</sup> and a reported incidence of 0.1-0.7% of all tuberculosis cases<sup>3</sup>. In Portugal, although the reported incidence of TB has decreased in recent years, the percentage of reported cases (26%) of extra-pulmonary tuberculosis is higher than the worldwide average<sup>4</sup>.

Infection by *Mycobacterium Tuberculosis* primarily affects the lung, but up to one third of cases present with extra-pulmonary involvement, including lymphatic, pleural, genitourinary and peritoneal. Late diagnosis of EPTB has been attributed to several factors including the unspecific clinical presentation or difficulty in obtaining tissue samples for diagnosis<sup>5</sup> and delay in the diagnosis and treatment is associated with worse prognosis<sup>6</sup>.

### CASE REPORT

A 53 year-old female with a known past medical history of arterial hypertension and anaemia (initially of unknown etiology but then it was related to chronic disease) presented to the emergency department with evening fever, night sweats, abdominal and pelvic pain and abnormal vaginal discharge during the two previous weeks accompanied by anorexia and weight loss over 3 months. On physical examination she presented with rebound lower abdominal tenderness and pelvic examination unveiled abundant leucorrhoea and painful cervical motion with no palpable adnexal masses. Laboratory results revealed a hypochromic microcytic anaemia (Hemoglobin 9.4 g/dl), normal leucocyte count ( $6.7 \times 10^9/L$ ), elevated (12.5 mg/dl) c-reactive protein (CRP) level. Transvaginal ultrasonography was normal except for high volume ascites. Abdominal computed tomography with contrast, held in the context of urgency, revealed loculated ascites and multiple intra-abdominal and enlarged pelvic lymph nodes. The diagnosis of pelvic inflammatory disease was assumed, the patient was admitted and started on intravenous antibiotics. Since no clinical and laboratory improvement was observed after three days of therapy an abdominal-pelvic magnetic resonance was ordered that showed a right pleural effusion and a diffuse thicken-

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ing and micronodular involvement of the peritoneum and secondary involvement of the greater omentum suggestive of peritoneal carcinomatosis. Due to these findings she underwent a work up for a metastatic cancer with unknown primary site. Upper gastrointestinal endoscopy, colonoscopy and bone scintigraphy were all inconclusive. The thoracic x-ray didn't have significant changes, except the moderate pleural effusion. Carcinoembryonic antigen (CEA) and alpha-fetoprotein (AFP) were normal and CA-125 increased (570 U/ml). Hepatitis B, hepatitis C virus and human immunodeficiency virus antibodies were negative. Ascitic fluid, obtained by paracentesis, revealed 4400 cells/ $\mu$ l with 53% polymorphonuclear leukocytes, sero-ascitic albumin gradient  $<1.1$  g/dl, adenosine deaminase (ADA) levels of 50.1 UI/L; cytology was negative for malignancy, no acid-fast bacilli were seen by microscopic exam and TB culture was negative. Pleural fluid analysis was compatible with an exudate, showing 45% of polymorphonuclear leukocytes, 35% lymphocytes and ADA level of 11 U/L. Cytological evaluation showed reactive mesothelial cells and no mycobacteria or atypical cells. Pleural biopsy findings were unremarkable. The Mantoux test was positive, with 23 mm of induration.

An exploratory laparotomy was performed: the adnexa were macroscopically normal and multiple millimetric implants were found at the peritoneal, intestinal and omentum surfaces. Peritoneal and omentum biopsies were retrieved. No complications were registered at or after the surgery, and there were a good cicatrization of the suture. Since the main suspected diagnosis was the peritoneal tuberculosis, due to the intraoperative findings and the Mantoux test positive, the follow up was performed by Infectiology. The histological results were compatible with a chronic inflammatory infiltrate with multiple granuloma with central necrosis and no microorganism or neoplastic cells were identified. After this results, 6 days after the surgery, she started on, empirically, antimicrobial therapy for *Mycobacterium Tuberculosis* – rifampin 600mg id, pyrazinamide 1000mg id, ethambutol 800mg id and isoniazide 300mg id. This was administrated during 6 months, with the first 15 days at the hospital. She showed clinical and imagiological improvement 1 month after starting the therapy.

## DISCUSSION AND CONCLUSIONS

The diagnosis of peritoneal tuberculosis requires a high

degree of clinical suspicion since the disease is usually insidious, clinical manifestations are nonspecific and laboratory finding can mimic other infectious or malignant diseases<sup>7</sup>.

The disease results either from haematogenous dissemination from a primary pulmonary focus or contiguous spread from adjacent organs<sup>8</sup>. Several risk factors have been described in association with PT including cirrhosis, diabetes mellitus, HIV infection<sup>5</sup> peritoneal dialysis, peritoneal carcinomatosis and ovarian cancer<sup>9</sup>. Interestingly, our patient presented none of the reported risk factors for PT.

The most common clinical manifestations include ascites, abdominal pain, weight loss and fever but diarrhoea and constipation may also be present<sup>3,10</sup>. Peritoneal affection has been classified into three different clinical forms: wet-ascitic, fibrotic-fixed, and dry-plastic form<sup>8</sup> although from a practical standpoint the clinical distinction between the three types is difficult and adds no prognostic or therapeutic information.

The most common laboratory findings found among PT patients were reported to be low haemoglobin and high CRP levels while leukocytosis was observed in only 10% of cases<sup>11</sup>. Interestingly, our patient had a normal leukocyte count and an elevated CRP level, but these features yield low specificity for the diagnosis of PT. An elevated serum level of CA-125 is a nonspecific marker of ovarian cancer that can also be elevated in multiple gynaecological and non-gynaecological conditions, including PT<sup>11</sup> and some authors even suggest that monitoring of CA-125 levels might be beneficial for the evaluation of treatment success<sup>12</sup>.

Other non-invasive test that can be adjunctive diagnostic tools to PT include the ADA levels in ascitic fluid<sup>13</sup> which increase due to stimulation of mycobacterial antigens. Some authors have demonstrated that it is a highly accurate diagnostic test, with a sensitivity and specificity of 100% and 97%, respectively, for a cut-off value  $>33$  UI/ml<sup>14</sup>. Interestingly, our patient presented with an ascitic fluid ADA level of 50.1 UI/ml, further supporting the diagnostic role of this test. Similar to our case, about 40-85% of patients with PT have a positive Mantoux test and this simple, non-invasive test can also provide useful diagnostic information<sup>15</sup>.

The radiologic features of PT, including ascites, irregular abdominal masses and omentum involvement are also detected in other diseases, such as primary malignant tumors, lymphoma and peritonitis<sup>16</sup>. Our patient presented omental and peritoneal thickening as

well as intra-abdominal lymphadenopathy, the latter being the least frequently reported finding in only approximately one third of patients<sup>11</sup>.

The gold-standard for diagnosis is culture growth of *Mycobacterium* on ascitic fluid or a peritoneal biopsy. While the presence of caseating granulomatous on histological examination may be a hallmark of PT, the diagnosis can also be confirmed by Polymerase chain reaction (PCR) of the infected tissues. The yield rate of culturing for *Mycobacterium tuberculosis* is low and make take up to 6 weeks, can be negative even in the presence of caseating granulomas<sup>17</sup>, causing a diagnostic and therapeutic delay. Therefore the search for *Mycobacterium Tuberculosis* on smears and cultures of peritoneal fluid is usually insufficient for a diagnosis<sup>18</sup>. In our case both the smear and ascitic fluid culture were negative for the identification of *M. tuberculosis* and unfortunately PCR tests for *M. tuberculosis* in biopsy tissue or culture were not performed, which could have been a useful alternative, allowing a more rapid diagnosis and treatment.

Laparoscopic or laparotomic examination of the peritoneum followed by histopathology can be used, allowing a more rapid diagnosis of PT compared to conventional microbiological assays<sup>19</sup>. Among these patients a broad spectrum of finding have been described, including thickened, hyperemic peritoneum with ascites and whitish granular nodules scattered over the peritoneum; ascites and adhesions; and thickened parietal peritoneum with possibly yellowish nodules and cheesy material, along with multiple thickened adhesions (i.e., the fibro-adhesive type). In various publications, laparoscopy has been reported to be superior to laparotomy and unguided percutaneous peritoneal biopsy, with a reported diagnostic rate of 80–95% with this method.<sup>19</sup>

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