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Peritoneal Carcinomatosis: An Unexpected Differential

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Abstract

Background: *Peritoneal tuberculosis is a disseminated form of mycobacterium tuberculosis infection that results in peritoneal thickening, abdominopelvic masses, ascites and elevated CA 125 that can mimic advanced stage gynecologic malignancy and while it is a rare diagnosis accounting for approximately 5% of all TB cases globally, a multidisciplinary approach is required for timely diagnosis and appropriate treatment. We hope that this will serve as a reminder to broaden the differential when faced with these findings and no underlying malignancy.*

Case: *We report a case of a 46-year-old healthy female who presented with abdominal pain, ascites and peritoneal thickening. Initial abdominal imaging revealed ascites and omental caking and carcinomatosis. Elevated cancer antigen 125 (CA-125) levels to 639 units per milliliter (U/mL) further raised suspicion of a gynecological malignancy. Multiple omental biopsies did not yield malignant tissue and subsequent investigations with Karis cell free DNA ultimately led to an unanticipated diagnosis and appropriate treatment.*

Conclusion: *Peritoneal tuberculosis (TB) is an uncommon diagnosis. This case highlights the critical role of histological analysis when radiological findings suggest malignancy; as well as the importance of utilizing a multidisciplinary approach for a comprehensive workup when the diagnosis is uncertain. Usage of cell free DNA assisted in accurate diagnosis is crucial for timely and appropriate management. Following treatment initiation, serial CT scans should be used for monitoring and to guide the duration of anti-tuberculous therapy.*

Keywords: Peritoneal Tuberculosis, Peritoneal Carcinomatosis Mimicry, Ascites and CA-125 Elevation, Histopathological Diagnosis, Multidisciplinary Approach

Teaching Points

1. Consideration of alternate strategies to obtaining specimens for pathologic diagnosis, when interventional radiology is unsuccessful i.e. surgical exploration and biopsies.
2. Consideration of peritoneal TB as a differential in the setting of suspected peritoneal carcinomatosis with persistent granulomas on biopsy.

1. Introduction

Peritoneal tuberculosis (TB) is a spectrum of TB-related conditions caused by infection with Mycobacterium tuberculosis that can affect various intraabdominal organs, and peritoneum [1]. Peritoneal TB accounts for approximately 5% of all TB cases globally. It is more commonly seen in individuals with immunocompromised states, such as those undergoing chronic corticosteroid use, as well as in patients with malnutrition, diabetes mellitus, HIV infection, and liver cirrhosis [2]. Peritoneal TB can result from the reactivation of latent TB or the dissemination of active TB. It is exceptionally rare for an otherwise healthy individual to develop abdominal TB. Case reports also show that 15%-25% of patients with peritoneal TB have concurrent pulmonary TB [3].

The clinical presentation of peritoneal TB can vary widely, depending on the specific organs involved. Typical presentations are with new-onset ascites, fatigue, fever, an abdominal mass, and weight loss [4]. In women, this clinical presentation often raises suspicion of intra-abdominal or gynecological malignancy such as advanced stage ovarian or primary peritoneal cancer. Peritoneal TB may arise through hematogenous spread from active pulmonary or military TB, or less frequently, transmurally though infected small intestines or contiguous spread from tuberculous salpingitis [3]. Timely diagnosis is crucial for improving patient outcomes, especially in female patients, where the clinical presentation can often be mistaken for a gynecological malignancy. We report a case of a 46-year-old healthy female who presented with

abdominal pain, ascites and peritoneal thickening. Initial abdominal imaging revealed ascites and omental caking and carcinomatosis. Elevated cancer antigen 125 (CA-125) levels further raised suspicion of a gynecological malignancy. However, subsequent investigations ultimately led to an unanticipated diagnosis.

2. Case Presentation

A 46-year-old female immigrant from Nigeria with no pertinent medical history presented to our gynecologic oncology clinic with abdominal distention, ascites on ultrasound and an elevated cancer antigen (CA) 125 to 639 units per milliliter (U/mL). Prior to this, she reported about 3 months of abdominal bloating and early satiety with an unintentional weight loss of about 15 pounds. She had no history of nocturnal fever or cough and no close contact with known active TB patients. Physical examination was significant for cachexia and abdominal distention with a fluid wave. CT imaging confirmed the findings on exam with peritoneal ascites as well as diffuse peritoneal thickening and omental caking suspicious for metastatic disease. The pelvic organs were overall unremarkable. Chest imaging was benign with no visible adenopathy, masses or lesions. Decision was made to proceed with diagnostic and therapeutic paracentesis for cytology and symptomatic relief and omental biopsy to obtain a tissue diagnosis. Initial paracentesis drew off 2 L of amber fluid with negative cytology. Omental biopsy demonstrated necrotizing granulomas, acid fast bacilli (AFB) and Grocott's methenamine silver (GMS) stains were negative with no evidence of malignancy. Given the high clinical suspicion for malignancy, the patient was scheduled for a diagnostic laparoscopy to obtain tissue sampling. Preoperative labs were significant for hyponatremia with a sodium value of 121 milliequivalents per liter (mEq/L). She was therefore admitted to our institution for treatment of her hyponatremia and optimization prior to her surgery. Other labs were significant for leukopenia of uncertain etiology. Upon admission, she was noted to be tachycardic to the 120s and subsequent CT angiography of the chest demonstrated new bilateral pulmonary emboli. She was therefore started on therapeutic heparin. Nephrology and critical care teams were consulted for management of the hyponatremia.

Her admission was complicated by subsequent septic shock on hospital day three. Workup was significant for bilateral pneumonia of uncertain etiology. She was persistently febrile despite broad spectrum antibiotics. Infectious disease was consulted who initiated a workup for Legionella as well as opportunistic infections given leukopenia. CD4 flow cytometry was sent in the setting of leukopenia noting CD4 count in the 40s cells per cubic millimeter (cells/mm3) signifying dangerously low levels. She was initiated on Sulfamethoxazole/Trimethoprim (Bactrim) for pneumocystis pneumonia (PCP) prophylaxis in the setting of critical CD40 count. Bronchoscopy was notable for negative cultures, AFB and GMS stains. HIV and HTLV1 testing were performed and were also negative. Repeat omental biopsy during this admission was again significant for only necrotizing granulomas and was negative for malignancy. Ultimately Karis cell free DNA next generation sequencing detected circulating TB DNA and confirmed the diagnosis of extrapulmonary TB. Given the recurrent necrotizing granulomas seen on biopsy along with critically low CD4 counts reflective of opportunistic infections, multidisciplinary consensus was to initiate TB directed therapy and the patient was then started on rifampin, isoniazid, pyrazinamide, and ethambutol (RIPE regimen) with subsequent improvement of her symptoms and discharge home for nine-month course of TB treatment. Currently that patient is 7 months into her treatment and continues to be managed on the RIPE regimen as an outpatient with resolution of her ascites, improved appetite with 12 lb weight gain and overall improvement in her functional status.

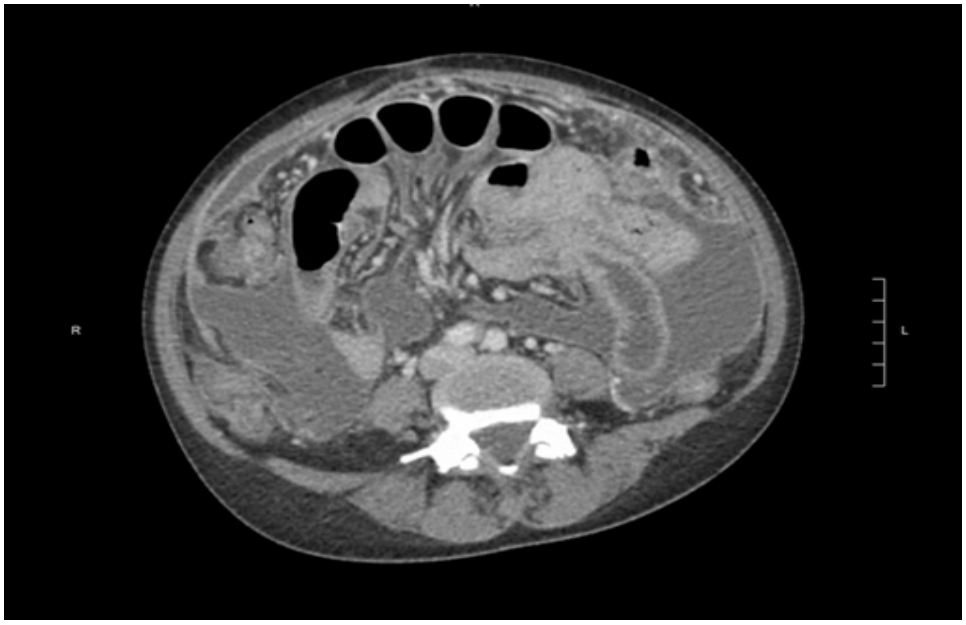

Figure 1: Initial Ct Scan Demonstrating Significant Ascites (*) and Omental Caking (Arrow)

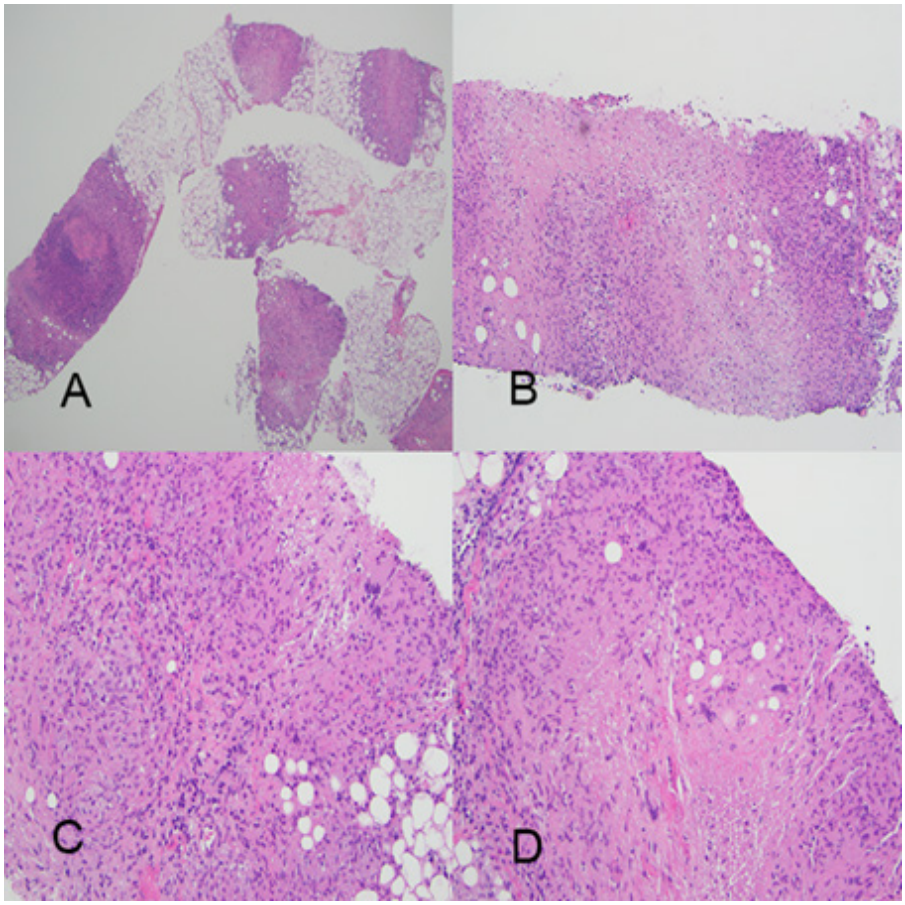

Figure 2: A: H&E Stain at 40x Magnification Showing Biopsy Cores with Necrotizing Granulomas B: H&E Stain at 100x Magnification Showing Epithelioid Macrophages Surrounding Area of Necrosis C, D: H&E Stain at 200x Magnification Showing Epithelioid Macrophages and Multinucleated Giant Cells Surrounding Area of Necrosis

3. Discussion

Our case of peritoneal TB presenting with clinical and radiographic features concerning for an underlying neoplasm underscores the importance of broadening the differential diagnosis when presented with patients with ascites and weight loss, particularly with possible demographic ties to endemic areas of TB such as India, Bangladech, Myanmar, Nigeria, Democratic Republic of the Congo and Papua New Guinea [5]. Although all pre-biopsy investigation strongly suggested metastatic disease, the final diagnosis was peritoneal TB, highlighting the challenge of distinguishing between the two conditions. An essential point to consider in the context of this case is the role of CA-125 as an exclusive biomarker for malignancy. This tumor marker is known to be nonspecific and unreliable in differentiating between malignancy and noncancerous conditions such as peritoneal TB. Elevated CA-125 levels are commonly observed in a range of peritoneal conditions, making it an unhelpful diagnostic tool in these cases. This observation is supported by a case report by Purbadi et al., where CA-125 levels were found to be 1,200 U/mL [6], significantly higher than found in our patient.

Several factors can influence CA-125 levels, as highlighted in a comprehensive review by Charkhchi et al., which identified numerous benign conditions such as endometriosis, uterine fibroids, peritoneal inflammation, menstruation, pregnancy, obesity, heart failure, and liver cirrhosis to name a few. Additionally, abnormal CA-125 levels are observed in multiple non-ovarian malignancies, including breast and lung cancers [7]. While imaging studies are critical for diagnosing diffusely metastatic disease, biopsy and histopathological examination remain of the utmost importance prior to initiating directed therapy. Aggressive surgery with laparotomy and a maximal debulking effort is a key component of ovarian cancer treatment in contrast to the medical treatment for peritoneal TB. If the initial workup for suspected ovarian cancer (IR guided biopsy, cytology etc.) is negative for carcinoma, it may be prudent to approach further diagnostic approaches in a minimally invasive fashion to spare the patient the morbidity of a laparotomy [8].

This was evident in our case, where clinical, biochemical, anatomical, and radiological findings initially suggested a malignant process and referral to our Gynecologic Oncologic office, with plan for a diagnostic laparoscopy, but the final diagnosis of peritoneal TB was established only after two histological evaluations. A key factor in aiding in this expeditious diagnosis was the initiation of a multidisciplinary approach with our primary team, medicine, critical care and infectious disease colleagues

as well as rheumatology consultation to aide in taking a global view of this patient and synthesizing all data points to determine the final diagnosis. Ultimately one of the keys to this diagnosis was her leukopenia which sparked a CD4 count workup. While the underlying etiology of her low CD4 count was uncertain in the context of negative HIV and HTLV1 tests, it drove the discussion around her underlying immunocompromised state, leading to the diagnosis of TB activation and dissemination.

Treatment for peritoneal TB is guided by the culture and sensitivity results of the isolated mycobacterial strain. In cases of fully sensitive organisms, the treatment approach is similar to pulmonary TB and response typically takes at least three months. In our case, the patient was prescribed a nine-month regimen, with directly observed therapy (DOT) upon hospital discharge. Traditionally, treatment is also guided by interval CT scans in monitoring peritoneal TB patients during follow-up, as they not only aid in assessing treatment response but can also guide the duration of anti-tuberculous therapy [9].

4. Conclusion

Peritoneal tuberculosis (TB) is an uncommon diagnosis. This case highlights the critical role of histological analysis when radiological findings suggest malignancy; as well as the importance of utilizing a multidisciplinary approach for a comprehensive workup when the diagnosis is uncertain. Accurate diagnosis is crucial for timely and appropriate management. Following treatment initiation, serial CT scans should be used for monitoring and to guide the duration of anti-tuberculous therapy.

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Authorship Contribution Statement

Sarah Werner: Investigation, Writing- original draft, review and editing, conceptualization
Fareed Rajack: Writing- review and editing, conceptualization
Nicole Gaulin: Writing- review and editing
Katherine Mager: Writing- review and editing
Karen Mc Lean: Writing- review and editing
Mohamed Desouki: Writing- review and editing, conceptualization
Emese Zsiros: Writing- review and editing, conceptualization
Peter Frederick: Writing- review and editing

Declaration of Competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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