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Single Case

Abdominal Ascites of Unknown Origin: Diagnostic Accuracy of Adenosine Deaminase for Tuberculous Peritonitis

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Abstract
The occurrence of tuberculosis (TB) is exceedingly rare in the United States (US), and incidence has steadily declined since 1993, but the pace of decline has slowed in recent years. The US TB rate during 2019 declined to 2.7 cases per 100,000 persons, the lowest level on record. The abdominal form is the sixth leading cause of extrapulmonary TB, after lymphatic, genitourinary, osteoarticular, miliary, and meningeal. Abdominal TB can infect any part of the gastrointestinal tract, including the peritoneum and the pancreaticobiliary system. We present a case of persistently elevated adenosine deaminase in peritoneal ascites of a young, healthy female with new-onset ascites. An extended diagnostic evaluation was performed to reach the diagnosis.

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Introduction

Abdominal tuberculosis (TB) is predominant in individuals <40 years of age, with a higher frequency in females [1]. The risk factors for developing peritoneal TB are HIV infection,

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cirrhosis, diabetes, malignancy, and receiving continuous ambulatory peritoneal dialysis [2]. The clinical presentation can be acute or chronically intermittent. Most patients (80–95%) have abdominal pain, 40–90% fever, 11–20% diarrhea and constipation, and 40–90% weight loss, anorexia, and malaise [3]. Peritoneal TB occurs in 3 forms: (a) wet type with ascites, (b) dry type with adhesions, (c) fibrotic type with omental thickening, and loculated ascites [3]. Patients with peritoneal TB manifest a slowly progressive abdominal swelling from ascites and abdominal pain. Approximately 90% of patients with TB peritonitis suffer from ascites [4]. Pathogenesis involves infection by tubercle bacilli (a) following reactivation via hematogenous spread from a primary lung focus, (b) via hematogenous spread from active pulmonary or miliary TB, and (c) through lymph channels from infected nodes. Peritoneal involvement may occur from infected contiguous lymph nodes, intestinal lesions, or fallopian tubes in women. Additionally, abdominal lymph nodal and peritoneal TB may develop without gastrointestinal involvement in 30% of cases [2].

Case Presentation

We are reporting a 32-year-old woman known to have diabetes mellitus who presented to the emergency department initially with a 2-week history of abdominal distention and increased abdominal girth associated with shortness of breath. She denied any nausea, vomiting, abdominal pain, loss of appetite, early satiety or unintentional weight loss, hematemesis, melena, or hematochezia. The patient denied any past surgical history. She was born and raised in the USA and never traveled outside the USA. Her social history was significant for active tobacco and marijuana smoking. She had no known allergies. Her initial vitals were blood pressure of 131/79 mm Hg, a pulse of 83 bpm, respiratory rate of 18, and temperature of 98.6°F. On examination, the abdomen was soft and distended with positive shifting dullness. Bowel sounds were normal.

Computed tomography (CT) scan of the abdomen and pelvis with contrast showed a large amount of ascites with normal hepatic architecture. Ultrasound of the pelvis showed large-volume ascites and normal appearing ovaries and uterus. The patient underwent paracentesis showing a low SAAG value (of 1 and repeat 0.6) with high protein (6.4 and repeat 7), neutrophilic predominance initially (total WBCs 6,760 with 95% neutrophils), then lymphocytic predominance (total WBCs 3,840 with 64% lymphocytes); cytology of ascitic fluid was negative for any malignant cells. Of note, she was found to have an adenosine deaminase (ADA) level of 113 in ascitic fluid; upon repeat testing, the level was 100.6. Acid-fast staining, MTB PCR, and mycobacterium cultures were negative in ascitic fluid. Ascitic fluid amylase level was 46 U/L, TAG level was 22 mg/dL, and LDH level was 554 U/L. HIV testing, HCV testing, HAV IgM, and auto-immune workup, including ANA, ANCA vasculitis antibodies, anti-smooth muscle antibodies, and liver kidney microsomal antibodies, were also negative. Serum pro-BNP was 40 pg/mL, lipase 37 U/L, ceruloplasmin level 38 mg/dL, alpha-1-antitrypsin level 144 mg/dL, ESR 100 mm/h, and CRP was 85 mg/L. Her serum immunofixation showed a dense polyclonal pattern suggestive of chronic inflammation. Urine testing for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* was negative. CT of the chest and CT of the abdomen and pelvis with contrast material were negative for any malignant focus. She underwent exploratory abdominal laparoscopy, which revealed fibrinous exudate on the peritoneal surface, and had a biopsy of the peritoneum. The pathology report from the peritoneal biopsy showed granulomatous inflammation with no malignancy (Fig. 1). PAP smear showed atypical squamous cells of

undetermined significance. Endometrial biopsy was also negative for any malignancy. Transvaginal ultrasound showed normal ovaries. She also had EGD and colonoscopy to rule out gastrointestinal malignancy and in view of the unknown origin of ascites. EGD and colonoscopy both were unremarkable, and biopsy reports were negative for any malignancy. The patient was lost to follow-up, and treatment was not initiated.

Case Discussion

An abdominal TB diagnosis can be challenging, especially for the peritoneal type, because the signs and symptoms are often very subtle. The differential diagnosis of peritoneal TB should be kept in mind in patients presenting with nonspecific symptoms of nausea, vomiting, and fever associated with ascites [4].

Ascitic fluid analysis is routinely performed in evaluating all patients presenting with ascites. The WBC in peritoneal TB varies widely, ranging from counts of <100 cells/mm^3 to as high as 5,000 cells/mm^3 [5]. The cells are predominantly lymphocytes. For unknown reasons, patients on peritoneal dialysis with tuberculous peritonitis may have a neutrophilic response [5]. The ascitic fluid protein content is usually >3.0 g/dL in the setting of tuberculous peritonitis [6]. Patients with tuberculous peritonitis (in the absence of underlying cirrhosis) typically have SAAG <1.1 g/dL; patients with underlying cirrhosis have SAAG ≥1.1 [2, 7]. The sensitivity of AFB smear and mycobacterial culture of ascites fluid is low (<2 and <20%, respectively) [8].

Measurement of ascitic fluid ADA levels can be a useful diagnostic tool for the diagnosis of TB peritonitis. Its diagnostic reliability increases in the absence of cirrhosis [9]. A meta-analysis study, including 264 patients, found that ADA levels had high sensitivity (100%) and specificity (97%) using cutoff values from 36 to 40 IU/L [10]. The sensitivity of ascites fluid ADA in patients with cirrhosis is approximately 30%. This low sensitivity is attributed to inadequate humoral and T-cell-mediated responses [7]. It is recommended to use lower thresholds (21–30 IU/L) in such cases [11, 12].

Obtaining biopsy specimens from the peritoneum is another diagnostic modality that can be used to diagnose TB peritonitis. In one systematic review, including 402 patients, the sensitivity and specificity of laparoscopic examination in making the diagnosis of peritoneal TB was 93 and 98%, respectively [2]. Gross laparoscopic findings expected in tuberculous peritonitis are (1) thickened peritoneum with yellow/white lesions with or without adhesions, (2) thickened peritoneum with or without adhesions, and (3) fibroadhesive pattern [13, 14]. Biopsy specimens should be sent for microbiological evaluation, including AFB smear, mycobacterial cultures, and PCR as well as histopathological evaluation. The sensitivity of AFB smear and mycobacterial culture for biopsy specimens is low (<50%) [15, 16]. If available, PCR is more sensitive and specific for the diagnosis of TB than AFB smear or mycobacterial culture, and often PCR results are available sooner [17, 18]. The presence of caseating granulomas is suggestive of TB but is not pathognomonic. Ascitic fluid ADA levels, along with clinical and epidemiological factors, can help establish a diagnosis under such circumstances.

Finally, it may not be possible to establish a definitive diagnosis of abdominal TB. For situations in which there is a high index of suspicion based on clinical, epidemiologic, and diagnostic findings (such as elevated ascitic fluid ADA and consistent findings in histology, with nondiagnostic mycobacterial culture), an empiric trial of antituberculous therapy is

reasonable. In general, the approach to antituberculous therapy for peritoneal TB is the same as for pulmonary TB [19, 20].

Measurement of ascitic fluid ADA levels is a valuable diagnostic tool for the diagnosis of TB peritonitis. ADA sensitivity and specificity increases in the absence of cirrhosis. After exhausting all the common and rare causes of new-onset ascites, our patient was found to have a persistent elevation of ADA. The patient had no underlying liver disease. Even though acid-fast staining, mycobacterial culturing, and PCR may be negative, it should not deter the physician from further evaluation and empirical treatment for TB.

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Statement of Ethics

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of Interest Statement

The authors of this article do not have any conflict of interest to declare.

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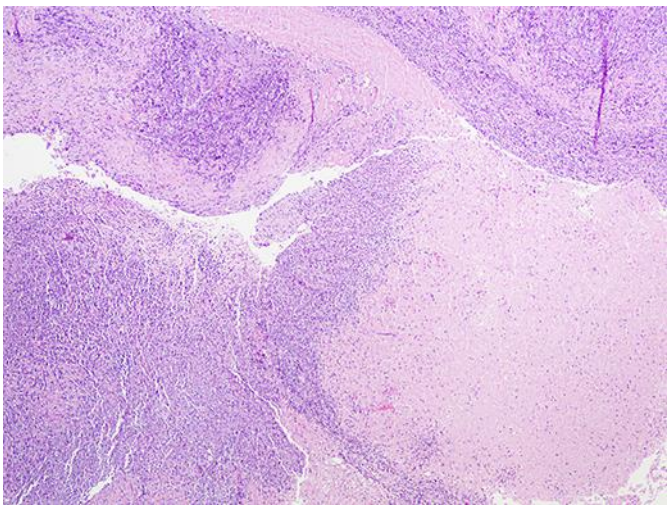

Fig. 1. Histological examination of peritoneum sample. Magnification ×10. Multiple necrotizing granulomas composed of central zone of necrosis/fibrinous, surrounded by epithelioid cells and lymphocytes.