Single Case

Measurement of Adenosine Deaminase in Ascitic Fluid Contributed to the Diagnosis in a Case of Tuberculous Peritonitis

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Keywords

Tuberculous peritonitis · Ascites · Adenosine deaminase

Abstract

A diagnosis of tuberculous peritonitis (TBP) is difficult because of nonspecific manifestation and limited effectiveness of conventional diagnostic tools. Recently, the usability of measurement of ascitic adenosine deaminase (ADA) was shown. We report here a case of TBP in which measurement of ascitic ADA contributed to the diagnosis. A 93-year-old male developed a large amount of ascites. Analyses of the ascitic fluid revealed exudation, though antibiotics treatment was ineffective. Using paracentesis, the ADA level in the ascites was measured and shown to be high. Under suspicion of TBP, an exploratory laparoscopy was performed and a definitive diagnosis of TBP was made.

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Introduction

The peritoneum is one of the most common extrapulmonary sites of tuberculous (TB) infection, with TB peritonitis (TBP) first cared for in a documented case from The New York Hospital in 1843 [1]. Thereafter, introduction of antituberculous chemotherapy and improvements in sanitation led to a decline in all forms of TB, including TBP. Recently, its prevalence has been rising due to the usage of more powerful immunosuppressant therapy, a greater number of HIV-positive individuals, and age-related diminution in immune function. According to a systematic review, TBP occurs in up to 3.5% of cases of pulmonary TB and comprises 31–58% of those of abdominal TB involving the esophagus, stomach, intestinal tract, hepatobiliary duct, pancreas, perianal area, and lymph nodes [2]. In Western Europe and North America, an association between TBP and cirrhosis has frequently been described [3, 4]. Other factors, such as chronic renal failure requiring continuous ambulatory peritoneal dialysis and HIV infection, have also been shown to be important risk factors [5, 6]. However, the diagnosis of this disease is difficult because of a lack of specific clinical features and the limited effectiveness of commonly used diagnostic tests. Isolation of mycobacteria from sampled ascitic fluid is also difficult, thus a laparoscopy is frequently needed for the diagnosis. Meanwhile, the usability of measurement of ascitic fluid adenosine deaminase (ADA) has recently been shown [7, 8]. Here, we report a case of TBP in which ascitic fluid ADA measurement contributed to the diagnosis.

Case Report

A 93-year-old male with chronic kidney disease came to our hospital with complaints of nausea, anorexia, and weight loss. Vital signs were unremarkable. A physical examination noted abdominal distension with a fluid wave. Laboratory tests showed normal liver function findings, while renal function was decreased with eGFR at 31.0 mL/min/1.73 m². White blood cell count was 3,510/μL, and C-reactive protein level was 5.27 mg/dL. A computed tomography (CT) scan revealed a large amount of ascites, as well as thickened walls of the ascending and transverse colon (Fig. 1a). In the chest, there was a linear scar-like lesion in the apex area of the left lung (Fig. 1b). Abdominal paracentesis was performed, and analyses of ascitic fluid revealed a high total protein level of 5.8 g/dL and low serum-ascites albumin gradient (SAAG) of 0.6 g/dL, suggesting exudative ascites. Furthermore, the white blood cell level in the ascites was above the measurement limit, thus antibiotics treatment (sulbactam/cefoperazone) was started for suspected bacterial peritonitis, though that had a scant effect. Paracentesis was performed again, and ADA in ascitic fluid was measured, which showed a high level of 108.2 U/L (reference range, 8.6–20.5 U/L). That measurement suggested TBP; thus, acid-fast staining and polymerase chain reaction (PCR) testing for *Mycobacterium tuberculosis* was performed, though those results were negative. To obtain a definitive diagnosis, an exploratory laparoscopy was performed, which revealed extensive, thickened adhesions between the peritoneum, omentum, and bowel. A yellowish-white thickened peritoneum and miliary nodules on the peritoneum were also observed (Fig. 2). Omental and peritoneal biopsy findings showed epithelioid granulomas with Langhans giant cells and infiltrating lymphocytes (Fig. 3). The results of 3 consecutive concentrated sputum smear tests for acid-fast bacillus were all negative, and a test for HIV infection was also negative. Treatment began with a 3-drug protocol of rifampicin, ethambutol, and isoniazid, due to reduced renal function. Eight weeks after starting treatment, a mycobacterial culture of obtained tissue was positive for *M.*

tuberculosis. One month later, ascites and associated symptoms were resolved, and the patient was discharged at 4 months after starting treatment.

Discussion

Peritoneal tuberculosis is reported to occur under 3 different conditions, with the most common reactivation of latent TB foci in the peritoneum established via hematogenous spread from a primary lung focus [9]. The next most common condition is hematogenous spread in the setting of active pulmonary TB or miliary TB, and the third condition is entrance into the peritoneal cavity in a transmural manner from an infected small intestine or via contiguous spread from TB salpingitis [10]. In our patient, chest CT imaging showed a linear scar-like lesion in the apex area of the left lung, which was considered likely to have a tuberculoid origin. This is consistent with speculations noted in past studies that TBP is usually secondary to hematogenous spread from a pulmonary focus.

Clinical manifestations of TBP are nonspecific, though affected patients in previous reports have often presented with ascites (93%), abdominal pain (73%), and fever (58%) [11]. The ascites in these cases is often exudative, with a SAAG <1.1 g/dL [2]. The present patient as well had a low SAAG value. His chief complaints of nausea and anorexia were considered to be due to ascites.

A diagnosis of abdominal TB is definitively established by demonstration of *M. tuberculosis* in peritoneal fluid or a biopsy specimen from an involved site, such as the peritoneum, intestine, or liver. However, the sensitivity of acid-fast staining (<2%) and mycobacterial culturing of ascitic fluid (<20%) is low, while results of liquid-based cultures are not available for at least 2–3 weeks, and solid egg-based culture results require 4–8 weeks [12, 13]. The utility of ascitic fluid PCR for the diagnosis of TBP has been reported [14], though it has not been well established. In the present patient, the results of acid-fast staining, mycobacterial culturing of ascites, and PCR were all negative. However, TBP cannot be denied even if these tests are not positive. Furthermore, Chow et al. [11] reported that TBP-associated mortality is high among patients waiting for results of mycobacterial cultures of ascitic fluid samples.

Measurement of ADA has been reported to be useful for the evaluation of patients with suspected TBP and to be the most reliable marker in the absence of cirrhosis [7, 8]. A meta-analysis found that ADA levels had high sensitivity (100%) and specificity (97%) when using a cutoff value of 36–40 U/L [7]. On the other hand, in patients with cirrhosis, the sensitivity of ADA measurement in ascitic fluid is only approximately 30%, likely due to poor humoral and T cell-mediated responses [15]. The ADA level in our patient was 108.2 U/L, much greater than reported cutoff values, which supported the diagnosis.

To obtain a definitive diagnosis, we performed a laparoscopic peritoneal biopsy, as the diagnostic yield of a laparoscopic examination is very high with sensitivity of the macroscopic appearance approaching 93% [2]. With disease progression, the peritoneum becomes studded with tubercles and ascites development for exudation of proteinaceous fluid from the tubercles is shown, which can be observed as thickened peritoneum with yellowish-white lesions.

As seen in the present case, diagnosis of TBP can be difficult. Nevertheless, it is important to consider TBP as a differential diagnosis in patients with ascites of unknown etiology and measure the ADA level. For a definitive diagnosis, an exploratory laparoscopy should be performed for patients with nondefinite diagnostic ascites analysis findings.

Statement of Ethics

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

Disclosure Statement

None of the authors have any financial conflicts of interest. All authors have confirmed that the article is not under consideration for review at any other journal.

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Author Contributions

All authors have made contributions to the article and have reviewed it before submission.

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Fig. 1. **a** Computed tomography (CT) image of the abdomen showed a large amount of ascites, as well as thickened walls of the ascending and transverse colon. **b** Chest CT image showing a linear scar-like lesion in the apex area of the left lung (arrow).

Fig. 2. Exploratory laparoscopy findings showing extensive, thickened adhesions between the peritoneum, omentum, and bowel. Furthermore, a yellowish-white thickened peritoneum and miliary nodules (arrowheads) on the peritoneum were also revealed.

Fig. 3. Omental and peritoneal biopsy results showing epithelioid granulomas with Langhans giant cells (arrowheads) and infiltrating lymphocytes (HE staining; $\times 100$).