Tuberculous Peritonitis Associated with Ovarian Teratoma Presenting as Peritoneal Carcinomatosis

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SUMMARY

Objective: Peritoneal tuberculosis (TB) is a fatal disease if not promptly diagnosed. We present a case of unexplained ascites with miliary peritoneal TB and a review of the literature.

Case Report: A 56-year-old woman was admitted to our hospital because of severe abdominal fullness for 20 days. Computed tomography scans of the abdomen showed massive ascites and a huge intrapelvic mass mimicking an ovarian dermoid cyst. Laboratory examinations revealed an elevated serum cancer antigen 125 level of 1,132.9 IU/mL and normal chest roentgenographic findings. About 5 L of ascitic fluid and many superficial whitish miliary deposits on the intra-abdominal and pelvic surfaces were found during exploratory laparotomy. A right ovarian cystic mass measuring 15 x 14 x 10 cm in size was noted and removed. Pathologic studies of the cyst revealed a mature cystic teratoma, and all the specimens from the peritoneum and the ovarian surface had chronic granulomatous inflammation with central caseous necrosis compatible with TB. She received postoperative anti-TB chemotherapy and was doing well 5 months after surgery.

Conclusion: Tuberculous peritonitis is not easy to diagnose. We suggest that tuberculous peritonitis associated with ovarian teratoma should be included in the differential diagnosis of peritoneal carcinomatosis. [Taiwanese J Obstet Gynecol 2005; 44(2): 164–167]

Key Words: ascites, ovarian teratoma, tuberculous peritonitis

Introduction

Tuberculosis (TB) is endemic in Taiwan; the incidence in 2000 was reported to be 62.7/100,000 population, which is an intermediate rate relative to the rest of the world. Most of these cases presented as pulmonary TB and TB pleuritis. Miliary peritoneal TB without pulmonary manifestation is a rare presentation of TB that can be confused with advanced ovarian cancer if it is associated with ascites and elevated levels of serum cancer antigen 125 (CA-125) [1]. Clinically, TB peritonitis is generally characterized by abdominal distension, anorexia, weight loss, fever, night sweats and abdominal pain, although these typical symptoms may be absent. Despite the introduction of effective anti-TB chemotherapy, mortality from TB peritonitis has remained high and may be related to the diagnostic difficulty of this great mimicker. Clinicians should consider peritoneal TB as part of the differential diagnosis in women with nonspecific abdominal symptoms, unexplained ascites, evidence of pelvic masses on imaging studies, and elevated levels of CA-125.

Case Report

A 56-year-old woman was admitted to our hospital with the chief complaints of severe abdominal fullness, poor appetite, oliguria, chillness and abdominal pain for 20
days. She was a hospital attendant and had recently taken care of a patient with lung infection. On admission, she was afebrile and chest roentgenographic findings were normal. However, abdominal sonography revealed massive ascites and a huge pelvic complex mass. Computed tomography (CT) scans showed ascites and a 10 x 7 x 8 cm mixed soft tissue tumor arising from the right ovary without lymphadenopathy. Laboratory examinations for CA-199, carcinoembryonic antigen and α-fetoprotein, liver function tests, and electrolyte levels were all within normal ranges. Serum CA-125 was abnormally high, with a level of 1,132.9 IU/mL (normal, < 35 IU/mL).

Ultrasound-guided aspiration of the ascites was performed. Ascitic fluid cytology was negative for malignancy. White blood cell count was 1,791/L, of which 98% were lymphocytes. Cultures for *Mycobacterium tuberculosis* were negative for growth; Ziehl-Neelsen stains were negative for acid-fast bacilli. Despite the negative cytology for malignancy, there remained a strong possibility of a malignant tumor arising from either the pelvic tumor or the peritoneum, and a laparotomy was arranged.

The laparotomy was performed through a midline incision with the intention for primary debulking. A 5.2 L volume of ascitic fluid was removed and submitted for cytologic examination. The peritoneum was inflamed, with innumerable superficial whitish miliary deposits measuring 1–3 mm in diameter on the peritoneal surfaces, the uterus, the adnexa, the pouch of Douglas, the serosal surfaces of the intestines, and on virtually every visible intra-abdominal and pelvic surface (Figure 1). A large right ovarian cystic tumor measuring 15 × 14 × 10 cm in size was found and total oophorectomy was performed. Deposits from the peritoneal surface were sent for frozen-section analysis. Frozen section of the ovarian tumor revealed mature cystic teratoma, whereas other specimens from the peritoneum and ovarian surface demonstrated a diffuse chronic granulomatous inflammation with central caseous necrosis and no evidence of malignancy (Figure 2). These findings were considered to be highly suggestive of TB. The abdomen was closed.

The final histology report confirmed granulomatous inflammation and central necrosis with areas of caseation. The findings were compatible with TB. Standard bacteriologic and mycologic cultures of the ascitic fluid were sterile. No acid-fast bacilli were seen by microscopy, and the results of TB polymerase chain reaction (PCR) analysis of the specimens were negative. The patient received quadruple anti-TB chemotherapy immediately after surgery, with daily dosages of: 5 tablets Rifater (rifampicin 120 mg, isoniazid 80 mg, pyrazinamide 250 mg), 1 g ethambutol, and 10 mg pyridoxine (vitamin B6). The patient’s general condition gradually improved over the next week and abdominal fullness subsided. She was discharged and anti-TB drugs were continued together with close monitoring of her progress.

A few days later, it was noted that the patient’s liver function was impaired. Alanine aminotransferase was 698 U/L (normal, 0–35 U/L). The quadruple anti-TB regimen was discontinued, and her liver function gradually improved over the next 2 weeks. Isoniazid and ethambutol, followed by rifampicin, were gradually reintroduced, with close monitoring of liver function. During the next 4 months of follow-up, she was in good condition and showed significant improvement.

**Discussion**

The incidence of extraperitoneal manifestations of TB varies widely, and a normal chest X-ray does not exclude
the diagnosis. This report strongly illustrates that peritoneal TB should be included in the differential diagnosis of all patients who present with ascites and pelvic mass in spite of a negative chest X-ray finding.

In developed countries, TB is commonly detected in immigrants, in patients with HIV infection, accompanying alcoholic cirrhosis of the liver, and as a complication of peritoneal dialysis. In developing countries, TB is one of the most common causes of non-cirrhotic ascites.

Peritoneal TB may mimic peritoneal carcinoma as it usually presents with vague symptoms and non-specific signs. Abdominal pain and malaise are the most frequent symptoms, while ascites is the most frequent sign at admission. CT imaging does not appear to be any more specific than ultrasonography for the diagnosis of this condition. Tumor markers such as CA-125 commonly reach very high levels, especially in cases with extensive miliary dissemination [1], and cannot aid in the differential diagnosis. Simsek et al showed that serum CA-125 level normalization correlated closely with the response to anti-TB therapy [2], which indicates that CA-125 could be used as a follow-up marker in patients being treated for tuberculous peritonitis.

Ascites of TB peritonitis is exudative and is commonly misdiagnosed as carcinomatous peritonitis, especially in the elderly. Cell count analysis of ascitic fluid can show either neutrophil or lymphocyte predominance. Levels of total protein and lactate dehydrogenase, and the serum/ascites glucose ratio in ascites fluid are usually insufficient to distinguish TB peritonitis from peritoneal carcinoma.

For a definitive diagnosis of tuberculous peritonitis, it has long been recognized that microbiologic and/or histologic confirmation is indicated. Direct smear for Ziehl-Neelsen stains is unhelpful, with reported sensitivity ranging from 0% [3] to 6% [4]. Culture of ascitic fluid takes up a considerable amount of time before results become available, and negative results occur in the majority of tuberculous ascites. Hence, peritoneal biopsy has a better diagnostic value than ascitic fluid analysis alone. The typical TB granuloma consists of a focus of epithelioid cells rimmed by fibroblasts, lymphocytes and Langhans giant cells, and commonly presents with central caseous necrosis.

With increasing incidence of TB epidemics, the low sensitivity and the length of time taken by traditional diagnostic modalities have hampered efforts to interrupt disease transmission. Introduction of other noninvasive diagnostic tools, such as ascitic adenosine deaminase (ADA) levels, elevated interferon (IFN)-γ concentrations, and direct identification of M. tuberculosis with PCR methods, has been suggested. In one series of 200 patients with undiagnosed ascites, laparoscopy proved to be a safe method of providing a diagnosis [5]. Nevertheless, port site metastases may complicate the use of laparoscopy in the diagnosis of ovarian cancer.

ADA was a helpful marker for tuberculous peritonitis; levels in the ascitic fluid above 30 IU/mL had a sensitivity and specificity of 94% and 92%, respectively [6]. However, false-negative results for ADA were quite common in cirrhotic patients with low-protein ascites [7]. In addition, ADA is a product of activated cells of the immune system rather than of M. tuberculosis, so it may be falsely positive in peritoneal carcinomas, spontaneous bacterial peritonitis and secondary peritonitis. However, in conditions that are difficult to diagnose, this easy, rapid, safe and reliable test may have a place in routine investigation.

IFN-γ, a cytokine associated with a Th1 type of cell-mediated immune response, has been found to be a reliable indicator for the presence of peritoneal TB [8]. Elevated IFN-γ concentrations in patients with tuberculous pleural and peritoneal effusions have been reported in a number of studies [8,9]. This has led to the proposal that IFN-γ may be used as a diagnostic tool for tuberculous exudates [10]. Use of a cut-off value of ≥ 3.2 U/mL has a sensitivity of 93% and a specificity of 98% [11].

Rapid nucleic acid amplification techniques such as PCR allow direct identification of M. tuberculosis in clinical specimens. The use of molecular techniques to assist in the diagnosis of pulmonary TB is well accepted. Molecular diagnosis of tuberculous peritonitis using nucleic acid amplification tests has been reported [12]. However, PCR has limited sensitivity in detecting M. tuberculosis due to lingering problems with specimen preparation.

Close monitoring of anti-TB treatment is required due to potential liver toxicity. If severe hepatitis is present, then all hepatotoxic anti-TB drugs must be temporarily discontinued and treatment changed to non-hepatotoxic anti-TB drugs such as streptomycin, ethambutol, and ofloxacin. When liver function returns to normal, the hepatotoxic drugs may be re-introduced one by one.

Nosocomial transmission of TB to two health care workers after exposure to infected peritoneal fluid was reported by Matlow et al [13]. If there is any evidence of concomitant pulmonary TB, precautions against airborne transmission are required, e.g. use of private rooms, negative air pressure ventilation, respiratory protective devices such as fitted respirator masks or high-efficiency particulate air filters.

Tuberculous peritonitis is difficult to diagnose. Identification of infected persons requires a high index
of suspicion. Ascitic fluid ADA activity is a rapid and reliable test for intra-abdominal TB. Peritoneal biopsy is still the most reliable method for the diagnosis of TB peritonitis. If laparotomy or laparoscopy is required for making the diagnosis, frozen-section analysis should always be considered, as extensive surgery prior to adequate antimicrobial treatment in patients with tuberculous peritonitis significantly increases postoperative complications such as bladder and intestinal fistula formation. More importantly, accurate diagnosis can reduce future complications from this infection and avoid unnecessary extensive surgery.

References