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Case Report

Tuberculosis peritonitis mimicking ovarian cancer in young women

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Abstract: Background: We aim to present two patients who were referred to our gynecological oncology clinic with the pre-diagnosis of ovarian and/or peritoneal cancer; however, they were diagnosed with peritoneal tuberculosis. Case presentation: The first patient was a 44-year-old female on whom we performed a diagnostic laparoscopy. There were approximately 500 cc of yellowish ascites fluid in the abdomen. There were multiple miliary-like lesions in both ovaries and in the peritoneum over the tuba uterinae and fossa ovarica. There were multiple nodules compatible with miliary tuberculosis in all peritoneal areas, in the liver, on the diaphragm, on the omentum and all over the small and large intestines. The second patient was a 22-year-old woman with no history of surgery and no alcohol. Her cervical smear was normal. The CA-125 level was 265 U/ml. The patient also underwent the consultation of the Interventional Radiology discipline and they performed percutaneous drainage procedures for ascites and pleural effusion. We performed tuberculosis culture, acid-fast staining, TB PCR tests on the ascites fluid. The results were positive and the patient was diagnosed with tuberculosis. We began anti-tuberculosis treatment. Conclusion: A multi-disciplinary approach should be established between clinicians and pathologists. Consideration of the fact that granulomatous infections like TB may exhibit similar characteristics to gynecological malignancies will enable us to avoid unnecessary and complicated surgical procedures, particularly in young patients.

Keywords: Mycobacterium tuberculosis, granulomatous inflammation, intra-peritoneal tuberculosis, ovarian cancer

Introduction

Granulomatous inflammation is a histological type of tissue reaction, which occurs following cell injury. Autoimmune, infection, allergic, toxic, drug and neoplastic disorders cause granulomatous inflammation. The clinical differential diagnosis and management are narrowed by the tissue reaction pattern. Necrotizing granulomas, non-necrotizing granulomas, suppurative granulomas, diffuse granulomatous inflammation and foreign body giant cell reactions are common patterns [1].

Tuberculosis (TB) is among the most important infectious causes of granulomatous peritonitis. Approximately 2 million individuals die from tuberculosis every year [2].

In recent years, individuals with low socio-economic status have led an intensive migration from Syria to Turkey due to the civil war. This condition may have caused an increase in number of tuberculosis patients. In 2013, the World Health Organization (WHO) reported approximately 9 million new cases and 1.5 million TB-related deaths worldwide [3]. Mycobacterium tuberculosis is the causative agent of TB, which primarily involves the lungs, but may also be found in any part of the body. While abnormal chest radiography is observed at a rate of 21-83% in patients with peritoneal TB, it is seen at a rate of 14% in active TB [4].

Two female patients who were referred to our gynecological oncology clinic with the pre-diagnosis of ovarian and/or peritoneal cancer; however, they were diagnosed with peritoneal TB under the light of the current literature and patient data.

Case presentation

The first patient was a 44-year-old female. She had a medical history of cholecystectomy, appendectomy and C/S (Caesarean section)

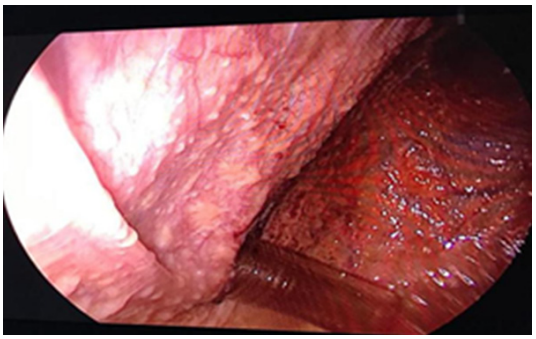

Figure 1. Laparoscopic appearance of pelvic miliary tuberculosis nodules.

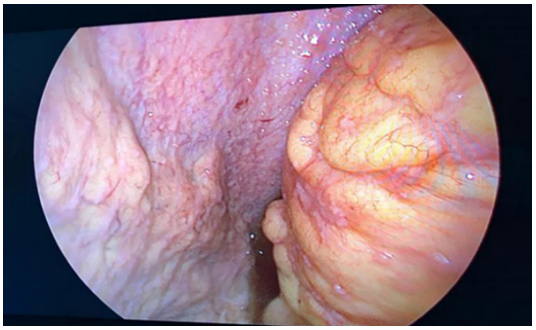

Figure 2. Gray-whitish diffuse nodular appearance in upper abdominal parietal peritoneum.

operations. She had no allergies. She did not smoke and did not consume alcohol. She had the complaints of abdominal bloating and distension. She had been pre-diagnosed with peritoneal tuberculosis in another hospital and anti-tuberculosis treatment was begun.

She was referred to our tertiary hospital due to suspicion of ovarian cancer and peritoneal tuberculosis. On the trans-vaginal ultrasonography, the endometrium was 4.8 mm in thickness. The ovaries could not be evaluated clearly bilaterally. Diffuse ascites in the abdomen and peritoneal irregularities were observed. She had undergone an Abdominal CT (computerized tomography) scan in another hospital. These scans underwent the consultation of our Radiology Division. Minimal pericardial effusion with a depth of approximately 4 mm in the pericardial area was observed. There was minimal pleural effusion with a depth of 6 mm at the base of the left hemithorax. Linear atelectatic band formations were observed in the upper lobe of the left lung and in the anterior part of the lower lobe of the left lung. Two to three pulmonary nodules, the largest having a diameter

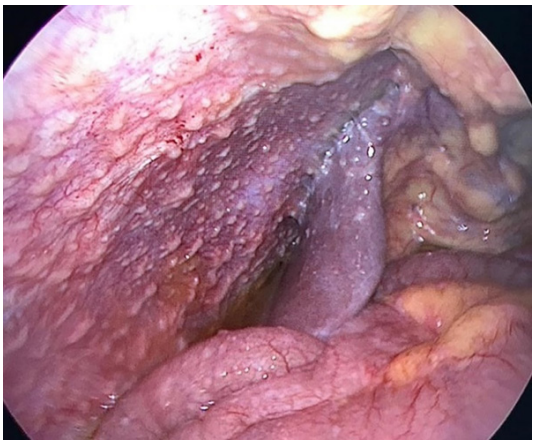

Figure 3. Dense adhesions secondary to peritoneal TB in the liver and the diaphragm.

of 4 mm, were observed in the lower lobe of the left lung. The radiology department recommended work-up for metastasis. We continued the anti-tuberculosis treatment while we were preparing the patient for surgery. The patient's Ca-125 (cancer antigen 125) level was 110 U/ml.

We performed a diagnostic laparoscopy. There were approximately 500 cc of yellowish ascites fluid. There were multiple miliary-like lesions in both ovaries and in the peritoneum over the tuba uterinae and fossa ovarica. There were multiple nodules compatible with miliary tuberculosis in all peritoneal areas, in the liver, on the diaphragm, on the omentum and all over the small and large intestines. We conducted multiple biopsies from the right anterior pelvic side wall and the right para-colic peritoneum (**Figures 1**-**3**). The pathology result revealed mature fat tissue, hyalinized connective tissue in one place or another, mononuclear inflammatory cells and multiple granulomas. There were giant cells, histiocytes, lymphocytes, eosinophils and neutrophils in the granuloma. No malignant cells were observed. This was interpreted as foreign body granuloma.

Cytological examination of the ascites fluid revealed chronic inflammatory cells within a proteinous background. The ARB (Acid-resistant bacteria) smear, the cultures and the PCR (polymerase chain reaction) of ascites fluid were negative.

A few days following surgery, the levels of the patient's liver function tests increased. We

requested the consultation of the Gastroenterology and the Pulmonology departments. They stopped the anti-tuberculosis treatment. Hepatic doppler USG (ultrasonography) was performed. There was a hemangioma measuring 23×17 mm in segments 5-8 of the right lobe of the liver adjacent to the portal vein. Hepatic artery flow velocity was normal. Hepatitis markers were negative. Dynamic CT was performed on which there was a hypodense lesion in the liver adjacent to the left part of the portal vein, minimal pelvic fluid and multiple retroperitoneal lymph nodes, the largest measuring 8 mm. The patient's liver enzymes returned to normal values.

The second patient was a 22-year-old woman with no history of surgery or alcohol consumption. She had been suffering from abdominal bloating and distension for two weeks. She was referred to our tertiary hospital with suspicion of ovarian cancer. The uterus was normal and the endometrium was linear on the trans-vaginal ultrasound. The ovaries were normal bilaterally. Widespread ascites was observed in the pelvis. Her cervical smear was normal. The CA-125 level was 265 U/ml.

She had undergone an abdominal CT scan in another hospital. These scans underwent the consultation of the Radiology department. Widespread free fluid and thickening of the peritoneal lines in the abdomen were observed. There were irregular densities and a nodular appearance in the omental area. Both ovaries were observed to be normal. We carried out a thoracic CT. There were bilateral apical cavitary lesions and an infiltrative appearance in the upper lobe of the right lung. The radiologists suggested consideration of tuberculosis and peritoneal carcinomatosis in the differential diagnosis.

The patient underwent the consultation of the Gastroenterology department. They performed colonoscopy, which was normal. Hepatic doppler USG revealed a 29×17 mm focal lesion in segment eight of the liver and grade one hepatosteatosis. The patient's ascites was not considered to have resulted from portal hypertension.

The patient also underwent the consultation of the Interventional Radiology department and they carried out percutaneous drainage of the ascites and pleural effusion. We performed tuberculosis culture, acid-fast staining and TB PCR tests on the ascites fluid, the rsults of which were positive. The patient was diagnosed with tuberculosis. We began anti-tuberculosis treatment.

Discussion

The histological identification of granulomatous inflammation is an indicator of the etiology. The clinical differential diagnosis can be narrowed by histological patterns (foreign-body, necrotizing, non-necrotizing, suppurative and a diffuse histiocytic reaction). A definitive diagnosis can be made with supportive testing with special stains and/or molecular diagnostics [1].

Although pulmonary TB is frequent in developing countries, peritoneal TB is rarely diagnosed due to diagnostic difficulties and is sometimes confused with other clinical conditions. Peritoneal TB develops from reactivation of TB areas in the peritoneum or hematogenous spread of pulmonary TB [5]. These patients should be screened for sexually transmitted diseases, particularly the Human Immune Deficiency Virus (HIV) infection.

Intra-peritoneal tuberculosis constitutes only 1-2% of tuberculosis cases [6]. There are four types of intra-abdominal tuberculosis: peritoneal, nodal, luminal and visceral [7]. The most common symptoms of intra-peritoneal tuberculosis are abdominal pain, cachexia, fever, anorexia, abdominal distension and ascites [6]. The most common symptoms associated with adnexal masses include pain and abdominal bloating, and urinary symptoms may indicate malignant rather than benign causes. More severe, frequent symptoms of shorter duration may also indicate cancer [8]. Due to the clinical and laboratory similarities between these two diseases, pelvic tuberculosis can be misdiagnosed as ovarian cancer. Pelvic tuberculosis can also mimic other pathological conditions including cancer, infectious diseases and bowel diseases [9].

Only half of the patients with early epithelial ovarian tumors and two-thirds of the patients with advanced tumors have increased CA 125 levels. Pelvic tuberculosis can increase the CA-125 levels. CA-125 levels are not very useful for the differential diagnosis of pelvic tuberculosis versus ovarian neoplasms [10].

While TB culture positivity is at a rate of 20-83%, PPD (purified protein derivative) test positivity may be seen at a rate of 24-100%. Anemia, increase in erythrocyte sedimentation rate, increase in CRP (C-reaktif protein) and hypo-albuminemia may also be observed. None of these tests are specific for peritoneal TB [11-13]. Acid-fast bacilli are limitedly revealed with PCR due to the problems in preparation [14]. Ultrasonography and computed tomography have a limited place in the differential diagnosis as peritoneal TB is of a miliary nature. Although clinicians may start empirical treatment in some cases with strongly suspected but not confirmed TB, this is not very effective and may lead to hepatic damage [15].

Laparoscopy and/or laparotomy with tissue biopsy are the gold-standard method in diagnosing intra-abdominal tuberculosis. It is important for the differential diagnosis of intra-abdominal lesions that the operation be performed by an experienced surgeon and specimens should be sent for intra-operative frozen examination. Thereby unnecessary bowel and organ removals may be avoided. In the first case of ours, laparoscopy revealed multiple diffuse involvement of the peritoneum, miliary nodule and plaque formation, fibrosis and ascites (**Figures 1**-**3**). Multiple peritoneal biopsies were obtained and confirmation of the histopathological diagnosis was attempted. Studies have shown that the sensitivity of laparoscopy is 92.7% and the specificity is 93% for TB peritonitis [4, 16].

Diagnosis is made with laparotomy or USG-guided biopsy if possible, where laparoscopy is not available and in the suspicion of widespread intra-abdominal adhesion [17]. We tried to exclude ovarian cancer/peritoneal cancer through performing laparoscopic biopsy in the first case and USG-guided biopsy in the second case as non-invasive methods, as the patients were not in advanced age when ovarian cancer is most frequent.

Female genital tuberculosis is rare, but its differential diagnosis should be done very well. Because, in order to protect patients from radical surgical procedures, especially in epithelial ovarian cancers, it may be recommended to perform more conservative diagnostic laparoscopy-like interventions in order to make a clear differential diagnosis of peritoneal tuberculosis. However, in a recent study, it was found that advanced age, adnexal mass, papillary structures, diffuse intra-abdominal acid, very high CA-125 elevation and HE-4 elevation were more prominent in epithelial ovarian cancer patients before all surgical interventions, and an algorithm was planned and implemented in clinical practice for this. It is recommended to be used in differential diagnosis [18].

Conclusion

A multidisciplinary approach should be established between the clinicians and pathologists. Consideration of the fact that granulomatous infections like TB may exhibit similar characteristics to gynecological malignancies will enable us to avoid unnecessary and complicated surgical procedures, particularly in young patients.

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Disclosure of conflict of interest

None.

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