

Peritoneal carcinomatosis versus peritoneal tuberculosis: a rare diagnostic dilemma in ovarian masses

Case Reports

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Summary

The incidence of tuberculosis is rising resulting in a simultaneous increase in the risk of TB peritonitis in surgical practice. This type of disease is fatal if it goes untreated. In women the symptoms may mimic ovarian carcinoma. We present, retrospectively, five cases during the period 1998-2002 from three hospitals in SW Greece, which presented with elevated CA 125 and vague symptoms as ovarian cancer. Five women 23-76 years old. In all five cases the patient revealed the presence of ascitic fluid and elevated CA 125. The initial diagnosis was ovarian cancer, but the final histological diagnosis confirms the TB peritonitis. We expose our experience in five cases of tuberculous peritonitis and we discuss the problems in differential diagnosis and treatment of this disease, the role of surgery and the impact of antituberculous chemotherapy upon the disease.

I. Introduction

Incidence of tuberculosis is sharply rising in the developing as well as in the developed countries and tuberculous peritonitis is often diagnosed late in the course of the disease, resulting increased patient morbidity and mortality. Despite the widespread impression that tuberculous peritonitis is rare today, the disease appears regularly on the surgical services worldwide. Its symptoms are insidious and non specific and often simulate symptoms of carcinomatous peritonitis (Lisehora et al 1996). It constitutes the third most common etiologic factor for ascites, after hepatic cirrhosis and neoplasm and it is the sixth most frequent cause of extra pulmonary tuberculosis in the USA, following lymphatics, genitourinary tract, bone and joint, miliary and meningeal tuberculosis. It may be associated with Human Immunodeficiency Virus, although the pattern of presentation seems to differ (Mehta et al 1991). It is often not considered in the differential diagnosis of abdominal pain and it is left untreated. Most often, especially in

women with abdominal pain, ascites, obstruction or peritonitis, the diagnosis is ovarian cancer (Gitt S et al 1992). In this article, we describe five case of peritoneal tuberculosis in Southwestern Greece, mimicking ovarian cancer. We expose our experience in diagnosis and treatment of this disease, with particular regard to the role of surgery and the impact of antituberculous chemotherapy upon the disease.

II. Case Reports

A. 1st Case

A 65 year-old female presented to the hospital with progressive symptoms of abdominal bloating and mild pain persisting for two months, a low grade fever of 37.5-37.8 °C every afternoon, weight loss of 3 kg, loss of appetite and night sweating. The patient had been exposed to Mycobacterium Tuberculosis continuously for few months preceding her admission, through her husband who was suffering active pulmonary TB without knowing

it (his diagnosis was made after the diagnosis of TB peritonitis was made in the female patient). During the physical examination, arterial blood pressure and pulse rate were normal and the body temperature was 37.2°C. There was no confirmation of lymphadenopathy. Ascites was present, but there was no edema of the extremities. Results of blood analysis on hospital admission were: Hct 39.6%, Hbg 13.1 g/dl, WBC 5,110/mm³ (PMN: 66%, LYM: 26%, MON: 8%) and a platelet count of 386,000/mm³. The Westergen sedimentation rate was 59 mm in one hour. Liver biochemistries included SGOT 33U/l, SGPT 16U/l and LDH 206U/l. Renal function laboratories and urine analysis were normal. CA-125 was highly elevated (465U/ml). CA-19 9 was 441 U/ml and a-FP was 2,721 U/ml. The chest radiograph was normal and the abdominal ultrasound and CT scan revealed fluid without organomegaly or peritoneal masses. Finally, the PPD skin test, which was made without clinical suspicion of TB infection, was negative. A preliminary diagnosis of peritoneal carcinomatosis due to ovarian cancer was made, based on the physical examination, the patient's history and the laboratory data. According to this diagnosis, the patient underwent laparoscopy on the fifth hospital day. During the procedure, several liters of ascetic fluid were drained, showing the peritoneum studded with nodules along with adhesion of the omentum, small intestine and transverse colon. The ovaries and uterus were covered with the same lesions. A bilateral oophorectomy was performed with simultaneous partial resection of the omentum and peritoneum along with suspicious lesions. The frozen section of the sample from the ovaries was negative for malignancy; instead it revealed granular lesions with necrosis. The cytology exam of the fluid was negative for tumor cells, as well the Gram and Ziehl-Neelsen stains. The patient had an uncomplicated postoperative course and on the sixth day, she began anti-tuberculosis treatment with daily doses of 300 mg INH, 600 mg rifampycin, 1,500 mg pyrazinamide and 10 mg B6. Four weeks after surgery, the ascetic fluid culture was negative for mycobacterium while the abdominal bloating and the sweating completely resolved during the second week. At twelve weeks of therapy, CA-125 level was within normal range. Ten months after the beginning of anti-tuberculosis treatment, the serum CA-125 level was still within normal range and the abdominal ultrasound was negative for ascetic fluid.

B. 2nd Case

A 67 year-old female was admitted to the hospital with facial edema, loss of appetite and muscular cramps. Physical examination revealed distended abdomen with drillness, indicative of ascites. Her personal history was significant for a partial hysterectomy and unilateral oophorectomy 20 years ago for non-malignant disease, as well as a history of suspicious pleural collection more than forty years ago. Laboratory data at presentation included the following: Hct 33%, WBC 7,200/mm³ (PMN: 74%, LYM: 18%, MONO: 8%), PLT: 450,000/mm³ and ESR was 97mm in one hour. Liver biochemistry included SGOT 55U/l, SGPT 82 U/l, LDH 180 U/l. Renal function analysis was within normal range. The serum CA-125

level was elevated (1,25U/ml) and CA 15-3 was highly elevated (415 U/ml). The chest radiograph was normal and the abdominal CT scan revealed a large abdominal mass in proximity to the anatomic site of the uterus and ascites. An initial diagnosis of peritoneal carcinomatosis from ovarian cancer was made and the patient underwent laparotomy. During the procedure, granules implanted in the surface of the parietal peritoneum and small bowel, were found. Microscopic examination of these lesions revealed tuberculous granulation tissue while the pelvic mass proved to be uterine leiomyoma, arising from the remainder of the uterus. The ovary was free of malignant disease. The patient had an uncomplicated postoperative course and on the 10th day, she began anti-tuberculosis treatment with INH, rifampycin for at least 10 months. She is well having until now.

C. 3rd Case

A 76 year old female patient presented with anemia, fatigue and abdominal meteorism for two weeks. Physical examination revealed distended abdomen with ascites. Laboratory data demonstrated: Hct 27%, WBC 7,100/mm³. The ESR was 102 mm in the first hour. The serum CA-125 level was highly elevated (5,354 U/ml). The chest X-ray was normal and the abdominal CT scan revealed ascites with lymph nodes enlargement without any mention of peritoneal masses. An exploratory laparotomy was performed under general anesthesia. During the operation, several liters of ascetic fluid were evacuated. Besides the ascites, the operative findings included nodules and adhesions implanted to the peritoneum, uterus, ovaries, small and large intestine. An ovarian carcinoma was speculated and a bilateral oophorectomy was performed, including the uterus and part of the omentum. Unfortunately, the patient died the 4th postoperative day, due to pulmonary embolism. The histological examination of the specimen was negative for malignancy and the final diagnosis was peritoneal tuberculosis.

D. 4th Case

A 23 year old female patient was admitted to the hospital complaining acute abdominal pain and high fever of 38-38.8°C. The physical examination revealed acute abdomen. Laboratory data at presentation included Hct 29%, WBC 12,000/mm³ (PMN: 70%, LYM: 20%, MON: 8%) and a platelet count of 420,000/mm³. ESR was 73 mm in the first hour. Liver and renal function analyses were within normal range. The tumor marker CA-125 was moderately elevated (200 U/ml). The chest X-ray was normal and the abdominal ultrasound and CT scan revealed peritoneal fluid with evidence of peritoneal masses. The patient underwent a broad spectrum antibiotic therapy but the fever persisted high, even on the 4th day of treatment. Based on the physical findings and the resistant fever, a preliminary diagnosis of intraabdominal infection or peritoneal carcinomatosis from ovarian cancer was made and the patient was subjected to exploratory laparotomy. The surgical findings and the frozen section of a sample from the ovaries and the peritoneum,

confirmed the diagnosis of peritoneal tuberculosis. The patient had an excellent postoperative course and on the 5th postoperative day, she began anti-TBC therapy, INH and rifampycin, for twelve months. The patient completed the treatment course of 1 year anti TB therapy and she is well having until now.

E. 5th Case

A 58 year old female patient was admitted to the hospital complaining colon obstruction. The physical examination revealed distended abdomen with ascites. Her personal history was significant for meningial tuberculosis in the age of twenty four, as well as “pneumonia” in the age of thirty two. Laboratory data at presentation included the following: Hct 31%, WBC 14,000/mm³ (PMN: 74%, LYM: 18%, MON: 8%) and a platelet count of 300,000/mm³. Liver biochemistries included SGOT 75U/l, SGPT 44U/l and LDH 187 U/l. Renal function analysis was within normal range. The serum CA-125 level was elevated (810 U/ml) and CA 15-3 was elevated (70 U/ml). The chest radiograph was normal and the abdominal CT scan revealed an abdominal mass in the pelvis, proximally to the anatomic site of the left colon and the presence of ascetic fluid. An initial diagnosis of ovarian cancer with colon invasion was made and the patient underwent laparotomy. The surgical findings and the frozen section of a sample from the mesentery and the peritoneum, confirmed the diagnosis of peritoneal tuberculosis. The patient had an excellent postoperative course and he received anti-tuberculosis treatment (starting the 7th postoperative day) with INH and rifampycin for nine months.

III. Discussion

The incidence of abdominal tuberculosis is extremely low in developed countries, but tuberculous peritonitis

accounts for 25-30% of the disease in the tropics and perhaps even more in immigrant patients living in developing communities. Large series have estimated the frequency of tuberculous peritonitis to range from 0.1 to 0.7% of all cases of tuberculosis, while the frequency in females is approximately twice than that found in males. It can be encountered, not only in the lowest socioeconomic classes, but also in any socioeconomic class and age, even without the coexistence of pulmonary findings of the disease (al-Quorain et al 1993; Hasanzadeh et al 2005). Abdominal tuberculosis has four major clinical presentations: mesenteric lymphadenopathy, ileocecal disease, peritonitis, colonic and anorectal disease. On the other hand there are three forms of tuberculous peritonitis: the “wet” (with ascites), the “dry” (peritoneal involvement without ascites) and the “fibroid” type (with profound omental thickening and extensive adhesion formation) (Groutz et al 1998; Bilgin et al 2001). In our cases, all five patients were presented with the “wet” type of tuberculous peritonitis; it represents the most common type and is attended by usually non specific clinical manifestations and may suggest an occult malignancy, especially ovarian carcinoma, or cirrhosis with ascites. (Table 1) (Lisehora et al 1996). The infection route of the peritoneum by the tubercular bacterium varies. Infection may occur by reactivation of a long-latent TB focus in the peritoneum from a primary focus in the lung or elsewhere, infected mesenteric lymph nodes, contamination from tuberculous enteritis or expansion of a tuberculous salpingitis in the female. (Sochocky 1967). The disease is insidious with mild symptoms and no specific signs and it can mimic ovarian cancer in women. If a patient presents with abdominal bloating and pain, low fever and weight loss persisting for more than a few weeks, then TB peritonitis must be added to the differential diagnosis.

Table 1. Main patients characteristics with peritoneal TB mimicking ovarian cancer

	AGE	Symptoms	Exposed to TB	Tumor Markers	CT Scan	Initial Diagnosis	Histological Diagnosis	Follow-Up
Case 1	65	Ascites Weight Loss Low Fever	+	CA-125: 465 CA 19-9: 441	Fluid No Mass	Ovarian Cancer	Peritoneal TB	Anti-TB treatment Alive until now
Case 2	67	Anemia Edema Loss of Appetite Fever	+/-	CA-125: 185 CA 19-9: 415	Fluid Abdominal Mass	S. Sjögren Ovarian Cancer	Peritoneal TB	Anti-TB treatment Alive until now
Case 3	76	Anemia Fatigue	-	CA-125: 5354	Fluid Lymph Nodes	Ovarian Cancer	Peritoneal TB	Death due to pulmonary embolism at 4 th postoperative day
Case 4	23	High Fever Abdominal Pain	-	CA-125: 200	Fluid	Abdominal Infection or Ovarian Cancer	Peritoneal TB	Anti-TB treatment Alive until now
Case 5	58	Bowel Obstruction	+	CA-125: 810 CA 19-9: 70	Fluid Mass	Ovarian Cancer	Peritoneal TB	Alive

Even more important, the disease must be considered when an elderly female patient presents with ascites and elevated serum CA-125 levels. In our cases, all patients presented with abdominal pain, fever and weight loss. The serum CA-125 levels were highly elevated in all patients, misleading the dominant initial diagnosis to the suggestion of an ovarian cancer in four of the five patients, preoperatively (**Table 1**). However a patient presented with symptoms of acute abdomen. In this case, the diagnosis first suspected only at laparotomy. In one autopsy series, a primary focus of the disease was demonstrated in 97% of patients (Simsek et al 1997; Straughn et al 2000). In our study, the evidence that the patient had been exposed to TB mycobacterium was clear in two cases, suspicious in another one and negative in two cases. The prognosis of the disease depends primarily on early suspicion and diagnosis, followed by immediate onset of the proper therapy. Since the introduction of anti-tuberculosis chemotherapy, the disease mortality decreased dramatically, from 49 to 7% (U-Bayramicli et al 2003). Diagnosis of tuberculous peritonitis is extremely difficult. Determination of serum CA-125 levels, serves as a useful marker for the diagnosis, the disease activity and also in evaluating the response to therapy in patients with peritoneal tuberculosis. In our study, CA-125 level, although high before the induction of TB chemotherapy, was measured within normal range as soon as the treatment course was completed, confirming the role of this marker in the clinical monitoring of the disease. However, serum CA-125 levels can also be raised in patients with ovarian cancer and other malignancies, chronic liver diseases and peritonitis. High CA-125 levels can be found in patients with diseases affecting the peritoneum and/or ascites, as well as in women during pregnancy or in benign diseases, e.g. endometriosis. In our cases, pelvic inflammation caused by tuberculous peritonitis produced raised CA-125 levels, which fell after anti-TB therapy took place. (Simsek et al 1996; Kucok, 1998) The correct diagnosis of tuberculous peritonitis depends primarily on the appreciation of the manifold clinical manifestation of the disease and on bacteriologic proof of tuberculosis somewhere in the body. TB infection cannot be ruled out based solely on sputum analysis, chest fluid, ascetic fluid or the gastric fluid analysis. It should be also noted that cultures of the ascetic fluid for tuberculous bacilli and the tuberculin skin tests often prove negative in patients with peritoneal TB. CT scan seems to be the most sensitive imaging modality. If there is a large amount of ascetic fluid (according to CT scan results), at least a litter should be aspirated in order to perform a Ziehl-Neelsen stain, culture for mycobacterium tuberculosis and cytological examination. If there is a minimum ascites on CT scanning or the stain for acid-resistant bacteria is negative, then peritoneal biopsy via laparotomy or, in selected cases, laparoscopy must be planned. (Rodriguez et al 1996; Vazquez Munoz et al 2004) Laparoscopy is probably contraindicated in advanced TB peritonitis, where the peritoneum may be more than 1 cm thick and is tightly adherent to underlying friable bowel. In our cases the abdominal CT scanning revealed only the presence of ascetic fluid and no intraperitoneal implants (false

negative examination), while in two cases revealed additionally the presence of pelvic mass. The extent and distribution of the implants often seen in TB peritonitis may lead the physician to the wrong diagnosis of a terminal stage ovarian cancer. Histological evaluation however may reveal mycobacilli and granulomas with epithelioid cells and giant cells and infiltration of lymphocytes in the periphery. Such implants were observed in the peritoneum of all our patients, frozen section of whom detected granulomas with central necrosis. The histological examination is very helpful in the setting of differential diagnosis from other forms of granulomatous peritonitis such as schistosomiasis or ascariasis that require a different therapeutic approach. Different studies demonstrate that adenosine deaminase activity levels of greater than 32.3 U/l in ascetic fluid are as high as 100% sensitive and 96% specific for the diagnosis of tuberculous peritonitis (Kadayifci et al 1996). It is important to establish the diagnosis of TB peritonitis at the operating table, in order to begin immediately the therapeutic measure, while waiting for the culture results to indicate sensitivity. Specific sensitivity to various medications must be known, in order to avoid the formation of resistant strain of mycobacilli, by using the correct regimen. The onset of therapy in our patients was delayed for a few days, waiting for histological examination that documented the diagnosis. In conclusion, unclear abdominal symptoms in a patient from a risk group should alert the surgeon to the possibility of abdominal tuberculosis.

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