

# Peritoneal tuberculosis mimicking ovarian carcinoma with ascites and elevated serum CA-125: Case report and review of literature

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## Summary

Peritoneal tuberculosis is rare in the western world, although its incidence has been increasing in recent years. The presenting signs and symptoms, imaging examinations and CA-125 status in peritoneal tuberculosis may resemble that of ovarian carcinoma. Thus, the possibility of peritoneal tuberculosis should be considered in the differential diagnosis of ovarian carcinoma, especially in women immigrants from countries with a high prevalence of tuberculosis. A case of peritoneal tuberculosis mimicking ovarian carcinoma in a young woman immigrant from India is described. The patient presented with ascites, abdominopelvic masses and elevated serum CA-125 (1,081 U/ml). Laparoscopy confirmed the diagnosis of peritoneal tuberculosis and no malignancy, and thereby unnecessary extended surgery was avoided. Following treatment with the 4-drug anti-tuberculosis regimen, the patient recovered with disappearance of ascites and abdominopelvic masses, and return of CA-125 to normal range. It is concluded that laparoscopy, if feasible, seems to be a sufficient and safe method to provide diagnosis of peritoneal tuberculosis.

*Key words:* Paracentesis; Laparoscopy; Laparotomy; Tuberculin test; Acid fast bacilli; Polymerase chain reaction.

## Introduction

Women presenting with signs and symptoms that include abdominal pain, ascites, abdominopelvic masses and elevated serum CA-125 should initially be thought to have ovarian carcinoma. However, these signs and symptoms may be the manifestation of peritoneal tuberculosis, especially in women immigrants from developing countries [1, 2]. Definitive diagnosis by examining ascitic fluid obtained by paracentesis and tissue samples obtained by laparoscopy or laparotomy is important to avoid unnecessary extended surgery. We describe a young woman with peritoneal tuberculosis who presented with signs, symptoms and serum CA-125 level resembling those of ovarian carcinoma and review the pertinent literature.

## Case report

A 32-year-old, gravida 2, para 2, married Jewish woman, who emigrated from India to Israel six months previously, presented in May 2001 with aggravating abdominal pain and swelling of four month's duration. Her medical history included tonsillectomy in childhood, two deliveries by cesarean section and bilateral tubal ligation performed at the last cesarean section four years before. Physical examination revealed an uncomfortable woman with stable vital signs and extensive ascites. Pelvic examination disclosed a normal sized non-mobile uterus, bilateral mildly enlarged adnexae (each sized 5 cm) and multiple irregular nodules (each sized 0.5 cm) densely lining the floor of the

cul-de-sac. The serum CA-125 level was 1,081 U/ml (normal range, 0 - 35 U/ml) and HIV test was negative. Chest X-ray demonstrated no abnormalities. Transvaginal ultrasound showed a considerable amount of fluid in the pelvis, normal sized uterus and mildly enlarged ovaries with normal blood flow. A computerized tomography (C.T.) scan of the chest, abdomen and pelvis revealed a small right pleural effusion, marked ascites, bilateral mildly enlarged solid ovaries and thickening of the omentum ("omental cake"). Ascitic fluid obtained by paracentesis was an exudate with lymphocytosis and no malignant cells. Culture of ascitic fluid demonstrated growth of acid-fast organisms and nucleic acid probe testing ("Gen-Prob") was positive for the *Mycobacterium tuberculosis* complex (This complex consists of the following species: *M. tuberculosis*, *M. bovis* BCG, *M. africanum* and *M. microti*). Gene probe testing cannot distinguish between these organisms because they contain closely related nucleic acids). A tuberculin skin test (Mantoux) showed an induration of 15 mm in diameter (an induration  $\geq 10$  mm is considered positive for immigrants from countries endemic for tuberculosis).

Although culture of ascitic fluid confirmed almost certainly the diagnosis of intra-abdominal tuberculosis, a decision was made to perform a laparoscopy to facilitate a definite diagnosis. At laparoscopy, the peritoneal cavity contained 1,000 ml of yellow-straw stained ascitic fluid. The parietal and visceral peritoneum were studded with numerous small whitened plaques and extensive adhesions causing conglomerations of the omentum, mesentery, bowel loops and pelvic organs. The uterus and adnexae were buried in a morass of dense adhesions and plaque, but grossly appeared normal. Biopsies taken from the peritoneum and right ovary showed multiple necrotizing epithelioid cell granulomas with multinucleated giant cells surrounded by lymphocytes (Figure 1). No acid-fast bacilli were seen by microscopy. Results of polymerase chain reaction

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(PCR) analysis of the IS6110 sequence specific for the *M. tuberculosis* complex and of the 65 KDa antigen gene common to all mycobacteria were positive.

Postoperative recovery was uneventful. Quadruple anti-tuberculosis chemotherapy was started with isoniazid 300 mg/day and rifampin 600 mg/day for six months, and ethambutal 1,200 mg/day and pyrazinamide 1,500 mg/day for three months. The patient tolerated anti-tuberculosis chemotherapy well, serum CA-125 level returned to normal range and to date, seven months after diagnosis of peritoneal tuberculosis, she is alive and well and without evidence of disease.

## Discussion

In the western world, due to increased immigration and with the increase in HIV infection and the number of immunocompromised patients, the rate of tuberculosis has in recent years increased [1, 3, 4]. Pulmonary tuberculosis has remained the most common and well-known form of presentation, whereas other forms of presentation, such as peritoneal tuberculosis, are less common [1, 3, 5]. Medical awareness of peritoneal tuberculosis in the western world is still lacking and many patients with this disease undergo unnecessary extended surgery. This patient was a new immigrant from India; a country with a high prevalence of tuberculosis. Her young age (32 years) corroborates studies that demonstrated that women with peritoneal tuberculosis are younger than those with ovarian carcinoma [2].

The clinical manifestations of peritoneal tuberculosis may resemble those of widespread intra-abdominal ovarian carcinoma with signs and symptoms that include abdominal pain, ascites, abdominopelvic masses and elevated serum CA-125 [1, 2, 3-9]. Ultrasound examination and computerized tomography (CT) scanning of the abdomen and pelvis may lead to the misdiagnosis of disseminated intra-abdominal ovarian carcinoma [2,4]. Thus, clinical discrimination between peritoneal tuberculosis and ovarian carcinoma may sometimes be extremely difficult [1]. In peritoneal tuberculosis, chest X-ray may be normal and the tuberculin skin test (Mantoux) is often nonreactive [1]. Even during laparoscopy or laparotomy, the gross appearance of peritoneal tuberculosis often can be similar to that of disseminated intra-abdominal ovarian carcinoma [1, 3, 5]. Thus, the preoperative and even intraoperative differential diagnosis of peritoneal tuberculosis versus ovarian carcinoma often is difficult and problematic. Only examination of ascitic fluid obtained by paracentesis and histopathologic examination of biopsies taken from the pelvic or abdominal lesions can provide the crucial information and correct final diagnosis [3]. Since chronic granulomatous reaction and inflammation are consistent but not diagnostic of tuberculosis, histologic confirmation of tuberculosis can be difficult [3]. The following laboratory tests of aspirates and biopsy specimens are needed to finally confirm the diagnosis of peritoneal tuberculosis: 1). Presence of acid fast bacilli (Ziehl-Nielsen staining positive); 2). Positive culture for *M. tuberculosis*; 3). PCR positive for *M. tuberculosis* complex [2, 7].

Ascites in women is most often associated with advanced-stage ovarian carcinoma. Ascites may also be caused by other conditions such as benign gynecological diseases, liver disease, heart failure, and infectious diseases including peritoneal tuberculosis [1, 2, 3-5, 8, 9]. Cytologically and biochemically, ascites associated with peritoneal tuberculosis is basically a lymphocytic exudate characterized by lymphocytosis, no malignant cells, high total protein content (> 25 g/l), a small serum-ascites albumin gradient (< 11 g/l) and an elevated LDH level (> 90 U/l) [4, 6, 7]. Sheth [10] has demonstrated that among 70 Indian women who had laparoscopy for ascites, 20 women had peritoneal tuberculosis with involvement of pelvic structures in 16 women.

CA-125 has been recognized as a marker of non-mucinous epithelial ovarian carcinomas. Elevated level of CA-125 can also be associated with benign intra-abdominal conditions such as pelvic inflammatory disease, endometriosis, adenomyosis, uterine myomas, hepatitis, pancreatitis and peritonitis including tuberculous peritonitis [2, 3, 8]. In this patient the serum CA-125 level was 1,081 U/ml; however, in most reported cases of peritoneal tuberculosis serum CA-125 levels were <500 U/ml [1, 2, 3-5, 8, 9]. In many of these women, elevated serum CA-125 levels had led to the misdiagnosis of ovarian carcinoma. Thus, the use of CA-125 in the differential diagnosis between peritoneal tuberculosis and ovarian carcinoma is inconclusive or even misleading. Simsek et al [11] have shown that serum CA-125 level normalization correlated closely with the response to anti-tuberculosis treatment and it has been suggested that serum CA-125 level could be used as a follow-up marker for monitoring the success of anti-tuberculosis therapy in patients with peritoneal tuberculosis. In this patient, serum CA-125 levels have returned to normal range during and after completion of anti-tuberculosis therapy.

The treatment of peritoneal tuberculosis and that of ovarian carcinoma differ markedly. Peritoneal tuberculosis is treated medically by anti-tuberculosis drugs, usually the 4-drug regimen consisting of isoniazide, rifampin, ethambutol and pyrazinamide, and no extended

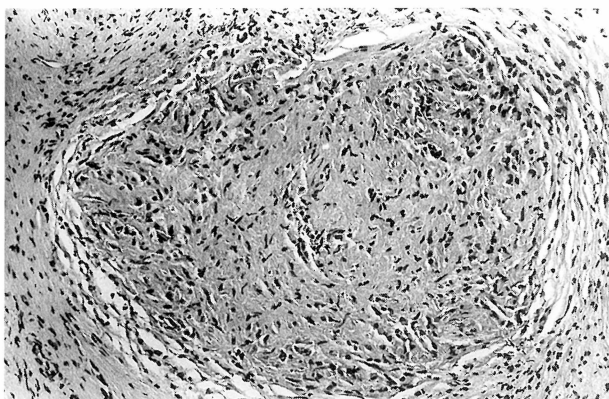


Figure 1. — Peritoneal tuberculosis. Epithelioid cell granuloma with multinucleated giant cells surrounded by lymphocytes (H&E x 200).

surgery is indicated. Ovarian carcinoma is treated by extensive debulking surgery followed by combination chemotherapy with cytotoxic drugs [7, 8]. Laparoscopy seems to be a sufficient and safe method to provide tissue samples for histologic and bacteriologic diagnosis of tuberculous infection [2]. If laparoscopy is not feasible, a laparotomy is usually necessary to obtain tissue samples for the diagnosis of peritoneal tuberculosis [2].

### Conclusion

The possibility of peritoneal tuberculosis should always be considered in the differential diagnosis of ovarian carcinoma, especially in women immigrants from developing countries. In the presence of ascites, cytologic examination and culture of ascitic fluid obtained by paracentesis may obviate the problem. If ascitic fluid can not be obtained or the cytologic examination and culture result are inconclusive, diagnostic laparoscopy is needed to seize the diagnosis through biopsy. If the performance of laparoscopy is impossible, exploratory laparotomy is performed and biopsies are taken for intraoperative frozen section examination and samples are sent for culture and PCR testing. If no carcinoma is detected and the diagnosis of peritoneal tuberculosis is confirmed, extended surgery is avoided and anti-tuberculosis treatment is started. If the diagnosis of ovarian or peritoneal carcinoma is confirmed, extended debulking surgery is performed.

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