

# Laparoscopy may be an effective tool in the diagnosis of peritoneal tuberculosis

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## Summary

In order to identify the effectiveness of laparoscopy in the diagnosis of peritoneal tuberculosis, we retrospectively reviewed the medical and pathology reports of 10 patients with peritoneal tuberculosis who were operated at our clinic with the suspicion of ovarian cancer during a 11-year period. The characteristics of the clinical picture, radiologic imaging studies, laboratory tests including polymerase chain reaction and the role of laparoscopy in the diagnosis of peritoneal tuberculosis were evaluated for differentiation of ovarian cancers and peritoneal tuberculosis. In conclusion, peritoneal tuberculosis should be suspected in young women with ascites with or without adnexal mass. Laparoscopy is an effective diagnostic tool in patients with no suspicion of adnexial masses.

**Key words:** Laparoscopy, peritoneal tuberculosis

## Özet

**Laparoskopi, peritoneal tüberküloz tanısında etkili bir yöntem olabilir**

Laparoskopinin peritoneal tüberküloz tanısında etkinliğini araştırmak amacıyla, son 11 yıllık periyod içinde over kanseri şüphesi ile kliniğimizde opere edilen 10

peritoneal tüberküloz olgusunun dosyası ve patoloji raporları retrospektif olarak incelendi. Klinik tablo özellikleri, radyolojik görüntüleme çalışmaları, laboratuvar testleri ve laparoskopinin peritoneal tüberküloz tanısındaki rolü, over kanseri ve peritoneal tüberküloz ayırımı için değerlendirildi. Sonuç olarak, adneksiyal kitlesi olsun ya da olmasın asiti olan genç bayanlarda peritoneal tüberkülozdan şüphe duyulmalıdır ve laparoskopi, adneksiyal kitle şüphesi olmayan hastaların tanısında etkili bir araçtır.

**Anahtar kelimeler:** Laparoskopi, peritoneal tüberküloz

## Introduction

Tuberculosis continues to be an important health problem in both developing and underdeveloped countries, though it is uncommon in the Western world (1). There are several case reports pointing out to an uncertainty in the preoperative differential diagnosis of female genital tuberculosis and advanced ovarian cancer, mainly due to the nonspecific nature of the common presenting symptoms, signs, and the further association of elevated CA-125 levels (2-12). A high index of clinical suspicion is mandatory for definitive diagnosis, since specific antituberculous therapy can obviate unnecessary laparotomies. This report of our experi-

ence with ten cases in the last eleven years, is concerned with the characteristics of clinical picture, radiologic imaging studies, laboratory tests and finally the role of laparoscopy in the diagnosis and management of peritoneal tuberculosis.

## Patients and Methods

Ten patients with peritoneal tuberculosis were operated at our clinic with suspicion of ovarian cancer during a 11-year period. Data were obtained from patients' files and pathology reports. The characteristics of the clinical picture, radiologic imaging studies, laboratory tests, including polymerase chain reaction and the role of laparoscopy in the diagnosis of peritoneal tuberculosis were evaluated for differentiation of ovarian cancers and peritoneal tuberculosis. Diagnosis of tuberculosis was based on the following histopathologic criteria: (1) the presence of a proliferative granulomatous lesion with central caseation necrosis surrounded by concentric layers of epithelial and giant cells with peripheral lymphocytes, monocytes and fibroblasts (8-13); (2) the presence of acid fast bacilli (Ziehl-Nielsen staining positive).

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## Results

The mean age of the patients was  $28.3 \pm 4.7$  years (median 28; range 22-37). All patients were referred to the gynecologic oncology unit with a history of abdominal swelling and pelvic-abdominal pain. The other symptoms were swelling in the legs and menstrual irregularity (in two patients); weight loss and lack of appetite (in one patient). Ascites was present in all patients, but no masses were palpable either abdominally or vaginally.

All patients had moderate iron deficiency anemia with a median hemoglobin level of 10.5 gr/dl; (range 9.7-11.1 gr/dl ) The white blood cell counts, platelet counts, erythrocyte sedimentation rates, liver function test results, urea concentration, and electrolyte levels were all within normal reference ranges. Intracutaneous injection of 5 tuberculin units of purified protein derivative caused a median skin induration of 11 mm for every patient (range 10-14 mm). A plain x-ray film of the chest showed normal appearance of the lungs, pleura, and mediastinum in all of the cases. All patients underwent abdominopelvic computerized tomography (CT), and transabdominal and transvaginal ultrasound examinations. All patients showed gross ascites and irregular thickening of the peritoneum. There were ovarian masses with heterogeneous textures of about 5 cm in size in two cases. Abdominal paracentesis was performed in the diagnostic work-up of all cases. Ascitic fluid was an exudate with lymphocytosis and no malignant cells. No acid-fast bacilli were seen by direct microscopy. Standard bacteriological and mycological cultures of ascitic fluids were negative. Results of tuberculosis polymerase chain reaction analysis of the ascitic fluid were negative. Sputum and urine cultures performed for all mycobacteria spe-

cies were negative. All patients had elevated serum CA 125 levels with a median of 162 U/ml, (range 75 to 500 U/ml). All patients had normal cervical smears and endometrial biopsies.

A diagnostic laparoscopy was performed in all cases. Ascites with a median of 4 liter (range 3 to 5.5 lt), miliary peritoneal lesions, and filmy adhesions throughout the peritoneal cavity were the major intraoperative findings. These findings were considered highly suggestive of tuberculosis. In two patients with ovarian masses documented by preoperative CT and ultrasound scans, exploration of the adnexae revealed corpus hemorrhagicum. Multiple biopsies were obtained from various parts of the peritoneum and the omentum. Frozen section examinations demonstrated granulomatous inflammation with necrosis, compatible with tuberculosis in all patients. Acid-fast bacilli were detected in the postoperative histopathological specimen of one patient. The postoperative courses of the patients were uneventful.

All the patients received antituberculous therapy with isoniazid, rifampicin, ethambutol and pyrazinamide. Treatment was started with a combination of four drugs for the first 3 months, and continued thereafter with three drugs for nine months. Preoperative high serum CA-125 levels were found to be within normal limits two months after the completion of therapy.

## Discussion

Although vaccination against the disease during early infancy is mandatory, tuberculosis is not a rare phenomenon in our country. Since the clinical pictures of the patients with peritoneal tuberculosis are similar to those of patients with ovarian cancer, we are used to consider peritoneal tuberculosis in the differential diagnosis of ovarian cancer. The most

common signs and symptoms were abdominal swelling, abdominopelvic pain, ascites and elevated serum CA-125 level (2,13) in our cases. Other infectious agents (e.g., Actinomyces species and other mycobacteria) may produce similar clinical pictures. Recently, a case of *Streptococcus milleri* infection mimicking ovarian carcinoma was reported (14). Age may also be used as a good clinical predictor in favour of peritoneal tuberculosis. The age range of our cases contributed to the findings of previous studies demonstrating that women with peritoneal tuberculosis were younger than those with ovarian carcinoma (2,15).

A strongly positive tuberculin test (Mantoux) is sometimes indicative of reactivation of tuberculosis (16). The 10 to 14 mm skin induration (+) of our cases seems to be related to prior vaccination. The results of chest X-rays and sputum cultures showed that these tests were not helpful in the diagnostic work-up, as reported by other authors (16,17).

In our cases, cultures of ascitic fluids failed to demonstrate the infection, in contrast with the cases reported by Irvin et al (15) and Piura et al (18). Guinea pig inoculation and culturing for tuberculosis have a turnaround time of about six weeks, which could be a detrimental delay in treatment in the case of the ovarian cancer patient. Combined use of guinea pig inoculation and culture also has a low sensitivity about 37% (19).

Ascitic fluid analysis for mycobacteria generally does not contribute to more than 25% of the tuberculous peritonitis diagnoses. Direct preparations of ascitic fluid were not found to be positive for acid-fast bacilli in our cases as previously demonstrated by Bilgin et al (17).

An elevated adenosine deaminase activity in fluids isolated from the serous cavities is considered to be

an excellent tuberculosis marker, though only a few centers use it as an exclusive measure for tuberculosis diagnosis (1). On histologic examination, epithelioid granulomatous lesions with necrosis are typically seen in cases of peritoneal tuberculosis. In one of our cases Ziehl-Nielsen stain revealed acid-fast bacilli, however this is not always the case and is not essential for diagnosis (6,20). Cytopathological evaluation of ultrasonographically guided peritoneal biopsies may be a diagnostic approach, though it was never practiced at our institution (21).

Polymerase chain reaction (PCR) for mycobacteria may be helpful for obtaining results earlier (22). However, tuberculosis PCR analyses failed to demonstrate the infection in ascitic fluid, in contrast to the cases reported by Irvin et al (15) and Piura et al (18). In our laboratory, IS6110 fingerprinting was performed using the standard reference protocol (23). It was an unexpected finding to see that all the PCR tests for tuberculosis on ascite fluids were negative even when one patient had acid-fast bacilli on histopathological examination. We could not find a reasonable explanation for this unusual finding.

Although ovarian carcinoma remains to be the first diagnostic choice in patients with elevated serum CA-125 levels, an elevation of CA-125 is not a guarantee of ovarian carcinoma, even in those women presenting with organic abdominal pathologies. Several reports have showed raised serum CA-125 levels, pelvic masses, ascites, or pleural effusions in cases of tuberculosis (6). In most reported cases, the CA-125 levels have been <500 U/mL, and in a study of 11 patients the mean level was 316.6 U/mL (6). In our cases both the median level, and the range of serum CA 125 (162 U/ml and 75 to 500 U/ml, respectively) were consistent

with the previous reports. Simsek et al noted that the association between elevated serum CA-125 levels, and peritoneal tuberculosis was not an incidental finding (24). Monitoring serum CA-125 levels is helpful to evaluate the effectiveness of medical treatment in patients with peritoneal tuberculosis. Serum CA-125 levels can be expected to normalize in two months as in our cases, and other relevant reports.

Sonographic features of tuberculous peritonitis may illustrate adnexal masses, adhesions and septated or particulate ascites. Omental and peritoneal thickening can also be seen (25). However, ultrasonography has conflicting results in previously reported cases, revealing ascites and complex pelvic masses (12,17). We detected adnexal pathology only in two cases and the sonographic features were not helpful in diagnosis.

In computerized tomographic examination, the presence of a smooth peritoneum with minimal thickening and pronounced enhancement suggests peritoneal tuberculosis, whereas nodular implants and irregular peritoneal thickening suggest peritoneal carcinomatosis (26). In a retrospective study, Ha et al showed that patients with tuberculosis were more likely to have mesenteric changes, macro-nodules (>5 mm in diameter), splenomegaly, and splenic calcification visible on CT imaging. Patients with carcinomatosis were more likely to show a more irregularly infiltrated omentum and to have the loss of the thin omental line covering the infiltrated omentum (27). They calculated the sensitivities of CT scan in the prediction of tuberculosis and carcinomatosis as 69% and 91%, respectively. However, CT imaging does not appear to be any more specific than ultrasonography for diagnosis of this condition, as consistently shown in our cases and

in other reports (18,28).

The most fruitful algorithm for the diagnosis of possible peritoneal tuberculosis remains to be established. In the case of a young patient with generalized ascites and no suspicious mass, an abdominal paracentesis may be the first step in the diagnostic algorithm. If direct cytologic examination, culture or PCR analysis of ascitic fluid are inconclusive, diagnostic laparoscopy should be performed to obtain multiple tissue samples. Paracentesis and laparoscopy are not only simple, effective and minimally invasive diagnostic tools but also can be therapeutic tools whenever uncertain conditions of massive ascites are noted. In one series of 200 patients with undiagnosed ascites, laparoscopy proved to be a safe method of providing a diagnosis (29). In another series of 135 patients with tuberculous peritonitis, 97% of cases were diagnosed on the basis of biopsy specimens taken during laparoscopy (24). Since the gross appearance of peritoneal tuberculosis may resemble that of a disseminated ovarian carcinoma, a frozen-section analysis should always be considered during the laparoscopy. If no carcinoma is detected, and histopathological examination is consistent with diagnosis of tuberculosis, unnecessary extensive surgery is avoided and a multi-drug anti-tuberculosis regimen should be started. In patients with a suspicious adnexal mass, performing paracentesis or laparoscopy may lead to recurrences in the needle tracts, and laparoscopic port sites in case of ovarian malignancy (30). In ovarian cancer patients with abdominal wall metastases, prognosis is reportedly worse (31). Therefore laparotomy seems to be reasonable in cases with adnexal masses. On the other hand Volpi et al emphasized the importance of laparoscopy for the differential diagnosis of tuberculosis in a

gynecologic cancer center (32).

In conclusion, our series of ten patients demonstrated that peritoneal tuberculosis should be suspected in young women with ascites with or without adnexal mass. Chest X-ray, PPD, sputum culture, direct preparation or PCR studies of ascitic fluid, CT and ultrasonography may be useful techniques in the diagnosis of peritoneal tuberculosis. Laparoscopy is an effective diagnostic tool in patients with no suspicious mass. Although elevated serum CA 125 levels are not helpful in the diagnostic period, it may be useful in the follow-up of patients.

### References

1. Marshall JB. Tuberculosis of the gastrointestinal tract and peritoneum. *Am J Gastroenterol* 1993; 88: 989-999.
2. Groutz A, Carmon E, Gat A. Peritoneal tuberculosis versus advanced ovarian cancer: a diagnostic dilemma. *Obstet Gynecol* 1998; 91: 868-871.
3. Gürkan T, Zeyneloğlu H, Urman B, Develioğlu O, Yaralı H. Pelvic-peritoneal tuberculosis with elevated serum and peritoneal fluid CA-125 levels. *Gynecol Obstet Invest* 1993; 53: 60-61.
4. Lachman E, Moodley J, Pitsoe SB. Peritoneal tuberculosis imitating ovarian carcinoma "special category". *Acta Obstet Gynecol Scand* 1985; 64: 677-679.
5. Miranda P, Jacobs AJ, Roseff L. Pelvic tuberculosis presenting as an asymptomatic pelvic mass with rising serum CA-125 levels: a case report. *J Reprod Med* 1996; 41: 273-275.
6. Nistal de Paz F, Herrero Fernandez B, Perez Simon R, et al. Pelvic-peritoneal tuberculosis simulating ovarian carcinoma: report of three cases with elevation of the CA 125. *Am J Gastroenterol* 1996; 91: 1660-1661.
7. Rao GJ, Ravi BS, Cheriparambil KM, Pachter B, Pujol F. Abdominal tuberculosis or ovarian carcinoma: management dilemma associated with an elevated CA-125 level. *Medscape Womens Health* 1996; 1: 2-7.
8. Sheth SS. Elevated CA 125 in advanced abdominal or pelvic tuberculosis. *Int J Gynecol Obstet* 1996; 52: 167-171.
9. Yoshimura T, Okamura H. Peritoneal tuberculosis with elevated serum CA 125 levels: a case report. *Gynecol Oncol* 1987; 28: 342-344.
10. Kiu MC, Hsueh S, Ng SH, et al. Elevated serum CA 125 in tuberculous peritonitis: report of a case. *J Formos Med Assoc* 1994; 93: 816-818.
11. O'Riordan DK, Deery A, Dorman A, et al. Increased CA 125 in a patient with tuberculous peritonitis: case report and review of published works. *Gut* 1995; 36: 303-305.
12. Penna L, Manyonda I, Amias A. Intraabdominal miliary tuberculosis presenting as disseminated ovarian carcinoma with ascites and raised CA125. *Br J Obstet Gynaecol* 1993; 100: 1051-1053.
13. Manidakis LG, Angelakis E, Sifakis S, et al. Genital tuberculosis can present as disseminated ovarian carcinoma with ascites and raised CA-125: a case report. *Gynecol Obstet Invest* 2001; 51: 277-279.
14. Branagan G, Woolas RP, Senapati A, Cripps NP. *Streptococcus milleri* infection mimicking ovarian carcinoma. *Br J Obstet Gynaecol* 1999; 106: 745-746.
15. Piura B, Rabinovich A, Leron E, Yanai-Inbar I, Mazor M. Peritoneal tuberculosis mimicking ovarian carcinoma with ascites and elevated serum CA-125: case report and review of literature. *Eur J Gynecol Oncol* 2002; 23: 120-122.
16. Bhansali SK. Abdominal tuberculosis: experiences with 300 cases. *Am J Gastroenterol* 1977; 67: 324-327.
17. Bilgin T, Karabay A, Dolar E, Develioğlu OH. Peritoneal tuberculosis with pelvic abdominal mass, ascites and elevated CA 125 mimicking advanced ovarian carcinoma: a series of 10 cases. *Int J Gynecol Cancer* 2001; 11: 290-294.
18. Irvin WP Jr, Rice LW, Andersen WA. Abdominal tuberculosis mimicking metastatic ovarian carcinoma. *Obstet Gynecol* 1998; 92: 709-714.
19. Bhargava DK, Shriniwas, Chopra P, Nijhawan S, Dasarathy S, Kushwaha AK. Peritoneal tuberculosis: laparoscopic patterns and its diagnostic accuracy. *Am J Gastroenterol* 1992; 87: 109-112.
20. Panoltkaltis TA, Moore DA, Haidopoulos DA, McIndoe AG. Tuberculous peritonitis: part of the differential diagnosis in ovarian cancer. *Am J Obstet Gynecol* 2000; 182: 740-742.
21. Mizunoe S, Morinaga R, Umeki K, et al. A case of tuberculous peritonitis diagnosed by ultrasonography-guided peritoneal biopsy. *Kansenshogaku Zasshi* 2000; 74: 589-593.
22. Ginesu F, Pirina P, Sechi LA, et al. Microbiological diagnosis of tuberculosis: a comparison of old and new methods. *J Chemother* 1998; 10: 295-300.
23. Van Embden JDA, Cave MD, Crawford JT, et al. Small, strain identification of *Mycobacterium tuberculosis* by DNA fingerprinting: recommendations for a standardized methodology. *J Clin Microbiol* 1993; 31: 406-409.
24. Simsek H, Savas MC, Kadayifci A, Tatar G. Elevated serum CA 125 concentration in patients with tuberculous peritonitis: a case-control study. *Am J Gastroenterol* 1997; 92: 1174-1176.
25. Yapar EG, Ekici E, Karasahin E, Gökmen O. Sonographic features of tuberculous peritonitis with female genital tract tuberculosis. *Ultrasound Obstet Gynecol* 1995; 6: 121-125.
26. Rodriguez E, Pombo F. Peritoneal tuberculosis versus peritoneal carcinomatosis: distinction based on CT findings. *J Comput Assist Tomogr* 1996; 20: 269-272.
27. Ha HK, Jung JI, Lee MS, et al. CT differentiation of tuberculous peritonitis and peritoneal carcinomatosis. *Am J Roentgenol* 1996; 167: 743-748.
28. Bankier AA, Herold CJ. Abdominal tuberculosis mimicking a gynecologic tumor (letter). *Am J Roentgenol* 1993; 161: 211-212.
29. Nafeh MA, Medhat A, Abdul-Hameed AG, Ahmad YA, Rashwan NM, Strickland GT. Tuberculous peritonitis in Egypt: the value of laparoscopy in diagnosis. *Am J Trop Med Hyg* 1992; 47: 470-477.
30. Gleeson NC, Nicosia SV, Mark JE, Hoffman MS, Cavanagh D. Abdominal wall metastases from ovarian cancer after laparoscopy. *Am J Obstet Gynecol* 1993; 169: 522-523.
31. Kruitwagen RF, Swinkels BM, Keyser KG, Doesburg WH, Schijf CP. Incidence and effect on survival of abdominal wall metastases at trocar or puncture sites following laparoscopy or paracentesis in women with ovarian cancer. *Gynecol Oncol* 1996; 60: 233-237.
32. Volpi E, Calgaro M, Ferrero A, Viganò L. Genital and peritoneal tuberculosis: potential role of laparoscopy in diagnosis and management. *J Am Assoc Gynecol Laparosc* 2004; 11: 269-272.