

Original Article

Pelvic tuberculosis, echinococcosis, and actinomycosis: Great imitators of ovarian cancer

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Aims: To evaluate the demographic, laboratory, clinical and imaging findings, surgical procedures and complications in women with final pathology results of pelvic tuberculosis (PT), pelvic echinococcosis (PE) or pelvic actinomycosis (PA) following exploratory surgery for suspicion of ovarian cancer.

Methods: Among 492 operations from January 2005 through January 2013, we retrospectively reviewed women with PT ($n = 15$), PE ($n = 6$), or PA ($n = 5$) mimicking ovarian cancer seen in an education and research hospital clinic.

Results: The mean ages of the women with PT, PE and PA were 34.2 ± 9.4 , 39.1 ± 11 and 46.3 ± 3.6 years, respectively. The serum CA-125 was elevated in 14 (93%), four (67%) and four (80%) women, respectively. The average CA-125 levels were 242.8 ± 240 , 104.3 ± 76.4 and 52.3 ± 18.6 IU/mL, respectively. The most common symptom was lower abdominal pain in 12 (87%), four (67%) and four (80%) women, respectively. The most common ultrasonography and computed tomography/magnetic resonance imaging finding was a pelvic mass in 11 (73%), six (100%) and five (100%) women, respectively. The most common surgical procedure was extensive adhesiolysis in 10 (67%), three (50%) and five (100%) women, respectively.

Conclusions: Pelvic tuberculosis, echinococcosis and actinomycosis must be included in the differential diagnosis of women suspected to have ovarian cancer with or without ascites and elevated CA-125 levels, especially in those living in endemic countries. During surgical exploration, frozen section analysis is important to avoid unnecessarily prolonged surgical procedures and retroperitoneal lymphadenectomy, which increases morbidity in women with these curable pelvic infectious conditions.

Key words: mimicking, ovarian cancer, pelvic actinomycosis, pelvic echinococcosis, pelvic tuberculosis.

Introduction

Although ascites, abdominopelvic masses and elevated serum CA-125 levels are most often associated with ovarian or gastrointestinal system malignancy, there are no pathognomonic signs, symptoms, markers or radiological criteria for diagnosing ovarian cancer.^{1–4} The diagnosis is usually made after performing an exploratory laparotomy or laparoscopy and conducting histopathological studies.^{3,4}

Tuberculosis, echinococcosis and actinomycosis are infections that have a propensity to spread to the adnexa and pelvic peritoneal surfaces. Their clinical manifestations and imaging findings can mimic ovarian cancer and create a diagnostic dilemma in gynaecological oncology.^{3–9} Consequently, some women can be subjected to an

unnecessary explorative laparotomy with an erroneous diagnosis of advanced ovarian cancer.^{3,4,7,9} Although pelvic tuberculosis (PT) and pelvic echinococcosis (PE) are common in the nonindustrialised countries, they can be detected in industrialised countries because of increases in global travel and immigrant populations.^{5,6,8} There is a growing amount of information concerning PT, PE and pelvic actinomycosis (PA) separately as imitators of ovarian cancer.^{3–9} However; at the time of our review, no published study had analysed and discussed these three nontumoural infectious conditions together in the pathological and gynaecologic oncological literature.

Therefore, we explored the clinical, laboratory, imaging and intra-operative features as well as the diagnostic surgical approaches for differentiating these three rare entities mimicking ovarian cancer based on our experiences and a literature review.

Materials and Methods

Our centre managed 492 women who underwent laparotomy or laparoscopy and frozen-section analysis for

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suspicion of ovarian cancer with or without ascites and elevated CA-125 levels as diagnosed by symptoms, clinical examination and imaging findings from January 2005 through January 2013. These cases were evaluated retrospectively. The clinical and imaging diagnostic criteria for suspicious complicated ovarian masses were as follows: (i) increased or unchanged size in eight weeks with the presence of severe pain, (ii) a palpable pelvic mass, (iii) abdominal swelling and (iv) a pelvic solid nodular or papillary mass of ≥ 5 cm, a multiloculated cystic mass with thick septation of >3 mm and an irregular appearance with or without ascites and elevated CA-125 values. Women with pathologically confirmed PT ($n = 15$), PE ($n = 6$), or PA ($n = 5$) were included in the study. At presentation, all women underwent computed tomography (CT) or magnetic resonance imaging (MRI) examinations of the abdomen and pelvis in addition to ultrasonography (USG), and all findings were available for review. The present study was approved by the institutional review board of Tepecik Education and Research Hospital, Izmir, Turkey.

The diagnosis of tuberculosis was made by finding a noncaseating granuloma with granulomatous inflammation histopathologically with acid-fast bacilli (positive Ziehl–Nielsen staining) and positive findings of tuberculosis at surgery (tubercles, caseation and adhesions). The diagnosis of echinococcosis was made by finding numerous daughter cysts on tissue sections and free scolices in the fluid aspirated from the cyst. Actinomycosis was diagnosed by finding acute and chronic inflammation and pathognomonic sulphur granules on haematoxylin and eosin staining.

Details of the study group were retrieved from the files and operation notes of the women, including demographic features (age, education status and intra-uterine contraceptive device (IUD) use), laboratory analysis (white blood count and CA-125 level), clinical features, USG and CT/MRI findings, intra-operative findings, surgical procedures performed and complications. Women's demographics and disease characteristics were presented as descriptive statistics calculated using MedCalc for Windows, Version 11.5 (MedCalc Software, Mariakerke, Belgium).

Results

Of the 492 women with a suspected pre-operative diagnosis of ovarian malignancy; 15, six and five women were found to have PT, PE and PA, respectively. The onset of symptoms ranged from four and 26 weeks prior to the surgery. The demographic, laboratory, clinical and preoperative imaging findings in PT, PE and PA are presented in Tables 1 and 2. The most common USG and CT/MRI finding was a pelvic mass in 11 (78%), six (100%) and five (100%) women, respectively.

None of the women with PT was receiving immunosuppressive therapy or had a family or personal history of tuberculosis. The mean age of the women with PT was 39.8 ± 9.5 (range, 27–59) years. Abdominal swelling and lower abdominal pain were the most common symptoms in women with PT. Fourteen (93.3%) of the women had elevated CA-125 levels (>35 U/mL). The mean CA-125 level was 242.8 ± 240 U/mL, and the mean adnexal mass size was 6.6 ± 2.3 cm. Chest X-ray

Table 1 The demographic, laboratory and clinical findings of women with pelvic tuberculosis, echinococcosis and actinomycosis

Characteristics	Pelvic tuberculosis ($n = 15$)	Pelvic echinococcosis ($n = 6$)	Pelvic actinomycosis ($n = 5$)
Age (years)†	39.8 ± 9.5	41 ± 9.9	49 ± 3.2
Leukocytosis‡	4 (27)	1 (17)	3 (60)
Ca-125 level (U/mL)†	242.8 ± 240	104.3 ± 76.4	52.3 ± 18.6
<35‡	1 (6.7)	2 (33)	1 (20)
35–200‡	8 (53.3)	4 (67)	4 (80)
200–1,000‡	6 (40)	–	–
Adnexal mass size (cm)†	6.6 ± 2.3	8.2 ± 2.4	7.4 ± 1.3
Education \leq eight years‡	13 (87)	4 (67)	3 (60)
IUD use and/or use history‡	5 (33)	3 (50)	5 (100)
Symptoms‡			
Menstrual disorder	5 (33)	2 (33)	1 (20)
Anorexia	4 (27)	–	1 (20)
Weight loss ($>10\%$)	4 (27)	–	1 (20)
Night sweats	2 (13)	–	–
Fever	3 (20)	–	2 (40)
Abdominal swelling	10 (67)	2 (33)	2 (40)
Lower abdominal pain	12 (80)	4 (67)	4 (80)
Constipation	1 (6.7)	–	3 (60)
Vaginal discharge	–	–	2 (40)

IUD, intra-uterine contraceptive device; SD, Standard deviation.

Values are expressed as †mean \pm SD, ‡ n (%).

Table 2 Pre-operative imaging findings of women with histological diagnoses of pelvic tuberculosis, echinococcosis and actinomycosis

Characteristics	Pelvic tuberculosis (<i>n</i> = 15)	Pelvic echinococcosis (<i>n</i> = 6)	Pelvic actinomycosis (<i>n</i> = 5)
USG, CT/MRI findings			
Ascites	11 (73)	–	–
Omental cake/thickening appearance	10 (67)	1 (17)	1 (20)
Unilateral pelvic mass	8 (53)	6 (100)	3 (60)
Bilateral pelvic mass	3 (20)	–	1 (20)
Peritoneal thickening	8 (53)	2 (33)	3 (60)
Bowel wall thickening	6 (40)	1 (17)	3 (60)
Peritoneal nodularity	8 (53)	–	–
Retroperitoneal lymphadenopathy	3 (20)	–	1 (20)
Pelvic retroperitoneal mass	–	–	1 (20)
Unilateral hydroureter	1 (6.7)	–	2 (40)
Unilateral hydronephrosis	1 (6.7)	–	1 (20)
Pleural effusion	1 (6.7)	–	–
Chest X-ray			
Normal	14 (93)	6 (100)	5 (100)
Abnormal	1 (6.7)	–	–

CT, computed tomography; MRI, Magnetic resonance imaging; USG, Ultrasonography.

All values are expressed as *n* (%).

was normal in 14 women, and one had minimal pleural effusion.

The mean age of the women with PE was 41 ± 9.9 [range, 29–57] years. Similar to PT, abdominal swelling and lower abdominal pain were the most common symptoms in the women with PE. Four of the six women in this group had elevated CA-125 levels (>35 U/mL). The mean CA-125 level was 104.3 ± 76.4 U/mL and the mean adnexal mass size was 8.2 ± 2.4 cm.

The mean age of the women with PA was 49 ± 3.2 (range, 44–52) years. Lower abdominal pain and constipation were the most common symptoms in these women. Elevated CA-125 levels (>35 U/mL) were seen in four women. The mean CA-125 level was 52.3 ± 18.6 U/mL, and the mean adnexal mass size was 7.4 ± 1.3 cm. Three women with PA were currently using IUD, and two had removed their IUD three months and one year earlier.

The intra-operative findings, performed diagnostic surgical procedures and intra- and postoperative

complications are demonstrated in Tables 3 and 4. A frozen-section determination at the time of surgery was not available in one woman aged 57 years who had a final pathological diagnosis of pelvic TB. This individual underwent complete staging surgery, including a total abdominal hysterectomy, bilateral salpingo-oophorectomy, appendectomy, infracolic omentectomy and pelvic and para-aortic lymphadenectomy because the lesions and view of the pelvis resembled those of advanced ovarian cancer. All women with pelvic tuberculosis, echinococcosis and actinomycosis completed anti-infective drug treatment successfully and were cured.

Discussion

This retrospective study reviewed the clinical, laboratory and diagnostic features of women with extra-ovarian infectious conditions that resembled ovarian malignancy. To the authors' knowledge, these three infectious

Table 3 Intra-operative findings of women with pelvic tuberculosis, echinococcosis and actinomycosis

Characteristics	Pelvic tuberculosis (<i>n</i> = 15)	Pelvic echinococcosis (<i>n</i> = 6)	Pelvic actinomycosis (<i>n</i> = 5)
Unilateral adnexal mass	9 (60)	6 (100)	3 (60)
Bilateral adnexal mass	3 (20)	–	1 (20)
Ascites	11 (73)	–	–
Caseous material	6 (40)	–	–
Peritoneal adhesions	11 (73)	3 (50)	5 (100)
Frozen pelvis	6 (40)	1 (17)	4 (80)
Peritoneal miliary nodules	10 (67)	–	–
Omental mass/thickening/caking	10 (67)	1 (17)	2 (40)
Retroperitoneal mass	–	–	1 (20)
Bulky retroperitoneal lymph nodes	4 (27)	–	1 (20)

All values are expressed as *n* (%).

Table 4 Surgical procedures, intra- and postoperative complications in women with pelvic tuberculosis, echinococcosis and actinomycosis

Characteristics	Pelvic tuberculosis (n = 15)	Pelvic echinococcosis (n = 6)	Pelvic actinomycosis (n = 5)
Surgical procedures			
Laparoscopy	6 (40)	1 (17)	2 (40)
Laparotomy	9 (60)	5 (83)	3 (60)
Extensive adhesiolysis	10 (67)	3 (50)	5 (100)
Total abdominal hysterectomy	1 (6.7)	–	2 (40)
Ovarian wedge biopsy	6 (40)	–	–
Unilateral salpingo-oophorectomy	4 (27)	6 (100)	3 (60)
Bilateral salpingo-oophorectomy	2 (13)	–	2 (40)
Omental biopsy	9 (60)	1 (17)	2 (40)
Multiple peritoneal biopsy	10 (67)	1 (17)	2 (40)
Pelvic abscess elimination	–	–	5 (100)
Retroperitoneal mass elimination	–	–	1 (20)
Appendectomy	1 (6.7)	–	1 (20)
Infracolic omentectomy	1 (6.7)	–	–
Pelvic + para-aortic lymphadenectomy	1 (6.7)	–	–
Intra- and postoperative complications			
Conversion to laparotomy	3/6 (50)	–	2/2 (100)
Intra-operative blood transfusion	1 (6.7)	–	1 (20)
Small bowel injury	1 (6.7)	–	1 (20)
Rectovaginal fistula	1 (6.7)	–	–

All values are expressed as *n* (%).

conditions mimicking ovarian cancer have not previously been discussed together.

Almost invariably, tuberculosis of the genital tract is secondary to disease elsewhere, usually in the lungs. Approximately 5–13% of women with pulmonary tuberculosis develop a genital infection.³ Tuberculosis remains a global health problem, especially in low-resource countries. Although it is uncommon in industrialised countries, it can be seen in immigrant populations who were born or travelled in areas where the tuberculosis incidence was high and in women infected with human immunodeficiency virus. Female genital tuberculosis is rare in some developed countries, but it is a frequent cause of chronic pelvic inflammatory disease and infertility in other parts of the world.^{5,6}

Peritoneal tuberculosis can mimic ovarian carcinoma, as it usually presents with vague symptoms and signs. The detection of free peritoneal fluid is common and can vary from a small pelvic collection to gross abdominal ascites. Pre-operative abdominal paracentesis and cytology may not aid in the differential diagnosis because only 57% of patients with intra-abdominal malignant tumours and ascites are positive for malignant cells.¹⁰ However, pre-operative abdominal paracentesis¹¹ and USG- or CT-guided tru-cut biopsy^{11,12} can be useful in selected young women suspected to have PT. In cases of tubal tuberculosis, an irregular adnexal mass might also be present, further complicating the pre-operative diagnosis. The CA-125 levels are commonly very high, especially in cases with extensive miliary dissemination.^{4,13} In our series, only one woman had a CA-125 level of <35 U/mL; it was

35–200 U/mL in eight cases and 200–1000 U/mL in six. Abdomino-pelvic imaging is often inconclusive and can be misleading.

In previous studies, women with PT were younger than women with ovarian carcinoma.^{3,4,11,12} In our study, the mean age of the women with PT was 39.8 ± 9.5 (range, 27–59) years. Although some reports have suggested performing a laparoscopic biopsy to achieve a histological diagnosis,^{4,5,13} a laparotomy might be more appropriate because the extensive adhesions in the abdomen caused by peritoneal tuberculosis can increase the risk of intestinal complications during laparoscopy.^{3,14} During laparoscopy or laparotomy, the gross appearance of peritoneal tuberculosis can resemble advanced ovarian carcinoma, and a frozen section is mandatory to discriminate the two clinical entities.^{3,11,12} Women without an intra-operative frozen-section evaluation sometimes undergo unnecessary extensive surgery.⁴ In our series, nine women were managed with laparotomy, and six underwent a laparoscopic evaluation. However, the laparoscopic evaluation revealed extensive adhesions in three women, and the operation was converted to a laparotomy. For one woman, no frozen-section determination was available at the time of surgery; this woman underwent extensive and complete staging surgery, including a total abdominal hysterectomy, bilateral salpingo-oophorectomy, appendectomy, infracolic omentectomy and pelvic and para-aortic lymphadenectomy because the lesions resembled an advanced ovarian cancer.

Actinomycosis is a chronic suppurative and granulomatous infection caused by *Actinomyces israelii*, a gram-positive, non-spore-forming anaerobic to

microaerophilic organism.^{15–18} PA accounts for about 3% of all actinomycotic infections and is commonly associated with IUD use. Ovarian involvement is distinctly uncommon.^{9,15–20} In our series, all of the women with PA had an IUD and/or had history of IUD use.

The diagnosis of actinomycosis is difficult to establish pre-operatively.^{16,19–21} The clinical symptoms are usually nonspecific and include a wide range of clinical presentations. Acute abdomen can develop following perforation or fistulisation; abdominal pain is present more frequently, as in the women with PA in our study. The CA-125 level can be elevated in women with PA, although not as much as in those with PT. In our series, 80% of the women had CA-125 levels higher than 35 U/mL. Many cases are diagnosed when infection is advanced, when hydronephrosis occurs due to ureteral compression by the pelvic abscesses, and when the disease becomes severe, with tubo-ovarian abscess formation leading to rectosigmoid colon obstruction and 'frozen pelvis' and mimicking pelvic cancer.^{15–21} Similar to PT, a frozen section is mandatory during the surgery to discriminate ovarian carcinoma and to avoid complete staging procedures and, pelvic and para-aortic lymphadenectomy.

Pelvic echinococcosis commonly presents as a suspected ovarian malignancy.^{3,7,8,22–26} The incidence of pelvic echinococcus cysts is 0.2–0.9% in endemic countries.^{23–25} In pelvic cases, the ovary is the most frequent location, followed by the uterus.^{8,24–26} This usually occurs through the transcoelomic spread of a ruptured liver cyst or rarely a splenic cyst. The symptoms of PE are nonspecific and include abdominal pain, swelling, menstrual irregularities, infertility and pressure symptoms involving adjacent organs, including the bladder and rectum.^{7,22,23} In our study of women with PE, low abdominal pain was the most common symptom.

The CA-125 level can be mildly elevated in PE. The CA-125 level was elevated in 67% of our cases of PE (35–200 U/mL). Radiological imaging techniques can be useful for making the preoperative diagnosis, although there are many imaging similarities between hydatid cysts and pelvic malignant diseases. Daughter cysts can resemble septal structures and mimic a multicystic ovarian malignancy such as cystadenocarcinoma.^{7,8,22–26} In our series, there was no evidence of hydatid disease of the liver or lung in the chest X-rays, USG or CT. Ozat *et al.*²³ stated that laparotomy is the gold standard treatment for PE. We performed an exploratory surgery in five with laparotomy and one with laparoscopy and detected unilateral adnexal masses in all women with PE. Similar to PT and PA, a frozen section is mandatory during the surgery to discriminate ovarian carcinoma.

Potential limitations of this study were its retrospective nature and relatively small sample size, especially for PE and PA. Moreover, all female patients were suspected to have ovarian malignancy (in view of the adnexal mass, ascites and/or elevated CA-125 level) and underwent surgery for the diagnosis. In addition, no cases pre-operatively resembled tubo-ovarian abscesses.

In conclusion, medical awareness of these infectious diseases in the differential diagnosis of ovarian malignancy is still lacking, especially in developing countries. Unfortunately, routine physical, radiological, and laboratory examinations are not sensitive enough to distinguish these nontumoural infectious diseases from advanced ovarian cancer. The important findings in our study were as follows: (i) PT should be considered in young women of low socioeconomic status living in endemic areas who present with symptoms such as a pelvic mass, ascites and elevated CA-125 levels; (ii) PA should always be considered in women of reproductive age with a pelvic mass, especially those with an IUD *in situ* or who recently had an IUD removed; (iii) PE should be considered in the differential diagnosis of pelvic masses, especially in women residing in or coming from endemic areas; and (iv) during laparotomy or laparoscopy, an intra-operative frozen section should be performed to achieve the correct diagnosis and avoid unnecessary surgical approaches and retroperitoneal lymphadenectomy, which increases morbidity in these curable nontumoural pelvic infectious conditions.

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