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Peritoneal tuberculosis mimicking ovarian cancer — diagnostic difficulties. A report of two cases

Abstract

Tuberculosis, and particularly its extrapulmonary location, still causes diagnostic difficulties. In 2007, 7.3% of newly registered cases of tuberculosis in Poland were located extrapulmonarily. Peritoneal tuberculosis is often misdiagnosed as ovarian cancer due to similar symptoms such as: abdominal pain, abdominopelvic masses, ascites and elevated CA-125 serum concentration. We present reports of two patients with suspected ovarian cancer at admission. The patients' complaints, as well as elevated serum levels of CA-125, suggested ovarian cancer. Chest X-rays showed a normal picture in one case and minimal fibrotic changes in the other. The results of additional tests were uncharacteristic. Based on the data obtained by diagnostic laparoscopy, observed clinical symptoms and the intraoperative picture, which all suggested ovarian cancer, a resection (total abdominal hysterectomy and bilateral salpingo-oophorectomy) was performed in both cases. Histological evaluation of biopsy specimens revealed peritoneal tuberculosis in both cases.

Key words: ovarian cancer, peritoneal tuberculosis, differential diagnosis

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Introduction

Tuberculosis (Tb) morbidity has recently decreased in most countries. Epidemiological data indicates that the incidence of tuberculosis in Poland in 2007 was 22.7/100 000, and cases of extrapulmonary location accounted for 7.3% of all newly registered patients [1]. Extrapulmonary Tb is regarded as a serious diagnostic problem and according to the international data it comprises around one in five of all forms of Tb. This may indicate a poor rate of Tb diagnosis in Poland or poor reporting of new cases to epidemiological databases.

Peritoneal Tb is considered a rare extrapulmonary form, but at the same time this location is five

or six times more frequent than the location in any other organs of the alimentary system. Peritoneal Tb is initiated by the infiltration from altered mesenteric or intestinal lymphatic nodes. There is also the possibility of its spreading via the bloodstream from the primary site in the lungs. Weakness, loss of appetite, fever, abdominal pain and enlarged abdominal circumference are the usual clinical symptoms. Physical examination reveals pathological lesions in abdominal cavity and ascites, while laboratory test shows increased serum concentration of antigen CA-125. Because of uncharacteristic symptoms, peritoneal Tb is often pre-surgically unrecognized and misdiagnosed in the female population as an ovarian cancer [2–8]. Increased concentration of antigen CA-125 may

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Table 1. Characteristics of patients with peritoneal tuberculosis

	Case 1	Case 2
Age	41	24
Gravidity/labor	2/2	1/1
Past medical history	Excochleation of the uterus, removal of breast fibroma	Hypothyreosis, rheumatic arthritis
Signs and symptoms	Hypogastric pain, sub-febrile body temperature	Hypogastric pain, sub-febrile body temperature, increased abdominal circumference
Gynecological examination	Muco-bloody excretion in cervical canal, normal size, mobile uterus, thickening of right uterine adnexa, normal left uterine adnexa	Fluid in Douglas pouch, cervical erosion, orange- size tumor at the left adnexal region
Chest rentgenogram	Normal	Fibrous changes at the apex of the left lung
Pelvic ultrasonography	Free fluid in abdominopelvic cavity, heterogenic right ovary, enlarged and heterogenic left ovary, structure corresponding to endometrial polyp in uterus cavity	Free fluid in abdominopelvic cavity, a cyst with dense content in the left ovary 55 × 39 mm (diameter: 37 mm), right ovary dimensions: 32 × 20 mm
Computer tomography	No examination	Enlarged bowel loop, a polycystic formation with fuzzy border located in the Douglas pouch and corresponding to pathological masses
CA-125 [IU/ml]	691	600

also be found in cases of pelvic inflammation, endometriosis, uterine fibroma, hepatitis and peritonitis. This means careful interpretation of antigen CA-125 results and comparison of these results with the patient's clinical status are needed [6, 8].

The results of ultrasound and computer tomography (CT) images are also uncharacteristic and frequently do not allow for the proper diagnosis [8–10]. The diagnosis of peritoneal Tb is established late, most often during diagnostic laparoscopy or laparotomy [11]. Histological examination of the peritoneal samples is of crucial importance [12].

In 2007, two patients with suspected ovarian cancer were admitted to our department. The pre-surgical clinical picture, high serum concentration of antigen CA-125, ultrasound and CT imaging, all suggested ovarian cancer, which resulted in the performance of total hysterectomy with adnexa, resection of greater omentum, and lymphatic nodes and appendectomy. Histological evaluation of a paraffin block specimen revealed peritoneal Tb. The demographic and clinical characteristics of the two patients are presented in Table 1.

Case 1

A 41 year-old woman had seen the doctor because of painful discomfort in the hypogastrium and a sub-febrile body temperature she had been suffering from for three weeks. Excochleation of the uterus cavity because of voluminous menstruation had been performed two years before and

breast fibroma was removed 15 years earlier. Nicotine, alcohol and drug addiction anamnesis were negative. The patient reported two uncomplicated spontaneous labors and regular menstruations. Her sister had died of cervical cancer.

Gynecological examination presented bloody mucosal excretion in the cervical canal. The normal size uterus was mobile, right adnexa were thickened and left ones non-palpable. Microbiological assessment of the vaginal smear showed *Staphylococcus epidermalis* and *Enterococcus spp.* Free fluid in peritoneal cavity, normal size but heterogenic structure of the right ovary and enlarged up to 5 cm in diameter, cystico-solid left ovary were revealed by ultrasound imaging. The uterus cavity contained a 0.5 cm long structure which might correspond to an endometrial polyp. Chest X-ray was normal. Laboratory tests were positive for HbS antigen and increased value of serum CA-125 (691 IU/ml; normal value is up to 35 IU/ml). Diagnostic laparotomy revealed the presence of 300 ml yellow-green liquid. Abdominal and pelvic peritoneum was covered with multiple small Tb nodules. The right ovary had an uneven papular surface. Retroperitoneal lymphatic nodes of small pelvis, located along iliac vessels on both sides, were enlarged up to 0.5–1.0 cm and poorly mobile. Because the clinical and intraoperative picture suggested an advanced stage of ovarian cancer, the patient underwent a total hysterectomy with adnexa, resection of greater omentum and pelvic lymphatic nodes, and appendectomy. Intraoperative inspection of right adnexa showed follicular

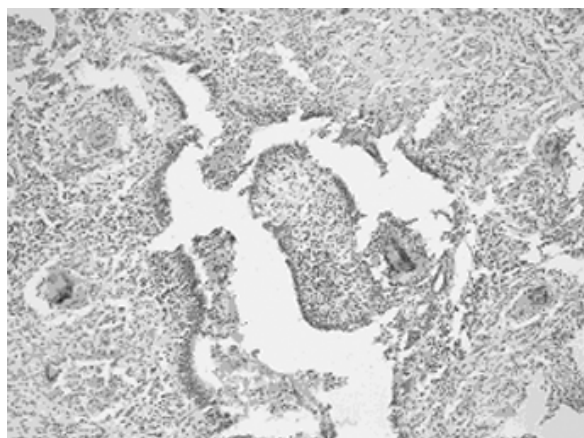


Figure 1. Histopathological picture of the uterine tube sampling. Numerous granulomas with Langhans giant cells. Staining HE. Magnification $\times 100$

cysts and cysts of corpus luteum, and pyosalpinx was suspected in the oviduct. Non-neoplastic focuses were found. The final diagnosis was not made before all surgically removed organs were checked. Histological evaluation disclosed multiple tuberculomas in all specimens taken from the peritoneum, omentum, lymphatic nodes, and also uterus disc, canal and cavity (Fig. 1). The oviduct was massively compromised by proliferative inflammation and caseous degeneration. It was impossible to perform Ziehl-Nielsen staining. Peritoneal Tb passing to reproductive organs was finally diagnosed. After discharge, the patient was given antituberculous treatment under the super-

vision of the Outpatient Clinic of Pulmonology in Zabrze.

Case 2

A 24 year-old woman was referred with a diagnosis of cystic tumor of the left ovary. Pain in the hypogastrium, sub-febrile body temperature and increased abdominal circumference had lasted for a month and were the reasons for admission to the municipal hospital. The patient had been treated for rheumatoid arthritis with non-steroid anti-inflammatory medications for the previous three years. She was not addicted to cigarettes, drugs or alcohol. Her obstetric history included one uncomplicated vaginal labor and regular, ample menstruations. Family history was unremarkable.

Ascites was revealed in physical examination as well as fluid in the Douglas pouch, cervical erosion and a 5 cm in diameter tumor in the projection of left adnexa were found by gynecological inspection. An abdominal ultrasound showed: large amount of free fluid in the peritoneum, a 40 mm in diameter cyst with dense content in the left ovary (55 \times 39 mm) and right ovary (32 \times 20 mm). Ambiguous clinical picture was the reason for pelvic CT, which disclosed expanded bowel loops and polycystic formation with partially blurred outline contour in projection of the Douglas pouch, corresponding to pathological masses (Fig. 2). The chest X-ray revealed fibrotic changes in the apex of the left lung. Serum antigen CA-125 concentration was 600 IU/ml (normal value < 35 IU/ml).



Figure 2. CT image of pelvis minor (case 2) — a polycystic formation in the projection of Douglas pouch

The miliaire spread covering the whole surface of the peritoneum, and multiple small tubercles particularly in the pelvis, as well as 300 ml of straw-colored fluid were found by exploratory laparotomy. The uterus was of normal size. The left ovary with nodular alterations and uneven surface, partially fused with the lamina of uterus broad ligament was localized in the Douglas pouch. In the small pelvis, retroperitoneal lymphatic nodes were 0.5 cm in diameter and poorly mobile. Based on the clinical and intraoperative picture, which suggested advance ovarian cancer, a total hysterectomy with resection of adnexa, greater omentum, and pelvic lymphatic nodes, appendectomy and peritoneal adhesions liberation were performed. Intraoperative inspection revealed a cyst, 50 mm in diameter, filled with bloody content, in the left ovary. Multiple giant cell granulomas were seen in the wall of the cyst. Neoplastic focuses were not found. Three units of fresh frozen plasma and three units of blood were transfused due to massive blood loss during surgery. The final diagnosis was made based on the histopathological evaluation of a paraffin block specimen of all organs removed during the surgery. All biopsy specimens of peritoneum, omentum, pelvic lymphatic nodes, and left adnexa showed proliferative inflammation and caseous degeneration, suggesting tuberculosis. Peritoneal Tb with the involvement of reproductive organs was finally diagnosed. The standard antituberculous treatment was administered after discharge and the patient was overseen by the Outpatient Clinic of Pulmonology in Zabrze.

Discussion

Peritoneal Tb comprises 1–3% of all cases of Tb [2, 7]. Body weight loss, weakness and sub-febrile body temperature are the commonest symptoms. Uncharacteristic symptoms of abdominal and pelvic involvement, such as: ascites, pathological abdominal masses and increased serum antigen CA-125 concentration, often suggest neoplastic process in an ovary. That is why peritoneal Tb is misdiagnosed as ovarian cancer, and patients undergo unnecessary extensive surgical removal of their reproductive organs [2–4, 10, 11].

In the study by Koc et al., among 1826 women hospitalized for suspected ovarian cancer, 22 were diagnosed with peritoneal Tb, 1.2% of all cases [4]. Whereas Bilgin et al. showed that the percentage of patients with peritoneal Tb, who were diagnosed with ovarian cancer during the 5-year follow-up, was 1.4% [8].

The two patients whose cases we report in this paper were admitted with a suspected neoplastic process in their ovaries. Both women presented uncharacteristic symptoms, such as sub-febrile body temperature and hypogastric pain. Furthermore, in the second patient there was an increase of abdominal circumference. Koc et al. revealed that the most frequent symptoms observed in women with peritoneal Tb were: increase of abdominal circumference (81%), hypogastric pain (54%) and body weight loss (27%). All patients had ascites and hypogastric pathological masses were found by palpation in 77% of women [4]. Gurbuz A. et al. showed that all patients with peritoneal Tb presented abdominal pain, pathological abdominal masses, decrease in body weight and ascites [2]. Such observations have been confirmed by other authors [5, 8, 10, 13]. It has to be emphasized however, that all these symptoms are unspecific and frequently found in women with ovarian cancer.

The other described woman had been treated for rheumatoid arthritis with non-steroid anti-inflammatory medications for three years. It is well known that steroid therapy raises the risk of Tb reactivation and occurrence of extrapulmonary tuberculous lesions. It was also suggested that rheumatoid arthritis by itself, even non-treated, remained a risk factor of Tb progression [14].

Additional tests in the case of peritoneal Tb unfortunately have low sensitivity and specificity. In peritoneal Tb, the ultrasound and CT images of abdominal cavity usually reveal ascites, pathological abdominal masses, thickening of the peritoneum and enlargement of retroperitoneal lymphatic nodes [3, 8, 10, 11, 15]. The patients hospitalized in our department had the above described changes in ultrasound imaging. CT performed in the second patient showed expanded bowel loops and polycystic formation with partially blurred outline contour in projection of the Douglas pouch, corresponding to pathological masses. The sensitivity of CT imaging in the diagnosis of peritoneal Tb and peritoneal neoplastic process is regarded as 98% and 70% respectively [16].

A non-specific marker (antigen CA-125) is used to diagnose ovarian cancer. It must be remembered however, that its increased serum concentration may also occur in women in the following clinical situations: inflammatory process in the pelvis, endometriosis, uterus fibroma, hepatitis, pancreatitis and peritonitis [6, 17, 18]. Koc et al. found elevated levels of antigen CA-125 in 90.1% of women with peritoneal Tb, and the mean value

was 565 U/ml [4]. This result has been confirmed by other researchers [8, 10, 11].

In both presented cases the concentration of antigen CA-125 was high. According to Simsek et al., serial determination of antigen CA-125 concentration in the group of women with peritoneal Tb may be helpful in the evaluation of disease activity and the response to antituberculous treatment [19]. This observation was verified by others [8, 10, 17], who showed a decrease of antigen CA-125 after antituberculous therapy. In the analysis made by Bilgin et al., including 10 patients with peritoneal Tb, the concentration of CA-125 was high in all cases and amounted to a mean value of 331 U/ml [8]. Moreover, in four cases pericentesis was performed and a high concentration of antigen CA-125 was found in ascitic fluid with a mean value of 855 U/ml. After completion of antituberculous therapy, the concentration of this marker decreased.

Peritoneal Tb usually spreads via the blood stream from the primary site in the lungs or by activation of the lesions located in mesenteric lymphatic nodes or secondary to intestinal tuberculosis [20]. It has to be emphasized that the chest X-ray of most patients with peritoneal Tb is normal [5, 16]. This was also the finding in the presented cases. Very often the microbiological culture of fluid obtained during the pericentesis and sputum may not be positive for acid-fast bacilli. Besides, a tuberculin test may be negative, and that makes correct diagnosis and initiation of the proper treatment even more difficult [2, 11].

The characteristic microbiological picture of tuberculoma lesions with central caseating necrosis and peripheral location of Langerhans giant cells are not always observed [16]. In the paper by Piura et al., in four female patients with peritoneal Tb, the typical tuberculomas were found in microscopic evaluation, but Ziehl-Nielsen staining did not reveal acid-fast bacilli. The PCR method however confirmed tuberculosis [10].

The similarity of clinical picture between peritoneal Tb and ovarian cancer, as well as the fact that results of laboratory tests and ultrasonography or CT images do not allow for final diagnosis, are reasons to perform diagnostic laparotomy [8, 11]. As in the presented cases, neither ultrasound nor CT imaging allowed preoperative recognition of peritoneal Tb.

The most frequent observations during the diagnostic laparoscopy and laparotomy in women with peritoneal Tb are ascites, diffused changes on the peritoneal surface and adhesions [8, 11].

According to Koc et al., preoperative diagnosis of peritoneal Tb in female patients admitted to

the hospital due to suspicion of ovarian cancer was possible only in two out of 22 patients [4]. In the others, laparotomy or laparoscopy with histological sampling was necessary to make a diagnosis. Piura et al. described four female patients with peritoneal Tb, but proper diagnosis based on laparoscopy was made only in one case, which made it possible to avoid surgery. Other patients underwent diagnostic laparotomy followed by surgical removal of the reproductive organs [10]. That is why the availability of intra-operative histological examination is of crucial importance. This diagnostic procedure in the majority of cases allows differentiation between a neoplastic process and a granulomatous inflammation. It helps avoid unnecessary surgical removal of uterus and adnexa. However, the diagnosis of Tb can be made only after histological evaluation of paraffin block samplings, based on characteristic microscopic picture and positive Ziehl-Nielsen staining. The growth of *Mycobacterium tuberculosis* in the microbiological cultures of samplings is the foundation of the decisive diagnosis of tuberculosis. The presented patients underwent a total hysterectomy with adnexa, greater omentum, and pelvic lymphatic nodes removal, and also appendectomy. The diagnosis was however possible on the basis of evaluation of paraffin block samplings. The study by Manidakis et al. proves that patients with a pathological picture of masses in the projection of adnexa should undergo exploratory laparotomy, but those with ascites may benefit from diagnostic laparoscopy [9]. As is emphasized by Gurbuz et al., the exclusion of peritoneal Tb is of crucial importance for women suspected of having ovarian cancer, who are considered for neoadjuvant chemotherapy [2].

The reported patients did not have Tb decisively confirmed by the positive culture of *M. tuberculosis*. Nevertheless, the result of histological evaluation and the subsequent course of treatment evidently supported this diagnosis.

Conclusions

1. Tuberculosis of the abdomen and reproductive organs should always be considered in the differential diagnosis of women with symptoms suggesting ovarian cancer.
2. Intra-operative histopathological evaluation of the samplings is of crucial importance in the diagnosis of peritoneal tuberculosis in women with suspected ovarian cancer and may guard against unnecessary surgical removal of reproductive organs.

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