Case Report

Peritoneal Tuberculosis Mimicking Ovarian Cancer: Gynecologic Ultrasound Evaluation with Histopathological Confirmation

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Abstract: Peritoneal tuberculosis (TBP) is a very rare condition, accounting for about 1–2% of all tuberculosis cases. The diagnosis of TBP can be easily mistaken for advanced ovarian cancer (AOC) or peritoneal carcinoma because of overlapping laboratory and clinical findings. We reported the ultrasound characteristics of a case of TBP in a 67-year-old woman who presented to our institute with a 1-month history of intermittent lower abdominal pain, fever, and asthenia. Overall, 20 biopsy-retrieved specimen histopathological features were suggestive of peritoneal tuberculosis. Gynecologic ultrasound revealed increased adnexa with multiple nodular formations spread across the surface, suggestive of caseous nodules. Although this is a rare occurrence, clinicians should consider TBP as a differential diagnosis of ovarian or peritoneal cancer.

Keywords: peritoneal tuberculosis; ovarian cancer; peritoneal disease; Mycobacterium tuberculosis; gynecologic ultrasound

1. Introduction

Worldwide, tuberculosis (TB) is still a very significant cause of morbidity and mortality [1]. About one-third of the world population, more than 2 billion people, is a carrier of latent infection with Mycobacterium tuberculosis and new cases amount to 9 million every year. Due to delays in diagnosis, inability to access drugs, or failure to adhere to prescribed regimens, approximately 1.5 million people die from TB each year [2]. TB is a chronic granulomatous infectious disease caused by Mycobacterium tuberculosis and commonly affects the respiratory system. For these reasons, lung disease is the most common TB presentation, but other manifestations are also possible depending on the duration and location of the disease [3]. Peritoneal TB (TBP) is rare, accounting for about 1–2% of all TB cases. TBP may rarely be transmitted sexually, with the majority of cases resulting from reactivation of latent TB foci in the peritoneum or from the lymphatic or hematogenous spread of primary pulmonary infection [4]. The diagnosis of TBP can be easily mistaken for advanced ovarian cancer (AOC) or peritoneal carcinoma because of overlapping laboratory and clinical findings, including elevated CA125 levels, abdominal pain, ascites, and pelvic mass [5–7]. Here, we present a case of peritoneal localization of tuberculosis in a 67-year-old patient who, due to diagnostic difficulties, represented a diagnostic challenge for the clinician and was then confirmed by histopathological analysis.
2. Case Presentation

A 67-year-old Italian woman (para 2) presented to our institute with a 1-month history of intermittent lower abdominal pain, fever, and asthenia. She had no medical, surgical, or family history of malignancy. Blood tests showed elevated levels of CA125 (671 U/mL, normal range 0–35 U/mL) and C-reactive protein (CRP) (220 mg/L, normal range < 2.9 mg/L). Complete blood count was normal. Gynecologic ultrasound revealed increased adnexa bilaterally with inhomogeneous echostructure (Figure 1). The right one was 52 × 39 mm, whereas the left one was 46 × 31 mm. Multiple nodular formations were spread across the surface (Figure 2).

Figure 1. Ultrasound revealed bilaterally increased adnexa with dishomogeneous echostructure.

Figure 2. Multiple nodular formations were spread across the surface.
The uterus was fixed. The peritoneum of the Douglas appeared obliterated. There was evidence of thickening of the meso-sigma-rectum, omental cake, and diffused packing of the small bowel. Abdominal-pelvic computed tomography (CT) confirmed that both ovaries were increased in volume with multiple nodulations with peripheral hyperdense labrum with diffused packing of the small bowel and lymphadenopathy. Chest X-ray and chest CT were negative. A laparoscopy was performed and thick white granulomatosis covering the uterus and partially filling the Douglas pouch was identified. The adnexa had transformed into tubo-ovarian complexes, with the salpinges were grossly dilated and tenaciously adherent to the ovaries with nodules on the surface. The small intestine was diffused and packed. Omental and peritoneum biopsies were performed.

Histopathological results revealed the presence of granulomatous lesions with central caseous necrosis and Langhans giant cells; there were also lymphocytes, plasma cells, fibroblasts, and histiocytes. Caseous necrosis was located in the center of the granuloma and consisted of amorphous acidophilic material with protein-rich granulations and lipids (Figure 3a,b).

Figure 3. (a) Histological preparation comprising foci of caseous necrosis surrounded by multinucleated giant cells together with lymphocytes and plasma cells (Hematoxylin-Eosin, original magnification 100×). (b) Details of previous microphotograph (Hematoxylin-Eosin, original magnification: 200×).
The patient was referred to the infectious disease unit. The woman started treatment with rifampicin, ethambutol hydrochloride, and moxifloxacin. After 6 months, CA125 and CRP were normal; after 18 months, gynecologic ultrasound evaluation revealed restitutio ad integrum of the pelvic organs.

3. Discussion

TBP often mimics the presentation of advanced OC. Therefore, the differential diagnosis may be challenging. Involvement of almost every organ has been described in extrapulmonary TB infection (EPTB), including lymphatic, pleural, bone and joint, genitourinary, and meningeal sites. TBP is the sixth most common site of EPTB, accounting for 4.9% of all EPTB cases [3,4]. TB may reach the peritoneum hematogenously through the lymphatic system by the ingestion of contaminated sputum from pulmonary TB, contaminated food (especially unpasteurized dairy in the case of Mycobacterium bovis), or through direct extension from adjacent foci of infection [8,9]. All those conditions compromise the immune system, such as liver disease and alcoholic liver disease, as well as HIV infection, peritoneal dialysis, and neoplasms [10,11]. The most common ultrasonographic and CT findings in patients with TBP are ascites with or without septations, peritoneal thickening, mesenteric and omental involvement, thickened ileal valve and bowel, mesenteric adhesions, and lymphadenopathy. Chest CT scans can be helpful in the diagnostic management of this disease. In a study of Liu et al. [12], an abnormal chest CT scan was found in 15/28 (53.57%) including 10 pleural effusions, 2 fibrocalcific, 1 enlarged mediastinal lymph nodes, 1 pleural thickening, and 1 thoracic vertebra TB. A report of Devi et al. [13] described seven patients with pelvic TB who had suspected diagnosis of ovarian cancer preoperatively. The mean age was 34 years (range, 20–52). The most common presentation symptoms were abdominal pain and distension. A history of fever was present in five patients (71%) and a clinically palpable adnexal mass was revealed in all of them. Six (85%) had ascites, which were investigated and found to be inconclusive for malignancy. One had a past history of pulmonary TB diagnosed 10 years earlier and had received a complete course of anti-TB therapy. CA125 levels were raised in six women with mean levels of 290 IU (range, 13–529). Chest X-rays were normal in all cases except the woman who had a past history of pulmonary TB. In women of childbearing age, the characteristics of the menstrual cycle may change. Clinically, female genital tract TB usually impacts menstruation, causing amenorrhea, oligomenorrhea, and infertility. Tuberculosis may erode the endometrium and severe body consumption may explain its mechanism [14]. The most common intraoperative findings in TBP are tubo-ovarian masses, ascites, pelvic adhesions, perihepatic adhesions, and caseous or granulomatous nodules. Sometimes the diagnosis of TBP can be made instantly when small tubercles (milia) are noted on the peritoneum, but when milia are not present, frozen section is also useful intraoperatively and can avoid unwarranted, extensive surgery [15]. Laparoscopic biopsies of the suspected lesions are an adequate and safe method to make available tissue samples for histologic and bacteriologic diagnosis of TB infection with sensitivity > 80%, especially in the presence of ascites [14,15].

4. Conclusions

Although this is a rare occurrence, clinicians should consider TBP as a differential diagnosis of ovarian or peritoneal cancer. The differential diagnosis is challenging, but an essential element of suspicion may be raised by the ultrasound or CT visualization of nodules spread on the ovarian surface, which must lead to suspect caseous nodules.

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References

1. Gopalaswamy, R.; Shanmugam, S.; Mondal, R.; Subbian, S. Of tuberculosis and non-tuberculous mycobacterial infections—A comparative analysis of epidemiology, diagnosis and treatment. *J. Biomed. Sci.* 2020, 27, 74. [CrossRef] [PubMed]

2. Adigun, R.; Singh, R. Tuberculosis. In *StatPearls [Internet]*. Treasure Island (FL): StatPearls Publishing; 2021 Jan; StatPearls: Orlando, FL, USA, 2020.

3. Migliori, G.B.; Tiberi, S.; Garcia-Basteiro, A.L.; Duarte, R. Tuberculosis and its future in the COVID-19 era: The Pulmonology series 2021. *Pulmonology* 2021, 27, 94–96. [CrossRef] [PubMed]

4. Sharma, J.B.; Jain, S.K.; Pushparaj, M.; Roy, K.K.; Malhotra, N.; Zutshi, V.; Rajaram, S. Abdomino-peritoneal tuberculosis masquerading as ovarian cancer: A retrospective study of 26 cases. *Arch. Gynecol. Obstet.* 2010, 282, 643–648. [CrossRef] [PubMed]

5. Wang, H.; Qu, X.; Liu, X.; Ding, L.; Yue, Y. Female Peritoneal Tuberculosis with Ascites, Pelvic Mass, or Elevated CA 125 Mimicking Advanced Ovarian Cancer: A Retrospective Study of 26 Cases. *J. Coll Physicians Surg Pak* 2019, 29, 588–589. [CrossRef] [PubMed]

6. Sophia De Saram, J.S.F. Gastrointestinal and Peritoneal Tuberculosis. In *Extrapulmonary Tuberculosis*, 1st ed.; Alper, S., Hakan, E., Eds.; Springer International Publishing: Cham, Switzerland; pp. 25–42.

7. Norbis, L.; Alagna, R.; Tortoli, E.; Codecasa, L.; Migliori, G.B.; Cirillo, D.M. Challenges and perspectives in the diagnosis of extrapulmonary tuberculosis. *Expert Rev. Anti-Infective Ther.* 2014, 12, 633–647. [CrossRef] [PubMed]

8. Hulnick, D.H.; Megibow, A.; Naidich, D.; Hilton, S.; Cho, K.C.; Balthazar, E.J. Abdominal tuberculosis: CT evaluation. *Radiology* 1985, 157, 199–204. [CrossRef] [PubMed]

9. Flores, L.S.; Solis, A.H.; Gutiérrez, A.E.; José, L.C.C.; Ortiz, I.C.; González, H.G.; Martínez, E.L.; Sabido, R.C. Peritoneal tuberculosis: A persistent diagnostic dilemma, use complete diagnostic methods. *Rev. Méd. Hosp. Gen. Méx.* 2015, 78, 55–61.

10. Koff, A.; Azar, M.M. Diagnosing peritoneal tuberculosis. *BMJ Case Rep.* 2020, 13, e233131. [CrossRef] [PubMed]

11. Guirat, A.; Koubaa, M.; Mzali, R.; Abid, B.; Ellouz, S.; Affes, N.; Ben Jemaa, M.; Frikha, F.; Ben Amar, M.; Beyrouti, M.I. Peritoneal tuberculosis. *Clin. Res. Hepatol. Gastroenterol.* 2011, 35, 60–69. [CrossRef] [PubMed]

12. Liu, Q.; Zhang, Q.; Guan, Q.; Xu, J.F.; Shi, Q.L. Abdominopelvic tuberculosis mimicking advanced ovarian cancer and pelvic inflammatory disease: A series of 28 female cases. *Arch. Gynecol. Obstet.* 2014, 289, 623–629. [CrossRef] [PubMed]

13. Devi, L.; Tandon, R.; Goel, P.; Huria, A.; Saha, P.K. Pelvic tuberculosis mimicking advanced ovarian malignancy. *Trop. Dr.* 2012, 42, 144–146. [CrossRef] [PubMed]

14. Martingano, D.; Cagle-Colon, K.; Chiaffarano, J.; Marcus, A.; Contreras, D. Pelvic Tuberculosis Diagnosed during Operative Laparoscopy for Suspected Ovarian Cancer. *Case Rep. Obstet. Gynecol.* 2018, 6452721. [CrossRef] [PubMed]

15. Sharma, J.B.; Roy, K.K.; Pushparaj, M.; Kumar, S.; Malhotra, N.; Mittal, S. Laparoscopic findings in female genital tuberculosis. *Arch. Gynecol. Obstet.* 2008, 278, 359–364. [CrossRef] [PubMed]