

# Diagnosis challenges of a patient with peritoneal tuberculosis masquerading as ovarian malignancy: A case report

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## Case Report

### Diagnosis challenges of a patient with peritoneal tuberculosis masquerading as ovarian malignancy: A case report

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## **ABSTRACT**

**Background:** Peritoneal tuberculosis (PTB) could mimic cases of advanced ovarian cancer making its diagnosis is challenging. Comprehensive and conscientious examinations for diagnosis are needed to differentiate such cases to avoid inappropriate treatment. We report a case of problematic diagnosis of PTB that mimic of ovarian malignancy.

**Case Presentation:** A 20-year-old female patients with history of multiple rehospitalization, presented with complaints of abdominal pain, nausea/vomiting, low grade fever, and weight loss in the last five months. In the first admission, patient was suspected with malignant ovarian cyst due to clinical features of malignancy with normal chest X-ray, abdominal USG suggested ovarian cyst in both ovaries, high levels of Ca125. However abdominal CT-scan showed thickening in peritoneum which suggested PTB. Patient was planned for urgent laparotomy while waiting for GenExpert result. On the second admission, patient presented with recurrent abdominal pain, GenExpert sputum and stool showed negative result, and planned for surgery but the patient refused. On the last admission, patient diagnosed with impending bowel obstruction and underwent abdominal CT-scan with contrast showed diffuse multiloculated cystic lesion in cavum pelvic and multiple prominent mesenteric lymph nodes that suggested abdominal TB with abscess in cavum pelvic. Exploratory laparotomy revealed conglomeration, pus and tubercles in the peritoneum. Based on pathology and microbiology examination from tissue biopsy and pus, a TB was confirmed.

**Conclusion:** We reported patient with PTB with unspecific clinical symptoms which suspected as ovarian malignancy. This study highlights the challenges in diagnosis PTB and therefore PTB could be considered as a differential diagnosis in patient suspected with ovarian malignancy in the TB endemic countries.

**Keywords:** diagnostic problems, peritonitis tuberculosis, ovarian malignancy, differential diagnoses

## INTRODUCTION

World Health Organization (WHO) estimates about 1.3 million deaths from tuberculosis (TB) infection around the world. In Indonesia, tuberculosis is one of main health problem.<sup>1</sup> A study conducted in 2014–2015 showed that Indonesia had around one million TB cases.<sup>2</sup> In 2018, 845,000 cases of TB was reported in Indonesia.<sup>3</sup> Peritoneal tuberculosis (PTB) accounts for about 0.1–0.7% of all TB cases representing 4–10% of extrapulmonary TB and 25–60% of abdominal TB.<sup>4</sup> PTB considered as challenging to be diagnosed due to the non-specific symptoms and may not have clear risk factors for infection with *Mycobacterium tuberculosis* (MTB).<sup>5,6</sup> In addition, due to low sensitivity of microbiological diagnostic tests for PTB, invasive tissue sampling for diagnosis is required.<sup>7</sup>

Extrapulmonary TB sometimes leads to a gynecologic oncology misdiagnosis such as advanced ovarian carcinoma.<sup>8,9</sup> Especially due to non-specific abdominal or pelvic symptoms such as masses, ascites, that can mimic cases of advanced ovarian cancer.<sup>10</sup> Ovarian carcinoma biomarker, Ca125, has been reported to be elevated in patients with pulmonary and extrapulmonary TB including PTB.<sup>2,11</sup> A study showed that the serum CA-125 level was elevated approximately 44% of patients with active pulmonary TB.<sup>2</sup>

Management and clinical outcomes between PTB and advanced ovarian cancer are very different.<sup>10</sup> PTB treated with anti-tuberculosis drugs, and can be cured. In contrast, advanced ovarian cancer should be treated with debulking surgery followed by cytotoxic drugs and with a worse clinical outcome.<sup>10</sup> Therefore, comprehensive and conscientious examinations are needed to differentiate such cases in order to provide proper treatment.<sup>8</sup> We report a case of problematic diagnosis of PTB with an initial suspicion of ovarian malignancy.

## CASE PRESENTATION

A 20-year-old female patient was consulted from the Department of Obstetrics and Gynecology with a diagnosis of suspected PTB with a differential diagnosis of malignant clinical ovarian cyst pro-exploratory laparotomy. Initially, the patient was managed by the Department Digestive Surgery with a diagnosis of suspected clinical malignant ovarian cyst and suspected TB abdomen with impending bowel obstruction, then transferred to the Department Obstetrics and Gynecology for diagnosis.

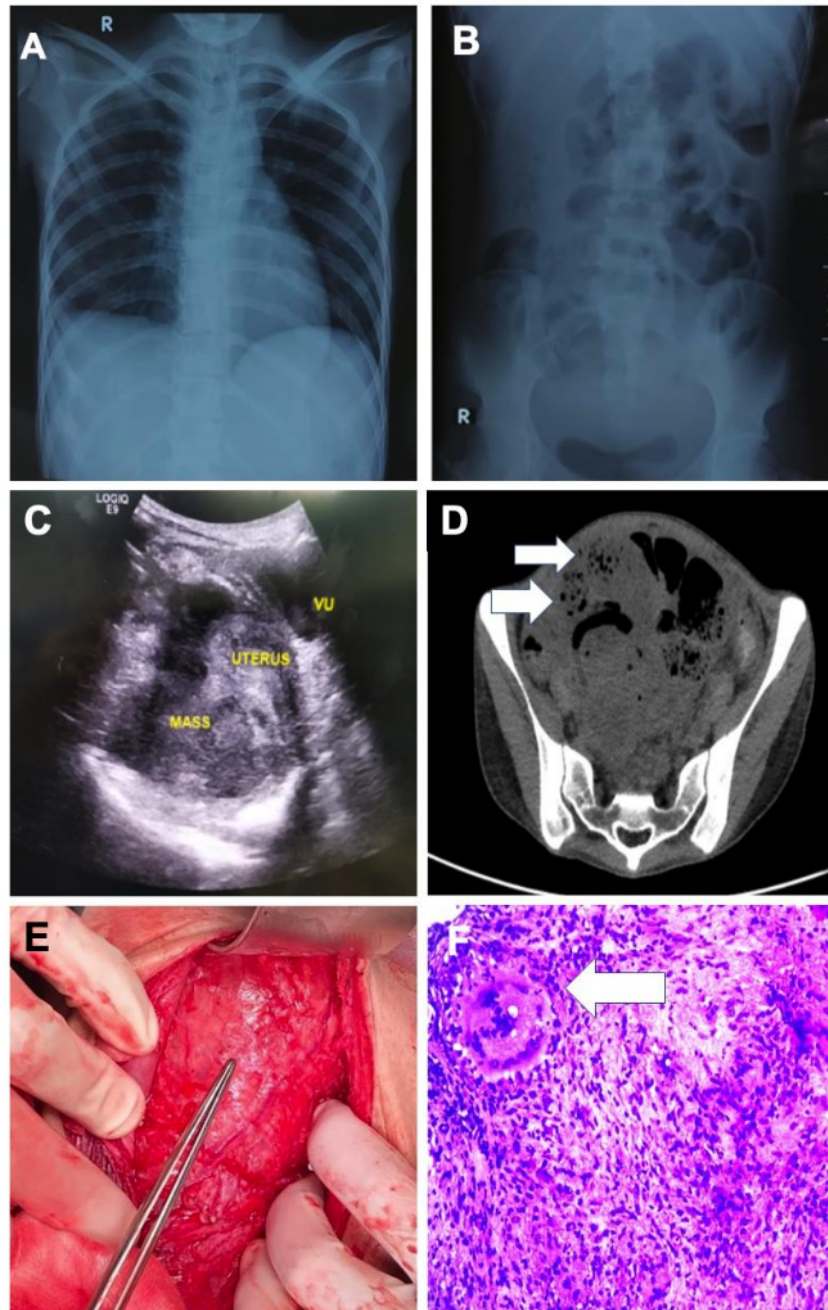
The patient had a history of repeated rehospitalizations with complaints of abdominal pain for 3 months, and worsened in the last one week. The pain was felt throughout the abdominal area, intermittent, and no lump was felt. Patient also complained nausea and vomiting for ten days prior to admission especially during consume food. Fever was also complained every day for five months ago accompanied by occasional cough with yellowish phlegm without blood, weight loss and loss of appetite. Shortness of breath denied.

Physical examination results showed general condition was fair, Glasgow comma scale was 4-5-6, blood pressure 110/80 mmHg, pulse 102x/min, regular rhythm, respiratory rate 20x/min, axillary temperature 36.8°C, weight 27 kg, height 150cm, BMI 12 kg/m<sup>2</sup>. Examination of the head and neck revealed that the conjunctiva was not anemic, the sclera was not jaundiced, and there was no cyanosis or dyspnea. There was no increase in jugular venous pressure and enlarged lymph nodes. Examination of the chest area showed symmetrical movement, no retraction was found. On cardiac examination, S1 and S2 were single, regular, no heart murmurs, gallop rhythm or pericardial friction were found. On lung examination, vesicular breath sounds were found in both hemithorax, no crackles or wheezing. Abdominal examination revealed a slight distended with normal bowel sounds. On palpation, a positive impression of muscular defense, tenderness in the umbilical region was found, but no chessboard phenomenon. The liver and spleen were within normal limits. Examination of the upper and lower extremities revealed warm, dry, no edema, dan no enlarged lymph nodes.

Abdominal TB manifestations in this patient were non-specific where there was no typical sign of abdominal TB infection in the form of a chessboard phenomenon, but the impression of peritonitis was observed. Based on the clinical presentation, the type of abdominal TB in this patient is more likely to suggest an abdominal obstruction.

Laboratory result revealed a low hemoglobin level (9.5 g/dL) with an MCV of 83.4 fL, MCH 26.2 pg indicated a suspicion of anemia due to chronic disease; increased of neutrophils (86.4%), elevated ESR (86mm/hr) and CRP (9.8) indicated a chronic inflammatory process. Chest x-ray and abdominal x-ray examination showed normal results (**Figure 1A** and **B**). Gynecological ultrasound (USG) revealed an indistinct mixed solid cystic lesion (6x7 cm) at superior-posterior of uterus (**Figure 1C**). Abdominal CT-scan with contrast revealed abdominal TB with abscess formation in the pelvic cavity, descending colon wall thickening, multiple subcentimeter lymph nodes in the mesentery (**Figure 1D**). After exploratory laparotomy was conducted due to impending bowel obstruction, the results showed a conglomeration of the entire intestine and peritoneum, tubercles in the peritoneum, omentum, and intestine, 200 ml of pus was found in the Douglas cavity, with grade IV interintestine adhesions (frozen abdomen) (**Figure 1E**). The uterus, right and left adnexa, tubes and ovaries were difficult to evaluate, adhesiolysis was performed, peritoneal and omental tubercles biopsy, pus culture, and drainage was performed. GenExpert sputum and stool examinations were negative. The results of acid-fast bacillus (BTA) staining from pus deep samples showed a formation of BTA positive bacteria and PMN +3 cells. Pathologic anatomy examination of peritoneal samples showed that there were pieces of connective tissue and fat with groups of epithelioid-shaped histiocyte cells that formed granulomas, the edges of which were scattered datia Langerhans cells and lymphocytes in the middle, caseous necrosis formed soft tubercles (**Figure 1F**). There were no signs of malignancy, so it was concluded as chronic granulomatous inflammation. Examination of tumor markers showed high Ca 125 results

(362.37 U/ml), by this result ovarian malignancy was suspected. ADA test was not performed because there were no signs of ascites. GeneXpert for sputum and stool examinations were negative.



**Figure 1.** Chest x-ray and abdominal x-ray revealed normal result (**A and B**). Abdominal USG showed a mixed solid cystic lesion in superior-posterior to the uterus (**C**). CT-scan showed diffused multiloculate cystic lesion in cavum pelvis (**D**). Conglomeration, suggestive tubercles, and pus in the peritoneum (**E**). PA result showed Caseous necrosis forming soft tubercles (**F**).



Based on the anamnesis, physical examination, and laboratory examination results, the patient was diagnosed with PTB. The patient treated with TB drugs category 1 in accordance with body weight (rifampicin, isoniazid, pyrazinamide, dan ethambutol) for 9–12 months (2HRZE/10HR). After two months, evaluation was conducted which showed an improvement of clinical conditions and laboratory results.

## DISCUSSION

PTB is one of the utmost ordinary type of extrapulmonary TB, including involvement of the peritoneal cavity, mesentery and omentum.<sup>12</sup> Women with PTB are usually younger than women with ovarian malignancies, ranging from 20–40 years, with a less progressive clinical picture than ovarian malignancies.<sup>13</sup> Most patients present with unexplained manifestation of abdominal pain (50–100% of cases), weight loss (50-61%), fever (13-59%), distension due to ascites (40–73%), abdominal mass, abdominal tenderness, and night sweats (65).<sup>7,14</sup> Due to slow progressivity of symptoms, patients tend to show symptoms for months before seeking medical care.<sup>7</sup>

In our case the patient had a history of repeated hospital admissions with complaints of abdominal pain that had been felt for more than five months which had worsened in the last one week. Pain was felt throughout the abdominal area, intermittent, and no lump was felt. Nausea and vomiting in the past ten days ago. Fever, loss of weight and appetite, occasional cough with yellowish phlegm for five months. Normal menstrual history, no changes in menstrual cycle or frequency, no severe pain during menstruation. Hair loss, joint pains, skin diseases, and canker sores were denied. From the history, it was more directed to the suspicion of chronic disease, namely TB infection, compared to ovarian malignancy which would have a worse clinical outcome and high disease progression.

In PTB, physical examination revealed ascites (73%) and abdominal tenderness (47.7%), doughy abdomen is rare (5–13%), hepatomegaly may also be found.<sup>15</sup> The chessboard phenomenon on physical examination is rarely found in abdominal TB infections.<sup>5</sup> In this patient, physical examination revealed a slight distended abdomen, muscular defenses by palpation, tenderness in the umbilical region, but no ascites, liver and spleen were within normal limits, and normal bowel sounds. PTB manifestations in this patient were non-specific where there were no typical signs of PTB in the form of a chessboard phenomenon, but peritonitis was found. Based on the clinical presentation, the type of PTB in this patient was more likely to suggest an abdominal obstruction. GenExpert sputum and stool examinations were negative although it has relatively high sensitivity and specificity.<sup>16</sup>

Cancer antigen 125 (Ca125) is found in the epithelium of the respiratory tract and female reproductive tract and can be elevated in both benign and malignant conditions including ovarian cancer.<sup>17</sup> It has been reported to be increased in peritonitis.<sup>17</sup> Average value of Ca125 was 104.9 IU/mL and the optimal cut-off value was 32.5 IU/mL



with 68.6% of sensitivity and 77.8% of specificity.<sup>18,19</sup> A study showed that both patients with peritonitis and patients with primary peritoneal cancer had elevated Ca125 levels which statistically higher in primary peritoneal cancer patients.<sup>19</sup> In this patient, examination of tumor markers showed high Ca125 (362.37 U/ml) and therefore it was suspected as ovarian malignancy.

Establishing a diagnosis of intra-abdominal TB such as PTB is a challenge, especially with uncommon manifestation.<sup>20,21</sup> Several criteria for diagnosing intra-abdominal TB includes: (i) positive smear or culture of peritoneal fluid; (ii) histological appearance of granuloma caseous; and (iii) good response to anti-TB drugs.<sup>17</sup> Ascitic fluid analysis is often performed for patients with suspected PTB.<sup>14</sup> BTA test from ascitic fluid is simple, but has a low positive rate (3%), while the sensitivity of bacterial culture ranges from 21–35%.<sup>14</sup>

Adenosine deaminase (ADA) measurement is useful to evaluate patients with suspected PTB.<sup>22</sup> ADA levels of ascitic fluid 40 IU/L show excellent sensitivity, although the specificity is relatively low for the diagnosis of PTB.<sup>22</sup> A meta-analysis found that ADA had high sensitivity (100%) and specificity (97%) using cut-off of 36–40 U/L.<sup>23</sup> In cirrhosis patients, the sensitivity is only 30% due to poor humoral and T-cell response.<sup>24,25</sup> However, in our patient, ADA test was not performed because there were no signs of ascites in the patient.

Various investigations are needed to establish the correct diagnosis and rule out the differential diagnosis. USG can be used to detect a low ascites, fluid collections, and thickening of the omentum and peritoneum.<sup>26</sup> CT-scan is favored to evaluate peritoneum and intra-abdominal viscera. A thickened mesentery with mesenteric lymph nodes could be as early characteristics of TB infection.<sup>27</sup> A study reported that CT-scan has 69% sensitivity for PTB.<sup>28</sup> However, those CT-scan findings can be seen in peritoneal carcinomatosis.<sup>29</sup> In patients with peritonitis, abnormal chest radiographs can be found in 21–83% of cases, with active pulmonary TB found in about 14% of cases.<sup>30</sup> However, neither of these findings is diagnostic for PTB and is only suggestive of a possible aetiology.<sup>25,30</sup>

Radiologically, if the ovaries are significantly enlarged in the definitive tumor, significant peritoneal infiltration indicates peritoneal metastasis.<sup>31</sup> But, if ovaries are normal in size in any patient with fatty insinuation of peritoneum, it would be challenging to diagnose benign or malignant peritonitis especially in areas where TB is endemic.<sup>31</sup> The CT-scan characteristics of female PTB and peritoneal carcinomatosis are very similar in endemic areas, so it is difficult to differentiate between the two diseases without surgical. Most cases with PTB can be diagnosed by laparoscopic exploration using frozen section for histopathological examination.<sup>32,33</sup>

In our case, interestingly, the chest X-ray examination showed normal results. However, gynecological USG showed a cystic lesion mixed solid with indistinct borders (6x7 cm) in the superior-posterior uterus. Abdominal CT-scan with contrast revealed

abdominal TB with a picture of abscess formation in the pelvic cavity, thickening of the descending colon wall, multiple sub centimeter lymph nodes in the mesentery which led to PTB.

We suspected that it was began with a focus infection in the lungs which could be overcome by the patient's immune response, but due to not achieving optimal treatment, there had been spread to extra-pulmonary organs, in this case the peritoneum. CT-scan has a fairly high level of sensitivity and specificity in establishing the diagnosis of abdominal TB, and there was a place for direct anti-TB regimens. However, due to various factors, especially adherence in this patient, the administration of anti-TB therapy was delayed.

If there was <sup>7</sup>diagnostic ambiguity, laparoscopy could be a solution due to its high sensitivity (92%).<sup>34</sup> Diagnostic laparoscopy with tissue biopsy is the gold standard for PTB that usually show multiple yellow-white tubercles, thickening of the omentum with ascites, fibrous bands in parietal to visceral peritoneum and abdominal cocoon.<sup>35</sup> Although the visual appearance has diagnostic in more than 90% of patients, histological and microbiological analysis of the tissue is required.<sup>35</sup>

Due to the impending bowel obstruction, it was decided to perform an exploratory laparotomy with the results revealed conglomeration of the entire intestine and peritoneum, tubercles in the peritoneum, omentum, and entire intestine, 200 ml of pus was found in the douglas cavity, grade IV inter-intestine adhesions (frozen abdomen). Uterus, right and left adnexa, tubes and ovaries were difficult to evaluate, adhesiolysis, peritoneal and omental tubercles biopsy, pus culture was performed.

Histopathological evaluation might expose the presence of caseous granulomas in 70-95% of patients. Microscopically, the important diagnostic clue is a large confluent granulomas with central caseous necrosis; while tissue PCR is positive in 25–70%.<sup>7,10</sup>

The results of BTA staining from the pus deep sample showed the formation of BTA positive bacteria and PMN +3 cells, the results of pathological examination showed pieces of connective tissue and fat with groups of epithelioid-shaped histiocyte cells that formed granulomas, with datia Langhans cells and lymphocytes scattered at the edges. In the middle, caseous necrosis appears to form soft tubercles. There were no signs of malignancy. In conclusion, this indicates a chronic granulomatous inflammation corresponds to TB.

PTB is treated as extrapulmonary TB with the 1<sup>st</sup> category of anti-TB drugs for 6–12 months.<sup>36,37</sup> The regimen consisted of rifampicin 10mg/kg, isoniazid 5mg/kg, pyrazinamide 25mg/kg and ethambutol 15mg/kg for two months followed by rifampicin 10mg/kg 3x/week and isoniazid 10mg/kg 3x/week for four months.<sup>38</sup> Response to therapy is usually seen within the first three months of treatment marked by resolution of any existing symptoms, including laboratory result. Surgery in PTB is recommended for cases with signs of bowel perforation, obstruction, fistula, abscess, and bleeding.<sup>14,39</sup> In our case, the patient was treated with anti-TB category 1 for 9–12 months (2HRZE/10HR).

After two months therapy, clinical evaluation and laboratory markers were carried out with the result that there was an improvement.

## **CONCLUSION**

We reported a case of PTB in a 20-year-old woman with a history of repeated hospital admissions with high Ca125 level with suspicion of malignant ovarian cyst and USG showed a mass in the pelvic cavity. Exploratory laparotomy should be conducted and biopsy supported the diagnosis of PTB that confirmed by acid-fast bacillus and pathology results. This case illustrates the challenges in establishing the diagnosis of PTB with clinical symptoms that are not typical and therefore that a comprehensive examination needs to be carried out. Enforcement of the appropriate diagnosis is very critical on the provision of therapy.

## **PATIENT CONSENT**

Written inform consent provided by the family member of the patient.

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## **DISCLOSURE OF CONFLICTS OF INTEREST**

There is no conflict of interest.

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None

## **AUTHOR CONTRIBUTION**

ASB contributed in concepting and designing the study, literature search, data collection, manuscript preparation and editing. UM contributed in intellectual content, manuscript editing and final editing.

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