

How to Cite:

Nirmawati, K., & Rusli, M. (2022). Case Report: Diagnostic approach of granulomatous inflammation with suspected peritoneal tuberculosis. *International Journal of Health Sciences*, 6(S6), 11126–11132. <https://doi.org/10.53730/ijhs.v6nS6.13055>

Case Report: Diagnostic approach of granulomatous inflammation with suspected peritoneal tuberculosis

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Abstract---The approach to diagnosing peritoneal tuberculosis in patients is complex and often overlaps with other obstetric and gynecologic diseases. A 27-year-old woman with complaints of abdominal mass went to the DOTS clinic after surgical removal of an ovarian mass. Clinical, laboratory, and histopathological abdominal CT scans showed a picture of tuberculosis. The patient was then treated with a TB regimen and as a result her clinical condition improved and the mass shrank.

Keywords---abdominal mass, ascites, peritonitis TB.

Introduction

Granulomatous inflammation is a histologic pattern of tissue reaction which appears following cell injury, it is caused by a variety of conditions including infection, autoimmune, toxic, allergic, drug, and neoplastic conditions. Common reaction patterns include necrotizing granulomas (Shah et al., 2017). Mycobacteria species are the most common etiologies of necrotizing granulomas worldwide (Miller, 1994). Peritoneal tuberculosis is an inflammation of the parietal or visceral peritoneum caused by the bacterium *Mycobacterium tuberculosis*. This disease often affects the entire peritoneum and organs of the gastrointestinal system, mesentery, and internal genital organs. This disease rarely stands alone, usually is a continuation of the tuberculosis process in other places, especially the lungs. However, it is often found when the diagnosis is made, the tuberculosis process in the lungs is no longer visible. Clinical symptoms vary, generally

complaints and symptoms arise slowly, often patients are not aware of this situation. The most common complaints are lack of appetite, cough, and fever. On physical examination, the most common symptoms are ascites, fever, abdominal swelling and pain, pallor and fatigue (Zain, 2014). Diagnosing abdominal TB remains a major challenge even for experienced clinicians. This disease is a great imitator that has an unusual presentation. A high index of suspicion is essential for the diagnosis. The clinical and radiological findings of abdominal tuberculosis are nonspecific (Abu-Zidan & Sheek-Hussein, 2019; Dawra et al., 2017). Peritoneal tuberculosis is a rare disease in the literature and will be discussed in this case report.

Case

A woman Mrs. A 27 years old, a medical worker (midwife), residing in Gresik, married, Javanese, came to the DOTS Poly for control. The patient initially complained that her stomach was getting bigger within 1-2 weeks, accompanied by complaints of intermittent fever, decreased appetite, weight loss, cough for 2 weeks, night sweats were denied and abdominal pain was denied. The patient had no complaints of hair loss, joint pains, skin diseases, or stomatitis. So far there have been no problems with menstruation or cycles. Then the patient was examined by the obstetrician poly at the nearest hospital. The obstetrician at the hospital suspected a mass in the patient's abdomen (suspected a mass in the uterine organs) and the patient was referred to the obstetrics poly at Dr. Soetomo Hospital. When he came to the Obsgyn Polyclinic after a series of examinations the patient was suspected of having an ovarian cyst. Then the patient underwent surgery. History of DM was denied, hypertension was denied, chronic cough was denied, history of hospitalization was denied. Currently, the patient has no complaints. Abdominal examination revealed a palpable solid mass in the right abdomen, measuring about 6x6 cm². A gynecological ultrasound was performed with a bilateral mass impression on the ovaries accompanied by ascites.

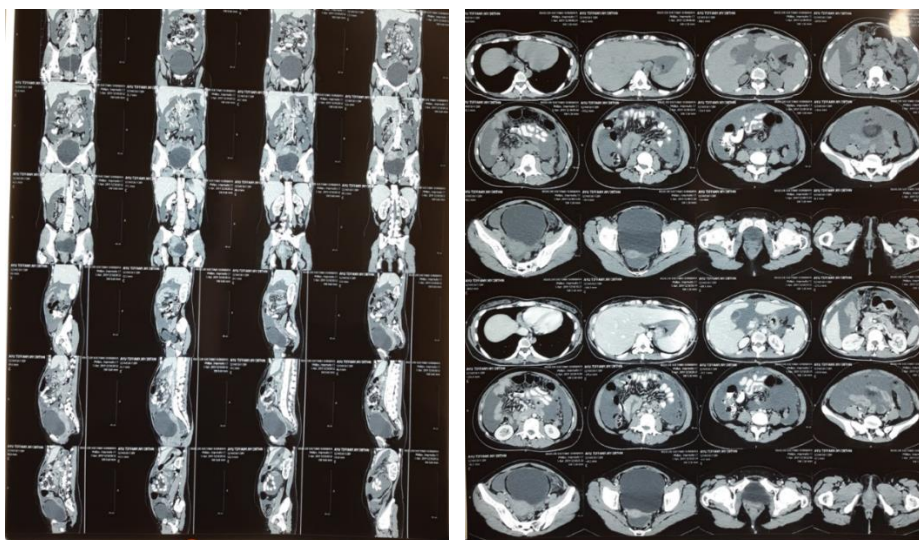


Figure 1. CT scan abdomen with contrast

Laboratory Examination at RSUD dr. Soetomo obtained CEA results of 0.62 ng/ml; CA-125 364 U/ml, LDH 256 U/L; B-HCG <2.00 mIU/ml, AFP 3.3, Hb 12.2 g/dL, leukocytes 7.510/mm³, platelets 527.000/mm³, Neutrophils 70.9%, SGOT 35 U/L, SGPT 15 U/L, HBsAg non reactive, anti-HCV non reactive, BUN 3 mg/dL, SK 0.53 mg/dL, Albumin 3.5 mg/dL, GDA 136 mg/dl, Na 135 mmol/L, K 5.0 mmol/L, Cl 96 mmol/L. Number of D 0.05 mg/dL, Number of T 0.30 mg/dL, PPT 11.2 seconds; APTT 30 seconds, INR 1.1. Ascitic fluid analysis WBC-BF 0.22x10³/L, RBC-BF 0.002x10³ / μ L, total protein 5.1 g/dL, glucose 75mg/dL, LDH 263 L, MN % 86.5%, PMN% 13.5%, albumin 3.0 g /dL. On a CT scan of the abdomen with contrast on April 5, 2019, an unenhanced image of multiple lobulated cysts, firm borders, irregular edges measuring \pm 2.52 x 2.92 x 2.69 cm in the pelvic cavity (impression of the right adnexa) was seen with the effect of space compression. The above leads to the appearance of an ovarian mass. There is ascites and hepatomegaly (Figure 1).

The results of histopathology examination of peritoneal wall biopsy tissue, tumors between the ovaries and tubes showed: 1) Peritoneal wall: showed pieces of tissue consisting of groups of epitheloid-shaped histiocyte cells forming granulomas, multinucleated Langhans giant cells were also seen, no signs of malignancy were seen (Figure 2). 2) Tumor between the ovary and tube: showing extensive pieces of necrotic tissue, no signs of malignancy were seen (Figure 3). Conclusion of PA results: granulomatous inflammation, according to tuberculous peritonitis.

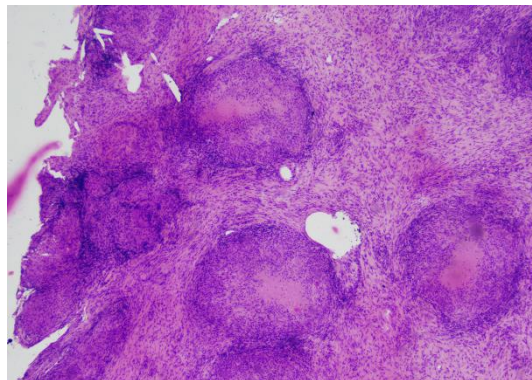


Figure 2. Granulomatous inflammatory process

Patients were given OAT category 1 outpatient therapy according to body weight, for 9-12 months (2HRZE/10HR). And the result in 12 months ascites reduced and the patient's clinical condition improved.

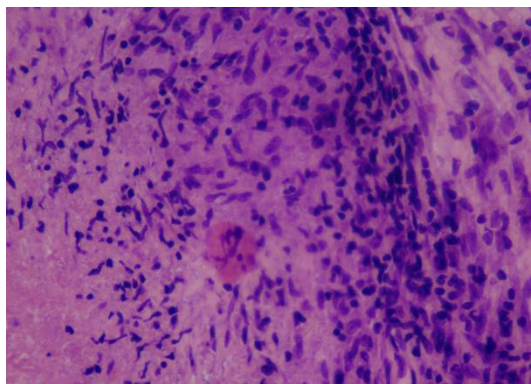


Figure 3. Large area of necrosis

Discussion

The main forms of abdominal TB are intestinal and peritoneal, but other nodal forms can also be found. In practice, various forms can occur together (Weledji & Pokam, 2017). Peritoneal tuberculosis is an inflammation of the parietal or visceral peritoneum caused by the bacterium *Mycobacterium tuberculosis*. This disease often affects the entire peritoneum and organs of the gastrointestinal system, mesentery, and internal genital organs. The peritoneum can be affected by tuberculosis in several ways: 1) Through hematogenous spread, especially from the lungs, 2) Through the wall of the infected intestine, 3) From the mesenteric lymph nodes, 4) Through an infected fallopian tube. In most cases, peritoneal tuberculosis occurs not as a result of continuous spread, but often due to reactivation of a latent process that occurs in the peritoneum acquired through hematogenous spread of the previous primary process (Zain, 2014).

Tuberculosis bacteria reach the gastrointestinal tract by hematogenous spread (from pulmonary foci acquired during primary infection in childhood), ingestion of infected sputum, or direct spread from infected adjacent lymph nodes and fallopian tubes. Ingested bacilli pass through Peyer's Patch from the intestinal mucosa and are transported by macrophages via the lymphatics to the mesenteric lymph nodes where they remain dormant. This reactivation of disease in the lymph nodes, especially in immunocompromised patients, includes diabetes, renal failure and malignancies which can lead to abdominal TB with spread of bacteria to the peritoneum or intestines. Peritoneal tuberculosis is usually caused by reactivation of tuberculosis foci in the peritoneum with concomitant pulmonary, intestinal, or genital TB (mainly from the fallopian tubes) (Weledji & Pokam, 2017).

Clinical symptoms vary, generally complaints and symptoms arise slowly, often patients are not aware of this situation. The most common disorders are: no appetite, cough, fever. On physical examination, the most common symptoms are ascites, fever, abdominal swelling and pain, pallor and fatigue. In women, peritoneal tuberculosis is often found accompanied by tuberculous processes in the ovaries or tubes, so that on examination of the genitals, signs of inflammation can be found which are often difficult to distinguish from ovarian cysts (Zain,

2014). In the high prevalence area of sub-Saharan Africa, the most common signs and symptoms were abdominal pain (76.6%); ascites (59.6%); weight loss (53.2%) and fever (29.8%). The median duration of symptoms was 3 months and 13% of patients had received previous pulmonary TB treatment (Akinkuolie et al., 2008).

Ultrasonography is the initial modality of choice that is useful in viewing lymphadenopathy, ascites, peritoneal thickening, omental thickening and bowel wall thickening in some cases (Debi, 2014). Ascitic fluid analysis and cytology are helpful in differentiating the type of ascites. Examination of ascitic fluid generally shows exudate, the cell count is 100-3000 cells/ml, usually more than 90% of lymphocytes, and the LDH is usually elevated. A SAAG value of less than 1.1 g/dL indicates that ascites is non-cirrhotic ascites. A comparison of ascitic and blood glucose less than 0.96 and a total protein of more than 3 g/dL may indicate tuberculosis infection. However, this value has a low sensitivity for the diagnosis of peritoneal TB (Tsao, 2017; Zain, 2014). Another test is to measure the concentration of CA-125 (cancer antigen 125) is an antigen associated with ovarian carcinoma, this antigen is not found in the ovaries of normal adults but has also been reported to be elevated in ovarian cysts, chronic renal failure, autoimmune diseases, pancreas, liver cirrhosis and peritoneal tuberculosis. Zain LH in Medan found that in 8 cases of peritoneal tuberculosis, the concentration of CA-125 was elevated with an average concentration of 370.7 /ml (66.2-907 /ml). Some researchers use CA-125 to see treatment response (Zain, 2014). Histological characteristics are the main means of diagnosis in 30-40% of cases, the remaining diagnosis is made on the basis of a combination of clinical, epidemiological, radiological and histological features as well as in response to antituberculosis therapy. Ascitic adenosine deaminase (ADA) 30 U/L has a sensitivity and specificity of more than 90% (Seram & Friedlan, 2019).

Many studies conclude that ultrasonography and computed tomography complement each other in detecting tuberculous ascites, as they provide different details. CT focuses on involvement of the peritoneum, omentum and mesentery (Suceveanu, 2017). In the past, exploratory laparotomy was a frequently performed diagnostic procedure, but nowadays many authors consider surgery to be only performed if other, simpler methods do not provide certainty of diagnosis or if there are urgent indications such as intestinal obstruction (Zain, 2014). FNAC / biopsy is done if the support that has been done previously is still doubtful to make a diagnosis (Debi, 2014). The typical histologic finding is the presence of caseating granulomas and acid-fast bacilli, however these are rare findings. The presence of noncaseating granuloma, although more sensitive, has lower specificity. In a meta-analysis of histologic findings, caseous necrosis was found to have a sensitivity of 21% and a specificity of 100% for the diagnosis of abdominal TB (Dawra et al., 2017). The diagnostic yield of histology is improved when samples are collected surgically by direct observation of the pathology.

Laparoscopy is widely used to investigate ascites or peritoneal thickening of unknown cause. In the case of peritoneal TB, the most common macroscopic findings at the time of surgery are ascites, yellow or white nodules of the peritoneum and parietal or visceral peritoneal adhesions. Visual appearance alone has been reported to have a sensitivity of 84–100% and a specificity of 96–100%. The sensitivity and specificity of examination of histological samples obtained

from surgical biopsies is 70-100%. In patients with peritoneal TB, the Ziehl-Neelsen stain of ascitic fluid is positive in only 3-6% of cases and positive cultures in only 16-35%. Meanwhile, peritoneal tissue gave higher yield with 50% positive on ZN staining and more than 70% positive on culture. The GeneXpert MTB RIF assay is an automated nucleic acid amplification assay that requires minimal operator time and expertise and can provide results in less than 2 hours. A meta-analysis found a sensitivity and specificity of 81.2% and more than 98% for extrapulmonary TB samples, respectively (Seram & Friedlan, 2019). There are 3 known forms of peritoneal tuberculosis, namely (Zain, 2014): exudative form (95%), adhesive form, and mixed form.

Treatment is the same as for pulmonary tuberculosis. Drugs such as streptomycin, INH, ethambutol, rifampin, pyrazinamide give good results, improvement will be seen within 2 months (Zain, 2014). The guidelines for peritoneal TB therapy in Indonesia are based on the regulator of the Ministry of Health (PERMENKES) number 67 of 2016. Peritoneal TB is treated with the first category of anti-tuberculosis drugs for 9-12 months. The regimen consisted of Rifampicin 10mg/kg, Isoniazid 5mg/kg, Pyrazinamide 15mg/kgBW and Ethambutol 15mg/kg for 2 months and continued with Rifampicin 10mg/kgBW 3x/week and Isoniazide 5mg/KgBW 3x/week for 7-10 months (Ministry of Health, 2016). Surgical procedures are required for symptomatic peritoneal TB of intestinal obstruction, perforation and peritonitis. Surgery is sometimes performed if conservative treatment fails (Wyers & Matthews, 2010). The prognosis for peritoneal TB is good as long as the patient receives adequate anti-tuberculosis drugs (Zain, 2014).

Conclusion

Diagnosing TB peritonitis is not easy, it is often misdiagnosed and overlaps with other obstetric and gynecological diseases. However, if used in conjunction of clinical, laboratory, radiologic and pathological examination may help increase diagnostic power in those with suspected peritoneal tuberculosis. The outcome of peritoneal TB treatment is good as long as the patient receives adequate anti-tuberculosis drugs.

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