

## Tuberculous Peritonitis Presenting Acute Recurrent Pancreatitis

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### ABSTRACT

*Tuberculosis (TB), one of the oldest diseases known to affect humans, is a major cause of death worldwide. TB is still a major problem in Indonesia. This disease, which is caused by bacteria of the Mycobacterium tuberculosis, usually affects the lungs, although other organs are involved in up to one-third of cases. Approximately 95% cases of TB and 98% death because of TB occur in developing country. Gastrointestinal tuberculosis is uncommon, making up 3.5% of extrapulmonary cases in the United States. This kind of TB may involve gastrointestinal tract, peritoneal, lymph nodes, or solid intraabdominal organs (viscera).*

*A 17 years old male admitted to hospital with TB peritonitis presenting unusual clinical manifestation. At the first admission patients was diagnosed with acute pancreatitis based on elevation of amylase and lipase level up to 285 and 2,046 U/L and after finishing further examination, patients suffered from tuberculous peritonitis which based on literature manifested some gastrointestinal disorders.*

*Diagnostic confirmation was accomplished by conducting serum-ascites albumin gradient (SAAG) of < 1.1 g/dL, peritoneal thickening and the presence of ascites with fine mobile septations on ultrasound, positive polymerase chain reaction (PCR) TB from ascitic fluid. Patients received conventional antitubercular therapy for 12 months of rifampicin, isoniazid, pyrazinamide, and ethambutol. The addition of corticosteroids for the first two or three months of treatment may reduce the incidence of late complications arising from adhesive disease, such as small bowel obstruction.*

**Keywords:** *mycobacterium tuberculosis, tuberculous peritonitis, PCR, serum-ascites albumin gradient*

### INTRODUCTION

Tuberculosis (TB), one of the oldest diseases known to affect humans, is a major cause of death worldwide. TB is still a major problem in Indonesia. This disease, which is caused by bacteria of the *Mycobacterium tuberculosis* complex, usually

affects the lungs, although other organs are involved in up to one-third of cases. In developing country, tuberculosis is associated with poverty, deprivation, overcrowding, illiteracy, and limited access to health care facilities. While in the developed world, tuberculosis is commonly accompanied with human immunodeficiency virus (HIV) infection. Approximately about one-third world citizens had suffered from *Mycobacterium tuberculosis*. In 1995, there were nine millions patients with TB and three millions death reported because of TB worldwide. Approximately 95% cases of TB and 98% death

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because of TB occur in developing country. It counts about 75% TB attack productive ages group economically (15-50 years of age). It predicted that adult TB patients may loss their average time of work, and may impact the decrement of annual income in 20-30%.<sup>1,2</sup>

Gastrointestinal tuberculosis is uncommon, making up 3.5% of extrapulmonary cases in the United States. This kind of TB may involve gastrointestinal tract, peritoneal, lymph nodes, or solid intraabdominal organs (viscera) and it constitutes up to 12% of extrapulmonary TB and 1-3% of total. This disease may mimic another sign and symptom, including inflammatory bowel disease (IBD), malignancy, dan another infection diseases pattern. Therefore it caused delay in diagnosing gastrointestinal tuberculosis. The delay does not only impact in high level of mortality, and also frequently cause unnecessary surgical procedure.<sup>3,4</sup>

TB may involve any part gastrointestinal tract from mouth to anus, the peritoneum and pancreatobiliary system. It can have varied presentation, frequently mimicking other organ and rare diseases. The clinician must look for TB, and confirm or exclude this treatable malady in any patients who presents with gastrointestinal disease.<sup>5</sup>

Both the incidence and the severity of abdominal tuberculosis are expected to increase with increasing incidence of HIV infection in India. About 0.4 million people in India are co-infected with HIV and tuberculosis. Extra-pulmonary form of TB which account for 10-15% of all cases may represent up to 50% of patients of AIDS. TB of the gastrointestinal tract is the sixth most frequent form of extrapulmonary site, after lymphatic, genitourinary, bone and joint, miliary and meningeal tuberculosis.<sup>3</sup>

This case report will discuss a case of tuberculous peritonitis presenting unusual clinical manifestation. At the first admission patients was diagnosed with acute pancreatitis and after finishing further examination, patients suffered from tuberculous peritonitis which based on literature manifested some gastrointestinal disorders.

## CASE ILLUSTRATION

A 17 years old man was being admitted in the internal medicine ward with the chief complaint of abdominal pain that became worsen since three months before hospital admission. Pain was felt around the umbilical and radiated to left lumbal regions and to the back. The stomach was also distended and patients was also complaint of losing his appetite, fever, nausea, vomit, cough with white sputum positive, night sweating positive, loss of six kilograms of body weight, and history of diarrhea, but patient was

not suffered from short of breath. Patient had himself examined by doctor, but there was little progress of his illness. The doctor stated that he suffered from typhoid fever and dyspepsia. There were not any problem of defecation and micturition. A week before hospital admission patient was brought to general practitioner, and he was suggested to undergo laboratory test and sonography examination. The result show that he had colonictuberculous. Two days before hospital admission patient complained of worsen abdominal pain, distended positive, cough with productive white sputum. There were no history of intravenous drug users, blood transfusion, tattoo and free sex.

On physical examination revealed that the patient look severely ill, his blood pressure was 110/80 mmHg, pulse rate 100 times/minutes, respiratory rate was 24 times/minutes, temperature was 37.5°celcius. Patient's nutritional status was poor, body weight 35 kg, height 160 cm, and the body mass index will be 14 kg/m<sup>2</sup>. His conjunctiva was not looked pale, no palpable lymph nodes. On lung examination, there were low sound in percussion in 1/3 lower of right lung and rhales in both lungs. On abdominal examination the stomach was distended, bowel sound was decrease, and the stomach was pain on palpations examination. Chess board phenomom of this patient was hardly assessed. The rectal touche examination revealed normal result.

On the beginning laboratory examination, blood examination suggested hemoglobin 9.8 mg%, leukocyte 8,200/uL, thrombocyte 264,000 /uL, MCV 73 fl, MCH 25 pg, MCHC 34 g/dL, erythrocyte sedimentation rate 95 mm, AST 58 U/L, ALT 15 U/L, albumin 2.7 mg/dL, blood glucose 93 mg/dL, ureum 29 mg/dL, creatinin 0.8 mg/dL, sodium 128 mEq/L, potassium 4 mEq/L, chloride 105 mEq/L, amylase 285 U/L, serum lipase 2046 U/L. Chest X-ray showed infiltrate positive and right pleural effusion positive suggested specific process. Electrocardiogram showed sinus tachycardia. Plain abdominal photo revealed a meteorismus without any sign of ileus.



Figure 1. Chest X-ray revealed infiltrate positive and right pleural effusion positive suggested specific process

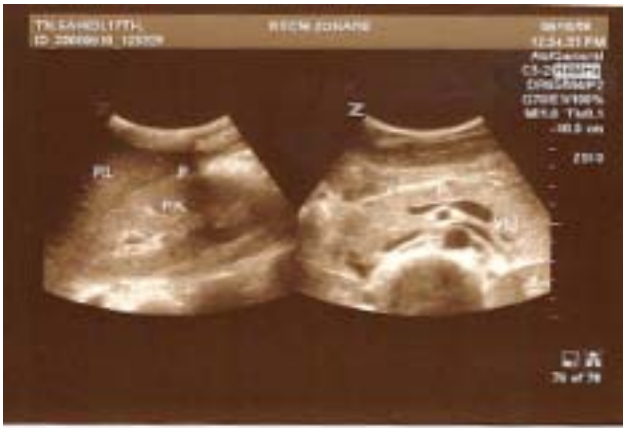


Figure 2. Sonography examination revealed suggested tuberculous peritonitis with the present of omental thickened and ascitic fluid accumulation

Patient had working diagnosis of abdominal pain ec suspicious acute pancreatitis diagnosis tuberculous peritonitis, pneumonia diagnosis pulmonary tuberculosis with right pleural effusion, anemia, hypoalbuminemia, hyponatremia, history of diarrhea and poor nutritional status.

Patients was treated with nasogastric tube insertion to decompress distended abdomen, total parenteral nutrition, antibiotic cefoperazon 3 x 1 gram, omeprazole 1 x 40 mg, sucralfate 4 x 15 cc. The production of nasogastric fluid had been evaluated to determine when the tubes should be removed. The nasogastric had been produced fluid  $\pm$  500 cc daily for about five days. The administration of antituberculous drug was being postponed to gain maximum result of medication until the the nasogastric tubes produced fluid less that 150 cc.

On the 5<sup>th</sup> day of hospitalization, the production of nasogastric fluid had decreased to 150 cc and bowel sound was positive, amylase and lipase level were 551 U/L and 443 U/L, therefore patient started having partial parenteral nutrition by administering fluid intake trough the tubes. The administration of anti-tuberculous drugs had been delay for diagnostic confirmation. Patient was consulted to the Division of

Hepatology and planned to undergo peritoneoscopy, but the Division of Hepatology disagree about the procedure because it is invasive procedure and highly risk for the patient and suggested to perform ascitic puncture guided sonography.

Several laboratory studies were performed, the result were anti HIV negative, elevation of C-reactive protein (CRP) level, serum iron 51  $\mu$ g/dL, total iron binding capacity 223  $\mu$ g/dL, ferritin 3,728 ng/mL, sodium urine 236 mEq/24 hours, potassium urine 84 mEq/24 jam, chloride urine 291 mEq/24 hours and urine osmolality 1,132 mosm/kg.

On the eight day of hospitalization, patient's stomach started to be distended and pain. Patient was retreated with total parenteral nutrition and nasogastric tube insertion. Nasogastric tubes produced 500 cc of fluid, amylase and lipase level raised 234 U/L and 1,435 U/L. After insertion of nasogastric tubes the complaint was getting better.

On the ten day of hospitalization patients underwent ascites puncture guided sonography and succesfully evacuated 75 cc of fluid contain pus and conducted an examination of ascitic fluid analysis, gram staining, MOR, BTA culture, and polymerase chain reaction (PCR). The result of ascitic fluid revealed yellow color, positive rivalta test, leukocyte count 1,600  $\text{mm}^3$ , and serum of ascitic albumin gradient (SAAG) was 0.53, confirming tuberculous peritonitis as the result of SAAG less than 1.1. The result of gram staining examination was negative, neither was the MOR examination. The PCR TB result was positive. Based on the diagnostic confirmation result, antituberculous drugs were started by administering regimen of rifampicin 300 mg, isoniazide 300 mg, pyrazinamide 1,000 mg, and ethambutol 750 mg. According to Division of Pulmonology round, additional corticosteroid should be given. Patient was prescribed methyl-prednisolon equal to prednison with dose 0.5-1 mg/kg body weight/day.

On the 20<sup>th</sup> day of hospitalization, there were an elevation of AST/ALT level became 166 U/L and 131 U/L, but the antituberculous drugs remain continued because the elevation were less than five times of normal limit. Patient was consulted to the Division of Pulmonology and suggested to recheck AST/ALT level every three days. In the next AST/ALT level, the result was raised 208 U/L and 314 U/L. The antituberculous drugs regimens changed into ESO regimens.

After the liver function test turned in normal range, patient started titration of anti tuberculous drugs. On the 35th day of hospitalization, the patient was clinically stable, abdominal pain was diminished and laboratory result confirmed the patient's condition in normal range.

## DISCUSSION

Tuberculosis is still common in the developing world; so that it must be considered in the differential diagnoses of a majority of the medical, surgical, and gynecological presentation.<sup>6</sup> Peritoneal tuberculosis is uncommon site of extrapulmonary infection caused by *Mycobacterium tuberculosis*. The risk is increased in patients with cirrhosis, HIV infection, diabetes mellitus, underlying malignancy, following treatment with anti-tumor necrosis factor (TNF) agent, and in patients undergoing continuous ambulatory peritoneal dialysis (CAPD). However, 20% of patients had no risk factor.<sup>7</sup> In addition, it is often misdiagnosed because of its insidious nature and the variability of its clinical presentation and the lack of pathognomonic findings, leading to delay the diagnosis and the treatment of tuberculous peritonitis.<sup>5</sup> Tuberculous peritonitis is a main differential diagnose in patients with fever, ascites and abdominal pain of uncertain origin.<sup>7</sup>

Abdominal TB may be enteric (intestinal involved itself), peritoneal, nodal (lymph nodes involvement) and solid visceral tuberculous like liver, spleen, kidney, pancreas or in any combination of these four varieties. Abdominal TB has diverse and non specific symptomatology. No single test is adequate for diagnosis of abdominal tuberculosis in all patients. Abdominal TB in non-HIV patients remains an ongoing diagnostic dilemma requiring a high index of clinical suspicion. This patients presented diverse symptom and high suspicion of abdominal TB. Above data direct further examination to confirm the diagnosis.<sup>2</sup>

Infection occurs most commonly following reactivation of latent tuberculous foci in the peritoneum that were established from hematogenous spread from a primary lung focus. It can also occur via hematogenous spread from active pulmonary or miliary TB. Much less frequently, the organisms enter the peritoneal cavity transmurally from an infected small intestine or continuously from tuberculous salpingitis in female patients. In this case, patient had a history of unexplained fever, loss of body weight, cough, and night sweats. The diagnostic confirmation on chest X-ray showed an infiltrate and pleural effusion dextra. This patient might be infected from hematogenous route or reactivation of latent tuberculous foci.<sup>3,4</sup>

As the disease progress, the visceral and parietal peritoneum become increasingly studded with tubercles. Ascites develops secondary "exudation" of proteinaceous fluid from the tubercles and more than 90% of patients with TB peritonitis have ascites at the time of presentation. The case presented an ascites and was confirmed by sonography studies.

Approximately 70% of patients have symptoms more than four months before the diagnosis is established. This is due in part to the insidious onset of the disease and because the diagnosis frequently unsuspected. In this case, patients had suffered from several symptoms of tuberculous peritonitis for about three months.

The most common features were ascites (93%), abdominal pain (73%), and fever (58%). Abdominal pain and ascites were also the most common presenting features in several other reports. Beside those common symptoms, there are other symptoms that are also frequently complained like distended abdomen, cough, night sweats, anorexia, fatigue, weight loss, and diarrhea. In this case, patients complained all of the symptoms that stated above, and had chief complain of worsen abdominal pain.

Gastrointestinal tuberculosis is uncommon, making up 3.5% of extrapulmonary cases in the United States. This kind of TB may involve gastrointestinal tract, peritoneal, lymph nodes, or solid intraabdominal organs (viscera) and it constitutes up to 12% of extrapulmonary TB and 1-3% of total. This disease may mimic another sign and symptom, including inflammatory bowel disease (IBD), malignancy, and another infection diseases pattern. Therefore it caused delay in diagnosing gastrointestinal tuberculosis. The delay does not only impact in high level of mortality, and also frequently cause unnecessary surgical procedure.<sup>4</sup>

TB may involve any part gastrointestinal tract from mouth to anus, the peritoneum and pancreatobiliary system. It can have vary presentation, frequently mimicking other organ and rare diseases. The clinician must look for TB, and confirm or exclude this treatable malady in any patients who presents with gastrointestinal disease. In this case, patients presented a symptom of acute pancreatitis in the beginning, therefore the treatment was focused on pancreatitis and antituberculous drugs was administered after the diagnostic confirmation of tuberculous peritonitis had been established.<sup>4</sup>

Clinical manifestation of tuberculous peritonitis has three form, serous type, adhesive type and mixed type. This case showed mixed type with the presence both of ascitic fluid and omental thickened, but chess board phenomenon hardly examined.<sup>3</sup>

Pancreatitis itself has numerous etiologies, biliary track diseases, alcohol, post ERCP, trauma, drugs, infection, hereditary, hypercalcemia, tumor, toxin, and autoimmune. Infection accounts for 1% of pancreatitis case. Bacterial causes of pancreatitis may come from *Mycobacterium tuberculosis*, *Salmonella*, *Compylobacter*, and *Mycoplasma pneumonia*. *Mycobacterium tuberculosis* was suspected as the causes of pancreatitis in this case.<sup>6</sup>

The diagnosis of peritoneal tuberculosis was particularly based on clinical suspicion.<sup>5</sup> Routine laboratory studies are nonspecific. A normal leukocyte count is presenting in most patients, a mild normocytic normochromic anemia is present in approximately 50% of patients. The laboratory data of the patients showed normal leukocyte count and mild normocytic normochromic anemia. Tuberculin testing with purified protein derivative (PPD) is positive in approximately 70% of patients, however a negative result is of no help in excluding the diseases. Patients with a known previous skin reaction to TB maybe anergic at the time of PPD reading.<sup>8</sup>

A chest X-ray may show evidence of old tuberculosis 20 to 30% of patients while features of active tuberculosis are much less common. Other radiologic features such as peritoneal thickening, omental caking, and the presence of ascites with fine mobile septations on ultrasound and CT imaging may suggest the diagnosis. In this case, ultrasound imaging revealed omental thickening confirming the diagnosis with the presence of ascites.<sup>8</sup>

Tuberculous peritonitis should be considered in all patients presenting with a serum-ascites albumin gradient (SAAG) of < 1.1 g/dL. The diagnosis can be difficult since the onset can be insidious, it can have a variable presentation, and since it can frequently be seen in patients with underlying liver or renal disease. The gold standard for diagnosis is culture growth of *Mycobacterium* on ascitic fluid or a peritoneal biopsy. In this case, patients presented SAAG 0.53 g/dL, but peritoneal biopsy under peritoneoscopy was cancelled to perform because of its complication.<sup>4,5,8</sup> Laparoscopic investigation of tuberculous peritonitis could fail in up to 1-16% cases, and is not without a risk. Intestinal perforation is the major complication beside ascites oozing and omental hemorrhage.<sup>9</sup>

Abdominal TB should be considered in all cases with ascites. Uzonkoy et al experience suggests that PCR of ascitic fluid obtained by ultrasound-guided fine needle aspiration is a reliable method for its diagnosis and should at least be attempted before surgical intervention.<sup>5</sup> The PCR of ascitic fluid of this patient was examined to confirm the diagnostic and the result was positive.

PCR assays, which amplify mycobacterial 16S ribosomal RNA, show promise of rapid detection of mycobacteria. The diagnostic sensitivity of TB PCR is for pulmonary and extrapulmonary specimens was 82.3% and 72.0%, respectively. Adenosine deaminase is a purine-degrading enzyme that is necessary for the maturation and differentiation of lymphoid cells. Adenosine deaminase activity (ADA) of ascitic fluid has been proposed as a useful non-cultured method of detecting tuberculous peritonitis. Sensitivity and

specificity of ADA level in tuberculous ascites have been reported as high as 100 and 97%.<sup>4,8,10</sup>

Barghava et al studied 87 patients with high protein ascites, of which 38 were diagnosed as having tuberculosis. They found visual appearances to be more helpful (95% accurate) than either histology, culture or guinea pig inoculation (82.3% and 37.5% sensitivity respectively). Caseating granulomas may be found in 85-95% of the biopsies. The laparoscopic findings in peritoneal tuberculosis can be grouped into 3 categories: (1) Thickened peritoneum with tubercles: multiple, yellowish white, uniform sized (about 4-5 mm) tubercles diffusely distributed on the parietal peritoneum. The peritoneum is thickened, hyperemic, and lacks its usual shiny luster. The omentum, liver, and spleen can also be studded with the tubercles; (2) Thickened peritoneum without tubercles; (3) Fibroadhesive peritonitis with markedly thickened peritoneum and multiple thick adhesions fixing the viscera.<sup>3</sup>

All patients should receive conventional antitubercular therapy for at least 6 month including initial 2 months of rifampicin, isoniazid, pyrazinamide, and ethambutol. A randomized comparison of 6 month short course chemotherapy with a 12 month course was conducted by Balasubramaniam et al and the cure rate was 99 and 94% in patients given short-course and the 12 months regimen respectively.<sup>34</sup> However, many physicians extend the treatment duration to 12 to 18 months. Two reports suggest that obstructing intestinal lesions may relieve with antitubercular drugs alone without surgery. Anand et al reported clinical and radiological resolution of tuberculous strictures with drug therapy even in patients with subacute intestinal obstruction.<sup>3</sup>

The addition of corticosteroids for the first two or three months of treatment may reduce the incidence of late complications arising from adhesive disease, such as small bowel obstruction. Fever usually resolves within one week of commencing anti-tuberculous treatment. More than 90% of patients have improvement in abdominal ascites within weeks of initiating treatment. In this case, patients was administered corticosteroid and the symptoms were resolved after treatment.<sup>8,10,11</sup>

Therapeutic surgery is indicated for complications like intestinal obstruction (acute, acute on chronic, chronic), perforation and peritonitis.<sup>6</sup>

Mortality ranged from 8 to 50% in various series. Advanced age, delay in initiating therapy, and underlying cirrhosis have been associated with higher mortality rates. Some patients develop complications such as small bowel obstruction related to adhesions.<sup>8,10</sup>

Tuberculous peritonitis may be fatal but is medically cured if diagnosed in a timely fashion.

Although both non-invasive and invasive tests have additional benefits, clinician suspicion is still the first step for the diagnosis of tuberculous peritonitis.<sup>5</sup>

This patient condition after receiving anti tuberculous therapy and additional corticosteroid had improved without any complications and clinically stable.

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