Caspian Journal of Internal Medicine 2024 (Autumn); 15(4): 735-742
DOI: 10.22088/cjim.15.4.735

Case Report

Concurrent peritoneal and pleural tuberculosis in an adult: A case report and literature review

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Received: 15 April 2023
Revised: 29 July 2023
Accepted: 27 Sep 2023
Published: 9 Sep 2024

Abstract

Background: The simultaneous involvement of the pleura and peritoneum with tuberculosis in the absence of pulmonary foci is an uncommon condition that may lead physicians to misdiagnose.

Case Presentation: Herein, we present a Persian male adult who manifested with epigastric pain, weakness, and a history of pleuritic chest pain two months prior to admission. The findings of the physical examination included vital signs within the normal range, unilateral fine crackle in the lung, abdominal distension with positive shifting dullness, and fluid wave test. Analysis of the ascitic fluid revealed a Serum-ascites albumin gradient (SAAG) of less than 1.1g/dl, indicating a non-portal condition. The results of the acid-fast bacilli (AFB) staining as well as the TB polymerase chain reaction (PCR) test were negative. However, the adenosine deaminase (ADA) level was 44 IU/L. A chest CT scan revealed mediastinal lymph node enlargement and pleural thickening with loculated pleural effusion. Three acid-fast bacilli smear of morning sputum were sent, and all three were negative. An abdominopelvic CT scan showed multiple periaortic and mesenteric lymph nodes of varying sizes with mesenteric haziness and accumulation of effusion in the peritoneal cavity. Eventually, peritoneal biopsy, the gold standard, was performed, which revealed multiple granulomatous lesions and areas of caseous necrosis surrounded by Langerhans giant cells and epithelioid cells.

Conclusion: It is worth noting that in cases of ascites and pleural thickening, especially in patients with poor socioeconomic status, simultaneous pleural and peritoneal TB should be considered, especially in third-world countries.

Keywords: Extrapulmonary, Tuberculosis, Pleural effusion, Ascites, Case report, Literature review.

Citation:
Barahimi E, Ghaeini Hesarooeyeh Z, Basham A, Karimi M, Heidari B. Concurrent peritoneal and pleural tuberculosis in an adult: A case report and literature review. Caspian J Intern Med 2024; 15(4): 735-742.

Extrapulmonary tuberculosis (EPTB) is the involvement of any organs within the body except lungs by *Mycobacterium tuberculosis* (MBT) (1) Sixteen percent of the 7.5 million notified TB patients have EPTB, ranging from 8% in the Western Pacific area to 24% in the Eastern Mediterranean area (2). Peritoneum is an uncommon site for developing TB. Fifteen percent of new TB cases are EPTB, and the peritoneum constitutes 4-10% of them (3). Peritoneal TB (PTB) can manifest with pain and distension in abdomen area, weakness, unintentional weight loss, night sweats, nausea, and vomiting (4).

Pleura is the second frequent site for EPTB. The incidence of tuberculous pleural effusion (TPE) among TB patients in developed countries is about 3-5% whereas in developing countries with high proportion of HIV-positive individuals reaches to 30% (5, 6). The effusion can range from completely benign which absorbed to complicated that thicken the pleura or other complications such as empyema and fibrothorax (7). Herein, we describe an uncommon case of extrapulmonary TB involving peritoneum and pleura presented with abdominal and chest pain.

Case Presentation

A 35-year-old Persian man, presented with epigastric pain and weakness for 10 days prior to admission. The pain was constant, non-radiating, and not associated with eating. He also had a history of chest pain since a month before admission, which was described as a burning pain during inhalation. The pain worsened with moving and coughing. He had no history of dyspnea. The patient had lost about eight kilograms during three months without changing his diet. Social history revealed he was addicted to heroin. Family history included multiple abdominal lipomas in his mother, and his sister died of Crohn disease.

The patient was oriented, ill but not toxic in general appearance with normal vital signs including respiratory rate (RR) of 18 breaths per minute, pulse rate (PR)of 96 beats per minute, blood pressure (BP) of 110/67 mmHg and temperature(T) of 36.9 °C. The patient had pale conjunctiva on physical exam. On chest examination, auscultation revealed unilateral fine crackle in the left lung and heart sounds were normal. Inspection and palpation of the chest were normal. On abdominal physical exam, the abdomen was distended, umbilicus bulged, bowel sounds decreased, and the epigastric area was tender. Shifting dullness and fluid wave tests were positive.

Laboratory (lab) tests requested for the patient that revealed white blood cell (WBC) count of 2.8×10^9 /L (4-11) (neutrophils 67.7% and lymphocytes 18.4%), hemoglobin (Hb) 8.5 g/dL (13-16), red blood cell (RBC) 3.22×10^6/µL, red cell distribution width 17.9%, estimated sedimentation rate 26 mm/hr (0-15) and C-reactive protein of 76.5 mg/L (0-6). The lab data within normal range are depicted in table 1. Lab tests regarding anemia (Hb: 8.5 g/dL) were requested to evaluate. According serum iron 45 µg/dL (50-160), ferritin: 321.95 ng/mL (21-284), total iron-binding capacity 238 µg/dL (250-450) and microcytosis in peripheral blood smear, the results were suggestive of anemia of chronic disease. Considering leukopenia (WBC:2.88×10^9 /L) and a history of addiction, we suspected to an immune deficiency condition in our patient, thus, we checked viral markers including human immune deficiency virus antibody (HIV), HIV-p24 antigen, hepatitis B surface antigen, and hepatitis C antibody that all were negative.

We also requested chest and abdominopelvic computed tomography (CT) scan. Chest CT scan revealed mediastinal lymph nodes and plural thickening with loculated pleural effusion in left side (figure 1). Abdominopelvic CT scan showed multiple periaortic and mesenteric varying size lymph nodes with mesenteric haziness (figure 2) and accumulation of effusion in peritoneal cavity (figure 3). The abdominal fluid aspirated under the guidance of ultrasound and sent to the laboratory for cell count, cell diff, level of albumin, culture, total protein, Gram stain and cytology. The fluid gross appearance was cloudy. A drainage catheter was also inserted. The result of ascites fluid analysis was as follows; WBC: 1150 (lymphocyte: 95% and polymorphonuclear: 5%), RBC: 3750, glucose: 88 mg/dL, protein: 4.61g/dL, albumin: 2.3 g/dL.

The culture of the fluid exhibited no growth after 48 hours. Simultaneous serum albumin content was 2.7 g/dL. Since Serum-ascites albumin gradient (SAAG) was <1.1g/dl, favored non-portal hypertensive causes. Our differential diagnosis included nephrotic syndrome, peritoneal carcinomatosis and abdominal TB. Further investigations on ascites fluid revealed negative acid-fast bacilli (AFB) staining, negative TB polymerase chain reaction (PCR) test, and adenosine deaminase (ADA) level of 44 IU/L. Moreover, three serial sputum smear examination was done that no AFB was seen.

Diagnostic laparoscopy found scattered whitish nodules over the peritoneum. Peritoneal biopsy was performed that revealed multiple granulomatous lesions and areas of caseous necrosis surrounded by Langerhans giant cells and epithelioid cells (figures 4a and 4b). The result of PCR on the biopsy sample was positive for MTB. Acid fast staining of the tissue biopsy was negative (figure 5).

Regarding pleuritic chest pain, with the suspicion of simultaneous involvement of pleura and peritoneum, we tapped pleural fluid. The appearance of the fluid was citrus yellow. Analysis of the liquid revealed LDH level 586 U/L, ADA 52 IU/L, protein 4.8 g/dL. Moreover, cytology exam revealed mononuclear predominance. All findings were in favor of pleural TB. Anti TB treatment and vitamin B6 started for the patient.

After two weeks of hospitalization, the patient general condition has improved. He gained weight; the appetite increased. The symptoms such as weakness, abdominal pain, chest pain relieved. Noteworthy, all procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee at which the studies were conducted (IR.HUMS.REC.1401.169) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Table 1. Laboratory data. Lab data within normal range is depicted here

Lab data	Amount	Normal range
BUN (mg/dL)	8.8	6-24
sodium (mEq/L)	130	135-145
potassium (mEq/L)	4.3	3.5-5
Blood sugar (mg/dL)	111	<140
Uric acid (mg/dL)	2.1	3.5-7.2
Alanine transaminase (U/L)	15	<41
Aspartate transaminase (U/L)	27	<37
Alkaline phosphatase (U/L)	209	100-360
Total bilirubin (mg/dL)	0.3	0.3-1.2
Direct bilirubin (mg/dL)	0.2	≤0.3
Prothrombin time (s)	16.1	12-14
Partial thromboplastin time (s)	35	25-45
International normalized ratio	1.5	<1.1
Lactate dehydrogenase (U/L)	372	120-460
Amylase (U/L)	64	<100
Lipase (U/L)	21	<60
Urine analysis	Normal	

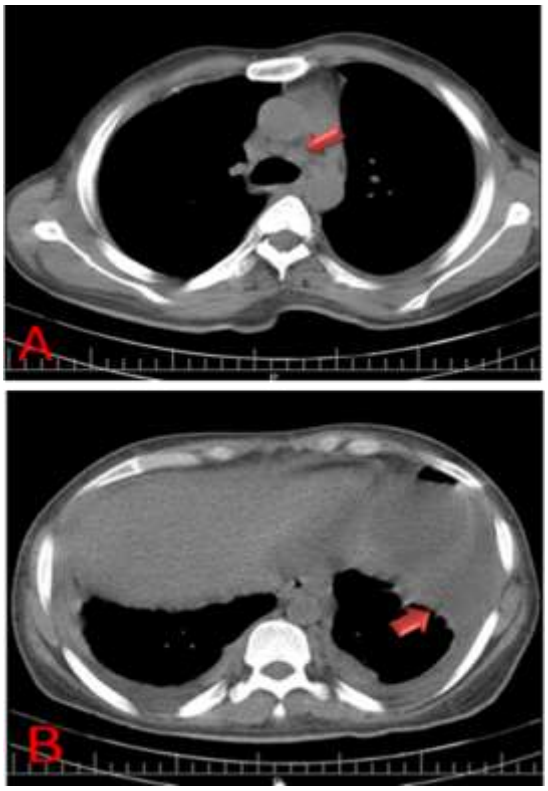

Figure 1. A shows mediastinal lymph nodes in chest CT-scan. B indicates Pleural thickening with loculated pleural effusion

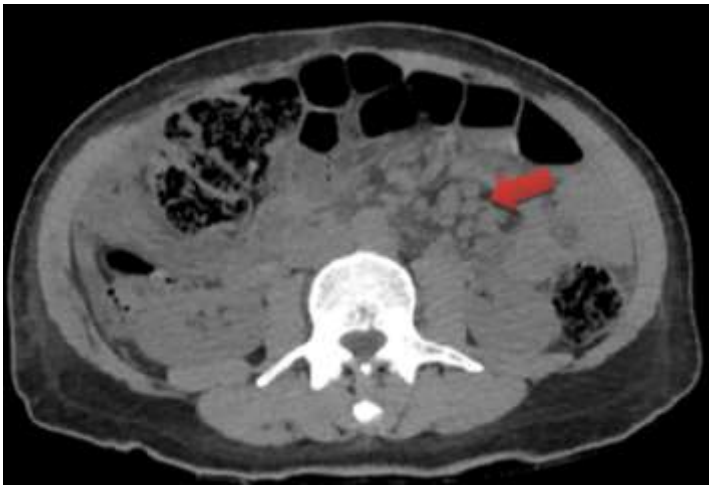

Figure 2. Multiple periaortic and mesenteric varying size lymph nodes with mesenteric haziness is seen

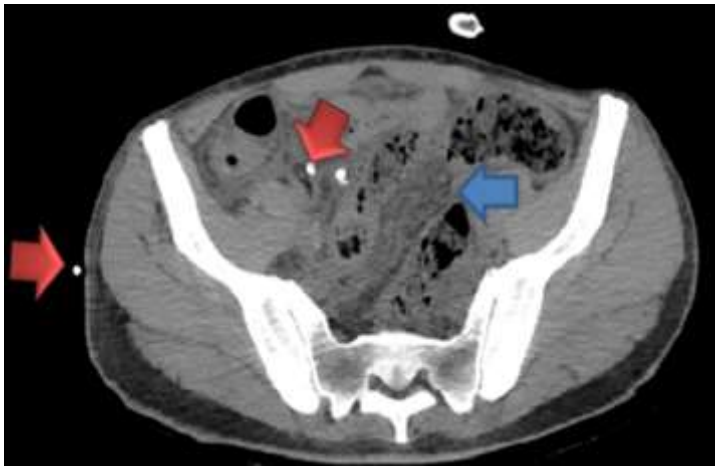

Figure 3. Blue arrow shows ascites fluid in peritoneal cavity and red arrows show indwelling peritoneal catheter for ascites drainage

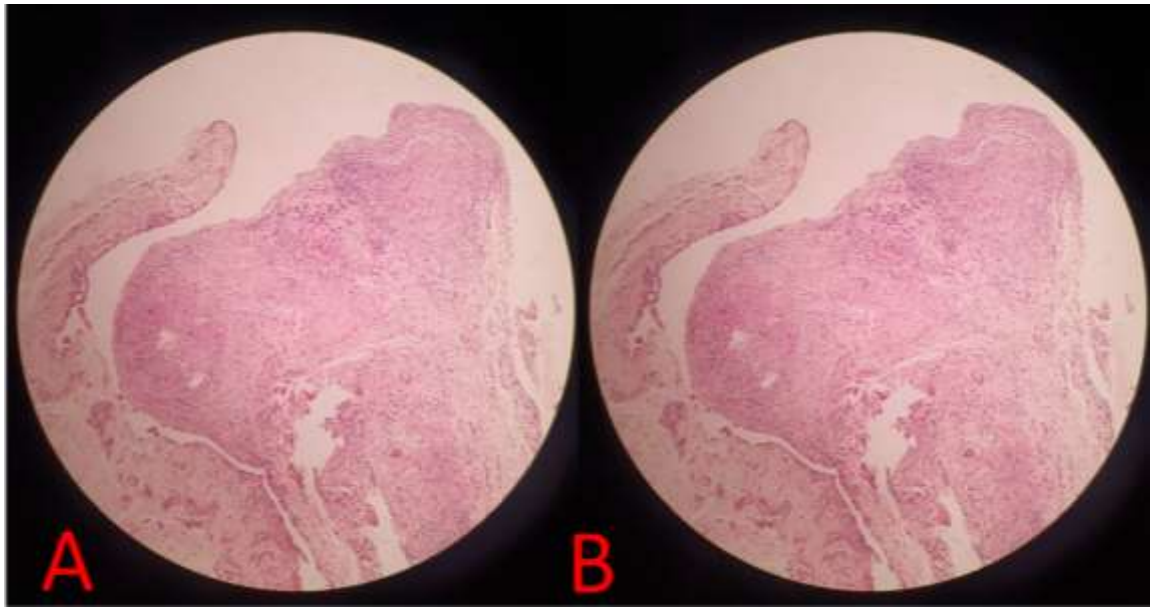

Figure 4. Peritoneal biopsy. A&B show multiple granulomatous lesions and areas of caseous necrosis (original magnification ×40)

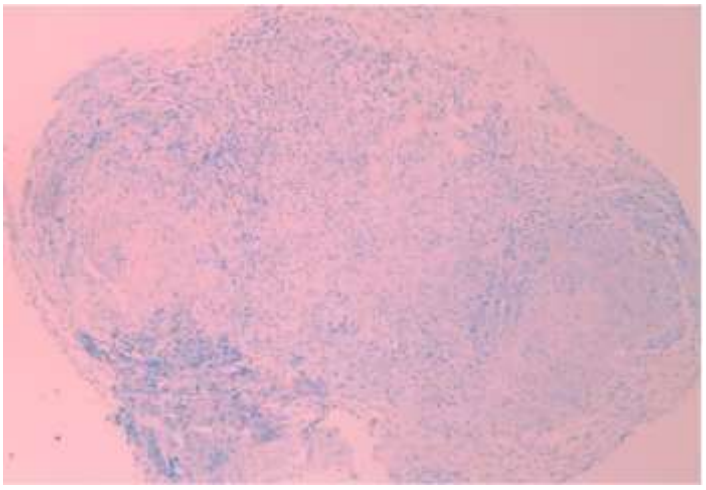

Figure 5. Acid fast staining. The image shows a negative acid-fast staining of peritoneum sample (Original magnification ×40)

Discussion

PTB patients commonly present with abdominal pain, weight loss, and fever. Other symptoms are abdominal mass or constipation, vomiting and signs of peritonitis such as abdominal tenderness and ascites. Our patient presented with epigastric pain, weight loss and weakness without any history of fever. PTB causes only 2% of all ascites; however, ascites in PTB is frequent (1, 8). The major route of dissemination to peritoneum is lymphohematogenous spread from a pulmonary focus (1); however swallowing sputum containing bacteria, ingestion of contaminated milk and directly transmission from infected adjacent sites could be other paths (2). CT scan is a helpful imaging modality to evaluate PTB suspected patients. Signs which are in favor of PTB including : 1) enhancement and regular thickening of peritoneum; 2) mesenteric macro nodules; 3) retroperitoneal and peripancreatic lymphadenopathy with hypodense center and ring enhancement; 4) enlargement and calcification of spleen (9).

Peritoneal TB is divided into three categories based on manifestations: 1) The wet-type, which presents with a large amount of loculated or high protein fluid; 2) The fibrotic type, which presents with adhesion in the bowel along the mesentery and omentum; 3) The dry plastic type, which presents with a gross inflammatory reaction characterized by scattered fibrous adhesions and nodules all over the peritoneum. Notably, PTB can manifest as a combination of these three types (2). Our case was the wet type due to the presence of ascites. PTB diagnosis is determined based on the combination of clinical presentation, ascites fluid microbiology, histopathology findings of peritoneum tissue sample, laboratory and radiological findings. Moreover, empirical antibiotic therapies with tight response monitoring are helpful to establish the diagnosis (10). Recent studies have found that acid fast bacilli (AFB) smear and ascetic fluid TB culture sensitivity is 2% and less than 20%, respectively; therefore, negative results could not rule out TB infection. TB fluid culture result takes 2–3 weeks, while early diagnosis is crucial to prevent complications. Other methods such as ADA level measurement, and PCR of ascetic fluid can be used to predict and detect mycobacterium TB, respectively. Both assays are non-invasive with high sensitivity (2, 9).

ADA, a purine metabolism enzyme related to T cell differentiation, increases following T cell differentiation in response to TB antigen. Therefore, it could be a useful marker for diagnosing PTB. Ascitic fluid ADA levels greater than 30 U/L have a sensitivity and specificity of more than 90% for peritoneal TB (2).

Gene amplification tests have tremendous potential in detecting MTB. The expert nested real-time MTB/rifampicin PCR (Cepheid Gene Xpert ® system, USA) was approved by WHO in 2010 for use in cases of pulmonary TB. In cases of EPTB, the Xpert MTB/RIF assay provides a sensitivity ranging from 31% in pleural tissue to 97% in bone or joint. Overall, this method is recognized as an excellent diagnostic tool. However, its sensitivity varies depending on the tissue sample. Instead, multiplex PCR that detects two specific gene sequences of the MTB genome, mycobacterial protein 64 and insertion sequence 6110, has a pooled sensitivity of approximately 94.5% in addition to lower cost compared to the Xpert MTB/RIF assay (2) The histopathology findings show necrotizing granulomatous inflammation with caseous necrosis, as well as the presence of Langerhans-type giant cells (11). In our case, peritoneal AFB smear was negative, however, ADA level of ascites

fluid (44 IU/L), peritoneum appearance in laparoscopy (scattered whitish nodules), histopathology evaluation of the tissue sample (caseating granuloma) confirmed PTB diagnosis. However, the result of the PCR test on the peritoneal fluid sample was negative. We summarized the case reports that similarly presented cases with pleural and peritoneal TB without any evidence of pulmonary foci in table 2. TPE is usually a typically acute to subacute illness that presents with fever (85%), unilateral pleuritic chest pain (75%), cough (70%), dyspnea (50%), night sweats (50%), and weight loss (25-85%) (6).

Our patient had pleuritic chest pain with no history of dyspnea. The pleural fluid in TPE has a citrus yellow appearance, but it could be cloudy. LDH levels elevate in 75% of patients and usually exceed 500 IU/L. Protein levels elevate to more than 30 g/L, which is present in 55-75% of cases. The cell count increases as neutrophils are dominant earlier on, but over time, lymphocytes, especially T-cells, become dominant, with the lymphocyte to neutrophil ratio being over 75% (6). Same as peritoneum, pleura is primarily involved by lymphohematogenous spread of mycobacterium TB. Another common rout of pleural infection is contact to a pulmonary source (12). Quantification of ADA level is a convenient and inexpensive method for TPE diagnosis. The ADA level elevates even in AIDS patients with low CD4+ counts. The most commonly accepted cut-off value for ADA is 40 U/L. The sensitivity and specificity are estimated to be 92% and 90%, respectively (5).

Interferon gamma is a useful marker for diagnosing pleural tuberculosis. Considering a cut-off point of 140 pg/mL provides sensitivity and specificity of 86% to 97% and 95% to 100%, respectively. The usefulness of this marker in diagnosing pleural TB is similar to that of ADA, with the added advantage of being highly specific for pleural fragments or pleural fluid. However, its high cost presents an obstacle to its routine use (12). The detection of MTB in pleural fluid by preparing conventional smear microscopy via Ziehl-Nielsen or Auramin stain has a low yield of less than 10%. The yield of MTB culture depends on the culture medium. For instance, solid media such as Lowenstein-Jensen medium provide a yield of less than 30%. On the other hand, the new liquid medium, the BACTEC MGIT (Becton-Dickinson, Franklin Lakes, NJ, USA), This method yields positive results in up to 70% of patients and requires a shorter time to get a positive result compared to solid medium (6). Nucleic acid amplification tests (NAAT) in the form of commercial and in-house tests are used to detect MTB-specific nucleic acid sequences in sputum and pleural effusion. The specificity of these tests is 97% and 91% for commercial and in-house kits, respectively. However, the poor and variable sensitivity in addition to its high cost limits its application as a useful diagnostic method (5). Pleural TB is typically diagnosed through the visualization of caseating granuloma or, more rarely, acid-fast bacilli in a biopsy sample. Thoracoscopy is the preferred method for collecting a sample in settings with adequate resources and expertise, as it can provide a sensitivity of up to 100%. However, a closed pleural biopsy under the guidance of sonography is a suitable option that can provide a sensitivity of 90% in shortage of such facilities (5).

In conclusion, we are presenting a case of extrapulmonary TB that involves both the pleura and peritoneum simultaneously. The takeaway from this case is that TB diagnosis can sometimes be delayed due to the similarity of its symptoms with other conditions. Therefore, physicians should include pleural and peritoneal TB in their list of differential diagnoses for patients who have pleuritic chest pain, abdominal pain, ascites, and constitutional symptoms, especially in developing countries.

Table 2. Summary of published reports regarding pleural and peritoneal tuberculosis. We excluded reports with military TB or primary pulmonary foci

Case	Manifestation	Diagnosis								
		Pleural TB					Peritoneal TB			
		ADA	Fluid AFB Stain/culture	AFB Sputum	MTB-PCR	Biopsy	ADA	Fluid AFB Stain/culture	MTB-PCR	Biopsy
A 4-year-old male patient (13)	Progressive abdominal distention, growth retardation, decrease in breath sounds, dullness to percussion in the lower part of the lung.	–	N	–	–	–	–	–	–	–

Case	Manifestation	Diagnosis								
		Pleural TB					Peritoneal TB			
		ADA	Fluid AFB Stain/culture	AFB Sputum	MTB-PCR	Biopsy	ADA	Fluid AFB Stain/culture	MTB-PCR	Biopsy
A 15-year-old male adolescent (12)	A generalized abdominal pain, fever, chills, night sweats and weight loss for 45 days, progressive abdominal distension, respiratory distress	P	N	_	N	P	P	N	N	_
A 19-year-old male (14)	High fever and shortness of breath for 1 month CT scan: left-sided encysted pleural effusion with mediastinal lymphadenopathy echocardiography: pericardial effusion ultrasonography: ascites & multiple enlarged lymph nodes in abdomen.	P	N/culture of fluid on BACTEC medium positive	N	_	P	_	_	_	_
A 21-year old woman with cystic lesion in right ovary (15)	Progressive abdominal swelling, fatigue, fever and dry cough for two weeks	_	_	N	_	P	_	N	_	_
A forty nine-year-old man living in TB endemic area & daily alcohol user for 20 years (16)	A case of covid-19 that after receiving treatment & recovery, still had intermittent fever, growing abdominal fluid, in addition to loculated pleural effusion & bilateral calcified hilar lymph nodes on chest CT scan	N	N	N	_	_	N	N/ Culture of fluid positive for MTB	_	_
A 50 -year old female (17)	A case of poly serositis presented with shortness of breath with pleuritic nature & lower limbs edema for three months, abdominal distension for 15 days, in addition to evidence of pericardial thickness3.0 mm & minimal pericardial effusion on echocardiography. The result of ascitic & pleural fluid analysis highly suggestive of TB	_	_	_	CBNAAT was negative	_	_	_	_	_

Acknowledgments

We wish to thank our counselors in the Clinical Research Center of Shahid Mohammadi hospital in Bandar Abbas.

Funding: The study did not receive any funding.

Consent for publication: The authors claim no conflict of interest.

Authors' contribution: EB, MK, and BH participated in the clinical reasoning and reviewed the manuscript. ZG and AB drafted the manuscript. All the authors read the manuscript and confirmed its content and accuracy in describing the case.

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