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Case Report

Tuberculous peritonitis in children: Two case reports highlighting the important role of imaging[☆]

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ABSTRACT

Tuberculous peritonitis is an uncommon extrapulmonary form of *Mycobacterium tuberculosis* infection, frequently presenting with nonspecific and insidious symptoms. Diagnosis is therefore difficult, unsuspected, and often delayed, especially in the pediatric patient without an obvious history of exposure to the pathogen.

This report presents a 9-year-old Hispanic girl and a 3-year-old African American boy presenting with nonspecific and insidious symptoms, such as abdominal pain, distention, and fever in whom computed tomography findings of peritoneal thickening and enhancement, high density ascites, lymphadenopathy, and bowel wall thickening acted as key components in establishing a final diagnosis of the condition. Computed tomography is an important clinical adjuvant in making this difficult diagnosis.

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Introduction

Although tuberculosis (TB) is on the decline in the United States, it remains a prevalent condition worldwide [1]. The disease is caused by the bacterium *Mycobacterium tuberculosis*, affecting nearly 10 million patients per year and causing approximately 1.5 million deaths [2]. While TB is typically known for affecting the lungs, the disease is also able to af-

fect other parts of the body, such as the pleura, lymph nodes, skin, joints, bones, and abdomen [3]. Abdominal involvement of TB occurs in approximately 11% of patients with extrapulmonary TB, and may present in areas such as the peritoneum, gastrointestinal tract, hepatobiliary tract, or lymph nodes [4]. Patients who are at a high risk for such involvement include those who are immunosuppressed, with approximately 12% of new diagnoses occurring in patients who are HIV positive [2]. Other high risk factors include patients with

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cirrhosis, use of continuous ambulatory peritoneal dialysis in patients with chronic renal failure, diabetes mellitus, malignancy, and immigrants from areas with high prevalence of TB [5,6].

Abdominal TB, while more common in the 25–45 year old age group, is rare in the pediatric population. Within the small subset of pediatric cases, peritoneal involvement is more common than gastrointestinal, with the most frequent presentation being that of abdominal pain, distention, and fever. It has been reported that the incidence of peritoneal TB in children under the age of 20 in the United States is as little as 0.3% [7]. In this article, we present 2 pediatric cases of peritoneal TB with insidious onset of symptoms in which the radiographic findings acted as key components in establishing the final diagnosis.

Cases

Patient 1

A 9-year-old Hispanic girl with a history of traumatic brain injury with resultant hydrocephalus at the age 2 years, ventriculoperitoneal (VP) shunt, and cochlear implant was admitted with a 9-day history of daily fever, change in behavior, and decreased appetite. The patient was nonverbal but was able to sign some words; her mother said that her daughter felt nauseated and had decreased appetite. She was admitted to our hospital for treatment of right middle and right lower lobe pneumonia 10 months prior to this presentation.

On admission, she was febrile to 38.3 °C and appeared nontoxic but fatigued and pale. Her examination was significant for a palpable cochlear implant and a palpable VP shunt reservoir with no overlying erythema. Her lungs were clear. Her abdomen was soft and nontender with no palpable masses at that time.

Initial laboratory findings on admission were total white blood cells (WBCs) 5500 with 43% polymorphonuclear leukocyte, 16% bands, 23% lymphocytes, 16% monocytes, 1% eosinophil, and 1% atypical lymphocytes. The hemoglobin was 10.6 gm/dL and the platelet count was 545,000. C-reactive protein was 11.75 mg/dL and erythrocyte sedimentation rate was 71 mm/h.

Admitting diagnosis was suspected VP shunt infection or meningitis. Lumbar puncture revealed clear and colorless cerebral spinal fluid (CSF). There were 2 WBCs and 519 red blood cells; the CSF protein was 29 mg/dL and the glucose was 61 mg/dL (serum glucose was 83 mg/dL). On the second hospital day, her VP shunt was tapped. The protein was 7 mg/dL, glucose 64 mg/dL. There were 2 WBCs and 0 red blood cells.

Her hospital course was complicated by poor oral intake, weight loss, and daily spiking fevers despite broad spectrum antibiotics. Multiple blood cultures were sterile. Her CSF and VP shunt fluid cultures were sterile and she had a negative urine culture. Her hemoglobin dropped and inflammatory markers remained elevated. A gamma interferon release assay for TB was equivocal. On the fourth hospital day, she developed abdominal distention and pain on palpation. She underwent a computed tomography (CT) scan of the abdomen and

pelvis (Fig. 1) revealing ascites, thickening, and nodularity of the omentum, as well as wall thickening of the small bowel loops without obstruction.

Based on the results of the CT scan, she underwent peritoneal fluid sampling by interventional radiology. The fluid had a protein of 4.9 mg/dL. The total WBCs were 1626 with 42% polymorphonuclear leukocyte, 27% lymphocytes, and 31% mono and/or macrophages. The Gram stain of the fluid showed no WBCs and no organisms. All cultures of the peritoneal fluid including routine, anaerobic, acid fast bacilli (AFB), and fungal were negative.

The patient was transferred to another institution for removal and replacement of her VP shunt and further work up. She was hospitalized at the second institution for 4 weeks during which time she continued to spike high fevers despite treatment with multiple broad spectrum antibiotics. Her VP shunt was externalized and ultimately replaced as ventriculoatrial shunt. Although afebrile at hospital discharge, her appetite and weight gain were poor.

The patient was readmitted to the referring hospital 10 days later with severe abdominal pain. She was taken to the operating room for exploratory laparotomy. Omentum was sent for histopathology and for culture. The histopathology revealed multiple giant cell granulomas, some of which were caseating. The AFB culture grew *M tuberculosis* complex, later confirmed as pan-susceptible TB. Peritoneal fluid also grew the *M tuberculosis*.

Patient 2

A 3-year-old African American boy with no known medical conditions was admitted for evaluation of daily fever of unknown origin for 4 weeks. He had presented to an outside hospital twice prior to arriving at our institution and was diagnosed with viral illness. His other symptoms included headache, chills, fatigue, and anorexia. For at least 3 weeks prior to admission, he had developed abdominal distention. He denied rash, cough, chest pain, adenopathy, nausea, vomiting, or diarrhea. Although born in the United States, he lived with his family in Sierra Leone, West Africa from the age of 10 months until 5 weeks prior to his illness onset and presentation at our hospital. He was behind on his vaccination schedule and had a 2 kg weight loss over the month prior to admission. On admission, he was febrile and ill-appearing but nontoxic. He was tachycardic and had subconjunctival and distal extremity pallor. His abdomen was distended and he had hepatosplenomegaly. Laboratory findings on admission were, hemoglobin 7.7 g/dL, platelet count 792,000, ESR > 100/h, and CRP 18.56 mg/dL. Blood and urine cultures were sterile. Malaria smears were negative. HIV 1 and 2 antibodies were negative. Flow cytometry showed no evidence of clonal B cell or T cell lymphoproliferative disorder.

An abdominal CT was performed (Fig. 2) revealing a large amount of ascites and nodular thickening and enhancement of the peritoneal lining. There was no free air. Following the CT, a diagnostic laparoscopy was performed to drain the ascites and sample the peritoneum. Proper precautions for peritoneal fluid were put in place during the procedure because peritoneal TB was on the differential diagnosis list.

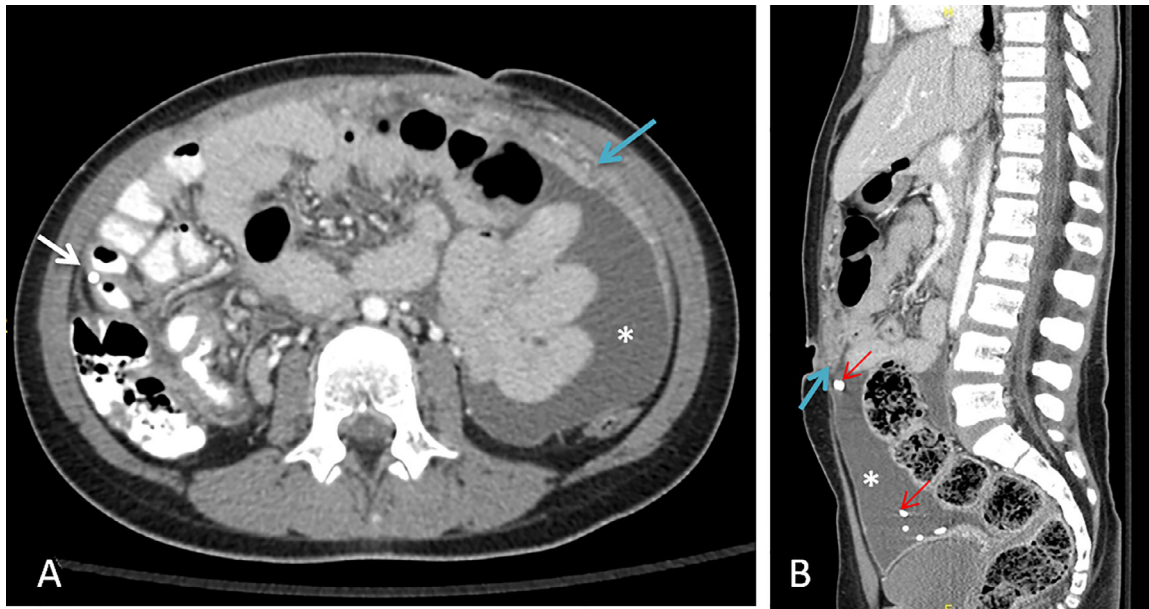


Fig. 1 – Patient 1–Axial (A) and sagittal (B) enhanced computed tomography of the abdomen and pelvis demonstrating thickening and nodularity of the omentum (blue arrow) with moderate volume ascites (white asterisks). There is also mild wall thickening of the small bowel loops within the right hemi-abdomen (white arrow) and a partially imaged coiled ventriculoperitoneal catheter noted within the ascitic fluid (red arrows). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

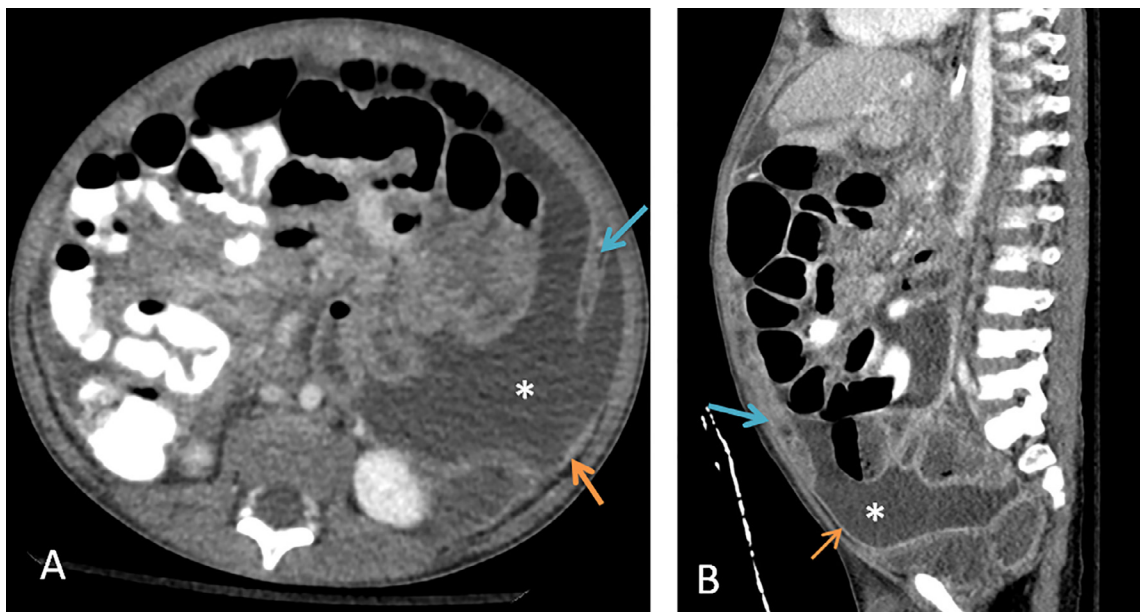


Fig. 2 – Patient 2–Axial (A) and sagittal (B) enhanced computed tomography of the abdomen and pelvis demonstrating abnormal peritoneal enhancement (orange arrow) and heterogenous thickening of the anterior abdominal peritoneal lining (blue arrows) with partially loculated large volume ascites (white asterisks). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

Cytology of the peritoneal fluid showed mixed inflammatory infiltrate with macrophages and cellular debris. There were no malignant cells. Histopathology of the peritoneal tissue revealed predominantly noncaseating granulomas with focal areas of necrosis and a few Langerhans giant cells. The peritoneal tissue grew AFB that was identified as pan-susceptible *M tuberculosis* complex.

Discussion

TB peritonitis is a common form of abdominal TB, and continues to be relatively prevalent in developing countries. The condition occurs in up to 3.5% of cases of pulmonary TB, and 31%–58% cases of abdominal TB [8]. The pathogenesis of peritoneal TB occurs most commonly via hematogenous spread after reactivation of latent TB involving primary lung foci, though it can occur during active pulmonary TB or miliary TB as well [9]. It can also result from rupture of mesenteric lymph nodes following hematogenous spread, gastrointestinal dissemination, or gynecologic involvement [10]. TB peritonitis can present with a variety of symptoms, including fever, night sweats, anorexia, weight loss, abdominal pain, and abdominal distention due to ascites [8,11].

Due to the nonspecific presentation of TB peritonitis and limited yield of diagnostic tests, diagnosis is often delayed [4,8,12]. There are a variety of clinical and laboratory investigations that may be performed, including tuberculin skin test, interferon gamma release assays, hematologic studies, peritoneal fluid analysis, laparoscopic biopsy of the involved site, mycobacterial culture, and nucleic acid amplification test. In areas where the disease has high prevalence and in particularly high risk patients with ascites, an evaluation and culture of ascitic fluid is standard for diagnosis [8].

Peritoneal biopsy performed by laparoscopy should also be considered as it can assist in making a rapid, specific diagnosis, with sensitivity rates approaching 93% [8,13,14]. Laparoscopic findings on peritoneal biopsy can include thickened peritoneum with yellow-white lesions and fibro-adhesive pattern [15,16]. The biopsy specimens can be sent for evaluation for AFB smear, culture, and polymerase chain reaction, with polymerase chain reaction showing the most sensitivity and specificity. Histologic visualization of caseating granulomas further contributes to a positive diagnosis [17].

Radiologic studies are of great value in making the diagnosis of peritoneal TB. In particular, ultrasound (US) and CT imaging, allowing evaluation of parenchymal organs, lymph nodes, and other affected sites [18,19]. Ultrasound changes can include complexity of the ascites visualized as fine mobile strands and/or septations or particulate matter within ascitic fluid. On CT, ascitic fluid has high attenuation value, with peritoneal and omental thickening, and nodularity [8,18]. Combining US and CT findings can yield strong diagnostic value in evaluating a patient for TB peritonitis. Radiological imaging with US and CT can also provide assistance for selecting and guiding an appropriate biopsy site and/or procedure, as well as monitor response to treatment [5]. In patients with TB peritonitis, chest radiographs can be abnormal up to 50%–75%

of the time, with 12%–63% of patients also having associated pleural effusion [20].

Due to variability of disease presentation and difficulty of making definitive diagnosis, treatment should be started if there is high index of suspicion based upon clinical, epidemiologic, and diagnostic criteria. Once the diagnosis is made, treatment of the condition can typically be performed with 6 months of therapy with anti TB drugs, while surgery is reserved for complications such as bowel perforation, fistula formation, intestinal obstruction, or bleeding [5]. Due to high morbidity and mortality rates associated with TB peritonitis, early diagnosis and treatment remain vital to improve prognosis.

TB peritonitis is uncommon in children, with some reports showing that 5% of total diagnoses were made in patients under the age of 14 years [20]. The clinical manifestations of general TB in children differ from those in adults, with the major factors in determining risk of progression being patient age and immunocompetency. The highest risk of disease complication is present in neonates due to their lack of fully matured immune systems. In infancy, miliary and meningeal involvement is common, and adolescents often present with progressive primary TB or cavitary disease. Extrapulmonary manifestations of TB are most common in patients who are immunocompromised [21].

The majority of children diagnosed with TB peritonitis present with abdominal distention, often accompanied by abdominal pain and fever. Other presenting symptoms may include pleural effusion in patients with coexisting pulmonary TB, cough, weight loss, night sweats, and failure to thrive. Many of these children have a family history of TB, with 1 report finding that 6 of the 9 pediatric patients with peritoneal TB had family members with prior TB diagnoses, and another showing that 10 of 12 had history of direct exposure [20,22]. Due to the severity of the disease, it must remain on a physician's differential diagnosis list especially in patients presenting with typical symptomatology and prior known exposure.

Just as in adults, ascitic fluid analysis is important for confirmation of the diagnosis, with ascitic fluid displaying exudative character. AFB, positive culture for *M tuberculosis*, and high adenosine deaminase activity in ascitic fluid may also be found. On laparoscopy, pediatric patients may have whitish tubercles with or without adhesions, as well as caseating granulomas on histological examination. Tuberculin skin testing should also be positive in many patients, but cannot be used to distinguish between latent infection and current disease, and must therefore be interpreted in the context of patient presentation [20,22]. Interferon-gamma release assay has been shown to have higher sensitivity and specificity in patients with latent TB, particularly in children younger than the age of 5 years [23].

Imaging with US or CT can be used to aid diagnosis in children. The most common findings on abdominal imaging include lymphadenopathy, high-density ascites with or without septations, omental and/or peritoneal thickening, and bowel wall thickening. Imaging can also reveal findings such as hepatomegaly, peritoneal or parenchymal abscess, or lymphadenopathy. Chest radiography is often abnormal in many patients, with 1 study involving 10 patients with a mean age

of 14.7 years showing that 9 of these patients had abnormal chest X-ray findings [20,24].

Once diagnosis is ultimately made, pediatric patients can be treated with 6-9 months of antiTB therapy and followed up appropriately to confirm resolution of disease. Since the fatality rate remains high in children with this disease if it is not diagnosed in time, early diagnosis with techniques including laparoscopy, peritoneal biopsy, imaging with US and/or CT, and ascitic fluid analysis continues to be crucial [20].

Conclusion

TB peritonitis in the pediatric patient is a rare, potentially fatal, extrapulmonary manifestation of *M tuberculosis* infection, most often presenting with fever, abdominal pain, and distention. Two companion cases demonstrate typical CT findings of an uncommon disease entity and highlight the importance of imaging in arriving at a prompt and accurate diagnosis.

REFERENCES

- [1] Miramontes R, Hill AN, Yelk Woodruff RS, Lambert LA, Navin TR, Castro KG, LoBue PA. Tuberculosis infection in the United States: prevalence estimates from the National Health and Nutrition Examination Survey, 2011-2012. *PLoS One* 2015;10(11).
- [2] Evans RP, Mourad MM, Dvorkin L, Bramhall SR. Hepatic and intra-abdominal tuberculosis: 2016 update. *Curr Infect Dis Rep* 2016;18(12):45.
- [3] Lee JY. Diagnosis and treatment of extrapulmonary tuberculosis. *Tuberc Respir Dis* 2015;78(2):47–55.
- [4] Rathi P, Gambhire P. Abdominal tuberculosis. *Assoc Physicians India* 2016;64(2):38–47.
- [5] Vaid U, Kane GC. Tuberculous peritonitis. *Microbiol Spectr* 2017;5(1).
- [6] Chow KM, Chow VC, Hung LC, Wong SM, Szeto CC. Tuberculous peritonitis-associated mortality is high among patients waiting for the results of mycobacterial cultures of ascitic fluid samples. *Clin Infect Dis* 2002;35(4):409–13.
- [7] Usta M, Urganci N, Dalgic N, et al. Clinical presentation in a series of eight children with abdominal tuberculosis: experience of a single-center in Turkey. *Iran J Pediatr* 2017;27(6):9766.
- [8] Sanai FM, Bzeizi KI. Systematic review: tuberculous peritonitis – presenting features, diagnostic strategies and treatment. *Aliment Pharmacol Ther* 2005;22:685–700.
- [9] Karanikas M, Porpodis K, Zarogoulidis P, Mitrakas A, Touzopoulos P, Lyraztopoulos N, Polychronidis A. Tuberculosis in the peritoneum: not too rare after all. *Case Rep Gastroenterol* 2012;6(2):369–74.
- [10] Da Rocha EL, Pedrassa BC, Bormann RL, et al. Abdominal tuberculosis: a radiological review with emphasis on computed tomography and magnetic resonance imaging findings. *Radiol Bras* 2015;48(3):181–91.
- [11] Manohar A, Simjee AE, Haffejee AA, Pettengell KE. Symptoms and investigative findings in 145 patients with tuberculous peritonitis diagnosed by peritoneoscopy and biopsy over a five year period. *Gut* 1990;31(10):1130–2.
- [12] Debi U, Ravisankar V, Prasad KK, et al. Abdominal tuberculosis of the gastrointestinal tract: revisited. *World J Gastroenterol* 2014;20(4):14831–40.
- [13] Marshall JB. Tuberculosis of the gastrointestinal tract and peritoneum. *Am J Gastroenterol* 1993;88:989–99.
- [14] Abdelaal A, Alfkey R, Abdelaziem S, et al. Role of laparoscopic peritoneal biopsy in the diagnosis of peritoneal tuberculosis. A seven-year experience. *Chirurgia* 2014;109(3):330–4.
- [15] Bhargava DK, Chopra P, Nijhawan S, et al. Peritoneal tuberculosis: laparoscopic patterns and its diagnostic accuracy. *Am J Gastroenterol* 1992;87(1):109.
- [16] Uzunkoy A, Harma M. Diagnosis of abdominal tuberculosis: experience from 11 cases and review of the literature. *World J Gastroenterol* 2004;10(24):3647.
- [17] Hickey AJ, Gounder L, Moosa MY. A systematic review of hepatic tuberculosis with considerations in human immunodeficiency virus co-infection. *BMC Infect Dis* 2015;15:209.
- [18] Demirkazik FB, Akhan O, Ozmen MN, Akata D. US and CT findings in the diagnosis of tuberculous peritonitis. *Acta Radiol* 1996;37(4):517–20.
- [19] Vazquez ME, Gomez-Cerezo J, Atienza Saura M, Vázquez Rodríguez JJ. Computed tomography findings of peritoneal tuberculosis: systematic review of seven patients diagnosed in 6 years (1996-2001). *Clin Imaging* 2004;28(5):340.
- [20] Dinler G, Sensoy G, Helek D, et al. Tuberculous peritonitis in children: Report of nine patients and review of the literature. *World J Gastroenterol* 2008;14(47):7235–9.
- [21] Cruz AT, Starke JR. Clinical manifestations of tuberculosis in children. *Paediatric Respir Rev* 2007;8(2):107–17.
- [22] Chavalittamrong B, Talalak P. Tuberculous peritonitis in children. *Progress in Pediatric Surgery* 1982;15:161–7.
- [23] Ge L, Ma JC, Han M, et al. Interferon-gamma release assay for the diagnosis of latent *Mycobacterium tuberculosis* infection in children younger than 5 years: a meta-analysis. *Clin Pediatr* 2014;53(13):1255.
- [24] Lin YS, Huang YC, Lin TY. Abdominal tuberculosis in children: a diagnostic challenge. *J Microbiol Immunol Infect* 2010;43(3):188–93.