Tubercular Peritonitis in a Former Correctional Facility Inmate

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Tuberculosis continues to be a major illness and cause of death throughout the world.[1] In the United States, the Centers for Disease Control and Prevention reported 14,517 cases of active tuberculosis in 2004, or 4.9 cases per 100,000 persons.[2] Although the 2004 data represent decreases in the number of new cases from previous years, there have been increases among foreign-born persons and new cases of multidrug resistant tuberculosis, both of which are contributing to the decelerating rate of decline in new cases of tuberculosis.[3] The annual rate of cases of tuberculosis decreased by 7.1% between 1993 and 2000, but only by 3.8% between 2001 and 2005.[3]

The pulmonary system is most frequently affected in cases of tuberculosis. Between 16% and 20% of tuberculosis cases occur in extrapulmonary sites;[4–6] the most common sites are the lymph nodes, the pericardium, and the genitourinary, skeletal, central nervous, and gastrointestinal systems. Gastrointestinal tuberculosis is the sixth leading site of extrapulmonary tuberculosis and can involve any organ in the abdomen, including the peritoneum or lymphatics; however, the ileum is the most commonly affected gastrointestinal site.[7,8] Patients at highest risk for gastrointestinal tuberculosis include immigrants, HIV-infected persons, elderly persons, the urban poor, and prison inmates.[6] This article describes the case of a man who was diagnosed with tubercular peritonitis after he presented to the emergency department (ED) with abdominal pain and weight loss approximately 8 months after being released from prison. Diagnosis and treatment of tubercular peritonitis are also reviewed.

CASE PRESENTATION

Initial Presentation and History

A 37-year-old man presented to the ED with a complaint of diffuse abdominal pain and weight loss. His symptoms had started 4 months earlier with epigastric and right upper quadrant pain. At the time, he visited a local clinic and was diagnosed with gastroesophageal reflux disease and possible peptic ulcer disease. He was treated with ranitidine and was scheduled for esophagogastroduodenoscopy (EGD). His abdominal pain improved somewhat with the medication; however, he did not want to undergo EGD, and he was lost to follow-up.

Two months later, the pain occurred again and progressed for an additional 2 months, until the patient presented to the ED. The pain, which had initially been in the right upper quadrant and had been relieved with ranitidine, gradually spread throughout the abdomen and progressed to nausea and vomiting for 3 days prior to the current ED presentation. The patient described the pain as a constant dull ache throughout the abdomen that was greatest in the right upper quadrant. The pain was worse after eating. He denied fever, chills, diarrhea, or cough. Although the patient noticed his abdomen had become significantly larger, he reported having lost 30 lb during the 4-month period since his initial presentation at a local clinic.

The patient's social history was positive for a 1-year period of incarceration; he had been released from prison 8 months prior to the current presentation. Upon admission to prison, he underwent purified protein derivative (PPD) testing for tuberculosis, the results of which were negative. He had not undergone repeat testing. The patient was not taking any medications at the time of presentation, and his medical history was not significant. He quit smoking 3 years prior but had previously smoked half a pack per day for 10 years. He admitted to binge drinking in college but stated that currently he was drinking alcohol only socially, approximately 1 to 2 times per week. He reported using marijuana for 21 years and only 1 incident of cocaine use. The patient was born in the United States and had no reported history of travel. His family history was negative for tuberculosis or other known chronic illnesses.

Physical Examination

On physical examination, the patient was a young man who appeared to be his stated age and had mild

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Table 1. Results of Emergency Department Laboratory Work-up of the Case Patient

Laboratory Study	Results	Normal Range
Calcium (mg/dL)	8.7	8.2–10.2
Sodium (mEq/L)	131	136–142
Hematocrit (%)	39.2	41–50
Hemoglobin (g/dL)	13.3	14.0–17.5
Mean corpuscular volume (fL)	75.6	80–100
Red blood cell count ($\times 10^6/\mu L$)	5.18	3.9–5.5
Red blood cell distribution width index (%)	13	11.5–14.5
Serum ferritin (ng/mL)	2452	15–200
White blood cell count ($\times 10^3/\mu L$)	5.9	4.5–11.0
Differential		
Granulocytes (%)	71.2	40–70
Lymphocytes (%)	13.2	22–44
Monocytes (%)	14.7	4–11

abdominal distress. The patient's vital signs were as follows: temperature, 103°F; pulse, 96 bpm; blood pressure, 118/68 mm Hg; and respiratory rate, 14 breaths/min. Lungs were clear bilaterally. On cardiovascular examination, point of maximal impulse was nondisplaced, jugular venous pressure was normal, and no murmurs or gallops were appreciated. His abdomen was distended with bulging flanks, and bowel sounds were hyperactive. There was mild shifting dullness and a positive fluid wave. No masses were appreciated, and the liver span was 9 cm. Abdominal tenderness was diffuse but greatest in the right upper quadrant and epigastrium, with mild voluntary guarding but no appreciable Murphy's sign. No peripheral edema or lymphadenopathy was appreciated.

Laboratory and Imaging Studies

The results of laboratory studies ordered for the case patient are listed in **Table 1**. The studies revealed a normal serum white blood cell (WBC) count with monocytosis, which is suggestive of chronic infection or malignancy. The hematocrit, hemoglobin, and mean corpuscular volume were low, which is indicative of a mild microcytic anemia. Testing of stool for occult blood was negative. There were no infiltrates or lesions on chest radiograph. Liver function tests, blood and urine cultures, hepatitis panels, HIV enzyme-linked immunosorbent assay (ELISA), and abdominal ultrasound were ordered.

Admission and Further Evaluation

The patient was admitted to the hospital with a working diagnosis of ascites due to hepatobiliary disease and started on ciprofloxacin for suspected spontaneous bacterial peritonitis. Abdominal ultrasound performed on hospital day 2 confirmed the presence of large ascites with no masses, but a thickened gallbladder wall was noted. Liver size was normal. On the third hospital day, liver function tests revealed hypoalbuminemia (albumin, 3.0 g/dL [normal, 3.5–5.0 g/dL]) but were otherwise normal, including the levels of aspartate aminotransferase, alanine aminotransferase, total protein, total bilirubin, and alkaline phosphatase and the prothrombin time and partial thromboplastin time. Serum lactate dehydrogenase (LDH) was 238 U/L (normal, 100–200 U/L), and the erythrocyte sedimentation rate (ESR) was 80 mm/hr (normal, 0–20 mm/hr), which is suggestive of inflammation due to either infection or malignancy. Blood and urine cultures revealed no growth, and the viral hepatitis panel was negative for hepatitis B and C. Serum ferritin was elevated at 2452 ng/mL (normal, 15–200 ng/mL).

Paracentesis was performed and ascitic fluid analysis revealed: protein, 5.8 g/dL (transudative, < 2.5 g/dL); LDH, 501 U/L (transudative, < 2/3 upper limit of serum level), and albumin, 2.6 g/dL with a calculated serum-to-ascites albumin gradient (SAAG) of 0.4 g/dL, which is consistent with malignancy or tuberculous ascites (< 1.1 g/dL). Further ascitic fluid analysis revealed mild leucocytosis with a lymphocytic predominance (WBC, 864/μL [normal, < 250–500/μL]; lymphocytes, 74% [normal, < 10%]). There were no acid-fast bacilli (AFB) organisms seen on the initial AFB smear of ascitic fluid. Fluid cytology was negative for malignant cells.

Although cholangiocarcinoma was entertained due to the finding of a thickened gallbladder wall, biopsy of the gallbladder was deferred due to the patient's young age and normal alkaline phosphatase level. By the fifth hospital day, the HIV ELISA was returned as nonreactive. PPD testing was ordered (hospital day 6) and the result was positive, with a 14- to 15-mm area of induration (hospital day 8). Further testing and treatment options were discussed with the patient, but he declined further invasive testing until the AFB culture of ascitic fluid returned in 4 to 6 weeks. Based on the positive PPD test, he was given a presumptive diagnosis of tubercular peritonitis. On hospital day 11, he was started on empiric 4-drug antitubercular medication with isoniazid, ethambutol, rifampin, and pyrazinamide, and he became afebrile by hospital day 16. As he demonstrated a history of poor medical follow-up, on discharge (hospital day 18) he was referred to state health authorities for directly observed therapy.

Follow-Up

Four weeks after discharge, the patient was seen on follow-up. AFB culture of ascitic fluid had returned positive for *Mycobacterium tuberculosis*, and the patient had gained 28 lb. Confirmatory laparoscopy with peritoneal biopsy to exclude malignancy found multiple nodular, 2- to 3-mm white implants throughout the abdominal cavity on the peritoneal surface and on the surface of the viscera, liver, and spleen. Frozen section analysis revealed inflammation with caseating granulomas with numerous Langhans giant cells and a lack of neutrophils suggestive of *M. tuberculosis* infection. AFB smear and culture of biopsy material were negative; however, the patient had been receiving empiric antitubercular medication at the time of biopsy. No malignancy was found, and he was scheduled to continue directly observed therapy with local health authorities.

DISCUSSION

Tubercular peritonitis is a treatable illness that responds well to medication if recognized early. However, this disease presents with nonspecific symptoms and mimics several other illnesses. Given the low incidence of tubercular peritonitis, a presumptive diagnosis of cirrhosis or malignancy is often made, leading to a delay in the correct diagnosis. Because delays in diagnosis can lead to complications (eg, adhesions, bowel obstruction, intestinal perforation) and death, it is necessary to have a high clinical index of suspicion for tubercular peritonitis in any patient presenting with chronic abdominal pain, fever, weight loss, and exudative ascites. Clinical suspicion should be further raised in individuals at risk for tuberculosis (**Table 2**).

Risk Factors for Developing Tuberculosis in the United States

The main risk factors associated with active tuberculosis in the United States now include incarceration in a correctional facility, immigration, HIV infection, and lower socioeconomic status (Table 2).[2–4,7,9–15] Incarceration in the US prison system poses a significant risk for contracting tuberculosis. The incidence of tuberculosis in prison inmates is roughly 4 to 6 times higher than that in the non-inmate population, with infection rates as high as 29.4 and 24.2 cases per 100,000 inmates in the federal and state prison systems, respectively, as compared with 6.7 cases per 100,000 persons in the non-inmate population in 1 study and the national rate of 4.9 cases per 100,000 persons.[3,4] Similarly, immigration from certain areas (primarily Mexico, the Philippines, Vietnam, India, and China[2,3]) is a major risk factor for tuberculosis. Most new tuberculosis cases in the United States now occur in foreign-born persons. As many as 54.3% of new tuberculosis cases diagnosed in 2005 occurred in the immigrant population.[3] HIV-infection continues to be a major risk factor for tuberculosis, although the number of new cases of tuberculosis occurring in HIV-infected persons is under control. In patients with HIV, the rates of extrapulmonary tuberculosis is increasing. Extrapulmonary tuberculosis accounts for approximately 16% to 20% of cases of tuberculosis in the general population[4–6] but for 53% to 62% of cases in HIV-infected persons.[5]

Table 2. Risk Factors for Developing Tuberculosis in the United States

HIV infection
Foreign-born person*
Correctional facility inmate (or a history of incarceration)
Lower socioeconomic status
Age > 65 yr
Cirrhosis
Peritoneal dialysis

*Countries endemic for tuberculosis: Mexico, the Philippines, Vietnam, India, and China.

TUBERCULAR PERITONITIS

Clinical Evaluation and Diagnosis

Approximately 20% of extrapulmonary tuberculosis cases occur in the peritoneum. Tubercular peritonitis is most commonly seen in people with HIV, cirrhosis, and peritoneal dialysis.[6] Symptoms of tubercular peritonitis, which are often vague and nonspecific, most commonly include ascites, abdominal pain, weight loss, and fever.[7,9–15] Tubercular peritonitis is not a common cause of ascites, accounting for fewer than 2% of cases. Between 80% and 85% of ascites are caused by chronic liver disease, and another 10% are caused by malignancy.[16,17] In several case reports, tubercular peritonitis was incorrectly diagnosed as liver disease or either primary or metastatic malignancy.[7,9–15] As such, invasive procedures to assess for malignancy were often performed, thus delaying both the diagnosis and the appropriate treatment for months, and in some cases until death. Due to vague symptoms and low incidence, the correct diagnosis of tubercular peritonitis requires a high index of suspicion.[5–16]

Likewise, diagnostic studies are often equivocal for tubercular peritonitis. PPD testing tends to be nonspecific and is positive in only 30% to 40% of patients.[11,14] Chest radiograph and sputum smear for AFB are often not helpful as only 15% to 20% of patients with tubercular

Table 3. Features of Tubercular Peritonitis

Abdominal pain
Fever
Weight loss
Exudative ascites with lymphocyte predominance (serum-to-ascites albumin gradient, < 1.1 g/dL)
Positive acid-fast bacilli culture of fluid taken from paracentesis and/or biopsy performed during laparoscopy or laparotomy

peritonitis have active pulmonary tuberculosis at the time of diagnosis.[9,14,15] Abdominal imaging studies with ultrasound or computed tomography scan are seldom helpful, often merely revealing a nonspecific mass lesion. Laboratory studies are also nonspecific. Patients tend to have a normal WBC count and may have a mild anemia as well as elevated ESR and LDH. Paracentesis most commonly reveals a calculated SAAG below 1.1 g/dL (exudative) with a lymphocytic predominance.[5–16] In most cases, AFB smear on ascitic fluid obtained at paracentesis is negative, yielding positive results in only 10% of patients. However, paracentesis with fluid AFB culture or biopsy remains the most sensitive and specific approach. The sensitivity of biopsy is further improved when performed by laparoscopy or laparotomy.[5–16] Laparoscopy or laparotomy is recommended for all patients with exudative ascites (SAAG, < 1.1 g/dL).[6–15] This procedure allows the operator to directly examine the peritoneal surface for the presence of white nodules that are characteristic of tuberculosis as well as to perform a biopsy, which reveals the caseating granulomas typical of tuberculosis. Biopsy may also exclude malignancy. Features of tubercular peritonitis are listed in **Table 3**.

Efforts to improve the diagnosis of tubercular peritonitis include measuring ascitic fluid adenosine deaminase (ADA) levels and testing ascitic fluid with polymerase chain reaction (PCR) for *M. tuberculosis*. ADA is an enzyme involved in nucleic acid metabolism. While present in most tissues, ADA levels appear to be highest in T-lymphocytes. ADA levels are increased in ascitic fluid of patients with tubercular peritonitis as a result of T-cell stimulation by mycobacterial antigens. Measurement of ADA levels in ascitic fluid samples has been suggested as a useful screening test where there is a high incidence of tuberculosis and in high risk patients; however, in populations with a low prevalence of tuberculosis the sensitivity and specificity of ADA levels are low.[9] An ADA level in ascitic fluid greater than 33 U/L is highly suggestive of tubercular peritonitis.[15]

Reports on the accuracy of PCR on ascitic fluid samples using 2 markers are encouraging, with some investigators recommending PCR testing routinely in the work-up of tubercular peritonitis.[8,9] The sensitivity of PCR testing varies from 95% in smear–positive samples to 48% to 53% in negative samples; however, in patients with a calculated intermediate or high index of suspicion for tuberculosis, sensitivity rises to 75% to 88%, with a specificity of 95% to 100%.[8] As results vary, PCR testing should not replace routine AFB smear and culture; however, PCR may aid in diagnosis in cases where there is a high clinical index of suspicion for *M. tuberculosis* in which AFB smear is negative and culture results are pending.[8] Caution should be taken when interpreting PCR results as this test detects nucleic acid material from both live and dead *M. tuberculosis*. As such, PCR testing should be used for initial diagnosis and not for follow-up or in cases where patients have already received antitubercular medications.[8]

Treatment

Treatment of extrapulmonary tuberculosis is similar to pulmonary infection, although treatment for 6 months is usually adequate with the exception of tubercular meningitis, which requires 9 to 12 months of multidrug treatment. Corticosteroids are also strongly recommended in the treatment of tubercular meningitis and pericarditis.[18] Treatment of tuberculosis involves initiation of a 4-drug regimen including rifampin and isoniazid in combination with 2 other antitubercular medications for 8 weeks until isolate sensitivities return. If the *M. tuberculosis* isolate is sensitive to rifampin and isoniazid, these 2 drugs may be continued alone for a complete course of 6 to 9 months.[18] In cases of isoniazid resistance, a 4-drug regimen that includes rifampin and pyrazinamide with 2 other antitubercular medications should be initiated, and rifampin should be maintained throughout the course of treatment.[18]

CONCLUSION

Although the incidence of tuberculosis in the United States remains relatively low as compared with developing countries, the rates of infection among prison inmates, foreign-born persons, persons with HIV-infection, and the urban poor remain significant. Tuberculosis will typically affect the pulmonary system but can also occur in extrapulmonary sites, such as the peritoneum. Tubercular peritonitis may also occur in those with cirrhosis or peritoneal dialysis. Tubercular peritonitis is a readily treatable disease, yet a correct diagnosis is often delayed, leading to increased morbidity and mortality. A high clinical index of suspicion and attention to risk factors are necessary to obtain an accurate diagnosis.

Any patient with appropriate risk factors for tuberculosis who presents with abdominal pain, fever, weight loss, and exudative ascites (SAAG < 1.1 g/dL) with a lymphocytic predominance should be worked-up for tubercular peritonitis. PPD testing and paracentesis with AFB cultures of fluid should be ordered. AFB cultures require 4 to 8 weeks to yield results and are often negative, leading to limited utility in diagnosis. If these initial tests are nondiagnostic, PCR testing should be performed to improve the sensitivity of testing. Additionally, biopsy with laparoscopy or laparotomy should be performed in all patients with exudative ascites to exclude malignancy and to visually confirm the diagnosis of tubercular peritonitis. **HP**

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