CASE REPORT

Extrapulmonary tuberculosis at an unusual site

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ABSTRACT

Tuberculosis remains a major public health problem. One-third of the cases diagnosed with tuberculosis have extrapulmonary disease. Here, we report a rare presentation of extrapulmonary tuberculosis involving the spleen. This isolate was a sensitive one and hence the patient responded to the standard regime. Traditional methods of diagnosis are time-consuming but accurate and should be mandatorily followed by drug susceptibility testing to rule out multidrug and extensively drug-resistant tuberculosis.

Key words: Line probe assay, LJ medium, *M. tuberculosis*, splenic tuberculosis

INTRODUCTION

Tuberculosis remains a major health problem worldwide and is second only to HIV as a cause of death resulting from a single infectious agent. There were 8.8 million incident and roughly 12 million prevalent cases reported in 2010 to the WHO (both pulmonary and extrapulmonary) of which 95% were from developing countries.[1] If properly treated, drug susceptible strains are virtually curable in almost all cases. When untreated or improperly treated, fatality rates approach 65% by 5 years. Only a third of all reported cases are extrapulmonary. Gastrointestinal tuberculosis constitutes only 3.5% of extrapulmonary cases. Focal splenic abscesses and mesenteric tuberculous lymphadenitis are rarer still; however, they are more common in the setting of immunodeficiency. In such cases, the yield of direct smear and culture are relatively low. The diagnosis is best established by culture of specimens obtained intraoperatively or by peritoneal or lymph node biopsies obtained by laparoscopy.

CASE REPORT

A 22-year-old male who is a chronic smoker presented with a history of recurrent fever, weight loss, loss of appetite and left-sided abdominal pain since 3 months. He gave a history of two prior hospitalisations, 3 months and 1 month back, respectively.

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The first visit was for complaints of fever and cough with expectoration. On evaluation, he was found to have an elevated erythrocyte sedimentation rate (ESR) (110 mm in the first hour) and positive Mantoux reaction. Subsequent evaluation for tuberculosis was inconclusive as his sputum was negative for acid fast bacilli on smear and culture. Ultrasonogram (USG) of the abdomen revealed a focal splenic lesion with peripancreatic adenopathy. A differential diagnosis of lymphoma was considered; however, the subsequent laboratory workup was negative for the same. A colonoscopy was done taking into account a previous episode of loose stools which lasted for 2 weeks. The study was normal. Since his symptoms subsided on antibiotics, he was discharged.

He presented 2 months later with recurrent symptoms and left-sided abdominal pain aggravated during inhalation. A repeat USG and contrast enhanced computed tomography (CT) of the abdomen showed residual peripancreatic adenopathy and focal splenic mass; however, the size of the splenic mass had reduced. In view of radiological response, he was discharged with further antibiotics and symptomatic medication. During his stay, he was investigated for meliodosis and brucellosis. An oesophago-gastro-duodenoscopy was done which was normal. He gave a history of drug abuse (marijuana), however, serum markers for hepatitis and retroviral infection were negative. A workup for collagen vascular disorders was also negative.

On the third visit, general examination was unremarkable except for tinia corporis and scabetic lesions. Two samples of splenic aspirate and two samples of blood were sent to our laboratory for culture and sensitivity.

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Laboratory diagnosis

The first splenic aspirate sample was received on 14 January 2014 which showed plenty of pus cells and gram-negative bacilli on Gram staining. Staining for acid fast bacilli (AFB) was negative. Culture yielded *Acinetobacter species* sensitive to cephalosporins, aminoglycosides, fluoroquinolones and Cotrimoxazole. Culture of two samples of blood received on 18 January 2014 was sterile. The second splenic aspirate sample received for culture and sensitivity one 1 week later was also sterile. The second splenic aspirate and blood samples were subjected to AFB culture and sensitivity.

The patient was put on intravenous Ceftazidime and Metronidazole; however, he showed little or no improvement. His condition deteriorated over the course of the next few days with persistent high-grade fever and abdominal pain. He was taken up for an emergency exploratory laparotomy to assess the splenic lesion. Intraoperatively, his spleen was found to be gangrenous with typical findings of tuberculosis. An intraoperative sample was sent to our laboratory for AFB culture and sensitivity and an emergency splenectomy was done. Post-operatively, he was given Pneumovac and started empirically on Category I anti tuberculous therapy (ATT).

Preoperative and intraoperative samples (total three) were inoculated onto Lowenstein Jensen (LJ) medium and incubated at 37°C. Direct microscopy with Ziehl Neelsen staining was done from all the three samples before and after concentration. Acid fast bacilli were not seen in any of them.

After 4 weeks, all three samples showed growth of dry, rough, tough, irregular, buff-coloured colonies showing waxy cauliflower appearance. Acid fast staining of the growth showed acid fast bacilli. The growth was further subcultured on LJ medium and kept at room temperature, 37°C and 42°C which yielded similar colonies.

The growth was taken to State Tuberculosis Centre, Thiruvananthapuram where line probe assay was done and growth was confirmed as *Mycobacterium tuberculosis* (*M. tuberculosis*) complex sensitive to Rifampicin and Isoniazid. The result was obtained within 7 hours of providing the sample. Immunochromatography card test was also positive for *M. tuberculosis*. This was obtained within 10 minutes.

The patient improved on Category I ATT and is now on follow-up with regular treatment.

DISCUSSION

The *M. tuberculosis* complex comprises seven species in the genus *Mycobacterium*, family *Mycobacteriaceae* and order *Actinomycetales*. Of the pathogenic species belonging to the *M. tuberculosis* complex, the most common agent of human infection is *M. tuberculosis*.[2] The other rarer culprits of human infection include *M. bovis, M. caprae, M. africanum, M. microti* and *M. canetti*.[3]

Tuberculosis of the gastrointestinal tract constitutes a very small percentage of extrapulmonary tuberculosis.[4] Moreover, intraabdominal tuberculous lymphadenitis and visceral abscesses are uncommon in immunocompetent patients. The usual route of spread is by direct seeding (swallowing sputum laden with bacilli), haematogenous dissemination or ingesting contaminated milk (*M. bovis*). Once affected, the terminal ileum and caecum are the most commonly affected sites. Symptoms often include abdominal pain, fever, weight loss, anorexia and night sweats. Rarely, patients present with an abdominal mass. Often surgery is required and the disease is best diagnosed by culture of intraoperative samples or by biopsy of the affected lymph nodes. This held true in our case also. Only the peroperative sample yielded AFB in culture, while preoperative blood and aspirate cultures were sterile.

Definitive diagnosis of tuberculosis depends on the isolation and identification of *M. tuberculosis* from a clinical specimen or identification of specific DNA sequences with nucleic acid amplification techniques.[5] Finding AFB on microscopy gives a presumptive diagnosis of tuberculosis; however, the sensitivity is reportedly low (40-60%). Tissue obtained for culture should not be collected in formaldehyde as for biopsy, but as such or in sterile saline. Culture is done on either egg- or agar-based media (eg., Lowenstein Jensen or Middlebrook 7H10) and incubated at 37°C. One of the limiting factors of this method is the time required. On average, a positive culture requires 4-8 weeks of incubation and various biochemical tests are used for speciation. The use of liquid culture for isolation and high-pressure liquid chromatography for mycolic acids have reduced this time by 2-3 weeks and are slowly gaining prominence in developing countries.

Once isolated, it is necessary to assess drug susceptibility of the strain, to Isoniazid and Rifampicin, to detect multi-drug-resistant (MDR) tuberculosis and to second-line antituberculous drugs, to rule out extensively drug-resistant (XDR) tuberculosis, if MDR tuberculosis is confirmed. This can be done by direct susceptibility testing on liquid media or indirect testing on solid media (3 weeks for the former and up to 8 weeks for the latter). Molecular methods like line probe assays detect genetic mutations that are associated with increased resistance to isonicotinylhydrazine (INH) and Rifampicin.[6] In this case,

diagnosis was obtained by conventional culture in 4 weeks and line probe assay provided confirmation and sensitivity testing within 7 hours. The completed result was thus given in 4 weeks.

The aim of therapy in diagnosed tuberculosis is both to render the patient noninfectious and thereby prevent transmission and also to reduce morbidity and mortality associated with the disease. Short-course treatment regimens that are currently used employ at least four first-line drugs, namely Isoniazid, Rifampicin, Ethambutol and Pyrazinamide for a period of not less than 6 months. Resistance to these requires addition or alternate use of Quinolones, Streptomycin, Ethionamide, Cycloserine or Para-aminosalicylic acid. Supervised or direct observed therapy is most effective and if treated adequately, susceptible strains are almost completely curable.

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