PUO - A Rare (And Forgotten) Cause!

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Abstract

Splenic tuberculosis is an extremely rare clinical entity and a frequently forgotten cause of pyrexia of unknown origin (PUO). We present the case of a 42 year old man who presented with fever of unknown origin. Ultrasonography revealed multiple hypoechoic areas within the spleen. As the abscesses did not respond to broad spectrum antibiotics splenectomy was done. The excised organ showed multiple cysts filled with pultaceous material. Histopathological examination revealed areas of granular caseating necrosis surrounded by epitheloid cells and Langhan's type giant cells consistent with splenic tuberculosis. There was no evidence of a primary focus in the lungs or in any other organ. The presence of isolated tubercular foci in the spleen without any evidence of tuberculosis in lung or other extra-pulmonary site prompted us to report this case.

Introduction

Globally, extrapulmonary cases (without concurrent pulmonary involvement) comprised 0.8 million cases (new and relapse) in 2011. This constitutes about 13% of the notified cases.¹ Among the extra pulmonary forms, tuberculosis of the spleen is an extremely rare clinical condition. Splenic tuberculosis is normally seen as a part of miliary tuberculosis and is rarely the sole presenting feature, thus prompting us to report this case.

Case Report

A 42 year old male, never smoker, presented to us with low grade fever since 2 weeks. He also complained of cough with scanty white mucoid phlegm since 2 years. He had no other symptoms. His appetite was normal and he denied any weight loss. He was a diabetic on oral hypoglycaemic agents since 4 years. He had no past history of TB, asthma or atopy. Patient consumed alcohol daily in moderation. General physical and upper airway examination was normal. Respiratory system examination did not reveal any abnormal findings. Chest radiograph was normal. Total leucocyte count was 9000 cells/mm³ (Differential cell count of N 78%, L 19%, E 03%, B 0%). Pulmonary function test was normal. Erythrocyte sedimentation rate was moderately raised (46 mm at 1 hr. by Westergren’s method). Post prandial blood sugar was 295 mg/dL (normal range 100-150 mg/dL) and glycosylated haemoglobin was 11.5 (normal range 4.8–6.0). Liver functions were mildly deranged; (total bilirubin 2.2 mg/dL, AST: 65 U/L, ALT: 28 U/L, ALP: 111 U/L, and prothrombin time- INR: 1.39). Blood culture was negative. Renal functions, urine analysis, 2D echocardiography and otorhinolaryngology evaluation were normal. A contrast enhanced computed tomography of chest and abdomen was done, which revealed splenomegaly (12 cm x 7.9 cm) with multiple hypodense areas (largest measuring 17 mm in diameter) suggesting the possibility of either multiple splenic abscess or granulomas (Figure 1). There were no other abnormalities. Blood samples sent for HIV and HBsAg were negative. An ultrasound guided fine needle aspiration from the splenic abscess/granuloma was attempted but deferred since the lesion was poorly accessible. In lieu of the abscess, documented high grade fever during the hospitalisation and uncontrolled sugars, patient was started on parenteral antibiotics (piperacillin-tazobactum with metronidazole) and plain insulin. A repeat ultrasound examination 72 hours later showed features of a resolving splenic abscess. Patient had turned afebrile and was therefore discharged on oral antibiotics and instructed to follow up after 10 days.

Patient returned with high grade fever and was readmitted. Ultrasound showed in
addition to earlier findings, a focal loculated collection adjacent to the splenic hilum and along the inferior and inner pole of the spleen suggesting an inflammatory collection. Patient was restarted on parenteral antibiotics (ceftazidime + metronidazole + amikacin), plain insulin and administered meningococcal vaccine. A General surgery consultation was sought and in lieu of lack of response to broad-spectrum antimicrobials, a splenectomy was carried out for definitive diagnosis.

Cut section of excised organ showed multiple cysts containing pultaceous material. Microscopic examination revealed areas of granular caseating necrosis surrounded by epitheloid cells, Langhan’s type giant cells and non-specific fibroid granulation tissue consistent with tuberculosis (Figure 2). Stain for acid fast bacillus was negative. Based on the histopathological appearance, a final diagnosis of splenic tuberculosis was made and patient was started on a 4 drug anti-tuberculous treatment (ATT) comprising of Isoniazid 300 mg/day, Rifampicin 600 mg/day, Ethambutol 1 g/day and Pyrazinamide 1.5 g/day under serial liver function monitoring. With splenectomy and 6 months of antitubercular treatment postoperatively, patient remained afebrile, his general condition improved and he gained weight.

Discussion

Splenic tuberculosis was first described by Winternitz (1912) who believed the gastrointestinal tract to be the portal of entry. In his series, most patients presented with vague left flank pains, weight loss, anorexia, a dragging sensation or occasionally a left hypochondrium mass. Review of Indian literature suggests that fever, anorexia, weight loss, abdominal pain and mild splenomegaly are the common symptoms.

The incidence of splenic abscess is very low (0.14 to 0.7%) and those due to tuberculosis are even more uncommon. In the period between 1965 and 1992 there were only six cases in five reports recorded in English, German and French literature. An Indian study by Potakkat B et al was able to establish a diagnosis of splenic tuberculosis in 10% (8/77) of patients who underwent diagnostic splenectomies. This high incidence was attributed to the overall high incidence of tuberculosis in our country.

Pathologically, two forms of the disease are seen. Commonly, the organ may be involved during miliary tuberculosis in immunocompromised patients, wherein it typically exhibits a multiple micronodular form. The second form is isolated splenic tuberculosis or solitary tuberculosis of the spleen (as in our patient) which is extremely rare, in which, macronodular lesions like tuberculoma or tubercular abscess are generally seen. Involvement of spleen is generally due to haematogenous seeding of the organ with tubercle bacilli; rarely it may be involved by contiguous spread of infection from other sites like vertebral/psoas/abdominal wall abscess.

Ultrasoundography (sensitivity 80-90%) and CT scan (sensitivity 95-100%) are useful diagnostic modalities. On ultrasound, a solitary lesion, anechoic mass, and lesions with highly echogenic foci (due to gas or calcification) suggest a benign entity. In one series, the radiological findings favouring tuberculosis included, in order of most common: single or multiple hypoechoic focal lesions, splenic abscess, calcifications (on CT), and isolated splenomegaly. Multiple regular hypoechoic lesions most likely represent multiple tuberculomas whereas irregular hypoechoic lesions represent splenic abscess.

With limited data available mostly as case reports, it is difficult to recommend one uniform treatment strategy for patients with splenic tuberculosis. While some authors advocate anti-TB medications as the first line treatment a few have observed that early splenectomy followed by anti-TB medications is a better approach. Splenectomy may become necessary if biopsy specimens are non-diagnostic, if
there is abscess formation, splenic rupture or non-responding patients.

Diagnosis of splenic tuberculosis is difficult and often gets delayed because of its vague clinical presentation. In the above case, the patient was a poorly controlled diabetic who had no past history of tuberculosis and investigations did not reveal evidence of tuberculosis in the lung or in the abdomen. Splenic abscesses were detected incidentally during a CT done for evaluation of PUO which was later proven to be tubercular only after the patient underwent a splenectomy for non-resolution.

The rarity of splenic tuberculosis coupled with the involvement of the spleen in isolation and outside the ‘miliary’ setting prompted us to report this case.

**Conclusion**

Although rare, splenic tuberculosis should be considered in the differential diagnosis of PUO with splenomegaly in a patient from an endemic area irrespective of the HIV status. Radiological investigations viz. ultrasound and CT abdomen are useful as a screening tool. However, confirmation lies in making a tissue diagnosis using fine needle aspiration/biopsy and where inconclusive, splenectomy.

**References**