Is it possible to encounter a patient with primary splenic tuberculosis during your career?

Mohammad Yahya Abdulrazaq[1]

ABSTRACT

Splenic tuberculosis is an extremely rare variant of extrapulmonary tuberculosis especially in immune competent person. It is usually presented as nonspecific symptoms leading to delay in the diagnosis. Here, we are reporting a 28 year-old female from Baghdad, who was presented with splenomegaly, fever and sweating of 4 months duration. After having a nonspecific laboratory investigation and poor response to broad spectrum antibiotics, splenectomy was done for her, and histopathological examination showed granulomas with caseation. The patient is diagnosed as primary splenic tuberculosis and was registered in the National Specialized Centre for Chest and Respiratory Disease.

Antitubercular medication was prescribed for her after splenectomy for a complete course of 6 months duration with a full improvement in the general condition of the patient. Tuberculosis is still a possible cause of splenomegaly and the patient should be treated with full course of anti TB medication even after splenectomy.

Key words: tuberculosis, spleen, caseated granulomas.

INTRODUCTION

In 2017, tuberculosis (TB) caused an estimated 1.6 million deaths, making it the leading cause of death from a single infectious agent worldwide and the tenth cause of death overall.[1]

This disease presents with diverse clinical symptoms, including both pulmonary TB and extrapulmonary TB. Extrapulmonary TB accounts for almost 15% of all cases. Among the extrapulmonary forms, majority are seen in lymph nodes, pleura, genito-urinary tract, bones, meninges, gastro-intestinal tract, peritoneum, and pericardium. Splenic TB is unusual. This form of TB is normally seen as part of miliary TB.[2] Isolated splenic tuberculosis is extremely rare, particularly in the immunocompetent patient.[3]

Even if tuberculosis is a familiar condition, an unusual presentation may disguise its correct nature, expressing itself as cases of unexplained fever and splenomegaly in TB endemic areas.[4] So, tuberculosis of spleen must be kept in mind while evaluating fever of unknown origin in any patient on immunosuppressant treatment or having HIV and even in immunocompetent patients as well. Treatment with antitubercular medication is rarely unsuccessful.[5]

Splenic TB is likely to be misdiagnosed as carcinoma of spleen, splenic abscess, lymphoma, or others. The misdiagnosis rate is high if there is no tuberculosis history in other organs.[6]

There are also some reports of spontaneous splenic abscess, causing acute abdominal pain and clinical hypersplenism with bleeding tendencies.[7]

At present there are few cases of solitary splenic tuberculosis reported in the literature internationally, and through the literature retrieval, there are no reports about splenic tuberculosis mortality rate data.[8]

1 *CABM, FIBMS, FRCP; Consultant pulmonologist & Consultant Internist at the National Specialized Centre for Chest and Respiratory Diseases. Baghdad, Iraq. E Mail: ntp.mohammad@gmail.com*

CASE PRESENTATION

A 28-year-old female from Baghdad was referred to the National Specialized Centre for Chest and Respiratory Disease to have an opinion regarding accidental histopathologic finding of caseating granulomas in a tissue specimen of spleen post splenectomy.

The history of the patient was dated back to 4 months before the splenectomy where the patient started to complain of pain in the left hypochondrial region and vague diffuse abdominal discomfort. Progressively patients developed low grade fever and sweating with vague ill health. Patient had no history of cough or significant weight loss. Initial medical consultation and simple laboratory investigation were not yielding to a diagnosis and treatment with antibiotic and analgesia failed to show any response.

Patient reported no significant medical, surgical and drug history. And her gynaecological history was unremarkable. She was not smoker has no history of contact with a patient known to have pulmonary tuberculosis or any other infectious diseases.

On clinical examination the patient was ill looking, with high temperature (37.8 °C), mild tachycardia with normal blood pressure. Cervical and axillary lymph nodes were not palpable. She was neither pale nor icteric. Chest examination was essentially normal while abdomen was distended with tender palpable spleen below the left costal margin and signs suggested of ascites.

Complete blood count was within normal limit. GPT, GOT, and alkaline phosphatase were mildly elevated, while renal function test, general urine examination, total serum bilirubin and serum albumin were within normal. Chest X ray showed no abnormality while abdominal ultrasound showed moderate splenomegaly with moderate ascites. Electrocardiography and echocardiography were within normal. The treating physician was thinking to exclude tumour like lymphoma or ovarian or other gastrointestinal malignancy. So, decision was made to do bone marrow aspiration which showed no significant pathology. Aspiration of peritoneal fluid which was exudative revealed cellular smear with moderate count of lymphocyte predominant mixed inflammatory cells and few hyperactive macrophages with no RBCs or atypical cell. Bacteriological examination of the peritoneal fluid was not yielding and unfortunately, Genxpert was not used to verified the diagnosis of Mycobacterium tuberculosis infection because TB was not suspected at this early stage.

Absent of response to treatment and non-specific investigation turned to decision to do splenectomy which was done under general anaesthesia. The gross pathological finding showed a spleen of 23x17x6 cm, brown in colour, and soft to firm consistency. Serial microscopic section showed splenic tissue with reactive lymphoid changes of white pulp and patchy replacement of red pulp by numerous small size non-caseating and minimally caseating active granulomas with Langerhans giant cells and secondary splenic fibrosis. With a suspicion of primary tuberculosis of the spleen.

At our centre, searching for latent or active pulmonary Tuberculosis were negative. Based on histopathological findings, poor response to preliminary antibiotics and absence of confirming diagnosis of malignancy the patient was diagnosed as a primary splenic TB and registered as an extra pulmonary TB case in the national TB program in Iraq. Antitubercular medication was prescribed for a complete course of 6 months duration started as 2 months initial phase with 4 tablets of combined fixed dose 4 drugs formula; Isoniazid 75 mg, Rifampicin 150 mg , Pyrazinamide 400 mg , and ethambutol 275 mg. Then followed by 4 months continuation phase with 4 tablets of combined fixed dose 2 drugs formula; Isoniazid 75 mg and Rifampicin 150 mg. Monitoring of the patient during the treatment course was uneventful. Progressively, the patient became clinical well without fever. Abdominal pain subsided and appetite has improved remarkably. Abdominal ultrasound post treatment was normal.

DISCUSSION

Tuberculosis continues to be a major health problem worldwide, despite considerable advances in the diagnosis and treatment of the disease.[9]

Abdominal TB which contributes to a mere 3% of all extrapulmonary TB encompasses

gastrointestinal tract, peritoneum, omentum, mesentery, regional lymph nodes and solid organs like liver, spleen and pancreas.[10] Isolated abdominal solid organ TB is rare in immunocompetent individuals. The incidence of splenic TB is 0.14-0.7% as per autopsy-based studies. [2, 11] A non-systematic review to search for published cases of splenic tuberculosis in immunocompetent patients between 2000 and 2019 found only 31 cases with tuberculous involvement of spleen.[12]

Although Iraq is endemic with tuberculosis, primary splenic tuberculosis is also extremely rare, and here we are reporting this case of isolated tuberculosis of the spleen which was presented with splenomegaly and ascites and it is the first reported case to the National Specialized Centre for Chest and Respiratory Diseases up to our knowledge.

Splenic TB occurs in two forms. The first form is part of miliary TB, which occurs especially in immunocompromised patients.[13] The second, and the unusual form is primary splenic TB where spleen is the is the primary site of involvement, as in our patient.[2] Splenic tuberculosis usually occurs secondary to haematogenous spread of a primary infection, as a part of disseminated disease.[14] morphologically, splenic tuberculosis occurs in five types miliary, nodular, spleen abscess, calcific and mixed type.[2]

Patients susceptible to acquiring splenic tuberculosis usually have one of the following risk factors: immunosuppression, preceding pyogenic infections, splenic abnormalities, prior trauma to the spleen, sickle cell disease and other haemopathies, and in the immunocompetent patient another body site infected by M. tuberculosis.[3] Study done by Dixit et al over a period of 3 years in an Indian hospital found only 16 patients (0.01%) with splenic involvement from a total of 9205 TB patients and were able to identify a cause for immunodeficiency in only 9 of those 16 patients (8 with HIV infection and 1 with myelodysplastic syndrome). Ten of those 16 patients in their study had pulmonary involvement too.[15]

In our report, we present a young immunocompetent female with primary splenic tuberculosis. Extensive history, comprehensive clinical examination and basic laboratory investigations failed to find any disease or condition that jeopardize her immune status. In addition, her lungs were free of tuberculous process.

Clinical manifestations are non-specific like anorexia, fever, malaise, weight loss, night sweats, abdominal pain and jaundice. Splenic TB can present as splenomegaly, hypersplenism, solitary splenic lesion or splenic abscess.[16,17,18] Rarely, patients can be asymptomatic and their diagnosis is delayed.[3] Other severe presentations include splenic rupture, portal hypertension with and without gastrointestinal bleed, and fulminant form involving rapid progression of fever, cachexia, haemorrhage and sepsis. Patients with splenic tuberculosis can also present with haematologic abnormalities: usually they are cytopenic due to hypersplenism, but cases of polycythemia have also been reported.[19,18,20] Our case was presented with nonspecific symptoms, pyrexia of unknown origin was the prominent presentation. Other constitutional symptoms were mild to moderate and this might be the cause of delay in the diagnosis. Also, clinical examination was normal except for splenomegaly and ascites.

Diagnosis of isolated splenic tuberculosis is difficult and often delayed because of vague clinical manifestations. In almost all the reported cases diagnosis was suggested by radiologic examination and confirmed by pathologic examination of fine needle aspiration, splenic biopsy or of splenectomy specimen. Some times the diagnosis was made by direct detection of the mycobacterium tuberculus bacilli.

Imaging studied by ultrasound and CT findings were very important to shift the diagnosis towards splenic tuberculosis. The imaging findings reported with splenic tuberculosis in their order of frequency are single or multiple hypoechoic focal lesions, splenic abscess, calcifications (on CT), and isolated splenomegaly. Ultrasound is not a sensitive tool to detect focal splenic lesions. In a study, five out of six patients with isolated splenomegaly on ultrasound were found to have lesions on CT.[21] Recently, the wide use of PET/Scan as a tool for searching for metastasis in patient with malignancy, who already have low immunity due to the malignancy itself or its chemotherapeutic treatment, has leading to accidental diagnosis of splenic tuberculosis. Mostly in FDG PET/CT examination, spleen tuberculosis is seen as

multiple lesions with increased FDG uptake.[22]

In our case the abdominal ultrasound was the only imaging technique used, and it showed splenomegaly without focal lesion. This of course is not enough to exclude presence of splenic nodules especially micronodules which would be detected if a CT scan had been used.

Real-time PCR is a very useful investigation for directly detecting the tubercle bacilli in clinical specimens.[7] Detection of Mycobacterium tuberculosis by XpertMTB/Rif assay in splenic aspirate, splenic tissues, or abscess fluid would confirm the diagnosis of tuberculosis.[7, 12] However, Sahoo et al in their review has found that 26 case out of 31 was diagnosed histopathologically and only 5 patients were diagnosed by direct detection of mycobacterium.[12] Therefore, histopathological examination is necessary for aetiological diagnosis. Histopathologically, tuberculous infection can be identified by presence of typical caseation along with granuloma of epitheloid cells and Langhans giant cells.[6]

In our case, Real-time PCR or XpertMTB/Rif assay were not used the diagnosis of tuberculosis in ascetic fluid because the TB was not highly suspected at that time and the diagnosis was raised after finding of caseating active granulomas with Langerhans giant cells. And probably this is the message that we want to send to our colleagues to think of extrapulmonary tuberculosis even in the rare sites whenever we encountered a nonspecific presentation and to broaden our differential diagnosis list to include it.

Purified protein derivative is a maker of the diagnosis of latent tuberculosis but not active tuberculosis. It is reported to be positive in patients with splenic tuberculosis.[20] However, tuberculin skin test was performed in our case and it was negative.

The first line treatment of splenic tuberculosis is anti- tuberculous drugs for at least 6 months with 4 drugs in the initial phase and two in the following maintenance phase.[20, 23]this attitude is still recommended even after total splenectomy.[3] In our patient the spleen was already removed and we started her on full anti-tuberculous therapy for 6 months. She responded nicely and fortunately without any adverse effects.

CONCLUSION

Yes, it is possible to encounter a patient with splenic tuberculosis during our career that TB is still a possible cause of splenomegaly and the patient should be treated with full course of anti TB medication even after splenectomy.

REFERENCES

1. People-centred framework for tuberculosis programme planning and prioritization, WHO ,2019.
2. Fooladi AAI, Hosseini MJ, Azizi T, Splenic tuberculosis: a case report. ***Int. J.Infect. Dis***. 2009;13(5):273–275.
3. Johanna V. Basa, Lilly Singh, Wassim Abi Jaoude, Gainosuke Sugiyama. A case of isolated splenic tuberculosis. ***International Journal of Surgery Case Reports*** 2015;8:117–119.
4. Azzam NA. Splenic tuberculosis presenting as fever of unknown origin with severe neutropenia. ***Annals of Clinical Microbiology and Antimicrobials*** 2013;12(1):13. **https://doi.org/10.1186/1476-0711-12-13**
5. Masoodi I. Splenic tuberculosis: Report of two cases and literature review. ***British Journal of Medical Practitioners***, 2017;10(1): 20-23.
6. Amin MA. Splenic Tuberculosis - A Rare Case Report. ***Glob J Medical Clin Case Rep*** 2017;4(3):072-073.
7. Kumar A, Kapoor VK, Behari A and Verma S. Splenic tuberculosis in an immunocompetent patient can be managed conservatively: a case report. ***Gastroenterology Report***, 2018;6(1),72–74.
8. Lin SF, Zheng L and Zhou L. Solitary splenic tuberculosis: a case report and review of the literature. ***World Journal of Surgical Oncology*** 2016;14:154.
9. Pramesh CS, Tamhankar AP, Rege SA, Shah SR. Splenic tuberculosis and HIV-1 infection. ***Lancet*** 2002; 369(9303):353.
10. Sharma SK, Mohan A. Extrapulmonary tuberculosis. ***Indian J Med Res*** 2004;120: 316-353.
11. Paris S, Weiss SM, Ayers WH, et al. Splenic abscess. ***Am Surg*** 1994;60:358-61.
12. Sahoo S, Naik S, Mishra B, Durgeshwar G, Panigrahi MK, Bhuniya S. Tuberculous splenic abscess in the immunocompetent host: a report and review of literature. ***Monaldi Archives for Chest Disease*** 2020; 90:79-85.
13. Reichel C, Theisen A, Rockstroh JK, Mu¨ller-Miny H, Spengler U, Sauerbruch T. Splenic abscesses and abdominal tuberculosis in patients with AIDS. ***Z-Gastroenterol*** 1996; 34(8):494—6.)
14. C.S. Ajithkumar, Tuberculosis of spleen: case report. ***Indian J Basic Appl. Med.Res***. 2013;6(2):619–622.
15. Dixit R, Arya MK, Panjabi M, et al. Clinical profile of patients having splenic involvement in tuberculosis. ***Indian J Tuberc*** 2010; 57:25-30.
16. Lim J, Yu JS, Hong SW, et al. A case of mass-forming splenic tuberculosis: MRI findings with emphasis of diffusion weighted imaging characteristics. ***J Korean Med Sci*** 2011; 26:457-60.
17. Mazloom W, Marion A, Ferron C, Lucht F, Mosnier JF. Tuberculose splenique:a partir d'un cas et revue de la literature.

Medecine et Maladies Infectieuse 2002; 32:444–6.

18. Rhazal F, Lahlou MK, Benamer S, Daghri JM, Essadel E, Mohammadine E, et al. Splenomegalie et pseudotumeur splenique d'origine tuberculeuse: six nouvelles observations. *Ann Chir* 2004; 129:410–4.
19. Hamizah R, Rohana AG, Anwar SA, Ong TZ, Hamazaini AH, Zuikarnaen AN. Splenic tuberculosis presenting as pyrexia of unknown origin. *Med J Malaysia* 2007;62(1):70–1.
20. Berady S, Rahbi M, Bahrouch L, Sair K, Benzaine H, Benkirane A, et al. La tuberculose splenique pseudotumorale. *La Revue de Medecine Interne* 2005;26: 588–91.
21. Sharma SK, Smith-Rohrberg D, Tahir M, Mohan A, Seith A. Radiological manifestations of splenic tuberculosis: a 23-patient case series from India. *Indian J Med Res*. 2007 May;125(5):669-78.
22. Cegla P, Spychala A, Marszalek A, Wierzchoslawska E, and Cholewinski W. Atypical spleen tuberculosis in a melanoma patient accidentally detected during a ^{18}F FDG PET/CT study: Case report. *Molecular and Clinical Oncology* 2018;8: 89-92.
23. Kumar S, Ajay G. Pai, Pravin N. Tungenwar, Ajay H. Bhandarwar. Isolated primary tuberculosis of spleen—A rare entity in theimmuno-competent patient . *International Journal of Surgery Case Reports* 2017;30:93–96.

Abbreviations list: Centimetre (**cm**), Computed tomography (CT), Degree Celsius (**°C**), Fluorodeoxyglucose-positron emission tomography. (**FDG PET/CT**), Glutamic oxaloacetic transaminase (**GOT**), Glutamic pyruvic transaminase (**GPT**), Human immunodeficiency virus (**HIV**), Milligram (**mg**), Polymerase chain reaction (**PCR**), Positron Emission Tomography (**PET**), Red blood cells (**RBCs**), Tuberculosis (**TB**).

Conflict of interest: Authors have nothing to declare.

Funding: Authors received no funds to complete this case presentation a part from self funding.