Background

TB infection is still common and can have a varied presentation and remains a differential diagnosis in cases of FUO. Hepatic TB is an extremely rare form of EPTB, constituting less than 1% of the cases of TB. Diagnosed radiologically through ultrasonography (USG) and computed tomography (CT), however, we present a case of a 52-year-old adult male with FUO diagnosed with primary hepatic TB through positron emission tomography/CT (PET/CT) scanning.

Case Report

A 52-year-old male presented with high-grade fever with 4 kg weight loss in the last 30 days. He has been a known case of type II diabetic mellitus, hypertension, and hyperthyroidism, taking regular treatment. On examination, he was conscious, oriented to time, place, and person. His pulse rate was 122/min, blood pressure 130/70 mmHg, respiratory rate 22/min, and temperature 101°F. The systemic examination was essentially normal.

A routine blood workup revealed normal hemoglobin (Hb 12.1 g/dL), neutrophilic leukocytosis (TLC 25.67 × 10⁹/L), and normal platelet count (441 × 10⁹/L). The liver function test showed transaminitis (SGOT 105 U/L, SGPT 84 U/L, ALP 194 U/L). The renal profile suggested acute kidney injury (serum urea 136 mg/dL, serum creatinine 1.4 mg/dL). The acute phase reactants were elevated (CRP 116.3 mg/dL, ESR 45 mm/h). Further workup as per protocol for FUO cases viz. typhi dot, malaria smear, and antigen, dengue NS1 and serology, widal, urine routine, and microscopy, paired blood cultures and urine culture, Mantoux
test, and Antistreptolysin O (ASO) titer were conducted and were inconclusive. Hepatitis B surface antigen (HbsAg), Hepatitis C virus (HCV), Human Immunodeficiency virus (HIV), and autoimmune workup viz. Antinuclear antibody (ANA), rheumatoid factor, and protein electrophoresis were negative. The chest X-ray PA view and Ultrasound of the whole abdomen revealed no abnormalities. Tests for Leptospira, Brucella, scrub typhus, and Cytomegalovirus Immunoglobulin M, Epstein-Barr Virus Immunoglobulin M were also negative.

Contrast-enhanced CT of the chest and abdomen showed a few subcentrimetric right paratracheal and prevascular lymph node, while there were a few well-defined hypodense subcentrimetric to centimetric mesenteric lymph nodes in the abdomen. He was initially started on piperacillin/tazobactam, doxycycline, and artemether + lumefantrine empirically. However, his fever continued unabated and as no potential diagnostic clue was forthcoming, a PET/CT scan was done which showed multiple Fluorodeoxyglucose avid (FDG) subtle hypodense lesions in both lobes of the liver [Figure 1] with mild FDG AVID few small lymph nodes in the periportal, portocaval, and aortocaval regions suggestive of active inflammatory/infective etiology or the lymphoproliferative disease.

We sent serum alpha-fetoprotein and serum Angiotensin-converting enzyme (ACE) levels which were normal. A USG-guided liver biopsy was performed. GeneXpert Mycobacterium Tuberculosis, Ziehl-Neelsen stains were negative, however histopathology revealed numerous caseating epithelioid granulomas in the portal region with scattered Langerhans giant cells suggesting necrotizing granulomatous inflammation [Figure 2] suggestive of tuberculosis. A diagnosis of primary hepatic tuberculosis was established.

He was treated with the conventional Anti Tubercular Treatment regimen Rifampicin, Isoniazid Pyrazinamide Ethambutol (RHZE) for 8 weeks followed by RHE for 28 weeks. He responded well to the treatment and is in good health at present.

**Discussion**

FUO is one of the greatest challenges in clinical practice and PET/CT should be utilized as a tool for diagnosing its etiologies such as infection, malignancy, and inflammatory diseases. Infections are the most common etiology of FUO, constituting 20–40% of the cases and one of the most important causes of infection is EPTB. The incidence of hepatic TB is less than 1% in all EPTB cases, making it an extremely rare form of EPTB. Hepatic tuberculosis was further classified into miliary TB, pulmonary TB with hepatic compromise, primary hepatic TB, focal or abscess TB, and tuberculous cholangitis by Levine. Miliary TB is the most common, involving the liver in 50–80% of the cases. Our case of primary hepatic TB is the rarest with an overall incidence of 0.3 and 0.16% as reported by Kok et al[5] and Chong, respectively. The pathogenesis of primary TB is hypothesized to be the mobilization of tubercle bacilli reaching the liver via the portal vein from the intestine leading to the formation of the granuloma in the portal region due to rich blood supply and reticuloendothelial system presence without interfering with the normal liver function, as evident in our case as well. The liver involvement in TB is rare due to low-oxygen tension making it an unfavorable site for mycobacterial growth.

Patients can present with varied clinical presentations making its diagnosis challenging. Most commonly, they present with constitutional symptoms including fever, malaise, weight loss, and abdominal pain, like our case. Hepatomegaly is observed mostly in association with splenomegaly although our patient had only mild hepatomegaly. The laboratory findings include an elevated level of serum alkaline phosphatase, aminotransferases with increased erythrocyte sedimentation rate. The histological findings include a variety of hepatic lesions including granuloma, casation, fatty changes, portal fibrosis, and acid-fast bacilli in the granuloma. The positivity rate of the AFB stain is only 7–59% primary hepatic TB and positive AFB culture yield is 10% primary hepatic TB. GeneXpert MTB has a higher chance of detecting Mycobacterium tuberculosis in the tissue sample with 82% sensitivity. However, the diagnosis is made classically based on the histopathological finding of caseating necrotizing granuloma in the tissue sample.

Due to non-specific signs and symptoms and lack of lesions in the USG and CT scans, diagnosing hepatic TB is very challenging, which in turn, leads to significant morbidity and mortality. In the recent algorithm of FUO, the PET/CT scan is placed superior.
to CT scan and other radiological scans given its ability to localize the key area to biopsy and make an accurate diagnosis. Similarly, in our case, the patient’s USG and CT scan were normal, however, the PET/CT scan revealed multiple lesions. Given the rarity of the disease, the challenges in the diagnoses and a low yield of microbiological testing, family physicians should consider employing imaging techniques for prompt and accurate management.

Conclusion/Key points

In conclusion, hepatic TB, although rare, should be kept in the differential diagnosis of FUO in the areas where TB is endemic. The PET/CT scan localizes the site for biopsy and makes an accurate diagnosis when the USG and CT scan are normal, placing the PET/CT scan superior in the algorithm of FUO, which will decrease the morbidity and mortality substantially in such cases.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship:

Nil.

Conflicts of interest

There are no conflicts of interest.

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