Case Report

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Liver Tuberculosis Presenting as an Uncommon Cause of Pyrexia of Unknown Origin: Positron Emission Tomography/Computed Tomography Identifies the Correct Site for Biopsy

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Key Words
Hepatic tuberculosis · Positron emission tomography · Computed tomography · Pyrexia of unknown origin

Abstract
Objective: To identify the correct site to biopsy in a case of pyrexia of unknown origin (PUO) caused by hepatic tuberculosis (TB). ***Clinical Presentation and Intervention:*** A 58-year-old man who developed hepatic TB presented with PUO. Ultrasonography (US) and computed tomography (CT) of the abdomen showed only calcifications in the liver, and positron emission tomography (PET)/CT showed diffuse increased metabolic activity in addition to focal areas of increased activity. A diagnosis of hepatic TB was confirmed by histological examination of liver tissues and interferon-γ release assays (IGRAs of T-SPOT/TB). The patient was treated with 4 anti-tubercular therapies (rifampicin, isoniazid, ethambutol and pyrazinamide). At the 3-month follow-up, the patient was disease free as confirmed by abdominal US. ***Conclusion:*** PET/CT was helpful in identifying a site to biopsy that led to the correct diagnosis.

Introduction

Tuberculosis (TB) infection is still common today and remains an important cause of morbidity and mortality [1, 2]. Abdominal TB is one of the most prevalent forms of extrapulmonary manifestation [3]. Hepatic involvement is uncommon and is categorized into 5 types: miliary, abscess, nodule, biliary invasion and serosal invasion. The manifestations range from abscesses and tuberculomas to hepatic calcifications. The manifestations can be non-specific and mimic many conditions. Ultrasonography (US) and computed tomography (CT) are the main radiological tools used for diagnosis. We describe a case of this type of hepatic TB in which the CT and US imaging findings were normal while the positron emission tomography (PET)/CT findings mimicked lymphomatous liver infiltration.

Case Report

A 58-year-old man presented to the outpatient department of our hospital with recurrent fever (38–41.2°C) and weight loss (up to 16 kg) for over 2 months and was admitted for pyrexia of unknown origin (PUO). At the time of admission, the physical examination revealed a conscious man with the following character-

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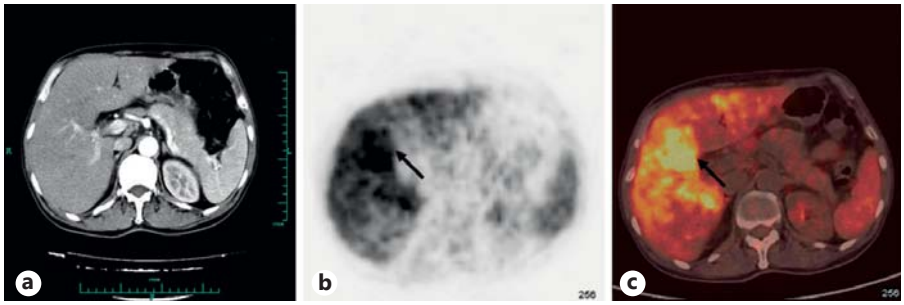

Fig. 1. a Contrast-enhanced CT scan of the abdomen in the arterial phase at the corresponding section revealing no comparable lesion. **b** PET scan showing abnormal diffuse hypermetabolic activity in the liver (arrow), especially in the junction of left and right liver. **c** PET/CT scan showing more hypermetabolic activity with more bright yellow colour (arrow).

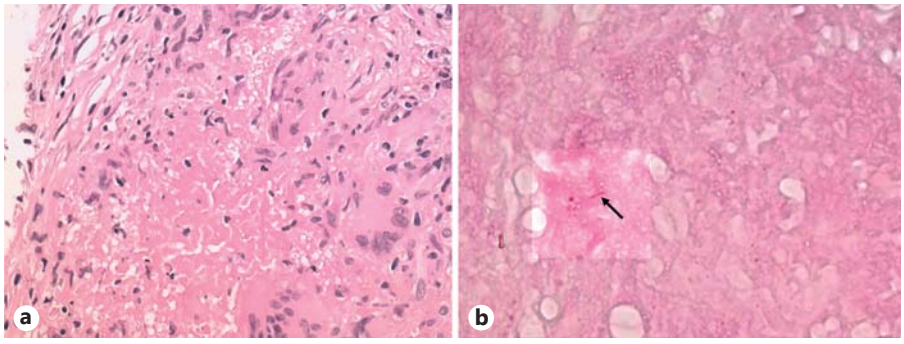

Fig. 2. Histological examination of the liver showing a TB follicle with central caseous necrosis surrounded by lymphocytes, multinucleate giant cells and epithelioid macrophages. **a** HES. ×40. **b** AFB. ×100. Acid-fast staining showed several positive bacilli. One of the acid-fast bacilli is marked by the arrow.

istics: temperature 39.6°C, pulse rate 102 beats/min, blood pressure 100/75 mm Hg and respiratory rate 22 breaths/min. There was no jaundice or lymphadenopathy. Abdominal examination revealed no tenderness or ascites and no hepatosplenomegaly or any other palpable mass in his abdomen. Laboratory analyses revealed the following data: haemoglobin 11.0 g/dl, white blood cells 7,600/mm^3 (70% neutrophils), blood platelets 207,000/mm^3, blood urea 3.7 mmol/l and creatinine 56 μmol/l. Liver enzymes showed a total bilirubin level of 17 mg/l with a direct component of 10 mg/l. Alanine aminotransferase and aspartate aminotransferase levels were 30 and 36 U/l, respectively (the normal range for alanine aminotransferase is 5–40 U/l and that for aspartate aminotransferase is 8–40 U/l), and alkaline phosphatase levels were 702 and 561 U/l (the normal range for γ-glutamyl transpeptidase is 11–50 U/l and that for alkaline phosphatase is 40–150 U/l). The C-reactive protein level was 56.8 mg/l (normal range 0.0–8.0 mg/l) and the erythrocyte sedimentation rate was 29 mm/h (normal range 0–15 mm/h for males). The levels of tumour markers, such as α-fetoprotein, carcinoembryonic antigen and carbohydrate antigen 19-9, were within the normal limits. The patient was non-reactive in HIV serology. A chest CT scan showed no lesion suggestive of TB but revealed mild bilateral hydrothorax and hydropericardium. US of the abdomen revealed a hepatic portal lymph node of 1.7 by 1.2 cm and gallbladder wall oedema. All other abdominal viscera appeared normal with no free fluid. An echocardiogram revealed moderate hydropericardium about 15 mm before the myocardium of the anterior free wall of the right ventricle. A contrast-enhanced CT scan of the abdomen revealed calcifications in the posterior segment of the right liver and lymph node enlargement in the hepatic portal, intraperitoneal and retroperitoneal regions (fig. 1a). Lymphoma, lymphatic TB and autoimmune tissue disease were initially suspected but the hydrothorax and hydropericardium were too small to obtain a sample, and the location of the intraperitoneal and retroperitoneal lymph nodes made them difficult to biopsy. Hence, the patient was referred for a whole-body PET/CT scan to find the lesion site for biopsy. The patient was injected with 350 MBq ^{18}F-fluorodeoxyglucose (FDG) and after 120 min he underwent a head-to-toe scan in a dedicated PET/CT scanner (Biograph, Germany) and a standard uptake value was calculated. Abnormal diffuse hypermetabolic activity in the liver was observed, especially in the junction of the left and right liver, with maximum FDG standard uptake values of 8.81 and 12.47 at the delayed scan (180 min after the injection) (fig. 1), and a nodular hypermetabolic lesion was found in segments V and VI. The standard uptake values of lymph nodes in the mesentery and retroperitoneal space were 7.17 and 9.11, respectively, at the delayed scan. Primary liver lymphoma and hepatocarcinoma were suspected. In order to establish a diagnosis, an ultrasound-guided percutaneous liver biopsy was performed in segments V and VI, and 2 strips of liver tissue were extracted from the liver.

Histological examination of the biopsy showed a TB follicle with central caseous necrosis surrounded by lymphocytes, multinucleate giant cells and epithelioid macrophages, revealing several acid-fast bacteria (fig. 2). To further confirm the diagnosis, a T-SPOT TB test was performed and it was highly positive for ESAT-6 (>20) and CFP-10 (>20). The diagnosis of hepatic TB was confirmed.

Four drugs for anti-tubercular therapy (rifampicin, isoniazid, ethambutol and pyrazinamide) with methylprednisolone 16 mg/day were started. At the 4-week follow-up the patient was asymptomatic and his body temperature had returned to normal. At the 3-month follow-up the patient had no hydrothorax or hydropericardium on chest CT and no enlargement of lymph nodes on abdominal US.

Discussion

PUO constitutes one of the greatest challenges in clinical practice, and PET/CT scans are mainly useful to classify its aetiologies such as infection, malignant, non-infectious inflammatory disease or unknown [4]. Infection is the most common cause and extrapulmonary TB remains an important cause. Localized hepatic TB is a distinct clinical form of extrapulmonary TB which is very rare even in countries where TB is an alarming public health problem and its diagnosis is usually difficult [5].

It is believed that the liver is affected in most cases of miliary TB, which usually occurs in association with miliary lung TB, mainly through haematogenous dissemination [6]. The manifestations range from abscesses and tuberculomas to hepatic calcifications. We found the lesions using US, CT or MR scans. Then, the diagnosis was confirmed via a biopsy or puncture. Occasionally the diagnosis may be made via laparotomy or autopsy. The symptoms and signs of hepatic TB, including fever, vague abdominal pain, anorexia and weight loss, are non-specific [1]. Hepatomegaly is a common physical finding. As in the case of our patient, because of the non-specific clinical presentation and the lack of hepatic lesions in the US and CT scan, diagnosing hepatic TB is quite difficult.

In order to determine the key area to biopsy and make an accurate diagnosis, the patient was referred for a whole-body PET/CT scan. ^{18}F-FDG uptake reflects glucose metabolism and can be present in high concentrations in tumour and inflammatory lesions [7]. PET/CT scanners currently allow quick and high-resolution imaging and can correlate the anatomical location with functional information, thus allowing detection of the lesion at an early stage. In our case, the hepatic TB might have been at a very early stage, so there was no anatomic abnormality in the US and CT scans but there was an extraordinary functional abnormality in the PET/CT scan. PET/CT scanning, which can produce whole-body imaging data and distinguish early high-metabolic liver lesions from normal liver tissues, is superior to CT and US which only visualize a limited portion of the body. Thus, PET/CT is advantageous in identifying the correct site for the diagnosis of hepatic TB as an unusual cause of PUO.

Conclusion

Hepatic TB without mass or miliary involvement on CT scans is very rare. PET/CT showed diffuse increased metabolic activity in addition to focal areas of increased activity, thus helping to identify a site to biopsy that led to the correct diagnosis.

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