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Isolated Tuberculous Liver Abscesses in Down Syndrome

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ABSTRACT

Isolated tuberculosis (TB) liver abscesses have rarely been documented in the literature. This report describes the challenging diagnosis of primary liver TB. We report on the case of a 10-year-old girl with Down syndrome, who had symptoms of fever and chills, anorexia and intermittent vomiting. The ultrasound and computed tomography (CT) revealed multiple abscess-like lesions in the liver. A diagnosis of TB should be considered in patients with hepatic abscesses, particularly in those patients who have possible immunodeficiency, such as Down syndrome.

Implication for health policy/practice/research/medical education:
This is the interesting case of TB for clinical physicians specially pediatricians.

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1. Introduction

Different organs can be involved in tuberculosis (TB) infection and a granulomatosis reaction of the liver in pulmonary and extrapulmonary disease is common. However, isolated TB of the liver in the form of multiple abscesses is extremely rare. Liver TB is usually accompanied by infectious foci in the lungs or gastrointestinal tract (1, 2). Of these, primary TB abscesses of the liver have been reported mainly in those who are; elderly, immunodeficient (e.g. AIDS) or with poor socioeconomic status (3, 4).

We present the case of a patient with Down syndrome, who developed multiple microabscess-like lesions in the liver without the involvement of any other organs. This report illustrates the challenging diagnosis of focal hepatic TB, which has never been described before in Down syndrome in the literature. This clinical manifestation of TB should be considered in patients who have non-recoverable liver abscesses, especially in patients with immunodeficiency, and who live in regions with the greatest prevalence of TB.

2. Case Presentation

A 10-year-old Iranian girl with Down syndrome was admitted to hospital with a history of fever, chills and intermittent vomiting. Due to her presentation at that time, suggesting sepsis, she underwent treatment with intravenous ceftriaxone and vancomycin for a period

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of two weeks. Because her condition did not respond to this antibacterial therapy, she was referred to a well-equipped center in another city. This patient was evaluated as having a fever of unknown origin (FUO) for ten days. Although all blood cultures were negative, she had the possibility of a congenital heart disease, so infective endocarditis was suspected and an echocardiogram was done. An intracardiac mass which might be related to a vegetation lesion was not reported. In further investigations, abdominal ultrasonography showed multiple hypoechoic lesions in her liver and supporting microabscesses. In that clinical setting, empirical antibiotic therapy with vancomycin and gentamicin was started, because the specific pathogen and its susceptibility had not been identified. However, there was no improvement in her general health and fever after 2 weeks of treatment.

At this stage the diagnosis was uncertain; the child was discharged with their parents' consent and referred to our Pediatric Medicine Center, the tertiary care hospital. At presentation, the patient complained of fever and chills, anorexia, intermittent vomiting and weight loss. Before this, she was well with no history of any infectious disease symptoms. In addition, their family had no serious infections during recent years. A physical examination on admission revealed that the child was conscious, but looked ill. The axilliary temperature was 39.5 °C, with tachycardia. Blood pressure and respiratory rate were within normal range, and auscultation of the heart and lungs was also normal. There was no lymphadenopathy or abdominal distention, but the upper abdominal area was slightly tender. The liver was enlarged 3 cm below the costal margins, and the edge and surface of the liver were soft and smooth. The clinical examination of other systems revealed no abnormal findings.

Laboratory reports showed a hemoglobin level of 12 g/dL with normochromic, normocytic indices, white cell count of 20800 with a differential count of 79% polymorphonuclears, 20% lymphocytes and 1% band cells, and a platelet count of 389000. Erythrocyte sedimentation rate (ESR) was 115 mm/1st hour. C-reactive protein (CRP) was 30 mg/dL. Liver function tests, serum albumin, prothrombin time, partial thromboplastin time and lactate dehydrogenase were within the normal range. Routine urinalysis was negative. Multiple blood, urine and sputum cultures were negative. Bone marrow aspiration with its culture was negative and/or normal differential counts. Sputum cultures of acid-fast bacilli (AFB) and TB polymerase chain reaction (PCR) were also negative. The tuberculin test and serological tests of Wright and Widal were negative. The workup of immune deficiency disorders (including chronic granulomatous disease) yielded normal immunoglobulin levels and nitroblue tetrazolium (NBT) test results. The two roentgenograms of the chest were normal at 3-week intervals. An abdominal ultrasonography and computed tomography (CT) scan revealed multiple hypoechoic and low density lesions in the liver, respectively.

Originally, multiple pyogenic liver microabscesses were suspected, because of the non-resolving fever, a biopsy of the liver was indicated. A percutaneous biopsy was impossible to perform under ultrasound or CT scan guidance due to the fact that the lesions were small and distributed. At first, the patient underwent a laparoscopy to obtain tissue for diagnosis, but it was not the most efficacious method. Therefore, a laparotomy was performed to establish a more precise diagnosis. Macroscopically, the appearance of small multiple abscesses-like lesions were observed. A specimen of liver containing a white nodular lesion was resected. Histologic examination of the liver tissue showed caseating granuloma with central necrosis. These findings were consistent with TB. Ziehl-Neelsen and Gram stain did not reveal any organisms such as AFB. Cultures of the liver tissue also yielded no AFB or any other organisms. However, a PCR assay of the liver biopsy specimen identified mycobacterium TB. The child was treated with antituberculous agents consisting of; isoniazid, rifampicin, ethambutol and pyrazinamide for two months. Several days after the initiation of antituberculous therapy, the patient's general condition improved and her fever was reduced. Following 2 weeks of therapy, the ESR and white cell counts decreased dramatically, the child became afebrile with a good appetite and general improved health, and she was discharged from our medical center. In outpatient follow-ups, her status was completely satisfactory. When seen 1 month later at the clinic, she was in good health, and the ESR was 13 mm/1st hour with no leukocytosis. A repeat CT scan of the abdomen 2 months post-therapy demonstrated healing of the lesions in the liver. The patient has been followed for 6 months, takes isoniazid and rifampicin and remains in good health 1 year after treatment.

3. Discussion

Extrapulmonary TB with isolated liver localization of TB and no evidence of other infected organs is rarely encountered, even in regions where TB is a relatively common and alarming public health problem. Overall, less than 100 TB hepatic abscesses have been reported in the literature, while primary liver involvement has been documented in only 17 previous cases up until 1991. In another study, it mentioned that 21 cases of isolated tuberculous abscesses of the liver had been found in the world literature, and two additional cases were described (2, 5-7).

TB in the liver usually occurs secondary to pulmonary or gut foci. Tubercles reach the liver via the hepatic artery or the portal vein and are often found in the portal areas, they may also spread to the spleen. It seems that infrequent cases of isolated liver TB are consistent with the oxygen tension of the liver tissue being too low for the growth of mycobacterium (7, 8). TB may affect the liver in three different morphological ways:

1) Military TB of the liver associated with generalized military or pulmonary TB, which is more commonly seen in; childhood, and the elderly.

2) Primary military TB of the liver without the involvement of other organs.

3) Primary single or multiple nodular lesions termed tuberculoma or frank abscess, which is uncommon (8, 9).

Clinically, tuberculous liver abscesses present with FUO, weight loss, anorexia and vague upper abdominal pain. Severe liver dysfunction and jaundice are uncommon in primary TB abscesses of the liver (7, 10). In patients with extrapulmonary TB, the most frequent abnormalities were; hypoproteinemia, elevated alkaline phosphatase and hypoglobulinemia (11). Our patient presented with these nonspecific symptoms as well as intermittent vomiting, and had hepatomegaly in physical examination. This manifestation was considered to be a result of sepsis in a girl with Down syndrome and no history of infectious disease. In further evaluations, laboratory tests revealed leukocytosis and elevated ESR and CRP levels which were in accordance with previous reports. However, all the liver function tests and serum protein profiles were within normal range.

Tuberculous of the liver is often confused with other infectious or inflammatory diseases and tumors (2, 7). The diagnosis of liver TB was delayed primarily because of the patient's background. Congenital heart defects related to Down syndrome induced suspicions of infective endocarditis. In addition, the preceding antibiotic therapy made the multiple blood cultures negative. Also, the CT scan showed multiple hypodense lesions in the liver and spleen consistent with abscesses. Therefore, antimicrobial therapy followed. When the patient was treated with different therapeutic regimes, and her general health and fever did not recover, the preliminary diagnosis of infective endocarditis was put in doubt. The chest X-rays showed no evidence of an active pulmonary disease. This clinical trend, involving only the liver, indicated the need for a liver biopsy.

The diagnosis of tuberculous liver abscess has been made in the majority of cases with a laparotomy. From 23 TB liver cases, 19 cases required surgical intervention to establish the diagnosis, because the mycobacteria in the percutaneous aspirate was not detectable (7). Actually, this fact reflects the difficulty in achieving a diagnosis when there is isolated liver TB. Tuberculous abscesses have been mistaken for; primary or metastatic carcinoma of the liver, pyogenic or amebic liver abscesses and empyema of the gallbladder (2). Some authors have reported that percutaneous liver biopsy using ultrasound-guided CT, or laparoscopy were adequate methods. However, the diagnosis still remains in doubt in some cases and more invasive investigations such as laparoscopy or laparotomy are required (2, 3, 12). In our patient, it was impossible to obtain the percutaneous biopsy of the liver tissue. Also, the laparoscopy method was unsuccessful due to the small, sparse lesions.

Histological examination of the liver biopsy specimen revealed caseating granuloma with central necrosis. AFB in the liver tissue and tubercle bacilli were not found elsewhere. The frequency of positive acid-fast smear and culture is low, with a higher frequency occurring among patients with military TB. However, in some reports the aspirate specimen of the liver has been flooded with mycobacterium (3, 13). Culture of the liver specimen, in this particular case yielded no AFB, which is in accord with previous reports. Detection of mycobacterium TB has been developed using a PCR assay of the liver biopsy specimen (14). In our patient, PCR assay of the liver tissue documented the TB diagnosis for a caseating granuloma.

The majority of isolated tuberculous liver cases have been found in patients with other underlying disorders. In patients with acquired immunodeficiency syndrome (AIDS), it has been observed that there is an increase in the incidence of extrapulmonary TB. In two prospective reviews involving 171 non-AIDS patients with hepatic TB, no isolated tuberculous liver abscesses were described (15, 16). Also, increased susceptibility to the hepatic TB is a well-known feature of uremia and liver cirrhosis (2). Actually, young children, the elderly and immunocompromised subjects are at high risk of extrapulmonary TB. In the literature, no case of isolated tuberculous liver has been described in a patient with Down syndrome. Down syndrome may be associated with immune system dysfunction including; an unusual morphology of the thymus with a decrease in the peripheral lymphocyte count, dysfunction of the phagocytic compartment, chemotaxis and intracellular killing deficiency (17). Also, it has been shown that the patients with Down syndrome have immature T lymphocytes due to a lack of thymic hormonal factors (18). Although our patient had normal immunoglobulin levels and NBT test, unknown phagocytosis dysfunction may have increased her susceptibility to multiple nodular microabscesses TB of the liver.

In conclusion, tuberculous involvement should be considered in a differential diagnosis of liver lesions in imaging studies, especially in immunocompromised or ill patients with prolonged nonspecific symptoms. In addition, patients with chromosomal abnormalities such as Down syndrome may be at increased risk of unusual forms of TB. Although the primary TB of the liver is usually misdiagnosed, it can be managed properly with systemic antituberculous therapy and result in a good prognosis.

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