Isolated Tuberculous Liver Abscess in a Patient With Asymptomatic Stage I Sarcoidosis

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Sarcoidosis is a multi-system disorder characterized by non-caseating granulomas. Depressed cellular immunity predisposes patients to infections with certain intracellular organisms, mostly fungi, Mycobacterium tuberculosis, and Nocardia species. Isolated liver tuberculosis is a rare condition, and atypical clinical presentation challenges the clinical acumen of the treating physician. Liver sarcoidosis is usually unsuspected and confused with primary or metastatic liver carcinoma. We describe a case of isolated tuberculous liver abscess without pulmonary spread in a patient with asymptomatic stage I sarcoidosis. Key words: sarcoidosis; granuloma; tuberculosis; liver tuberculosis; liver carcinoma; liver abscess. [Respir Care 2010;55(12):1751–1753. © 2010 Daedalus Enterprises]

Introduction

Sarcoidosis is a multisystem granulomatous disorder of uncertain etiology, characterized pathologically by non-caseating granulomas in involved tissues.1 Approximately half of cases are diagnosed incidentally from abnormalities on routine chest radiograph. Depressed cellular immunity predisposes patients to opportunistic infections with certain intracellular organisms, mostly fungi, Mycobacterium tuberculosis, and Nocardia species. Moreover, in patients with early-stage untreated disease these organisms are rather infrequent. As these infections are mainly insidious and difficult to differentiate from the underlying disease, a possible misdiagnosis may lead to fatal complications.2 We describe a patient with diagnosed asymptomatic stage I sarcoidosis for at least 2 years before his admission for a 2-week history of fever and abdominal pain, in whom we found an isolated tuberculous liver abscess. This case highlights the high index of suspicion required to identify tuberculosis liver infection in a patient with diagnosed asymptomatic sarcoidosis.

Case Report

A 40-year-old, non-smoking, non-diabetic man was diagnosed with stage I sarcoidosis of the lung, in the course of a routine medical checkup in July 2007, during a work-related visit to China. The diagnosis was made on the basis of bilateral paratracheal, pretracheal, and hilar lymphadenopathy on computed tomogram (Fig. 1). Mantoux test was negative, he had elevated angiotensin-converting enzyme, and biopsy of the right supraclavicular lymph node found non-caseating granuloma. After diagnosis he was completely asymptomatic for 2 years, during which he took no medications (eg, steroids).

In May 2009 he presented to our respiratory clinic with 2 weeks of upper-abdominal pain, high fever and chills, and rigor. The onset was gradual, with increasing weakness and deterioration of general health. At admission he looked ill and anemic, and had moderate fever, a heart rate of 120 beats/min, and blood pressure of 110/70 mm of Hg. There was no jaundice, clubbing, lymphadenopathy or edema of the feet. His liver was palpable about 2 cm below the right costal margin; the margin was sharp, the surface was smooth and soft, and the liver was tender to palpation. The spleen was not palpable. There was no ascites nor palpable abdominal mass. Respiratory and cardiovascular examination revealed no abnormalities. Complete hemogram was normal except for elevated erythrocyte sedimen-
tation rate and C-reactive protein. A liver function test found only mildly elevated alkaline phosphatase (497 U/L). Enzyme-linked immunosorbent assay (ELISA) for human immunodeficiency virus I and II was negative. Chest radiograph was normal. Ultrasonography found a solid space-occupying lesion in the right lobe of the liver. Computed tomogram (Fig. 2) showed an ill-defined hypoechoic mass in the right lobe of the liver. Sputum test for acid-fast bacilli smear was negative on 3 consecutive days. Fine-needle biopsy of the liver lesion showed caseating epithelioid granuloma (Fig. 3), and Ziehl-Neelsen stain showed the presence of acid-fast bacilli. Testing of the biopsy specimen for \textit{M. tuberculosis} with a mycobacteria detection system (BACTEC MGIT 960, Becton Dickinson, Sparks, Maryland) and the polymerase-chain-reaction test were both positive.

Our diagnosis was isolated tuberculous liver abscess in a patient with stage I sarcoidosis. We started him on category I tuberculosis (TB) therapy (short-course directly observed treatment) in June 2009. On follow-up, ultrasonogram showed that the liver lesion had shrunk, and his symptoms had improved. He completed the 6 months of TB therapy. A recent ultrasonogram showed that the liver lesion had completely resolved.

**Discussion**

Diagnosis of tuberculous liver abscess is difficult. Usual symptoms and signs, in order of frequency, are fever, chills, and soft cystic enlarged liver.\textsuperscript{3} Jaundice is seldom encountered.\textsuperscript{4} Smear and culture bacteriologic confirmation in suspected cases has also been very rare. Histology of the liver abscess is valuable to establish the diagnosis.\textsuperscript{5} In our patient the diagnosis was made possible by the smear examination of the biopsied pus and confirmed by culturing \textit{M. tuberculosis}. The polymerase-chain-reaction test for \textit{M. tuberculosis} can also increase diagnostic sensitivity and accuracy in hepatic TB: its sensitivity is 58\%, and its specificity is 96\% in diagnosing hepatic granuloma. The importance of correct diagnosis cannot be overstated, since untreated abdominal TB carries a 50\% mortality.\textsuperscript{6}

The majority of immunocompetent patients control mycobacterial infection efficiently, because of efficient coordination of the immune response by the cytokine network. Leukocyte migration to the site of mycobacterial focus, and initiation of the granulomatous lesion are mediated by chemokines and pro-inflammatory cytokines. Infected macrophages and dendritic cells produce interleukin-12, the crucial cytokine in controlling early \textit{M. tuberculosis} infection, which regulates the immune system toward a T-helper response with production of interferon gamma and down-modulation of interleukin-10 and interleukin-4. Formation and sustaining of the architecture are supported mainly by tumor necrosis factor alpha, interferon gamma, transforming growth factor beta, and lymphotoxin alpha 3.

A test for latent \textit{M. tuberculosis} infection, QuantiFeron-TB Gold (Cellestis Limited, Carnegie, Victoria, Australia), uses
peptide mixtures that simulate early secretory antigenic target-6 and culture filtrate protein-10 proteins to stimulate cells in heparinized whole blood. Detection of interferon gamma via ELISA is used to identify in vitro response to early secretory antigenic target-6 and culture filtrate protein-10, which are associated with \textit{M. tuberculosis} infection. The QuantiFeron-TB Gold assay is very helpful in diagnosing latent TB infection and excluding atypical mycobacterial infection where it is prevalent, but if \textit{M. tuberculosis} infection is confirmed by clinical findings or other tests (eg, culture), there is no need for the QuantiFeron-TB Gold test.

There are 3 forms of hepatic TB. Diffuse hepatic involvement with pulmonary or miliary TB is the most common form, seen in 50–80% of patients who die of pulmonary TB. Diffuse hepatic infiltration without recognizable pulmonary involvement is the second form. The third, very rare, form presents as a focal/local tuberculoma or abscess. Isolated tuberculous liver abscess is extremely uncommon, with a prevalence of 0.34% in patients with hepatic TB.\textsuperscript{7} Kok and Yapp reported an overall incidence of 0.3% for isolated hepatic TB.\textsuperscript{8} Hepatic TB lesions that appear as masses larger than 2 mm in diameter are referred to as macronodular or pseudotumoral TB. On the basis of imaging alone, these lesions are virtually indistinguishable from many other focal lesions of the liver, such as hepatocellular carcinoma, metastases, and Hodgkin disease, so pathology examination is necessary for diagnosis.\textsuperscript{9}

Isolated hepatic TB results from tubercle bacilli gaining access to the portal vein from a microscopic or small tuberculous focus in the bowel. The clinical presentation of isolated TB liver abscess is so rare and atypical that it challenges the clinical acumen of the treating physician.\textsuperscript{10}

The association of sarcoidosis with TB is complex, although it has been thoroughly studied. TB has been described as both preceding and coexisting with sarcoidosis, and as an opportunistic infection in sarcoidosis patients who are on corticosteroids, which depress the disordered cell-mediated immunity.\textsuperscript{11,12}

Although the prevalence of TB is high in India, hepatic TB is rare. Primary involvement of the liver in TB is especially rare due to the low tissue oxygen level, which makes the liver inhospitable for the bacilli. Only few cases of TB in patients with sarcoidosis have been reported in the world literature, and all of them had a course of corticosteroids or were immunosuppressed. To our knowledge, our patient was unique, as he had never taken corticosteroids.

\textbf{REFERENCES}