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Sclerosing cholangitis-like changes in hepatobiliary tuberculosis

Hepatobiliyer tüberkülozda skerozan kolanjit benzeri değişiklikler

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Atypical presentations of tuberculosis might cause difficulties in diagnosis, especially in developing countries. Primary hepatobiliary tuberculosis is a rare condition and the diagnosis of this condition necessitates a high index of suspicion. In this report, we present a case with obstructive jaundice, dilated intrahepatic bile ducts and lymphadenopathies in the porta hepatis. Endoscopic retrograde cholangiopancreaticography showed irregularities, strictures and dilatations both in the intra- and extrahepatic bile ducts resembling sclerosing cholangitis. The liver biopsy showed caseous granulomatous hepatitis and Langhans giant cells compatible with tuberculosis, and a lymph node biopsy obtained from the left cervical region demonstrated caseating confluent granulomas with abundant acid-fast bacilli. The present case shows that primary hepatobiliary tuberculosis may mimic primary sclerosing cholangitis and should be considered in the differential diagnosis of patients with sclerosing cholangitis-like changes on endoscopic retrograde cholangiopancreaticography.

Key words: Tuberculosis, sclerosing cholangitis, jaundice

Özellikle gelişmekte olan ülkelerde tüberkülozun atipik klinik sunumları teşhiste güçlük yaratmaktadır. Primer hepatobiliyer tüberküloz nadir karşılaşılan bir tablodur ancak ayırıcı tanıda her zaman akılda tutulmalıdır. Bu yazıda obstrüktif sarılık, intrahepatik safra yollarında genişleme ve porta hepatiste lenf adenopatisi olan olan olguda endoskopik retrograd kolanjiyopankreatikografide intra ve ekstra hepatik safra yollarında sklerozan kolanjite benzer şekilde irregülarite, dilatasyon ve striktürler saptanmıştır. Hastaya karaciğer biyopsisi yapılınca tüberküloz ile uyumlu olacak şekilde Langhans tipi dev hücreler ve kazeöz granulamatöz hepatit saptanmıştır. Hastanın sol posterior servikal bölgesinden eksize edilen lenf nodunun incelemesinde kazeifiye granülomatöz lezyonlar içinde Zehl – Nielsen boyası ile bol miktarda aside dirençli basil gösterilmiştir. Bu olgu hepatobiliyer tüberkülozun primer sklerozan kolanjiti taklit edebileceğini ve endoskopik retrograd kolanjiyopankreatikografide sklerozan kolanjit benzeri bulgular saptanan olgularda ayırıcı tanıda düşünülmesi gerektiğini göstermektedir.

Anahtar kelimeler: Tüberküloz, sklerozan kolanjit, sarılık

INTRODUCTION

Tuberculosis is one of the most prevalent infections in developing countries and its incidence has been rising in developed countries in the past couple of decades (1). The majority of cases have pulmonary tuberculosis, while biliary tuberculosis is extremely rare (2). In an old autopsy series, Stemmerman (3) found only 45 instances (3%) of biliary tuberculosis in 1500 cases with tuberculosis. Furthermore, jaundice was present in only 3 (6.7%) of these 45 cases.

Primary hepatobiliary tuberculosis is difficult to diagnose and treat. Obstructive jaundice can be caused by many different clinical conditions, and tuberculosis of the bile ducts is rarely taken into account in the differential diagnosis of this condition. In this article, we report a case who presented with obstructive jaundice and progressive sclerosing cholangitis–like cholangiograms, who was diagnosed to have biliary tuberculosis.

CASE REPORT

A 43-year-old female presented to a local hospital with the complaints of malaise and itching. She was found to have elevated liver enzymes and bilirubin and was referred to our hospital. Her past medical history was unremarkable. On physical examination, sclera was subicteric and the liver was palpable 2 cm below the costal margin. An enlarged lymph node measuring 1 x 1 cm was detected at the left posterior cervical region. The rele-

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vant laboratory data were as follows: aspartate aminotransferase (AST): 67 U/L (0-38), alanine aminotransferase (ALT): 63 U/L (0-41), gamma glutamyl transpeptidase (GGT): 146 U/L (8-61), alkaline phosphatase: 1189 U/L (0-270), bilirubin (direct/total): 2.05/3.0 mg/dl (0-0.3/0.1-1), hemoglobin: 12.4 g/dl (12-15), and white blood cell count: 7600/mm^3 (3600-11000). The erythrocyte sedimentation rate was 35 mm/hour. Liver sonography revealed focal areas where the intrahepatic bile ducts were dilated. The wall of the common bile duct was thickened (5.4 mm). The liver was increased in size and the parenchyma was irregular. Several lymphadenopathies, the largest being 30 mm, were observed in the porta hepatis.

An endoscopic retrograde cholangiopancreaticography (ERCP) was performed and showed irregularities, strictures and dilatations both in the intra- and extrahepatic bile ducts resembling sclerosing cholangitis (Figure 1). A 7 French nasobiliary drainage catheter was placed in the left bile duct. The pancreatic duct was normal.

A liver biopsy was performed and showed caseous granulomatous hepatitis with Langhans giant cells (Figure 2). The cytologic and polymerase chain reaction (PCR) examination of the bile obtained from the drainage catheter was negative for tuberculosis bacilli. The patient was screened for pulmonary tuberculosis but no evidence for pulmonary involvement was found. The posterior cervical lymph node was excised. The pathological examination showed caseating granulomas, and inset Ziehl-Neelsen stain demonstrated abundant acid-fast bacilli in the granulomas (Figure 3). Antituberculosis treatment with isoniazid 300 mg/day, rifampicin 600 mg/day, pyrazinamide 1500 mg/day, and ethambutol 900 mg/day was started. Pyrazinamide and ethambutol were planned to be discontinued after two months. Isoniazid and rifampicin were continued for nine months. At the end of this period, it was observed that the liver function tests were improved [AST: 25 U/L (0-38), ALT: 29 U/L (0-41), GGT: 104 U/L (8-61), alkaline phosphatase: 287 U/L (0-270), bilirubin (direct/total): 0.1/1 g/dl (0-0.3/0.1-1)]. A magnetic resonance cholangiography showed focal stenosis in the proximal portion of the choledochus, and patchy irregularities in intrahepatic bile ducts.

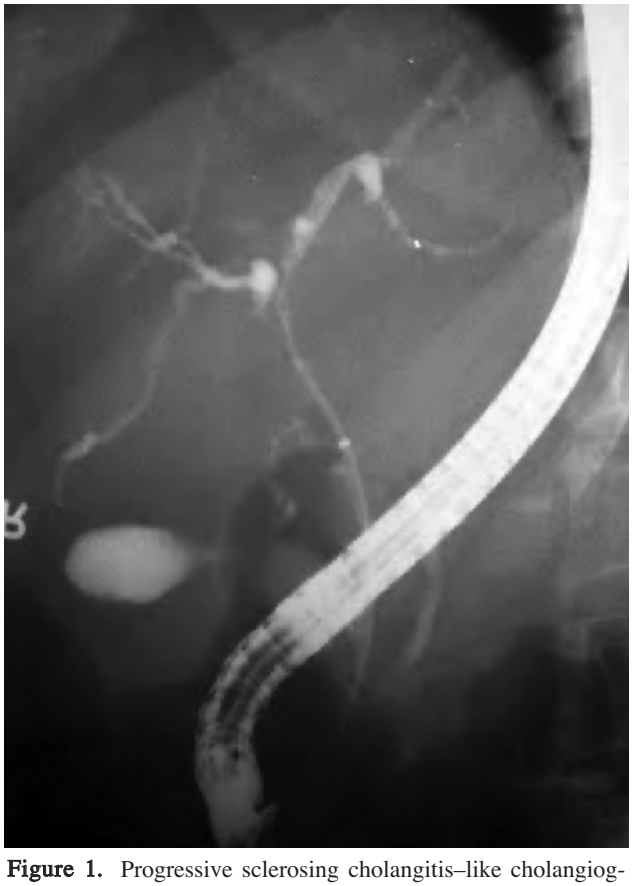

Figure 1. Progressive sclerosing cholangitis–like cholangiograms.

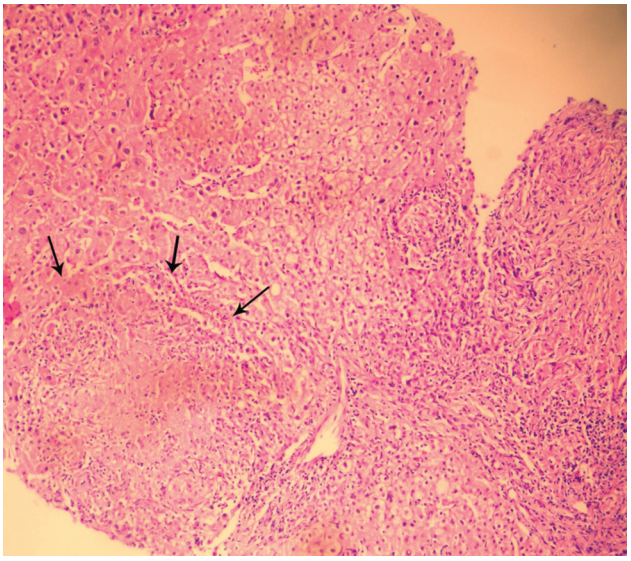

Figure 2. Arrows: Caseating granulomas in parenchyma and in portal tracts of the liver (hematoxylin and eosin [HE] stain, X20).

DISCUSSION

Abdominal tuberculosis is not uncommon in countries with high prevalence of pulmonary tuberculosis, and its incidence is about 12% in some countries (4). It is usually a primary disease of the gastrointestinal system, and active pulmonary tuber-

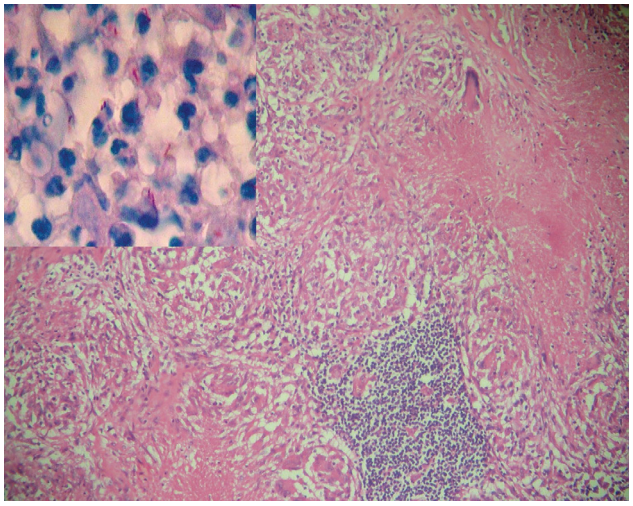

Figure 3. Microscopic examination of the lymph node revealed caseating confluent granulomas (HE). Inset Ziehl-Neelsen stain demonstrated abundant acid-fast bacilli.

culosis has been found in only 6–38% of the cases with abdominal tuberculosis (5).

Three types of liver involvement in hepatobiliary tuberculosis have been defined by Alvarez (6): 1) miliary, 2) granulomatous hepatitis or tuberculous hepatitis (with fever, jaundice, liver function abnormalities, and caseating granulomas on biopsy) and 3) localized hepatic tuberculosis or hepatobiliary tuberculosis (with bile duct involvement due to invasion by involved periportal lymph nodes and/or involvement of the epithelium of the bile duct or without biliary involvement).

Our patient did not have a history of tuberculosis and had no evidence for pulmonary tuberculosis. Since isolated hepatic tuberculosis is a very rare condition, we re-evaluated our patient for an evidence of tuberculosis after finding caseating granulomas in the liver biopsy. We found an enlarged lymph node in the posterior cervical region. This lymph node was excised and the pathological examination showed caseating granulomas, and inset Ziehl-Neelsen stain demonstrated abundant acid-fast bacilli in the granulomas. This finding verified our diagnosis. Thus, she had primary gastrointestinal tuberculosis presenting as granulomatous hepatitis (Type 2 according to the classification mentioned above).

Granulomatous hepatitis can be seen in the course of autoimmune diseases such as sarcoidosis or primary biliary cirrhosis, systemic infections such as tuberculosis, cryptococcosis, Q fever or brucellosis, malignant diseases such as Hodgkin's and non-Hodgkin's lymphoma or renal cell carcinoma, and secondary to some drugs such as allopurinol, sulphur drugs or quinidine.

Tuberculosis is the most common systemic infection causing granulomatous hepatitis. Active tuberculosis most typically presents with pulmonary symptoms, and the diagnosis can usually be made by microbiological examination of the material obtained from bronchi. However, if a patient presents more atypically, as did our patient, clinicians may not suspect tuberculosis as the initial diagnosis.

The clinical presentation of hepatobiliary tuberculosis is usually slow and insidious. Men and women are affected equally and the symptoms are non-specific. The most common symptoms are reported to be abdominal pain, malaise, jaundice, anorexia, weight loss, and fever (1, 7). In concordance with the literature, our patient had nonspecific symptoms such as malaise and itching.

The ERCP of our patient revealed features suggestive of sclerosing cholangitis. A stenosis, dilatation or irregularity in the intra- and/or extrahepatic biliary ducts is defined as sclerosing cholangitis. This condition is referred to as primary sclerosing cholangitis provided that no other associated conditions are present. Primary sclerosing cholangitis is characterized with progressive sclerosing fibrosis of the bile ducts. Progressive sclerosing cholangitis–like cholangiograms are also defined in some other conditions such as solid tumor metastasis, leukemia, lymphoma, and amyloidosis of the liver (8).

In the literature, it is reported that the clinical and cholangiographic features of tuberculous biliary stricture are usually not helpful in differentiating tuberculosis from other common causes of endoluminal biliary stricture, such as primary sclerosing cholangitis or cholangiocarcinoma. Alvarez and Sollano (9) described four characteristic cholangiographic features for hepatobiliary tuberculosis: 1) a tight hilar stricture with dilated intrahepatic ducts, 2) a long smooth stricture involving the distal bile duct, 3) pruning of the distal intrahepatic ducts, and 4) sclerosing cholangitis-like changes.

The diagnosis of biliary tuberculosis is difficult. Recent reports have suggested the usefulness of the examination of the bile obtained during ERCP by cytology or PCR-based techniques for the demonstration of the bacilli (2, 10). However, the diagnostic accuracy of these techniques has not been confirmed, and it is reported that only 1 of 5 pa-

tients with biliary tuberculosis had positive cytologic results (1). The diagnosis was made by liver biopsy in our patient. The cytologic and PCR-based examination was negative.

In conclusion, primary hepatobiliary tuberculosis should be considered in the differential diagnosis of patients with cholestasis and sclerosing cholangitis-like findings on ERCP. Heterogeneity of the liver parenchyma on ultrasonography should warrant liver biopsy in these patients.

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