

A STUDY OF HISTOPATHOLOGICAL AND BIOCHEMICAL CHANGES OF LIVER IN TUBERCULOSIS

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ABSTRACT

BACKGROUND

Infection with mycobacterium tuberculosis is most often found in well-oxygenated areas of the body such as the apices of the lung and renal cortex, it does affect liver in many ways. This kind of infection in the liver is usually secondary from TB of the lung or other organ.

The aim of this study is to assess the liver function test abnormalities and histopathological changes on liver biopsy in tuberculosis and to correlate with biochemical and histopathological changes in tuberculosis patients.

MATERIALS AND METHODS

This cross-sectional observational study was carried out on 50 cases of tuberculosis patients admitted in medical wards at KIMS Hospital, Hubli. Out of 50 study participants, 40 were suffering from pulmonary and remaining 10 from disseminated tuberculosis. The need for liver biopsy was clinically assessed by the evaluating hepatologist following a complete physical examination and appropriate radiological imaging. Vitamin K 5 mg/day was given IM for three consecutive days prior to liver biopsy ruling out all contraindications and coagulation or bleeding disorders.

RESULTS

In this study, male-to-female ratio was 3.5:1 with peak incidence among 20-40 years of age. Chest x-ray revealed nonhomogenous fibrocaseous lesions in 86% followed by cavitary lesions in 52% of cases. Hepatic granuloma was 12% all being seen in disseminated tuberculosis. Nonspecific changes were seen in 88% of cases. Most common being fatty infiltration (64%) and lymphocytic infiltration (68%).

CONCLUSION

This study concluded that the incident of hepatic granuloma was seen in disseminated tuberculosis. Diagnosis of hepatobiliary tuberculosis should be considered in any patient with hepatomegaly, especially if accompanied by weight loss and in suspicious cases, a liver biopsy should be performed without delay, since this condition responds well to early antituberculous therapy.

KEYWORDS

Liver Biopsy, Histopathology, Tuberculosis.

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BACKGROUND

Tuberculosis (TB) is a major health problem worldwide particularly in developing countries. Abdominal tuberculosis is rare manifestation among various forms of extrapulmonary TB. The diagnosis of abdominal TB is made based on the demonstration of tubercle bacilli in the gastrointestinal tract, peritoneum or intra-abdominal solid organs. Liver TB is considered very rare among abdominal TB patients. Usually, it is associated with foci of infection in the lungs or gastrointestinal tract.^{1,2}

Disseminated TB is defined as TB that involves two or more non-contiguous sites. It is a life-threatening condition, which is often a challenge to diagnose. The clinical presentation maybe chronic and nonspecific (with signs and symptoms such as fever, weight loss, anorexia and weakness) or acute (as fulminant disease). Clinical signs depend on organ involvement and in order of frequency include hepatomegaly, pulmonary findings, lymphadenopathy and splenomegaly.³ Fever is the most common (50-90%) symptom followed by abdominal pain (45-66%, mainly in the right upper quadrant).

The most common miliary consists of small nodules of 0.5 to 2 mm in diameter. It is found in 80-100 percent of autopsies of patients with disseminated tuberculosis and in 50-80 percent of all patients dying from chronic pulmonary tuberculosis. The organism reaches hepatobiliary tract by haematogenous route from a tuberculous infection of the lungs (which maybe active or inactive) via the hepatic artery.

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In some cases, infection could reach liver via the portal vein especially if there is concomitant gastrointestinal TB.⁴

Laboratory parameters and imaging methods in the local form of hepatic tuberculosis are frequently abnormal, but nonspecific. Definitive diagnosis of this condition can be very difficult. It relies on histological and/or bacteriological findings of the liver tissue obtained by biopsy.⁵

Patients with hepatic tuberculosis have variable clinical presentations and no consistent clinical and biochemical findings, which makes diagnosis difficult. The presenting symptoms are usually nonspecific and are mainly constitutional in nature. They include fever, night sweats, malaise, anorexia, weight loss and abdominal pain.^{6,7,8} When such evidence is lacking, a correct diagnosis can be extremely difficult.

Hence, the aim of this study was to assess the liver function test abnormalities and study the histopathological changes on liver biopsy in tuberculosis and to correlate with biochemical and histopathological changes in these patients.

MATERIALS AND METHODS

This cross-sectional observational study was carried out on 50 cases of tuberculosis patients admitted in medical wards at KIMS Hospital, Hubli. Out of 50 study participants, 40 were suffering from pulmonary and remaining 10 from disseminated tuberculosis. A written ethical approval was obtained from the ethical committee of the hospital. A written informed consent was obtained from all the patients prior to participation in study. All the study participants underwent routine biochemical and haematological investigations. Also, liver biopsy was obtained using Vim-Silverman needle. To assess the extent of disease, a chest x-ray posterior anterior view was taken as per the thoracic society diagnostic standards. Patients with history of alcoholism, diabetes and on hepatotoxic drug treatment were excluded.

The need for liver biopsy was clinically assessed by the evaluating hepatologist following a complete physical examination and appropriate radiological imaging. Vitamin K 5 mg/day was given IM for three consecutive days prior to liver biopsy ruling out all contraindications and coagulation or bleeding disorders. The site of biopsy was infiltrated with local anaesthetic and Vim-Silverman’s needle was inserted and the depth of puncture was limited to 6.5 to 7.5 cms. After obtaining adequate specimen, it was stained with haematoxylin and eosin. Special stains like Ziehl-Neelsen staining was done for acid-fast bacilli in cases showing granulomatous lesions.

Statistical Analysis

The results were analysed using Z statistical test.

RESULTS

The following observations were made from this study. A total of 50 patients were included and the incident was high among age group of 20-40 years. The incident was more among males (n=39) than females (n=11). Most of the patients were from lower economic status (Table 1). Fever,

cough with expectoration and weight loss were most common with 92%, 94% and 82%, respectively (Table 2). Hypoproteinaemia was observed in 22% of individuals (Table 5). Hypoalbuminemia in 98% (Table 6) and hyperglobulinemia in 10% of individuals (Table 7). Hepatic granulomas were evident in 12% of individuals who were suffering from disseminated tuberculosis (Table 11). Nonspecific changes were seen in 44 patients. Most common finding was fatty infiltration (64%) and round cell infiltration in 68% of patients followed by portal fibrosis (24%) (Table 12).

Age	Male (%)	Female (%)
12-20	1 (2)	4 (8)
21-30	18 (36)	4 (8)
31-40	11 (22)	1 (2)
41-50	06 (12)	2 (4)
51-60	02 (4)	0 (0)
>60	01 (2)	0 (0)

Table 1. Age and Sex Distribution of Study Population

Symptoms	Number of Patients (%)
Fever	46 (92)
Cough	47 (94)
Expectoration	45 (90)
Breathlessness	20 (40)
Loss of weight	41 (82)
Chest pain	03 (6)
Haemoptysis	06 (12)
Swelling in neck	7 (14)
Abdominal pain	4 (8)
Distended abdomen	2 (4)

Table 2. Symptoms Associated with the Study Participants

Diagnosis	Number of Patients
Cavitary TB	19
Noncavitary	21
Pleural effusion	07
Consolidation	06
Fibrosis	06
Bronchiectasis	01
Pneumothorax	02
Hydropneumothorax	02
Collapse	06

Table 3. Respiratory Diagnosis on Examination

Radiological Features	Number of Patients
Consolidation	43
Cavity	26
Fibrosis	6
Pneumothorax	2
Hydropneumothorax	2
Miliary shadows	3
Collapse	6
Pleural effusion	5

Table 4. Radiological Findings

Serum Protein (gm/dL)	Number of Patients
<5.5	11
5.5-8.0	35
>8.0	04

Table 5. Total Protein

Serum Albumin (gm/dL)	Number of Patients
<3.5	07
3.5-5.5	36
>5.5	07

Table 6. Serum Albumin

Serum Globulin (gm/dL)	Number of Patients
<2.0	16
2-3.5	29
>3.5	05

Table 7. Globulin

Serum Bilirubin (gm/dL)	Number of Patients
0.3-1.0	31
>1	19

Table 8. Serum Bilirubin

Alkaline Phosphatase (IU/L)	Number of Patients
<35	07
35-130	36
>130	07

Table 9. Alkaline Phosphatase

SGOT	No. of Patients	SGPT	No. of Patients
5-40	32	5-35	39
>40	18	>35	11

Table 10. SGOT and SGPT

Changes	Pulmonary	Disseminated	Percentage
Granuloma	0	6	12
Caseation	0	6	12
AFB	0	6	12
Culture	0	0	0

Table 11. Specific Changes

Changes	Pulmonary	Disseminated	Total (%)
Fatty changes	25	7	32 (64)
Focal Kupffer cell hyperplasia	9	1	10 (20)
Round cell infiltration	34	0	34 (68)
Nonspecific reactive hepatitis	0	3	03 (06)
Portal fibrosis	10	2	12 (24)
Focal cell necrosis	8	0	08 (16)
Cirrhosis	2	2	04 (8)

Table 12. Nonspecific Changes

DISCUSSION

Normally, the liver is an inhospitable place for tubercle bacillus owing to its low tissue oxygen tension. Hepatic TB is reported to occur in 50-80% of patients who are dying of pulmonary TB. But, most of cases are usually clinically silent. Liver is a common site for granuloma formation owing to its rich blood supply lying at the distal end of portal circulation and large number of reticuloendothelial cells. A majority of granulomas are usually located near the portal tract and there is only mild perturbation of hepatic function, so most patients are minimally symptomatic or asymptomatic. Primary hepatic TB is rare because low oxygen tension in the liver is unfavourable for growth of mycobacteria.⁹

In this study of the 50 patients, all had parenchymal tuberculosis and 10 had dissemination to other organs, 10 patients had pleural effusion, 2 had abdominal and one case of CNS involvement. Localised hepatic tuberculosis is a distinct clinical form of tuberculosis with signs and symptoms related only to the hepatic injury with minimal or no extrahepatic involvement. Hepatic tuberculosis constitutes less than 1% of all cases of this infection.¹⁰ Liver involvement may occur in the primary and secondary forms of tuberculosis and is particularly frequent in patients with disseminated miliary tuberculosis. In autopsy, series of disseminated tuberculosis, liver involvement was found in 80-100% of the cases.² Kok et al⁷ reported that hepatic tuberculosis was isolated in 0.3% of 1,678 new cases of tuberculosis.

Our study reported granuloma in 12% of patients with disseminated tuberculosis and 60% of these individuals had granuloma with caseation and all had positive staining for acid-fast bacilli. According to a review of several series of granulomatous hepatitis, tuberculosis is the second most common single cause of hepatic granulomas (10%-53% of the cases), and it is by far the main cause of granulomatous hepatitis among infectious diseases. Certain distinctive features can identify tuberculous granulomas in the liver. These include acid-fast bacilli within the lesion, caseating necrosis with destruction of the reticulin framework, irregular contours with a particularly dense cuff of lymphocytes surrounding the lesion and few lesions with a tendency to coalesce.¹¹ However, the aetiology of hepatic granulomas can seldom be established by histological appearance alone. Some authors suggest that in a consistent clinical picture, which is frequently somewhat nonspecific, the finding of granulomas especially with caseating necrosis constitutes histopathological evidence of tuberculosis.¹²

Abnormalities of the liver function tests are nonspecific and hence not diagnostic. Alkaline phosphatase maybe markedly elevated, particularly in those cases presenting with obstructive jaundice. Hypoalbuminaemia with polyclonal hyperglobulinemia are present in approximately 80% patients. In general, abnormalities in liver chemistry parameters confirm the presence of hepatic involvement, but their levels have no correlation with the extent of involvement.¹³

Histopathological examination of liver tissue obtained by biopsy is the most reliable diagnostic method. Imaging methods are of little value, because the findings are nonspecific. Ultrasonography, computerised tomography and magnetic resonance imaging are very sensitive for the detection of hepatosplenic nodules, but differential diagnosis from other conditions such as metastases, fungal abscesses and lymphomas is difficult.

Up to 90% of all patients with miliary tuberculosis have hepatic granulomas as well as a significant proportion of the HIV population especially in the developing world. Classic symptoms of fever, night sweats and weight loss maybe present as well as hepatomegaly and right upper quadrant pain. Laboratory abnormalities include elevated bilirubin and

aminotransferases with a disproportionately high alkaline phosphatase.¹⁴

However, Cucin et al compared the roles of liver biopsy and bone marrow biopsy in the diagnosis of disseminated TB and concluded that bone marrow biopsy was less hazardous.¹⁵

Percutaneous blind aspiration liver biopsy is more useful for the miliary form and tuberculous granulomatous disease of the liver where the success rate of a correct diagnosis is better. In the localised form of hepatic tuberculosis, ultrasound, CT or laparoscopic-guided liver biopsy yields a higher success (nearly 100%) than blind aspiration liver biopsy (67%).¹⁶

Histologically, the finding of caseating granuloma (found in 30-67%) in the liver biopsy specimen is considered diagnostic of tuberculosis.¹⁷ However, it has also occasionally been reported in brucellosis, coccidioidomycosis and Hodgkin's disease, but the clinical presentation is different.

CONCLUSION

The diagnosis of hepatobiliary tuberculosis should be considered in any patient with prolonged fever and chronic right upper quadrant pain associated with hepatomegaly, especially if accompanied by weight loss, and in suspicious cases, a liver biopsy should be performed without delay, since this condition responds well to early antituberculous therapy.

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