Value of Liver Biopsy Findings in AIDS Patients

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Abstract : From the year 1997 to 2000, 146 liver biopsies were performed in 140 AIDS patients, admited to Bamrasnaradura hospital with prolonged fever (73.6%), hepatomegaly (71.4%) and abnormal liver function test (69.3%) being the principle indications. The findings of liver biopsies included TB (18), MAC (14), Cryptococcosis (10), Histoplasmosis (6), Penicillosis (4), CMV (2) and 7 granulomas in which no organism was identified. Opportunistic infections were found in 61 of 146 biopsies (41.8%). Neoplasm was seen in 22 biopsies (15.1%); the most common neoplasm was hepatocellular carcinoma, found in 16 biopsies (11%). Other findings included chronic active hepatitis (3), cirrhosis (3) and alcoholic hepatitis (1). The liver biopsy is a helpful diagnostic tool in AIDS patients with prolonged fever, hepatomegaly or abnormal liver function tests.

เรื่องย่อ : การตรวจชิ้นเนื้อตับช่วยวินิจฉัยโรคในผู้ป่วยภูมิคุ้มกันบกพร่อง

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จากปี พ.ศ. 2540 ถึง 2543 ได้ศึกษาชิ้นเนื้อตับโดยวิธีใช้เข็มเจาะผู้ป่วยภูมิคุ้มกันบกพร่อง จำนวน 140 ราย ที่ได้รับไว้รักษาในโรงพยาบาลบำราศนราดูร ผู้ป่วยมารับการรักษาด้วยเรื่องไข้เรื้อรัง 73.6%, ตับโต 71.4%, และผลการตรวจเลือดแสดงการทำงานของตับผิดปกติ 69.3% จากการตรวจชิ้นเนื้อตับ พบการติดเชื้อฉวยโอกาส 61 ราย (41.8%), เนื้องอก 22 ราย (15.1%) มะเร็งตับชนิด hepatocellular carcinoma เป็นเนื้องอกที่พบบ่อยที่สุด 16 ราย (11%) การตรวจพบอื่น ๆ ได้แก่ภาวะตับอักเสบเรื้อรัง, ภาวะตับแข็ง, ภาวะตับอักเสบจากแอลกอฮอล์ และภาวะตับอักเสบไม่จำเพาะ

การศึกษานี้ชี้แนะว่าการเจาะเนื้อตับตรวจในผู้ป่วยภูมิคุ้มกันบกพร่องมีประโยชน์ในการวินิจฉัยโรคผู้ป่วยที่มีไข้เรื้อรัง, หรือผลการตรวจเลือดแสดงการทำงานของตับผิดปกติและภาวะตับโต

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INTRODUCTION

Hepatobiliary diseases occur frequently in patients with Acquired Immunodeficiency Syndrome (AIDS). They frequently have biochemical, serological or morphological evidences of parenchymal liver disease. Significant increases in liver function tests (transaminases, alkaline phosphatase) have been found in up to 65% of patients at some point during the course of AIDS.[1] Hepatomegaly may be detected by physical examination in up to 73% of patients.[1] These disorders result from a variety of opportunistic infections and neoplasms; as well as drug-induced liver disease, alcohol consumption or a combination of factors.[2] The purpose of this study was to evaluate the value of liver biopsy in AIDS patients who had prolonged fever, abnormal liver function tests (L.F.T.) and or hepatomegaly.

MATERIALS AND METHODS

From 1997 to 2000, 140 AIDS patients admitted to Bamrasnaradura hospital underwent liver biopsies for evaluation of prolonged fever, abnormal L.F.T.; and or hepatomegaly. This included 128 males and 12 females with ages ranging from 17-70 years in males and 21-61 years in females. Mean age was 37 years and 30 years for males and females respectively.

Each pateint's clinical record was reviewed. Liver function tests included alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase and total bilirubin level. Laboratory values used for analysis were those obtained closest to the day of biopsies.

All liver biopsies were performed percutaneously, fixed in 10% formalin, embedded in paraffin, 3 micron-cut and stained with Hematoxylin and Eosin (H&E). Stains for Masson's trichrome, Gram for detection of bacteria, Gomori-methenamine silver for detection of fungi, and Ziehl-Neelson for detection of acid-fast organisms were done. Three unstained sections were also available for additional stains as appropriate. Prolonged fever was defined as body temperature above 38°C for at least 2 weeks. Abnormalities of liver function tests were defined as an elevation of transaminase (ALT, AST), alkaline phosphatase, or total bilirubin greater than 1.5 times the upper limit of normal values. Hepatomegaly was defined clinically by the physician. The liver's size in some cases was confirmed by ultrasonography.

RESULTS

A total of 146 diagnoses from 140 AIDS patients who underwent percutaneous liver biopsies were available. One hundred twenty eight (91.4%) were males and 12 (8.6%) were females. Ages ranged from 17 years up to 70 years old in males and 21 years - 61 years in females. Eighty-eight percent of males and 83% of females were between ages 20-49 years.

Information regarding previous infections and opportunistic infections were available in 21 patients. These were 7 with pulmonary tuberculosis, 6 with extrapulmonary tuberculosis, 4 with cryptococcal meningitis and one each with Pneumocystis carinii pneumonia (PCP), Cytomegalovirus (CMV) infection, Penicillosis and cerebral toxoplasmosis. There was no correlation between previous infections and findings on the present liver biopsies.

The diagnostic findings from liver biopsies were shown in table I. Granulomatous hepatitis was found in 39 biopsies: Mycobacterium tuberculosis (MTB) was seen in 18 biopsies, Mycobacterium avium complex (MAC) in 14 biopsies, and 7 showed granulomatous changes without any identified organism.

Other infections found on biopsies included cryptococcosis in 10 biopsies, Histoplasmosis in 6, Penicillosis in 4 and CMV in 2 biopsies.

The most common neoplasm found on liver biopsy was hepatocellular carcinoma (16), followed by adenocarcinoma (3) and large cell lymphoma (3). In 3 patients with chronic active hepatitis, diagnosed by biopsy, serologies were not available. The other 3 biopsies showed the liver to be cirrhosis, none of which had available hepatitis viral serology. One patient had a history of heavy alcohol consumption, confirmed by histological evidence of liver damage by alcohol.

Miscellaneous liver biopsy findings included steatosis (19) nonspecific reactive hepatitis

(15), cholestasis (5) and nonspecific change in 17 biopsies. None of biopsies showed normal liver histology. Thus 90 (61.6%) of liver biopsies in our series yielded a histopathological diagnosis. There were double infections in 6 biopsies.

Table 1. 146 diagnostic findings on liver biopsies of 140 AIDS patients.

Diagnosis	No. of biopsies	Percentage (%)
Granulomatous hepatitis (39)		
MTB	18	26.7
MAC	14	
AFB negative, granulomatous hepatitis	7	
Fungus (20)		
Cryptococcosis	10	15.1
Histoplasmosis	6	
Penicillosis	4	
Virus (2)		
CMV	2	
Neoplasia (22)		
Hepatocellular carcinoma	16	15.1
Adenocarcinoma	3	
Lymphoma	3	
Chronic active hepatitis	3	2.1
Cirrhosis	3	2.1
Alcoholic hepatitis	1	0.7
Miscellaneous (56)		
Steatosis	19	38.2
Nonspecific reactive hepatitis	15	
Cholestasis	5	
Nonspecific change	17	

DISCUSSION

The pertinent symptoms and signs in 140 AIDS patients, admitted to Bamrasnaradura hospital in this study, were prolonged fever (73.6%), hepatomegaly (71.4%) abnormal L.F.T.'s (69.3%), wasting (27.1%) and right upper abdominal pain (12.1%).

This study showed the value of liver biopsies for etiologic diagnosis in AIDS patients with prolonged fever, hepatomegaly and or abnormal L.F.T. The yield of diagnosis by biopsies (61.6%) in this series was higher than that previously reported for autopsies (17-23%),[3,4] and for other antimortem studies reported by Kahn et al (57%),[5] and Cappel et al (50%).[6] Diagnosis of infection including special stains can be made within 12-72 hours after biopsies. Eighteen of thirty-nine hepatic granulomas (46%) in our study showed well formed granulomas with rare acid-fast bacilli consistent with MTB. Fourteen of the granulomas (36%) were composed of diffuse, poorly defined, pale-blue striated histiocytes filling with numerous mycobacteria. This was the classic histological appearance on H&E stain of MAC disease in AIDS.[7,8,9,10] The striations within the histiocytes represent large numbers of AFB as demonstrated on Ziehl-Neelsen staining. The other

seven hepatic granulomas showed no identifiable organism. The antibiotic and antiretroviral agents used in AIDS therapy may produce hepato-toxicity, including granulomas,[11] cholestasis, hepatitis[12] and microvesicular fatty change.[13] Macrovesicular fatty change[14] has been associated with AZT administration and has been also seen with liver failure in HIV-I positive patients.[15] The presence of fatty change in liver tissue of AIDS patients may also reflect the presence of HCV infection or alcoholic abuse.[16]

HIV can directly infect hepatocytes and also have an indirect effect on the liver through associated T-cell abnormality.[17] Hepatic infection with HIV may be via the CD4 receptor, which has been discovered on Kupffer cells and endothelial cells lining sinusoids.[18] The other possible causes of nonspecific liver pathology include malnutrition, with or without the use of total parenteral nutrition, as well as exposure to hepato-toxic drugs. Up to 90% of patients with AIDS are treated with at least one drug which has hepato-toxicity. These can contribute to hepatic abnormalities. Steatosis is the most common nonspecific finding, but the cause remains unclear. It may be related to several factors, such as alcoholic intake, polypharmacy, nutritional status, chronic disease, or be secondary to direct hepato-biliary infection with HIV.

The association of granulomatous disease of the liver with significantly elevated alkaline phosphatase has been reported.[19,20,21] This is presumably due to its infiltrative nature causing obstruction of terminal branches of the biliary tree. This study was not designed to determine whether liver biopsy should be attempted in all AIDS patients with prolonged fever, hepatomegaly or abnormal L.F.T. of uncertain etiology. What it does reveal is that in liver biopsy performed in AIDS patients with the above characteristics 61.6% were diagnosed, in which a majority of the diagnoses were treatable.

In conclusion, the liver is a common site of pathology in AIDS patients and liver biopsy is a sensitive, rapid, and relatively simple method for establishing the diagnosis and identifying the infection in AIDS patients who have unexplained fever, hepatomegaly and/or abnormal L.F.T.

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