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Hepatitis C Virus Infection in Hepatic Schistosomiasis

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Abstract

Thirty patients with bilharzial liver fibrosis, splenomegaly and hepatocellular failure (jaundice, ascites, gynecomastia, spider nevi) were studied. Colonic swab showed bilharzia ova and colonic bilharziasis in all of them. Upper endoscopy showed esophageal varices in 22 cases. Disturbed biochemical liver functions were present in all cases. 16 patients (53.3 %) had positive anti HCV antibodies by second generation ELISA test and 6 patients (20%) had positive HBsAg. Three cases had both anti HCV and HBsAg. All cases were negative for antinuclear and antismooth muscle antibodies. Liver biopsy showed histological changes of cirrhosis in 20 cases (66.7%) and chronic active, chronic lobular hepatitis in the remaining cases. Bilharzial pigment and or/schistosoma ova, granuloma were present in all cases. 8 cases (26.7%) showed histopathological changes of chronic hepatitis C and 5 cases (16.7%) showed ground glass appearance with positive orcein stain characteristic of HBsAg. In conclusion, the presence of positive markes of HCV in patients with hepatic schistosomiasis may contribute to liver cell failure. However, it may reflect only a chronic carrier state of anti HCV, in such cases liver biopsy can differentiate by the presence of histopathological changes characteristic of chronic hepatitis C.

Introduction

HEPATIC Schistosomiasis produces periportal fibrosis and hepatic parenchyma is well preserved both structurally and functionally [1]. Almost all mortality in patients with hepatic schistosomiasis is due to portal hypertension and bleeding esophageal varices, rather than hepatocellular failure. However, many patients develop progressive liver cell failure and cirrhosis [2]. It is not clear whether the cause of liver cell failure is due to schistosomiasis itself or an associated hepatitis viral infection [3].

Hepatitis B is endemic in Egypt. The exposure rate (HBsAg and/or anti HBaAg) for HBV infection in general population in rural areas was found to be up to 52% in lower Egypt and 44% in upper Egypt [4]. El Rooby [5] showed a high prevalence of hepatitis B viral infection on the top of bilharzial liver, with a high morbidity. Delta hepatitis virus infection on the top of he-

patic schistosomiasis causes deterioration of liver cell functions [6].

Kamel et al. [7] showed the prevalence of hepatitis C virus (HCV) infection to be 10.9% in 2164 apparently healthy, male Egyptian University students, who donated one unit of blood in 1992.

They were generally middle class and unpaid donors. Since ELISA-confirmed HCV positivity is frequently viraemic [8], potentially 10% of the recipients could contract HCV infection. About 50% of those infected with HCV are at high risk of cirrhosis in 3-5 years time [9].

Concomitant infection with both HCV and HBV in Egypt approaches 20% of cases of viral hepatitis [10].

The role of HCV infection in causing progressive liver cell dysfunction in patients with schistosomal liver fibrosis is unknown and the studies on this subject are few [11].

The aim of the present work is to determine the role of HCV infection in patients with proven bilharzial liver fibrosis and hepatocellular failure.

Material and Methods

Thirty male patients with a mean age 43±7 years and having endemic bilharzial liver disease with manifestations of liver cell failure (jaundice, ascites, spider nevi, gynecomastia, edema) were the subject of study.

The following investigations were done for all patients:

1- Routine urine, stool examination and full blood picture.

2- Sigmoidoscopy with mucosal scraping for detection of bilharzia ova.

3- Upper endoscopy.

4- Ultrasound examination of abdomen.

5- Complete liver function tests including total serum bilirubin, serum alanine and aspartate aminotransferases (by calorimetric method [12]), serum alkaline phosphatase (by calorimetric method [13],) serum total proteins (by biuret method), serum albumin (by bromocresol green method [13]), with calculation of serum globulin and prothrombin time (by thrombotest technique [14]).

6- Serum immunoglobulins IgG and IgM levels (measured by nephelometric assay [15]).

7- Detection of serum HBsAg by enzyme linked immunoassay (ELISA) [16].

Detection of anti-HCV in sera of patients by second generation enzyme linked immunoassay with recombinant four antigens (C_{100-3}, C_{33c}, C_{22-3} and C_{200}) from Abott [11].

8- Serum was tested for antinuclear antibodies (ANAs) and antismooth muscle antibodies (anti SMA) by indirect immunofluorescence technique [18].

9- Liver biopsy specimens stained with H and E., Mason trichrome stain for fibrous tissue and Gordon and Sweets silver stain for reticulin.

Results

All cases had a past history of bilharziasis and antibilharzial therapy. Bleeding esophageal varices was present in 12 cases and blood transfusion was given in 7 of them. Sclerotherapy was done in 8 cases.

Past history of previous surgery was

obtained in 4 cases and past history of jaundice in 7 cases. Upper endoscopy showed esophageal varices in 22 cases from grade 1 to grade 4. Evidence of colonic bilharziasis and/or bilharzia ova in mucosal swab was present is all cases.

Ultrasound of the abdomen showed periportal liver fibrosis and splenomegaly with dilated portal vein diameter.

Laboratory results: (Table 1,2).

16 patients (53.3%) had positive anti HCV and 6 patients (20%) had positive HBsAg.

Immunological markers, (ANA and Anti SMA) were negative in all cases. Hypergammaglobulinemia with raised IgG level above 18 gm/L were detected in 5 patients. Disturbed biochemical liver functions were present in all cases.

Liver biopsy: (Table 3) (Figs. 1,2,3,4,5).

Periportal fibrosis, bilharzial pigment and schistosoma ova or granuloma in portal tract could be detected in almost all cases. Liver cirrhosis with loss of hepatic architecture was present in 20 cases. The remaining cases showed evidence of chronic active or lobular hepatitis with focal cell necrosis or bridging necrosis, portal and lobular infiltration by lymphocytes. Ground glass appearance of hepatocytes with positive orcein stain for HBsAg could be detected in 5 out of 6 cases with positive serum HBsAg. 8 out of the 16 cases with positive anti HCV showed histological features suggestive of chronic hepatitis C affection as patchy fatty change, acidophilic hepatocytes, portal tract lymphoid aggregation or follicles, sinusoidal free lymphocytes, kupffer cell hyperplasia and bile duct affection [19].

Table (1): Biochemical Features of 30 Patients with Bilharzial Decompensated Liver Cirrhosis. (Mean ± S.D.).

Serum bilirubin	4.2±1.8 mg/dL
Serum ALT enzyme	155±46 U/L (Reference value up to 45 U/L)
Serum AST enzyme	143±36U/L (Reference value up to 40 U/L)
Serum alkaline phosphatase	16 K.A. units/dL±2.9 (Reference value up to 13 K.A./dL)
Prothrombin time	22±3.4 seconds (Reference value 10.5-12.5 sec.)
Serum albumin	2.8±0.8 gm/dL (Reference value 3.7-5.3 g/dL)
Serum globulin	4.1±0.7 gm/dL (Reference value 1.8-3.6 gm/dL)
Serum IgG	20 gm±3.6 gm/L (Reference value 6.5-15 gm/L)
Serum IgM	3.2±1.1 g/L (Reference value 0.4-3.5 g/L)

Table (2): Hematological and Immunological Features of 30 Patients with Bilharzial Liver Fibrosis (Mean ± S.D.

Hemoglobin	12.2 gm/dL.±2.1
Total white cell count	4.1 10^3/Cmm
Platelet count	170 10^3/Cmm
No. of positive HBsAg cases	6(20%)
No. of Positive anti HCV	16(53.3%)
No. of ANA and anti-SMA positive cases	Zero

Table (3): Histopathological Data of 30 Patients with Schistosomiasis and Hepatic Cirrhosis.

Chronic active hepatitis	8 cases
Chronic lobular hepatitis	2 cases
Liver cirrhosis (inactive)	14 cases
Chronic active hepatitis with cirrhosis	6 cases
Chronic hepatitis type B (Positive orcein stain)	5 cases
Chronic hepatitis type C (with fatty change, acidophilic cytoplasm, lymphoid follicles and bile duct damage).	8 cases

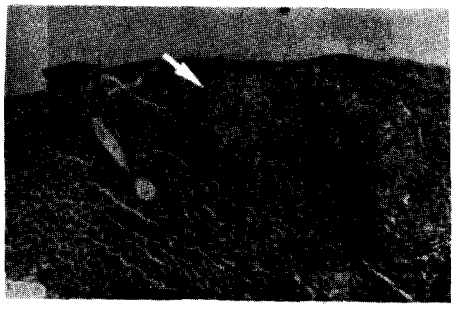

Fig. (1): Parenchymal bilharzial fibrocellular granuloma (arrow), Masson trichrome x 100.

Fig. (2): Marked fibrosis of the portal tract with bilharzial granuloma (arrow), H and E x 40.

Fig. (3): Two cirrhotic nodules surrounded by dense lymphocytic infiltrate and lower nodule shows irregularity of margins, features of activity in cirrhosis (H and E) x 40.

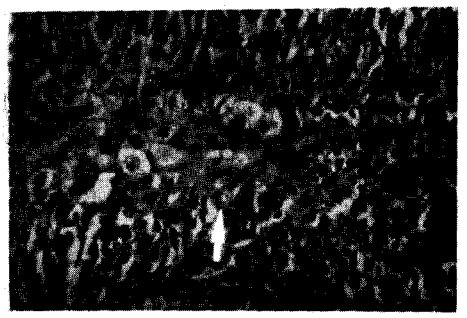

Fig. (4): Limiting plate destruction by lymphocytic infiltrate. Piece meal necrosis (arrow). A case of cirrhosis with activity (H and E) x 400.

Fig. (5): Cirrhotic nodule with scattered foci of fatty change, Masson trichrome x 40.

Discussion

Schistosomiasis characteristically leads to portal hypertension with preserved parenchymal functions. Occasionally hepatic decompensation occurs. The cause of decompensation in many cases is unknown. In Egypt, there is a high incidence of hepatitis-B virus infection on the top of bilharzial liver fibrosis [20].

In this study 6 patients (20%) were HBsAg positive, 5 of them showed ground glass appearance of hepatocytes characteristic of presence of HBsAg. Histopathological changes characteristic of chronic hepatitis C was detected in 8 patients (26.7%) while 16 patients (53.3%) had anti HCV antibodies in their sera.

Hepatitis C virus can progress to chronic liver disease and cirrhosis in 20-40% of cases and within only 3-5 years [9]. It may predispose to hepatocellular failure in patients with hepatic schistosomiasis. However, the association between bilharzial liver and anti-HCV may represent a false positive "anti-HCV" or anti HCV carrier state independent of cirrhosis.

False positivity of anti HCV has been reported in autoimmune chronic active hepatitis and it was attributed to hypergammaglobulinemia [21]. This occurs with the first generation of tests of anti-HCV.

Aceti and Taliam [22] reported 27 patients with urinary bilharziasis without liver disease, nine were anti-HCV positive by the ELISA (Ortho diagnostic) test. The positivity of anti-HCV correlated in their study with serum IgG levels, and they can not rule out false positive anti HCV results.

In our study, we used second generation anti HCV test which is more specific and more sensitive. Patients with second

generation positive ELISA test are frequently viraemic [2] as proved by polymerase chain reaction which detects HCV-RNA.

Five of our patients showed raised serum IgG levels, however, none of them had positive ANA or anti SMA.

Anti HCV carrier rate was reported to be 10.9% [7] in unpaid healthy blood donors of middle class and in the same study the prevalence of HBsAg was 3.4%. In rural areas and among paid blood donors in Egypt, the prevalence of hepatitis B and C virus infection is much higher.

Concomitant hepatitis B and C virus infection in one study in Egypt occurred approximately in 20% of cases of viral hepatitis [10]. In our study, three patients (10%) had both positive HBsAg and anti-HCV antibodies.

Liver biopsy is indicated for determining etiological diagnosis of liver cell failure.

The presence of pathological changes characteristic of chronic hepatitis C could be detected in only 8 out of 16 cases with positive anti HCV in our study. However, the presence of ground glass appearance and positive orcein stain for HBsAg could be detected in 5 out of 6 cases with positive serum HBsAg.

Liver biopsy is also important in determining disease activity and staging [23]. Grade 0 and 1 represents portal inflammation only while grade 2,3,4 represents focal cell necrosis, limiting plate necrosis up to severe bridging necrosis. Stages 1 and 2 represent periportal fibrosis with preserved architecture and stages 3 and 4 represent loss of hepatic architecture and cirrhosis.

Decompensated liver cirrhosis is a contraindication to antiviral therapy for hepatitis B or C [24].

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