CHRONIC HEPATITIS IN PATIENTS OF CHRONIC RENAL FAILURE

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KEYWORDS :

Case Report

A 42-year old male presented with symptoms of anorexia, vomiting and swelling of face and feet of three months duration. Clinical examination showed pallor, edema of face and feet and BP of 180/110 mm Hg. Systemic examination was unremarkable. Investigations showed Hb 7.5 gm/dl, and on urinalysis there was protein 3+, RBC 4-5, WBC 2-3 and occasional granular casts per high power field. The 24 hours urine protein was 2.8 gms/L. Blood biochemistry revealed urea 170 mg/dl, SGPT 20 IU/L. The HbsAg and anti HCV antibody were negative and on ultrasound both kidneys were small and contracted.

The patient was vaccinated against Hepatitis B virus and taken up for intermittent dialysis in addition to the other supportive measures. Seven months later he developed hepatocellular jaundice, the serum bilirubin was 1.8 mg/dl, SGPT 110 IU/L and alkaline phosphatase 20 KA units/dl. The HbsAg and HbeAg were positive. Over the next two weeks the liver function tests returned to normal, however, the HbsAg and Hbe antigenemia persisted. One year later prior to a kidney transplant he was re-evaluated. Clinically, the liver was palpable 2 cms below the right subcostal margin, it was soft and the surface was smooth. There was no ascites and spleen was not palpable. There were no oesophageal varices on upper GI endoscopy and on ultrasound the echotexture of the liver was maintained. A liver biopsy was done which showed chronic hepatitis grade II, stage I. The liver function tests showed serum bilirubin, 0.8 mg/dl, SGPT 16 IU/L and alkaline phosphatase was 24 KA units/dl. The HbsAg and IgM anti HBe were positive while anti HBs and anti HBe were negative. The patient was continued on intermittent dialysis and interferon therapy was considered.

To summarize, this patient has chronic glomerulo-nephritis with chronic renal failure and while on dialysis developed HbsAg positive chronic active hepatitis.

Q1. What is the prevalence of hepatitis B virus infection in the dialysis population?

The occurrence of HbsAg positivity in patient on dialysis is variable. The prevalence is influenced by the duration of dialysis, number of blood transfusions, the infection control measures like segregation of dialysis machine for HbsAg positive patients and the use of Hepatitis B vaccination. In USA the prevalence is

1.4 per cent with an annual incidence of 0.1 per cent [1]. In areas endemic for HBV infection like India the reported incidence varies from 7.7 per cent to 11.6 per cent [2].

Q2. What is meant by chronic hepatitis grade II, stage I.

To avoid intraobserver variation Schewer et al [3] have designed an objective and easily reproducible histological scoring system. Liver histology in chronic hepatitis was 'Graded' from zero to four based on the inflammatory activity and 'Staged' from one to four based on the degree of fibrosis. Grade II refers to mild limiting plate necrosis and stage I designates no fibrosis or fibrosis limited to enlarged portal tracts.

Q3. How effective is the Hepatitis B vaccine in patients of chronic renal failure on dialysis?

In early trials using conventional 20 mcg, with three dosages of plasma derived vaccine in haemodialysis patients and the staff, only 60 per cent patients developed protective anti Hbs titres > 10 mIU/ml in contrast to 93 per cent of staff members [4]. Even following an adequate anti HBs response haemodialysis patients have a poor ability to maintain protective antibody levels [5]. The current recommendation in the dialysis population is to use 40 mcg dose in a schedule of 0, 1, 2 and 6 months [6]. To increase the response rate to Hepatitis B vaccination in this population co-administration of immunomodulators such as gamma interferon, thymopentine and adjuvant interleukin-2 are under study [7].

Q4. What is the effect of renal transplant and associated immunosuppressive therapy on the course of HBV related liver disease?

In patients with HBV infection prior to transplant, the immunosuppressive drugs predispose to an in-

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creased virus replication with reappearance or increase in serum of HBV DNA and HBeAg following apparent clearance of previous HBV infection. Renal transplant accelerates the progression of liver disease and there is an increased risk of developing cirrhosis and death.

In patients acquiring HBV infection after the transplant, liver failure and death is frequent, probably related to intense immunosuppression [8].

Q5. What is the effect of HBV on graft and patient survival?

The effect of HBV infection on graft survival is controversial. Some workers have reported increased morbidity and mortality, others have demonstrated similar patient and graft survival rates, while still others have demonstrated improved graft survival rates [7]. In an important study Dienstag [9] observed the renal graft survival over a two to three years period was 82 per cent in HbsAg positive recipients but only 61 per cent in HbsAg negative patients. However in those patients who were HbsAg negative in serum but HBV-DNA positive in hepatic tissue and renal graft, survival was intermediate at 75 per cent. The reported difference in the effect of HbsAg on graft survival may reflect the unrecognised presence of HbsAg negative/HBV-DNA positive renal transplant recipients in whom graft survival, is superior to that of truly negative recipients. The elimination of HBV from the host is primarily dependant on cell mediated immunity. The failure to clear the virus and development of a chronic carrier state reflects hyporesponsiveness is probably responsible for the improved graft survival rates in HbsAg positive patients.

Q6. Can recombinant alpha interferon be used in managing chronic HBV infection in such patients?

Alpha Interferon acts by two mechanisms. (a) It has an antiviral effect (b) An immunomodulatory action.

In immunocompetent hosts recombinant alpha interferon leads to loss of HBeAg in upto 50 per cent of treated patients with associated improvement in liver histology [10]. Detailed information is not available about the role of alpha interferon in dialysis and transplant population. In one study alpha interferon in usual doses used to treat chronic hepatitis was well tolerated and efficacious in a group of HD patients [11]. However in a group of 13 post transplant patients treated with standard doses of interferon, two patients developed deteriorating graft function due to acute rejection and drug induced acute tubular necrosis. Overall, serum aminotransferases decreased during therapy but the response was not sustained once therapy was

stopped and side effects were common. Thus at present alpha interferon is reserved for controlled trials of anti viral therapy in post renal transplant patients.

Q7. What is the current recommendation regarding renal transplant in chronic renal failure with HBV infection?

At present decision about renal transplant in chronic HBV infected patients should be based on both the severity of liver histology and results of testing for markers of viral replication, like HbeAg and HBV-DNA [7].

Patients with severe chronic active hepatitis or established cirrhosis [7] on liver biopsy are at a high risk for hepatic decompensation following renal transplant and in these patients renal transplant should be avoided especially if markers for active viral replication are present. Given the favourable outcome in many patients with HBV infection, and less histologically severe liver disease such as chronic persistent hepatitis, renal transplant should not be precluded in these patients [12].

Q8. What are the hepatic morphological changes that can occur in a HbsAg positive renal transplant recipient? What is their significance in predicting the future course of liver disease?

Percutaneous liver biopsies of 77 renal transplant recipients have shown the following hepatic histological lesions : fat metamorphosis, chronic persistent hepatitis (CPH), chronic active hepatitis (CAH), hemosiderosis and micronodular cirrhosis. Long term follow up studies have shown that hepatic morphology can be a useful marker in predicting the course of liver disease in these patients. The calculated annual mortality from hepatic failure was 6.1 per cent in patients with early CAH, 9.6 per cent with hemosiderosis and 10.5 per cent with advanced CAH. In contrast patients with fat metamorphosis or CPH did not show evidence of clinical progression [13].

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