Nodular regenerative hyperplasia of the liver with membranous glomerulonephritis

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Summary

Nodular regenerative hyperplasia of the liver is an uncommon disorder, the main consequence of which is portal hypertension, hepatocellular decompensation being uncommon. A case associated with membranous glomerulonephritis is reported, in which death was caused by fulminant hepatic failure.

Introduction

Membranous glomerulonephritis occurs in association with neoplasms of several organs (Lee Yamaucki and Hopper, 1966) and also with non-malignant hepatic lesions including HB_s and HB_e antigenaemia (Takekoshi *et al.*, 1979), primary biliary cirrhosis (Rai *et al.*, 1977), alcoholic cirrhosis (Callard *et al.*, 1975) and chronic active hepatitis (Cogan, Graber and Connor, 1977). The nephritis is thought to be a consequence of circulating immune complex deposition in the kidney. The association of nodular regenerative hyperplasia has not, so far as can be ascertained, previously been reported.

Case report

The patient developed nephrotic syndrome at the age of 45 years and renal biopsy at that time showed membranous glomerulonephritis. During follow-up plasma creatinine was stable at 150 μ mol/l and urinary protein did not exceed 5 g/24 hr, but he developed discharging skin lesions which improved with erythromycin and histologically showed no evidence of vasculitis. After 2 years he presented as an emergency, semi-comatose, with a 2-week history of nausea and vomiting. On examination he was mildly dehydrated but there was no pyrexia, lymphadenopathy or jaundice. Fluctuant discharging skin lesions were noted, particularly over his knees and elbows and there were perianal ulcers. There was a little ascites but no clinically detectable hepatic or splenic enlargement and no oedema. There were no

abnormal neurological signs. Investigations showed (normal values in brackets): Hb 20.4 g/dl, MCV 100 fl, HCT 0.524 l/l, ESR 5 mm/hr. Blood film showed target cells and bone marrow examination was normal. Creatinine 196 μ mol/l (53-124); urea 7.4 mmol/l (2.5-7.0); glucose 3.6 mmol/l; calcium 1.88 mmol/l (2.25-2.75). Phosphate 1.21 mmol/l (0.6-1.30); alkaline phosphatase (liver origin) 338 i.u./l (28-92); aspartate amino transferase 57 i.u./l (2-21); albumin 16 g/l (34-50); total protein 54 g/l (60-80). Bilirubin 14 μ mol/l (17); prothrombin time 13 sec (control 13). Immunoglobulins: IgG 15.25 g/l (9.5-16.5), IgM 1.55 (0.65-2.00), IgA 6.90 g/l (0.90-4.50). HB_sAg was negative. Alphafoetoprotein was 59 MRC units/ml (up to 6 may be insignificant). C₃ 0.84 g/l (0.8-1.4). C₄ 0.38 g/l (0.1-0.4). Urinary protein excretion was 1.6 g/24 hr. Blood, urine and sputum cultures were sterile as were skin swabs. Chest X-ray was normal. IVP showed poor concentration of contrast but was otherwise normal. Barium swallow showed small varices. Barium meal and follow-through was normal. Liver scan showed small liver with little uptake of colloid. The spleen was enlarged. Percutaneous and later per laparoscopic liver biopsies showed irregular proliferation of hepatocytes with scanty fibrous septae and the laparoscopy had shown several umbilicated lesions on the liver surface.

He subsequently developed rapidly deteriorating renal function, deepening jaundice, hyponatraemia, hypoglycaemia, gastrointestinal bleeding and he died 6 weeks after admission to hospital.

Post-mortem examination showed haematomas in muscle, subcutaneous tissue and lung. Chronic pancreatitis was noted and the liver appeared macroscopically involved in diffuse hepatocellular carcinoma. The histological appearance of the liver, however, was of nodular regenerative hyperplasia with superadded acute focal damage to hepatocytes

FIG. 1. Renal biopsy. On the epithelial surface of the basement membranes are numerous spikes, characteristic of membranous glomerulonephritis (PASM stain, $\times 800$).

but no true hepatitis. Immunoperoxidase staining for alphafoetoprotein was negative but carcino-membryonic antigen was detected in the needle biopsy liver sample.

Discussion

Nodular regenerative hyperplasia (NRH) is an uncommon hepatic lesion of which portal hypertension is the main consequence. Manifestations of severe liver failure are usually absent but associated

features include rheumatoid arthritis; the calcinosis cutis-Raynaud's phenomenon-sclerodactyly-telangiectasia (CRST) syndrome; bacterial endocarditis; and monoclonal gammopathy (Rougier *et al.*, 1978). Although there was no direct evidence of active immune complex disease in the present patient, it is postulated that, in view of the above 'immune' associations of NRH, his membranous glomerulonephritis was associated with NRH by more than chance.

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