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Hepatitis B Virus Recurrence Following Orthotopic Liver Transplantation: Pathogenesis and Chemotherapy of Severe Infection. S Locarnini, DS Bowden, P Angus, M Richards, J Ireton, R Sinclair and R Jones. Virology Department, Fairfield Hospital, Fairfield, Victoria 3078; Liver Transplant Unit and Anatomical Pathology Department, Austin Hospital, Heidelberg, Victoria, Australia.

Post orthotopic liver transplant (OLT) recurrence of hepatitis B virus (HBV) is common and frequently results in graft failure. In particular, some patients develop a rapidly progressive illness, fibrosing cholestatic hepatitis (FCH), which usually results in irreversible graft dysfunction within 6-8 weeks of onset. In these cases the disease post transplant is characterised by extremely high viraemias (> 10,000pg HBV DNA per ml of serum) and abnormal liver function test (LFT) profiles. Histological examination of liver biopsy material reveals very high levels of hepatitis B core antigen (HBcAg) in the nucleus of virtually all hepatocytes with prominent hepatitis B surface antigen (HBsAg) in the cytoplasm. We have shown that the disease can be successfully treated using ganciclovir, a nucleoside analogue and DNA polymerase inhibitor, in combination with phosphonoformate, a known reverse transcriptase inhibitor. Within 4 weeks of therapy there was a 20 to 40 fold reduction in serum HBV DNA and HBsAg levels and a sustained improvement in LFT's with an associated clinical benefit. Histological examination of liver tissue showed a significant decrease in cytoplasmic HBsAg, however, there was little change in nuclear or cytoplasmic HBcAg. Progression of the lesion of FCH was also halted during therapy. These studies implicate cytoplasmic HBsAg as an important pathogenic marker rather than nuclear HBcAg, and have developed a potentially useful chemotherapeutic regime for the management of post transplantation recurrence of HBV infection.

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CLINICAL FEATURES AND RESPONSE TO INTERFERON IN PATIENTS WITH DIFFERENT HCV GENOTYPES IN ITALY

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It has recently reported that different HCV genotypes have peculiar characteristics in terms of disease activity and of response to interferon (IFN). We have cloned and sequenced the 5' noncoding region of HCV genome in 21 consecutive Italian patients with chronic hepatitis C and 4 distinct groups were identified, according to published literature (Cha et al, PNAS 89,7144,1992). 38% of the patients had genotype(s) GI/II, 48% genotype GIII and the remaining 3 patients genotypes GIV and GV. In patients infected with GI/II, GIV and GV liver disease activity was significantly milder in terms of biochemical and of histologic features, compared to cases infected with GIII. Mean values of three consecutive ALT determinations were 120$\pm$ 95.32 in the former and 310.90$\pm$327$\pm$34 ($p<0.05$) in the latter group, while CPH was present in 89% of the former and in 33% of the latter group and the corresponding features for CAH, with or without cirrhosis, were 11% and 67%, respectively. Fourteen patients were treated with recombinant IFN alpha 2a (3MU/3 times weekly for 6 months) and 7 out 9 (78%) patients with GIII isolate, but none of the remaining patients were long term responders, indicating that HCV genotyping can be useful in clinical management of HCV infection.