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Anti-pre-S antibodies in patients with fulminant hepatic failure

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Fulminant hepatic failure due to viral infection is a severe complication of acute viral hepatitis (Brechot et al., 1984). The reasons for acute infection to persue a fulminant course are yet to be ascertained. Occurrence of massive hepatic necrosis in patients with fulminant hepatic B has been attributed to an enhanced immune response against the HBV antigens and both cell mediated immunity as well as the humoral immunity have been implicated in the pathogenesis of liver (Zuckerman, 1984: Trepo et al., 1976). In context to the demonstration of high levels of anti-HBs and anti-HBe in the patients with fulminant hepatitis, the need to study the presence and significance of antibodies directed against pre-S proteins (anti-pre-S antibodies) have gained importance. In the present report, attempts have been made to establish a relation between the prevalence of anti-pre-S antibody and the HBV replication during the course of illness using specific ELISA.

38 patients with fulminant hepatitis including 28 cases with viral hepatitis B (IgM anti-HBc positive) and 10 cases of hepatitis non-B (IgM anti-HBc negative but HBsAg positive) were included in the study. All the patients developed hepatic encephalopathy within 10 days of the onset of symptoms and signs of acute hepatitis in the absence of any pre-existing liver

disease and the samples were collected within one week of the onset of encephalopathy.

HBsAg, anti-HBs, IgM anti-HBc and HBV-specific DNA-polymerase activity were tested in the serum as detailed earlier (Irshad et al., 1987). Anti-pre-S antibody in serum was tested by ELISA as described elsewhere (Irshad et al., 1988). The test is based on competitive binding between anti-pre-S and horse radish peroxidase labelled polymerised human serum albumin (HRPO-pHSA) for the pHSA receptor site on HBsAg molecule fixed to a solid surface. Serum samples from healthy subjects without HBV markers served as control group. Any test serum causing an inhibition of more than 50% was considered positive for anti-pre-S antibody.

The present series of 38 patients with fulminant hepatitis demonstrated a low prevalence of anti-HBs but moderately high prevalence of HBV-specific DNA-polymerase. A high proportion of sera samples showed the presence of anti-pre-S antibody (Table-I) in comparison to non-fulminant hepatitis B (4.2%) in our earlier report (Irshad et al., 1988). These findings indicate a brisk immune response to pre-S proteins in fulminant hepatitis B patients, resulting in an early appearence of anti-pre-S antibodies i.e. even before the disappearence of pre-S proteins or HBV replications. Low anti-HBs positivity in fulminant patients indicate that brisk immune response is present exclusively to pre-S proteins and not to HBsAg.

The presence of anti-pre-S antibody in group of patients which represent either a non-B infection in HBsAg carrier or an early stage of HBV-infection, indicate an early appearance of anti-pre-S , i.e. before the development of IgM anti-HBc (Table-I). Low levels of anti-pre-s in group of patients positive for

both HBsAg and IgM anti-HBc correspond to the declining phase of its appearance in a biphasic pattern (Okamoto et al., 1984). In group of patients representing the late stage of the disease i.e. presence of IgM anti-HBc in absence of HBsAg, anti-pre-S appeared in second phase representing IgG type of antibodies. Absence of HBsAg in this group of patients may be ascribed to the neutralizing effect of anti-pre-S present in high level as is supported by the fact that the anti-HBs levels were very low. Anti-pre S does not seem to arrest HBV-replication as was evident from high DNA-polymerase activity, suggesting that anti-pre-S clears off only the released HBsAg from hepatocytes without interfering in HBV-replication. The clearance of HBsAg by anti-pre-S predominates over its production.

Anti-pre-S antibody in fulminant patients seems to play a major role in clearing off HBsAg from circulation. Its function is different from that of anti-HBs which is more involved in the pathogenesis of liver than the clearance of HBsAg.

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Table-I

Hepatitis B markers in patients with fulminant hepatitis.

Groups	No.	anti-HBs +	anti-pre-S +	DNA-P +
HBsAg(+), IgM anti-HBc(-)	10	1(10.0)	5(50.0)	3(30.0)
HBsAg(+), IgM anti-HBc(+)	8	0(nil)	1(12.5)	4(50.0)
HBsAg(-), IgM anti-HBc(+)	20	3(15.0)	15(75.0)	7(35.0)

values in parenthesis show per cent value

DNA-P : HBV-specific DNA-polymerase