Summary and Conclusion

The host immune response have been suggested to play a role in liver injury occurring in patients with chronic hepatitis C. Several studies suggest that HCV by itself may not be cytopathic, and by comparison with the hepatitis B virus, the pathogenesis of HCV - induced liver damage might be mediated by the immune system itself (Liaw et al., 1995).

The aim of this study was to gain further insight into the relationship between the host immune response and HCV in patients with chronic hepatitis C in Egypt, and to asses if there is particular lymphocyte subsets in both the liver and peripheral blood of these patients.

We also aimed to find a correlation between the proportion of these lymphocyte subsets and each of the level of serum Alanine amino transaminase level (ALT) and the histopathological activity index (Knodell's Score).

This study carried out on twenty-one patients with chronic hepatitis C (patients group) and twenty individuals who are non reactive to anti-HCV antibodies (control group). The following investigations were carried out to both groups; liver function tests, complete blood picture, serological tests for HCV including anti- HCV antibodies and PCR. Flow cytometry was used to analyze both the intrahepatic and peripheral blood lymphocytes using monoclonal antibodies for CD3, CD4, CD8, CDI9, and CD56.

The results of the present study showed that although there was no difference in the intrahepatic $CD3^+$ lymphocytes between the patients and control group, there was a significant difference in the T lymphocyte

subsets distribution between both groups. The $CD8^+$ (cytotoxicT) lymphocytes were the predominant cells at the intrahepatic compartment in patients group.

Although $CD4^+$ lymphocytes proportion was smaller than the $CD8^+$ at the intrahepatic compartment in the patients group, they still significantly higher in patients than the IH $CD4^+$ lymphocyte proportion in the control group. This resulted in significantly higher $CD4^+/CD8^+$ IHL ratio in patients than in control group.

There was also a significant difference between the intrahepatic NK cells between the patients and the control groups.

There was no significant difference between IH CD19 (B lymphocytes) between the patients and control group. No significant difference was found between the intrahepatic and peripheral blood B lymphocytes in patient group.

We found a positive correlation between the proportion of intrahepatic $CD4^+$ lymphocytes and the histopathological activity index (Knodell' s Score), while there was no significant correlation between the lymphocyte subsets and the serum level of alanine aminotransferase (ALT).

In conclusion, after infection with HCV, multiple factors influence the virus-host interaction, resulting in a unique, individual disease pattern. Our data showed that compared to control group, although $CD8^+$ IHL remained higher than the PBL, patients with chronic hepatitis C had increased proportions of $CD4^+$ IHL. This revealed that the specific response of $CD4^+$ T lymphocytes directed against certain viral proteins are an essential part of the antiviral effectors mechanism, and the significant

increase in the CD4+ cells observed in the IHL of patients group compared to control group might reflect the important role played by the cytokines they produce. Also the positive correlation between the proportion of CD4+ cells & Knodell' score reflects the pivotal position of these cells in the immune system. Our data also lends a further suggestion that the cytotxic T-cells and NK cells compartalize in liver and are involved in the local host response to hepatitis C virus and play an important role in pathogeneses of chronic hepatitis C.

Recommendations

The significant positive correlation between the proportion of intrahepatic and peripheral blood CD4+&CD3 and the histological lesions leads us to propose that evaluation of the accessible peripheral blood population could be used as an indicator test for the severity of histological lesions in chronic hepatitis C.

Further studies are recommended on larger groups of patients, including functional studies of the various lymphocyte subsets and their proliferation and activation to different epitomes of the HCV - virus. Also we recommend studies of these cell subsets in response to - interferon treatment.