Vigorous peripheral blood cytotoxic T cell response during the acute phase of hepatitis C virus infection

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After infection by hepatitis C virus (HCV), a minority of patients develop acute symptomatic disease and some of them are able to clear the virus. In this study, we analyzed peripheral blood mononuclear cells from nine patients with acute symptomatic disease with respect to their cytotoxic T lymphocyte (CTL) response using a panel of HCV-derived peptides in a semiquantitative secondary in vitro culture system. We could detect early CTL responses in 67% of these patients. The CTL responses were directed against multiple viral epitopes, in particular within the structural (core 2-9, core 35-44, core 131-140, and core 178-187) and nonstructural regions of the virus (NS3 1073-1081, NS3 1406-1415, NS4 1807-1816, NS5 2252-2260, and NS5B 2794-2802). We compared the CTL responses displayed by recently and chronically infected HLA-A2-positive patients. Virus-specific CTLs were detectable in chronic carriers but the percentage of positive peptide-specific CTL responses was significantly higher in recently infected patients (P = 0.002). Follow-up of recently infected patients during subsequent disease development showed a significant decrease in the values and proportions of positive peptide-specific CTL responses (P = 0.002 and 0.013, respectively). Patients with limited viral replication exhibited significantly more vigorous early responses (P = 0.024). These data suggest a protective role for the early antiviral CTL response in HCV infection.