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## IS INTERFERON ALPHA 2b EFFECTIVE ON CRYOGLOBULINAEMIA RELATED TO HEPATITIS C VIRUS ?

*To the Editor*

Recently, mixed cryoglobulinaemia (MC) associated with hepatitis C virus infection (HCV), responsive to interferon, has been reported (1). During the same time, we observed 31 cases of chronic HCV associated with type II or III cryoglobulinaemia. Eight of them were treated with low dose interferon α2b (3 million units subcutaneously, three times per week for 6 months). The patients included 5 men and 3 women (average age 63). In five of them, a risk factor engendered by a previous transfusion precedence was present. All patients had the typical clinical triad of purpura, weakness and arthralgias, as well as a pronounced increase in serum aminotransferases. They had very low serum complement activity and increased rheumatoid factor. All the serum were anti-HCV positive by a second generation Abbot's anti-HCV enzyme immunoassay. Liver biopsy showed persistent hepatitis in 2 patients, active hepatitis in 5 patients and active cirrhosis in 1 patient. All the patients had type II MC with IgM monoclonal component. Five of the 8 patients (62.5%) treated with interferon dropped out after a median of 3 months (2-5 mo) because of inefficacy (4 pts) or intolerence (1 pt). The clinical symptomatology cleared up in the three other patients (37.5%). Aminotransferases levels, rheumatoid factor and serum complement activity returned to the normal range and cryoglobulinaemia disappeared in the first two months of administration. During six months of follow-up, no relapse was observed. Our observations have been supported by at least three preliminary reports (1,2,3). Long-term results of therapy with interferon-α for type II essential mixed cryoglobulinaemia have been recently reported by Casato et al (4). Of 16 patients observed for more than 1 year, 11 remained in remission for 14 to 40 months. These observations were published before an association between HCV infection and MC was demonstrated (5). Indeed, actually, a high prevalence of HCV infection in MC has been found in at least six different centers (6). In the first complete reported study (7), Ferri et al. have applied polymerase chain reaction to detect HCV RNA in sera from 42 of their MC group and found that 86% were positive. This enables us to believe that certain essential mixed cryoglobulinaemia from the Casato study (4) were in fact related to HCV infection. In patients with chronic hepatitis, the rate of complete remission (CR) at the end of a 6-month administration of recombinant interferon α is ~ 45% (8). In our patients, the rate of CR at the end of administration of interferon 37.5% did not differ from the one of cryoglobulinaemia negative patients. The similarity of the response to interferon in patients with HCV infection whether or not associated with MC is in accordance with the view that the effect of the treatment on HCV infection with cryoglobulinaemia is more likely to be due to the antiviral effects than to the immunomodulatory effect of interferon α. This study confirms preliminary reports and shows that consideration should be given to recombinant interferon therapy in MC associated with HCV infection. These conclusions, which are based on a relatively small number of patients, must however, be considered with caution.

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