letter to the editor
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LOW PREVALENCE OF HEPATITIS E VIRUS IN TYPE II MIXED CRYOGLOBULINEMIA

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Sir,

the relationship between hepatotropic viruses and mixed cryoglobulinemia (MC) has long been studied because of the frequent association of this lymphoproliferative disorder with chronic liver disease.[1]

Initially, a link with hepatitis B virus (HBV) was proposed, but a recent survey of a large series of cryoglobulinemic patients did not support this theory.[2] Moreover, evidence of hepatitis A virus (HAV) exposure has occasionally been recorded in MC.[3] At present, MC is considered a hepatitis C virus (HCV)-related disease since anti-HCV seroprevalence is very high (>80%) and HCV-RNA has been demonstrated in plasma and cryoprecipitate, as well as in blood and bone marrow mononuclear cells from MC patients.[4]

Another hepatotropic virus, i.e. hepatitis E virus (HEV), is the major etiological agent of non parenteral non-A, non-B hepatitis; it is responsible for large epidemics in developing countries and sporadic disease outbreaks in the industrialized world.[5] Although hepatitis E is a typical feco-orally-transmitted infection, other routes of contagion can be hypothesized, owing to the high prevalence of anti-HEV antibodies found in polytransfused and hemodialysis patients.[6,7] Moreover, a striking association between HCV and HEV infections was demonstrated in some selected populations.[8,9]

Therefore, we examined anti-HEV serology in 40 anti-HCV positive (second generation test) patients affected with type II MC (7 males and 33 females; mean age of 59 yrs, range 29-78; cryoprecipitate composed of monoclonal IgM κ plus polyclonal IgG in all cases).

Detection of anti-HEV antibodies was carried out by a commercially available EIA kit (Abbott Laboratories, North Chicago, IL, USA), utilizing two recombinant antigens (SG-3 and 8-5) derived from the structural region of the Burmese HEV strain expressed in *Escherichia coli*.

One female patient, aged 62 yrs, suffering predominantly from severe cryoglobulinemic peripheral neuropathy, was found to be HEV seropositive (serum sample optical density/cut-off repeatedly >1.50). Interestingly, this patient at the age of 45 and before the occurrence of MC had a history of acute jaundice, which could be attributed, at least in a presumptive way, to a community-acquired sporadic HEV infection. In fact, at that time no apparent risk for HAV was retrospectively documented and serum markers of prior HBV exposure are at present absent, thus making a diagnosis of HAV or HBV infection unlikely. In addition, this episode of acute jaundice could not be ascribed to HCV infection since most patients with acute hepatitis C are quite asymptomatic.[10]

This fact may be indirectly inferred by considering all the other patients belonging to our series, none of whom had a history of previous jaundice, thus indicating a silent clinical course for acute HCV infection. The lasting persistence of anti-HEV antibodies that we hypothesize in our HEV seropositive patient is in agreement with some data demonstrating that IgG anti-HEV can be detected for long periods, even more than 14 yrs after the HEV exposure.[11]

According to our results, although in MC HEV seroprevalence seems to be higher than in the normal healthy Italian population (2.50% vs 0.74%),[12] it can be concluded that HEV infection is documented only occasionally in this HCV-related lymphoproliferative disorder. Moreover, the previously described association

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between HCV and HEV infection can be ruled out, at least in type II MC patients.

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