CORRESPONDENCE

Monoclonal Gammopathies and Hepatitis C Virus Infection

To the Editor:

In recent years, a high prevalence of both anti-hepatitis C virus (anti-HCV) antibodies (HCVAb) and HCV RNA has been documented in series of patients affected by cryoglobulinemia.1-3 Moreover, it has been shown that in type I and II symptomatic cryoglobulinemias, both essential and secondary, the cryoglobulins, with cryocrit exceeding 1% to 2% and characterized by immunofixation techniques, are monoclonal IgS.3 The histologic as well as immunocytochemical analysis of the bone marrow of several patients frequently showed the presence of a clear expansion of a B-lymphocyte population, suggesting a minimal lymphoproliferative disease or a localized immunocytoma that in time, according to some investigators, may evolve in an overt lymphoma.4

On the basis of these observations and of the reported high prevalence of HCV infection markers in Waldenström’s macroglobulinemia,5 we analyzed 201 cases of monoclonal gammopathies (MGs) for the presence of HCVAb using enzyme-linked immunosorbent assay and second generation recombinant immunoblot assay (RIBA) tests (Ortho Diagnostic Systems, Raritan, NJ). The cases were divided in two groups on the basis of the presence or absence of cryoglobulinemic activity. The first group included 94 patients, all affected by type II (monoclonal IgMκ and polyclonal IgG) cryoglobulinemia, subdivided into (1) 62 so called ‘‘essential’’ cryoglobulinemias, (2) 12 cryoglobulinemias associated with overt lymphoproliferative diseases (3 Waldenström’s diseases, 6 immunocytomas, 2 chronic lymphocytic leukemias, 1 centoerytic lymphoma), and (3) 20 cryoglobulinemias associated with autoimmune disorders (9 Sjogren’s syndromes, 6 undifferentiated connective tissue diseases, 4 systemic lupus erythematosus, 1 systemic sclerosis). In 38 patients of this group, the presence of the HCV RNA in peripheral blood mononuclear cells was investigated by a reverse transcription-polymerase chain reaction technique using primers already described.6 The second group included 107 subjects (70 MGs of uncertain significance, 21 myelomas, 12 Waldenström’s diseases, 4 immunocytomas) with MGs without cryoglobulinemic activity (46 IgGκ, 28 IgGλ, 18 IgMκ, 7 IgMλ, 4 IgAκ, 4 IgAλ).

In so called ‘‘essential’’ mixed cryoglobulinemias, which were frequently associated with features of bone marrow B-lymphocyte clonal expansion, we found a very high prevalence of HCVAb (83.9% RIBA-positive cases). All the RIBA-positive cases, including 2 Waldenström’s diseases resulted positive when tested for the presence of HCV RNA in peripheral blood mononuclear cells. A similar result was obtained in the cryoglobulinemias associated with overt lymphomas (83.3% RIBA-positive cases), whereas no strict relation was found between HCV infection and cryoglobulinemias secondary to autoimmune diseases (15% RIBA-positive cases; see Table 1).

In MGs without cryoglobulinemic activity, the prevalence of HCVAb was very low in all the subgroups studied except for the immunocytomas, in which a firm conclusion is prevented by the low number of cases available for the study (Table 1). It must be observed that, contrary to what has already been reported in literature,6 our patients affected by Waldenström’s disease without cryoglobulinemia were HCV-negative.

Our overall data on 201 patients confirm the strict association between HCV infection and MGs with cryoglobulinemic activity, with the exception of those associated with autoimmune diseases. This relation does not seem to exist with the MGs without cryoglobulinemic activity, such as in MGs of uncertain significance, multiple myeloma, and Waldenström’s disease.

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REFERENCES

Table 1. HCVAb Prevalence in MGs

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<th>MGs With Cryoglobulinemic Activity</th>
<th>MGs Without Cryoglobulinemic Activity</th>
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<tr>
<td></td>
<td>EMC</td>
<td>LD</td>
</tr>
<tr>
<td>No. of patients</td>
<td>62</td>
<td>12</td>
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<td>RIBA+ (%)</td>
<td>52 (83.9)</td>
<td>10 (83.3)</td>
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Abbreviations: EMC, “essential” mixed cryoglobulinemia; LD, overt lymphoproliferative diseases; AD: autoimmune diseases; MGUS, MG of uncertain significance; MM, multiple myeloma; WD, Waldenström’s disease; IC, immunocytoma.


Monoclonal gammopathies and hepatitis C virus infection [letter] [see comments]

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