Primary Hepatosplenic Lymphoma: Association With Hepatitis C Virus Infection

To the Editor:

Several Italian investigators showed that hepatitis C virus (HCV) infection might be a cause of lymphoid malignancy such as Waldenström’s macroglobulinemia (WM), non-Hodgkin’s lymphoma (NHL), and monoclonal gammapathies with cryoglobulinemic activity. Recently, we reported a high incidence of HCV infection in B-cell NHL cases, suggesting that HCV is also related to the pathogenesis of B-cell malignancy in Japan. However, there are few reports on the relationship between a subset of NHL with some clinical characteristics and persistent HCV infection.

We experienced 83 cases of malignant lymphoma (54 cases of B-cell NHL, 20 cases of non-B-cell NHL, and 9 cases of Hodgkin’s disease) at first admission since November 1992, when the assay system of HCV (second generation enzyme immunoassay) was available in our institute. The antibodies against HCV (HCVAb) were not detected in any cases of non-B-cell NHL and Hodgkin’s disease. On the other hand, 12 of 54 B-cell NHL cases (22.2%) were positive for HCVAb. HCVAb positivity in the cases of B-cell NHL was significantly higher than that of non-B-cell NHL (P < .05; Fisher’s exact test). Of these 12 HCVAb-positive cases, 4 (33.3%) were B-cell NHL that originated from the liver and/or the spleen and were classified as diffuse large-cell type. In these 4 cases, radiographic findings suggested no other involvement than in the liver and spleen. Therefore, these cases were diagnosed as primary hepatosplenic lymphoma (PHSL), which is rare in NHL. There were no HCVAb-negative cases of PHSL in our study. The incidence of PHSL in HCVAb-positive NHL cases was significantly higher than that in HCVAb-negative NHL cases (P < .01; Fisher’s exact test). Persistent HCV infection was documented by reverse transcription-polymerase chain reaction (RT-PCR) assay, as described previously.

Coexisting liver diseases in these 4 PHSL cases were as follows: 3 cases with cirrhosis and 1 with chronic active hepatitis. The genotype of HCV based on Okamoto’s classification was II in 3 cases and III in 1 case, respectively. Genotype II is commonly observed in HCV carriers in Japan. Cryoglobulinemia was not detected in any of these four cases.

The direct causal relationship between the occurrence of PHSL and chronic HCV infection is unclear. The previous case reports suggested that splenic NHL and hepatosplenic lymphoma might be related to chronic hepatitis. However, HCV infection was not documented by RT-PCR assay in these previous reports. We detected persistent HCV infection by HCV immunoassay and RT-PCR assay in all these cases. Recently, De Vita et al noticed 2 cases of hepatic lymphoma with persistent HCV infection.

HCV-related lymphoma has been reported only from Italy and Japan. Further studies including the identification of HCV-RNA in the lymphoma cells are needed to clarify the causal relationship between the occurrence of PHSL and persistent HCV infection.

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REFERENCES
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