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CASE REPORT | LIVER

Lymphoma Remission by Interferon-Free HCV Eradication Without Chemotherapy

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Abstract

Epidemiologic studies have suggested an association between hepatitis C virus (HCV) infection and antigen-driven lymphoproliferative disorders, in particular marginal zone lymphomas. Antiviral therapy has been shown to exert an anti-lymphoma effect in these indolent B-cell lymphoproliferations, with survival gains observed. However, these protocols have traditionally incorporated interferon. We describe a patient with chronic hepatitis C, immune thrombocytopenia, and splenic marginal zone lymphoma who, after eradication of HCV with sofosbuvir and ribavirin, exhibited complete remission of both hematologic conditions. With the numerous new potent drugs currently available, the future looks positive with highly efficacious interferon-free regimens for HCV therapy.

Introduction

Hepatitis C virus (HCV) infection is a major public health issue worldwide, affecting an estimated 3–4 million people globally, with 170–200 million carriers with hepatotropic sequelae such as liver cirrhosis and hepatocellular carcinoma.[1] HCV has also been shown to be a lymphotropic virus, as epidemiologic studies have demonstrated an increased prevalence of B-cell lymphomas among people with chronic hepatitis C, predominantly indolent B-cell lymphomas such as marginal zone lymphoma and lymphoplasmacytic lymphoma.[2,3]

Case Report

A 70-year-old woman presented to our institution with a platelet count of 4 x 10^9/L and mucocutaneous bleeding. On examination, she lacked stigmata of chronic liver disease, lymphadenopathy, or splenomegaly. In the diagnosis of idiopathic thrombocytopenic purpura (ITP), genotype 2 HCV was ascertained for the first time. She had a high HCV RNA viral load of 6.6 log IU/mL. Cryoglobulins were negative. She had chronic, mild microcytic anemia in keeping with beta-thalassemia trait. Peripheral blood and bone marrow testing revealed an aberrant monoclonal B-cell population with an indolent immunophenotype (CD20+, CD19–, CD5wk, CD10–, CD11c–, CD38–). Clinicoradiologic review was negative for lymphoma and cytometry, thus identifying a monoclonal B-cell lymphocytosis of uncertain significance. Liver and renal biochemistries were unremarkable. Fibroscan result was 6.8 kPa, suggesting minimal liver fibrosis. Abdominal CT demonstrated a fatty liver.

Her ITP proved to be refractory to a variety of corticosteroid regimens, intravenous immunoglobulin, *Helicobacter pylori* eradication, azathioprine, and platelet transfusion. She required multiple, short-stay admissions

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over several months with recalcitrant thrombocytopenia. She underwent splenectomy which revealed marginal zone lymphoma, presumed in retrospect to have been driven by the HCV. Thrombocytopenia prevented the use of interferon and she was granted compassionate access to sofosbuvir 400 mg daily, with ribavirin 1,000 mg for 12 weeks. She had a rapid virological response and HCV RNA was undetectable by week 4 of treatment and at post-therapy weeks 0, 12, and 24, indicating sustained virological response. Repeat flow cytometry for residual monoclonal B-cell lymphocytosis remained negative 22 weeks after treatment, and the ITP remained in remission 83 weeks after treatment. Combination sofosbuvir and ribavirin was well-tolerated, with no side effects, and resulted in complete remission of marginal zone lymphoma and ITP more than 83 weeks after cessation of antiviral therapy.

Discussion

This is the second case report of lymphoma remission after HCV eradication with an IFN-free regimen.[4] IFN with or without ribavirin has been proven to be effective in the treatment of HCV-positive patients affected by indolent lymphoma, as lymphoma development may be related to chronic antigenic stimulation from the hepatitis C virus. Arcaini et al published the largest multicenter study on the anti-lymphoma efficacy of antiviral therapy, concluding that viral load suppression with interferon results in tumor regression.[5]

IFN has been assumed to be beneficial in remitting lymphoproliferative disorder due to its immunomodulatory effects.[6] However, the side effects may be detrimental to patients who have contraindications to IFN, such as advanced age or presence of liver cirrhosis (with potential precipitation of liver decompensation and/or failure), or other co-morbidities including cytopenias, which was a challenge in our patient. Our patient demonstrated a rapid and sustained virologic response without IFN, and remained in hematologic remission out to 70 weeks post therapy, which illustrates that perhaps the antiviral rather than the anti-proliferative activity of IFN is the mainstay of treatment.

Disclosures

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