

Exploring the role of viral hepatitis in plasma cell disorders

Elizabeth O'Donnell

Dana-Farber Cancer Institute, Boston, MA, USA

Correspondence: E. O'Donnell
Elizabeth_odonnell@dfci.harvard.edu

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Multiple myeloma (MM) is a malignant plasma cell disorder characterized by the proliferation of abnormal plasma cells in the bone marrow. Monoclonal gammopathy of undetermined significance (MGUS) and smoldering multiple myeloma (SMM) are precursors to MM. While the exact mechanisms are not yet fully understood, several studies have demonstrated an association between chronic viral hepatitis and the development of MM and other monoclonal gammopathies.¹⁻⁶

Viral hepatitis, caused by hepatitis B (HBV) and hepatitis C (HCV) viruses, has been a major global health concern for several decades. These viruses can lead to chronic infections that increase the risk of various liver diseases, including cirrhosis and hepatocellular carcinoma. However, recent research has shed light on the link between viral hepatitis and the development of certain hematologic malignancies, particularly MM and other monoclonal gammopathies.¹⁻³ In this issue of *Haematologica*, Rodriguez-Garcia and colleagues explore the role of HBV in patients infected with HBV and diagnosed with monoclonal gammopathy, and evaluate the impact of antiviral therapy on outcomes for patients with HCV and HBV infections and MM.⁷

Hepatitis C virus infection has been implicated in the pathogenesis of MM. Chronic HCV infection induces chronic inflammation, immune dysregulation, and clonal B-cell expansion, all of which can promote the development of B-cell malignancies.⁸ Furthermore, HCV infection has been associated with an unfavorable prognosis and reduced survival in patients with MM.⁹ However, in patients with HCV whose monoclonal protein reacted against HCV, treating the HCV infection improved MGUS and MM disease.¹⁰

Similarly, an increased prevalence of HBV infection has been reported in patients with MM compared to the general population.¹¹ In this issue, Rodriguez-Garcia and colleagues evaluated patients with monoclonal gammopathy who had been infected with HBV and found that, in 36.7% of the HBV-infected patients, the target of the monoclonal

Ig was the HBV, suggesting that the HBV infection initiated the clonal gammopathy. They then went on to evaluate the overall survival of patients with MM with HBV and HCV who had been treated with antiviral therapy *versus* those who had not. They found statistically significant differences between the treated and untreated cohorts for both HBV and HCV. Their findings strengthen previous findings that anti-HCV therapy may improve outcomes in plasma cell dyscrasias, and extends these to include HBV. The recognition of the association between viral hepatitis and MM and monoclonal gammopathies has important clinical implications. The authors highlight that if the target of a patient's monoclonal protein can be identified and eliminated, chronic antigen exposure disappears, leading to control of the clonal plasma cells. Not only would antiviral therapy improve outcomes and the morbidity associated with viral hepatitis, but it could also potentially mitigate the monoclonal gammopathy and the risk of progressing to symptomatic disease.

As such, there is a need for increased awareness and screening for viral hepatitis in patients with MM and monoclonal gammopathies. Early identification of viral hepatitis in these individuals can lead to appropriate antiviral therapy and subsequent improvement in outcomes. The management of patients with MM with concomitant viral hepatitis requires a multidisciplinary approach. Treatment decisions should consider both the hematologic malignancy and the viral hepatitis, taking into account potential drug-drug interactions and the impact of underlying liver disease on treatment tolerability. Close collaboration between hematologists/oncologists and hepatologists is essential to optimize treatment outcomes and minimize complications. Prevention strategies are also crucial in mitigating the impact of viral hepatitis in patients with MM and other monoclonal gammopathies. Vaccination against HBV should be encouraged in individuals at risk, including patients with MM and those receiving immunosuppressive therapy. In addition, raising awareness about safe injection practices, blood screening,

and the importance of antiviral therapy for viral hepatitis can reduce the incidence and transmission of these infections.

The association between viral hepatitis and the development of MM and other monoclonal gammopathies has emerged as an important area of research. Chronic HBV and HCV infections contribute to the pathogenesis of these hematologic malignancies, warranting increased awareness, screening, and management strategies. Early identification of viral hepatitis in patients with MM and

monoclonal gammopathies can lead to improved outcomes through appropriate antiviral therapy and tailored treatment approaches. Moving forward, continued research, collaboration between specialists, and comprehensive prevention efforts will be crucial in reducing the burden of viral hepatitis in this patient population, and in improving their overall prognosis and quality of life.

Disclosures

No conflicts of interest to disclose.

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