The controversy of hepatitis C and rituximab: A multidisciplinary dilemma with implications for patients with pemphigus

Sir,

Kanwar *et al.*'s recent report of the successful treatment of two patients with pemphigus and concomitant hepatitis C infection using rituximab brings to light an important controversy widely discussed in the oncology, hepatology and rheumatology literature.[1] Given the increasing use of rituximab in dermatology, the potential for hepatitis C reactivation following rituximab warrants further discussion.

Rituximab is a monoclonal antibody targeting the B-cell marker CD20 that has been demonstrated to be efficacious in the treatment of pemphigus in numerous studies.[2-4] CD20 is expressed on the surface of all B-cells starting at the pro-B-cell phase until they develop into plasma cells. Thus, rituximab leads to the destruction of B-cell progenitors but not plasma cells. Though rituximab has traditionally been viewed as a second- or third-line agent,[5,6] its use early in the disease course leads to improved long-term clinical outcomes and decreased relapse rates.[7,8] As such, some authors have suggested that rituximab be considered a first-line drug for pemphigus.[9-11] Regardless, rituximab plays an important role in disease refractory to non-biologic immunosuppresion.[6]

Several studies have demonstrated the risk of hepatitis C reactivation following treatment with rituximab.[12] These studies have almost exclusively been from the oncology literature. Results from oncology studies looking at hepatotoxicity and viral loads must be taken with caution, however, as these studies often use the R-CHOP protocol (rituximab, cyclophosphamide, vincristine, doxorubicin and glucocorticoids) which in itself is hepatotoxic.[13] Given the high mortality associated with these viral flares, much caution has been raised regarding the use of rituximab in patients with hepatitis C.[14] However, in patients who have reached a sustained virologic response to antiviral therapy, rituximab containing chemotherapy regimens do not induce viral replication.[15]

Only a few cases of hepatitis C reactivation following rituximab use have been reported in the rheumatology literature, further suggesting that hepatitis C reactivation in oncology patients is due to the additional hepatotoxic and immunosuppressant medications given.[16] Rituximab has been successfully used as a monotherapy in hepatitis C-related mixed cryoglobulinemia[17,18] demonstrating improvements in the manifestations of cryoglobulinemia as well as a favorable safety profile with an added benefit of hepatic improvement in some cases.[19] As such, it would be more appropriate to approximate the risk of hepatitis C reactivation in pemphigus patients to that of rheumatology patients rather than oncology.

The risks and benefits of alternative therapies must also be weighed, as the use of corticosteroids has been associated with increased viral loads and transaminases, though the clinical significance of these changes remains questionable.[20,21] Likewise, the commonly used adjuvant azathioprine is a well-documented hepatotoxin.[22]

As such, the presence of hepatitis C infection is not a contraindication to using rituximab but rather an additional comorbidity necessitating a multidisciplinary approach to patient management. Although the theoretical risk of viral reactivation in the pemphigus patient treated with rituximab appears to be relatively low, it is nonetheless recommended that patients be screened for hepatitis B and hepatitis C infection, in addition to tuberculosis before beginning treatment with rituximab.[23] As Kanwar *et al.* discussed in this patient population, close patient follow-up and collaboration with a hepatologist can allow for pemphigus patients to be safely treated with rituximab.[1]

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Conflicts of interest

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