Chronic Viral Hepatitis and TNF-α blockade

Sir, We read with interest the article by Roux et al. [1] regarding the use of tumour necrosis factor-α (TNF-α) blocking agents in patients with hepatitis B virus (HBV) and hepatitis C virus (HCV). The authors describe three patients with chronic HBV infection (all surface antigen positive) who were successfully treated with TNF-α blockade, in conjunction with lamivudine, with no evidence of HBV reactivation at follow-up of between 10 and 32 months. The article’s key message was ‘Anti-TNF-α appeared to be safe when administered to patients with HBV or HCV infection. However, concomitant treatment with lamivudine or adefovir is necessary in hepatitis B.’

We have previously described our initial successful experience of using anti-TNF-α therapy in two patients with HBV without the use of lamivudine or adefovir [2], and can now report on long-term follow-up of 2 and 3 yrs. These two cases were: a 50-yr-old woman with RA and chronic HBV infection [HBV surface antigen negative (HBsAg), HBV core antibody negative, HBV surface antibody positive] who had failed treatment with five disease-modifying anti-rheumatic drugs (DMARDs), and was commenced on etanercept without combination DMARD therapy. She did not receive any antiviral therapy prior to or during anti-TNF-α treatment, and has now completed 3 yrs of treatment with no evidence of HBV reactivation—HBV surface antigen is negative, HBV DNA undetectable, and liver function tests are normal. Etanercept was switched to adalimumab due to concerns that this may have been causing diarrhoea, however, the patient has since been successfully switched back to etanercept due to a lack of efficacy of adalimumab. The second case is a 62-yr-old woman with RA and chronic HBV infection (HBsAg negative, HBV core antibody positive, HBV surface antibody positive) who had failed treatment with three DMARDs. She was commenced on etanercept in combination with 15 mg methotrexate s.c. No antiviral therapy was given prior to or during treatment with etanercept, and we have seen no evidence of HBV reactivation to date—HBV surface antigen is negative and LFTs are normal. She has now had 2 yrs of treatment with etanercept with no complications.

A recent review of HBV in rheumatic diseases by Calabrese et al. [3] summarized the published experience of patients with rheumatic disease and underlying HBV infection treated with biological agents and discussed strategies for screening and prophylaxis. The benefit vs risk of prophylactic antiviral therapy in patients receiving a prolonged course of immunosuppression is undetermined, and prolonged treatment with lamivudine may be linked with the development of lamivudine resistant strains of HBV [4]. Calabrese et al. [3] concluded that prophylactic antiviral therapy may not be necessary routinely, providing decisions are made on an individual patient basis and that regular follow-up takes place.

The article by Roux et al. [1] helps to further clarify the risks of HBV reactivation in patients treated with anti-TNF-α therapy. However, our clinical experience is not in keeping with the article’s key message that ‘…concomitant treatment with lamivudine or adefovir is necessary in hepatitis B’. We believe that the currently available data suggest that TNF-α blockade is a therapeutic option in patients with RA and chronic HBV infection, though the risk/benefit ratio must be carefully assessed in each patient. Prophylactic antiviral therapy is indicated routinely in HBsAg-positive patients, but our experience is that anti-viral prophylaxis may not be necessary routinely in HBsAg-negative patients requiring an extended course of immunosuppressive therapy. As HBV is the commonest chronic viral infection in humans, this is scenario that many rheumatology centres are likely to encounter at some point. Further reporting of such cases is vital to further inform and clarify on an area where there is still a paucity of data.

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