Hepatitis B reactivation following treatment with abatacept in a patient with past hepatitis B virus infection

Sir, Abatacept (CTLA4-Ig) is a T cell co-stimulation modulator approved for the treatment of RA [1]. In contrast to the published experience with anti-TNF agents, data on the safety of abatacept regarding reactivation of hepatitis B virus (HBV) are scarce [2, 3]. Here we report a case of HBV reactivation following abatacept treatment in a patient with past HBV infection.

A 68-year-old woman with a 2-year history of RA was started on abatacept treatment on December 2010. Her symmetric erosive polyarthritis proved refractory to oral MTX treatment for 1 year and monthly i.v. abatacept was added as step-up therapy due to persistent high disease activity (DAS28 5.63).

Baseline HBV serology at the initiation of abatacept treatment was HBsAg negative, anti-HBc Ab positive, anti-HBs Ab negative and HBeAg negative/anti-HBe Ab positive. Liver function tests were normal. HBV viral load was not determined. Due to cost limitations, common practice in our centre for this subset of patients (anti-HBc positive), when administering biologic agents is to monitor HBsAg together with alanine aminotransferase (ALT) every 3 months in order to detect HBV reactivation (HBsAg positive). A mild ALT elevation [1.5 × upper limit of normal (ULN)] 6 months after the initiation of abatacept was attributed to drug toxicity by isoniazid (given for treatment of latent tuberculosis due to positive PPD testing); ALT returned to normal after isoniazid discontinuation. HBsAg at the time remained negative. Four months later, while ALT remained at the ULN, routine repeat HBsAg testing returned positive (1346 mIU/ml). γ-glutamyl transpeptidase (γ-GT) and ALP were within normal limits, as was the synthetic function of the liver. Serum HBV DNA was found to be $1.1 \times 10^6$ IU/ml (COBAS AMPLICOR assay). Treatment with abatacept was immediately discontinued.

Consultation with a hepatologist was requested and a liver biopsy was performed. Histological examination revealed evidence of mild active hepatitis and the absence of fibrosis. The patient was immediately started on tenofovir 300 mg/day. Shortly after tenofovir initiation, aspartate aminotransferase (AST)/ALT showed an elevation up to 8-fold the ULN, but quickly returned to normal within 2 months. Repeat HBV DNA was 565 IU/ml and became undetectable after 5 and 8 months on tenofovir (Fig. 1). Therapy for RA has not been reinstituted at the patient’s request.

Currently, no formal guidelines exist regarding optimal monitoring of rheumatic patients with past HBV infection (HBsAg negative, anti-HBc Ab positive, anti-HBs Ab positive or negative) receiving biologic agents. HBV DNA represents a highly sensitive yet costly test and HBsAg can serve as a suitable alternative. Data from anti-TNF agents have been conflicting. Based on studies from Asia [4] (an area with a high prevalence rate of HBV infection and few reported cases of viral reactivation in this subset of patients), serial HBV viral load measurements in anti-HBc-positive patients have been proposed [5]. However, data from Europe are more reassuring, with three recent studies showing no such reactivation in a total of more than 100 patients [6–8]. Differences in HBV epidemiology as well as in the assays used for HBV DNA measurements may have accounted for this discrepancy. Few such data exist regarding the use of abatacept or rituximab in patients with rheumatic disorders. Until more data are available, frequent monitoring of HBsAg and ALT levels (every 3–6 months) seems a realistic and cost-effective approach to detecting early HBV reactivation in this subset of patients with rheumatic disorders [9].

In summary, we describe a case of HBV reactivation with abatacept in a patient with past HBV infection, the second in the literature to date [2]. In a recent retrospective report, all four HBsAg-positive patients administered abatacept without concomitant antiviral prophylaxis experienced HBV reactivation, indicating the potential of this agent to reactivate HBV infection [3]. The case illustrates the value of careful baseline screening and prompt recognition of HBV reactivation by HBsAg and/or HBV DNA monitoring during biologic therapy, which led to immediate initiation of antiviral therapy and prevention of a potentially threatening hepatitis flare.

Fig. 1 Kinetics of AST/ALT and HBV viral load before and after tenofovir administration.

D/c: discontinuation.
Rheumatology key message

- Diligent monitoring for possible HBV reactivation is required in patients with past HBV infection receiving abatacept.