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CASE REPORT

Reactivation of chronic hepatitis B virus infection following rituximab administration for rheumatoid arthritis

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Introduction

In chronic hepatitis B virus infection, immune suppression has been linked with potential activation and, in a number of cases, acute liver failure and fatal outcome; patients with haematologic or other malignancies under chemotherapy were mostly affected [1]. In the same cohort of patients the incidence of HBV reactivation rose significantly in the past decade, after the introduction of rituximab, a monoclonal antibody targeted against the CD20(+) lymphocytes [2, 3]. In this setting, reactivation was recorded even in HBsAb(+) patients [4]. In patients with rheumatic diseases, analogous cases are still mainly anecdotal. Taking into account the increasing application of rituximab in the treatment of autoimmune diseases, and the global prevalence of chronic hepatitis B virus infection, cases of treatment-induced reactivation need to be recorded, in order to formulate prophylaxis and treatment guidelines, and to safely establish the safety profile of these agents in analogous circumstances [5].

Case report

A 56-year-old female patient with a 21-year-history of severe rheumatoid arthritis (cervical fusion surgery, hip and knee arthroplasty) and arterial hypertension received the 1st cycle of rituximab in July 2008. The patient had received etanercept (monoclonal antibody targeted against the soluble TNFa receptor) in 2002 for 1 year with good response; treatment was discontinued after setting the diagnosis of chronic HBV infection (HBsAg+, HBeAg−, HBeAb+) and the patient was started on lamivudine, steroids and DMARDs (cyclosporine) with moderate response in terms of the primary disease until May 2007. In May 2007 infliximab, and adalimumab were initiated sequentially (HBV DNA PCR < 6 IU/ml). Both were discontinued shortly after initiation, due to failure of response. The patient developed an allergic reaction to abatacept and gave her informed consent to receive rituximab (at initiation DAS28 was 6.28, the biochemical profile was normal, and PCR for HBV DNA was 9.6×10^2 IU/ml).

One month after administration of rituximab ($2 \times 1{,}000$ mg) the patient presented with fever (38°C) and elevated transaminases (SGOT 110, SGPT 150U/l). HBV DNA was $>1.1 \times 10^8$ IU/ml and antibodies for HDV were negative. Tenofovir was added to the concomitant lamivudine. Transaminases normalised 1 month after initiation of tenofovir, and, 10 months later, HBV DNA was 46 IU/ml. The patient was in good clinical condition and liver morphology (by imaging studies) and function remain normal.

Discussion

An unrecognised HBV infection may lead to serious complications in patients receiving DMARDs and/or biologics (e.g. TNFa antagonists, rituximab). On the other hand, a diagnosed chronic HBV infection may cause delay to or undertreatment of patients with rheumatic diseases. Reactivation of chronic HBV infection has been reported with

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anti-TNF agents [6, 7]. However, under prophylactic antiviral treatment these agents seem, at least in a restricted number of patients and under short-term follow-up, to be relatively safe [8, 9]. Longer follow-up of the patients involved is needed to safely extrapolate this conclusion. Experience with rituximab in analogous patients is scarce [10]. Current guidelines suggest avoidance of this biologic in patients with chronic HBV infection (HBsAb−), based on experience from oncological patients and its interference with B-lymphocyte biology. In cases in which all other therapeutic options have been excluded and the patient consents to its use, treatment requires close monitoring of the patient (clinical and laboratory) under concomitant antiviral treatment, and prompt reevaluation of the latter with early signs of viral reactivation.

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