



**HAL**  
open science

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

Athina Pырpasopoulou, Stella Douma, Themistoklis Vassiliadis, Sofia Chatzimichailidou, Areti Triantafyllou, Spyros Aslanidis

### ► To cite this version:

Athina Pырpasopoulou, Stella Douma, Themistoklis Vassiliadis, Sofia Chatzimichailidou, Areti Triantafyllou, et al.. Reactivation of chronic hepatitis B virus infection following rituximab administration for rheumatoid arthritis. *Rheumatology International*, 2009, 31 (3), pp.403-404. 10.1007/s00296-009-1202-2 . hal-00568311

**HAL Id: hal-00568311**

**<https://hal.science/hal-00568311>**

Submitted on 23 Feb 2011

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

**Reactivation of chronic hepatitis B virus infection following  
rituximab administration for Rheumatoid Arthritis**

A. Pyrpasopoulou, S. Douma, T. Vassiliadis, S. Chatzimichailidou, A. Triantafyllou,  
S. Aslanidis

*2<sup>nd</sup> Propedeutic Department of Internal Medicine, Hippokration General Hospital,  
Thessaloniki, Greece*

Address correspondence to:

Spyros Aslanidis, MD

Consultant Rheumatologist

2<sup>nd</sup> Propedeutic Dept of Internal Medicine

Hippokration Hospital

Konstantinoupoleos 49

54642 Thessaloniki

Greece

Tel: +302310892117

Fax: +302310892117

e-mail: [saslan@med.auth.gr](mailto:saslan@med.auth.gr)

## **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-yr-old female patient with a 21-yr-history of severe rheumatoid arthritis (cervical fusion surgery, hip and knee arthroplasty) and arterial hypertension received the 1<sup>st</sup> cycle of rituximab in 7/08. The patient had received etanercept (monoclonal antibody targeted against the soluble TNF $\alpha$  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 5/07. In 5/07 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  $9.6 \times 10^2$  IU/ml). One month after administration of rituximab (2x 1000mg) the patient presented with fever ( $38^\circ$  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 is 46 IU/ml. The patient is 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 TNF $\alpha$  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 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.

## REFERENCES

1. Yeo W, Chan PK, Zhong S, Ho WM, et al.

Frequency of hepatitis B virus reactivation in cancer patients undergoing cytotoxic chemotherapy: a prospective study of 626 patients with identification of risk factors.  
J Med Virol 2000;62:299-307.

2. Tsutsumi Y, Kanamori H, Mori A, et al.

Reactivation of hepatitis B virus with rituximab.  
Expert Opin Drug Saf 2005;4:599-608.

3. Yeo W, Chan TC, Leung NW, et al.

Hepatitis B virus reactivation in lymphoma patients with prior resolved hepatitis B undergoing anticancer therapy with or without rituximab.  
J Clin Oncol 2009;27:605-11.

4. Sera T, Hiasa Y, Michitaka K, et al.

Anti-HBs-positive liver failure due to hepatitis B virus reactivation induced by rituximab.  
Internal Medicine 2006;45(11):721-4.

5. Furst DE.

The risk of infections with biologic therapies for rheumatoid arthritis.  
Semin Arthritis Rheum 2008 Dec 29 (epub ahead of print)

6. Zingarelli S, Ario P, Frassi M, et al.

Prophylaxis and therapy of HBV infection in 20 patients treated with disease modifying antirheumatic drugs or with biological agents for rheumatic diseases.

Reumatismo 2008;60:22-7.

7. Nathan DM, Angus PW, Gibson PR.

Hepatitis B and C virus infections and anti-tumor necrosis factor-alpha therapy: guidelines for clinical approach.

J Gastroenterol Hepatol 2006;21:1366-71.

8. Calabrese LH, Zein N, Vassilopoulos D.

Safety of antitumour necrosis factor (anti-TNF) therapy in patients with chronic viral infections: hepatitis C, hepatitis B, and HIV infection.

Ann Rheum Dis 2004;63 Suppl 2:ii18-ii24.

9. Roux CH, Brocq O, Breuil V, Albert C, Euller-Ziegler L.

Safety of anti-TNF-alpha therapy in rheumatoid arthritis and spondyloarthropathies with concurrent B or C chronic hepatitis.

Rheumatology 2006;45(10):1294-7.

10. Salliot C, Dougados M, Gossec L.

Risk of serious infections during rituximab, abatacept and anakinra treatments for rheumatoid arthritis: meta-analyses of randomized placebo-controlled trials.

Ann Rheum Dis 2009;68:25-32.