We suggest that in chronic inflammatory arthropathies, if the haemoglobin is low, then MCH is a better marker of iron deficiency than MCV. We therefore propose that MCH in conjunction with serum ferritin is a better predictor of IDA in patients with chronic inflammatory rheumatic diseases.

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Accepted 1 September 2004

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Reactivation of a latent precore mutant hepatitis B virus related chronic hepatitis during infliximab treatment for severe spondyloarthropathy

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Ann Rheum Dis 2005;**64**:788–789. doi: 10.1136/ard.2004.031187

We report a case of hepatitis B virus (HBV) reactivation following the use of anti-tumour necrosis factor α (TNFα) antibodies that illustrates the need for careful viral monitoring and pre-emptive antiviral treatment in such patients.

CASE REPORT

A 35 year old white woman presented with a history of chronic hepatitis B without an increase in serum alanine aminotransferase (ALT) or detectable HBV DNA by a hybridisation technique since its diagnosis (in 1993); she was thus considered to be an asymptomatic HBV carrier. Her serological status was as follows: hepatitis B surface antigen positive, hepatitis B e antigen negative, hepatitis B e antibody positive, suggesting HBV precore mutant. Her rheumatological history began in September 2001 with oligoarthritis, inflammatory low back pain, limitation of motion, and anterior chest wall involvement. Symptoms improved incompletely with non-steroidal anti-inflammatory drugs. Biological inflammation (erythrocyte sedimentation rate 62 mm/1st h, C reactive protein 53 mg/l), positive HLA-B27 typing, and sacroiliitis on *x* ray examination completed the picture.

The patient did not respond to successive methylprednisolone boluses, sacroiliac injections of steroids, salazosulfapyridine, and methotrexate (15 mg/week) then associated with pamidronate infusions. No changes in transaminases or HBV DNA load were detected during this period.

Infliximab was started (5 mg/kg/infusion at weeks 0, 2, and 6) in August 2003, while she continued to receive methotrexate and non-steroidal anti-inflammatory drugs, with good response (over 50% improvement of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)) and return to a normal C reactive protein.

Follow up showed a progressive increase in serum transaminases, together with an increase in HBV DNA load assessed by quantitative real time polymerase chain reaction (TaqMan; fig 1), with persistent negativity of hepatitis B e antigen and positivity of hepatitis B e antibody. A 100 mg/day course of lamivudine treatment was promptly started in January 2004, while continuing infliximab every 8 weeks. This was followed by return to normal transaminase level, and undetectable HBV DNA load.

DISCUSSION

In this case of severe spondyloarthropathy, anti-TNFα treatment was, as expected, efficacious for treatment of the disease, but was followed by the first episode of HBV reactivation associated with hepatic cytolysis. In this case, infliximab was probably the culprit. Firstly, our patient was an asymptomatic HBV carrier, without any increase in serum ALT recorded over a long follow up period. Secondly, although she received methotrexate, which may favour HBV reactivation through its immunosuppressive properties[1] and induce subfulminant HBV reactivation after its withdrawal,[2 3] no change in HBV DNA load was seen during the 9 months of methotrexate monotherapy.

Although the mechanism involved in anti-TNF antibody induced HBV reactivation is not fully understood, it is well known that TNFα as well as interferon γ, is produced during the innate immune response in the liver[4] and has antiviral properties by inhibiting the replication of HBV DNA.[1] Moreover, inactivation of TNFα mediated apoptosis of cytotoxic lymphocytes by anti-TNFα antibodies may account for more severe liver disease.[5 6]

Our report is consistent with previously published cases of HBV reactivation after the use of infliximab.[1 7] In the first case, it occurred 16 months after starting infliximab for rheumatoid arthritis and was controlled with both lamivudine treatment and discontinuation of infliximab[1]; in two cases of Crohn's disease, reactivation of chronic hepatitis B occurred after withdrawal of infliximab.[7] Conversely, in another case of severe ankylosing spondylitis with chronic hepatitis B, a 1 year course of infliximab and methotrexate

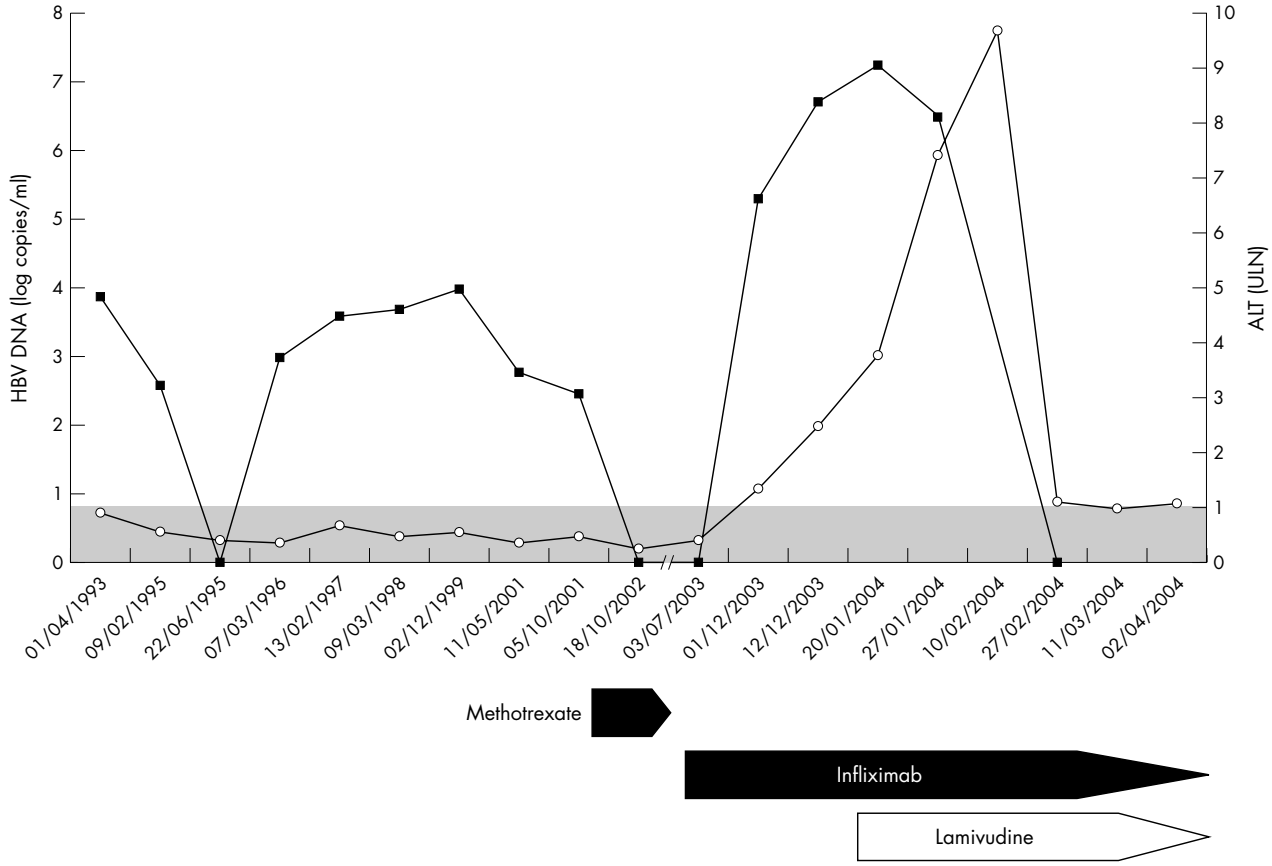

Figure 1 Outcome of serum HBV DNA (black squares) expressed in log copies per millilitre, and serum ALT (white circles), expressed in times over the upper limit of normal range (ULN). Serum HBV DNA was quantified using an in-house real time polymerase chain reaction (TaqMan) with primers and probe located in the core region and conserved among HBV genotypes.

had no deleterious effect on liver biochemistry or HBV DNA load. It is noteworthy that in this latter case with favourable outcome, concomitant lamivudine treatment had been started 1 year before infliximab and controlled HBV replication.[8] Hence, in HBV positive patients, further studies are needed to investigate the room and the timing for preventive lamivudine treatment.[7] Moreover, pre-emptive lamivudine treatment (that is, started after the detection of a significant increase in serum HBV DNA load), as in our case, should also be able to control HBV reactivation in patients receiving infliximab, while continuing this treatment.

ACKNOWLEDGEMENTS

We thank Alain Bourgeois, Carine Dirand, and Dominique Thomasset for their technical help in the quantification of serum HBV DNA.

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Accepted 24 September 2004

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