LETTER TO THE EDITOR

Infliximab-induced acute hepatitis during Crohn’s disease therapy: Absence of cross-toxicity with adalimumab

Hépatite aiguë à l’infliximab au cours du traitement d’une maladie de Crohn : absence de toxicité croisée avec l’adalimumab

The gold standard treatment of severe Crohn’s disease is a Tumor Necrosis Factor α antagonist such as infliximab. Hepatitis is a rare complication of treatment with TNFα antagonists [1—5]. We report the case of a patient who developed acute cytolytic hepatitis during infliximab treatment for Crohn’s disease. Once the hepatitis resolved, the patient was treated with adalimumab with no recurrence of hepatitis.

A 46-year-old man was referred to our unit in 2008 with a history of mouth and colon ulcers resulting in diagnosis of Crohn’s disease. The patient quickly became steroid-dependent, so treatment was begun with azathioprine. Therapy was stopped one month later due to intestinal intolerance with nausea. The patient’s alanine aminotransferase (ALT, N < 35 IU/L), aspartate aminotransferase (AST, N < 35 IU/L), gamma glutamyltransferase (γGT, N < 60 IU/L), alkaline phosphatase (AP, N < 280 IU/L) and bilirubin (N < 13.2 μM/L) values were normal.

He suffered from a severe relapse of Crohn’s disease, so treatment with 5 mg/Kg intravenous infusions of infliximab at zero, two and six weeks was started without concomitant treatment. Ten days after the first infusion at a dose of 325 mg, serum levels showed an increase in AST (107 IU/L), ALT (284 IU/L) and γGT (108 IU/L). AP (267 IU/L) and bilirubin (13 μM/L) values were normal. Laboratory tests on samples taken two weeks after the second infliximab treatment showed a slight decrease in liver enzymes (ALT 172 IU/L and AST 48 IU/L) without normalization (Fig. 1). Infliximab therapy was continued. Liver blood tests after the third infusion showed a relapse with an increase in ALT (528 IU/L), AST (143 IU/L) and γGT (128 IU/L) with no significant change in AP (277 IU/L) and bilirubin (14 μM/L). Hepatitis was severe with a decrease in prothrombin time to 52%. Liver toxicity due to infliximab was suspected and all other causes of acute hepatitis were ruled out. The patient was asymptomatic. He had no history of alcohol abuse and he was only receiving treatment with infliximab. Serological tests or polymerase chain reaction for hepatitis C virus, hepatitis B virus, hepatitis A virus, hepatitis E virus, HIV and cytomegalovirus were negative. Anti-smooth muscle, antinuclear, antimitochondrial and antiliver/kidney microsomal antibodies were not detected. Abdominal ultrasound showed no signs of biliary obstruction or any other abnormalities. A liver biopsy was performed. The histopathological study showed acute toxic hepatitis with areas of converging necrosis associated with inflammatory infiltration without bile duct damage. These histological findings did not suggest autoimmune hepatitis. No cytomegalovirus nuclear inclusion was found. Infliximab therapy was stopped. Six weeks after infliximab was discontinued, serum ALT, AST and γGT activities were normal. The patient was treated with adalimumab (40 mg/2 weeks) with no recurrence of liver test abnormalities after a follow-up of six months.

We believe that this is the first published case showing the absence of hepatic cross-toxicity between infliximab and adalimumab. The originality of this case is the absence of any confounding factors. We obtained a certain diagnosis...
by reintroduction and a control liver biopsy. Hepatotoxicity induced by infliximab has been described in patients treated for rheumatoid arthritis, psoriasis or ankylosing spondylitis [1—4]. Five published reports in the literature described successful retreatment of these patients with etanercept and good hepatic tolerance [1—5]. Etanercept is not suitable for treating Crohn’s disease but adalimumab produced good results in this case. Our report showed that adalimumab is a treatment option in patients with severe Crohn’s disease who develop toxic hepatitis to infliximab.

Conflict of interest statement

None.

References


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Available online 26 February 2010