Hepatotoxicity due to etanercept abated after dose reduction in a patient with pustular psoriasis and without compromised efficacy

Dear Editor,

We were interested to read the recent report on successful treatment with infliximab in a patient with rheumatoid arthritis (RA) following etanercept and adalimumab-related hepatotoxicity (1). We have also experienced etanercept-related hepatotoxicity, although in a patient with pustular psoriasis.

Case report

A 26-year-old man had an 8-year history of pustular psoriasis. He had received systemic conventional therapies, including oral acitretin, cyclosporine or methotrexate, and achieved partial remission. In April 2011, he was admitted with a further exacerbation of psoriasis. Baseline biochemistry tests were normal, and the HCV-antibody and HBV markers were negative. Etanercept was commenced at 50 mg/week subcutaneously. After the third dose, the psoriasis showed noticeable clinical improvement. However, the biochemical tests showed liver dysfunction, which progressively deteriorated over the next 6 weeks. Laboratory tests revealed an ALT level of 305 U/L (normal up to 40 U/L), AST level of 72 U/L (normal up to 40 U/L), and GGT level of 153 U/L (normal up to 40 U/L); the bilirubin and alkaline phosphatase were within normal range. Blood screening for autoantibodies and virological markers was negative. Etanercept was withdrawn and liver function tests returned to normal limits. Subsequently, the patient’s psoriasis re-flared and etanercept was reintroduced at 25 mg twice weekly. Routine biochemistry showed liver enzymes increased again. Suspicion of drug-induced hepatitis and the limited treatment options available for this patient led to etanercept being reintroduced but at a lower dosage (25 mg/week). Two months after the reduction of etanercept, all elevated liver enzymes had returned to within the normal range (Fig. 1). Thereafter, liver function tests showed values within normal range, and psoriasis remained stable during the following 10 months of uninterrupted etanercept treatment and follow-up.

Discussion

The mechanism of hepatotoxicity induced by TNF-α antagonist has not yet been clarified. Predisposing genetic background, underlying liver diseases, and consumption of alcohol may be contributing factors (2,3). Unpredictable idiosyncratic drug-induced liver injury seems most likely, and study had suggested that humoral and cell-mediated immune responses are important in this pathogenesis (2). In our case, it seems highly likely that etanercept was responsible for the liver dysfunction since the liver function test was normal at baseline, the onset of hepatotoxicity appeared after three injections, no evidence of another cause of hepatitis was found, and the liver dysfunction regressed after drug withdrawal and hepatitis recurred upon re-challenge with etanercept. Previously published data have suggested an absence of hepatic cross-toxicity among the different TNF-α antagonists (1,2). Unfortunately, both infliximab and adalimumab were unavailable in our hospital at the time, and we had to use a strategy of lowering the dose of etanercept in an attempt to alleviate the hepatotoxicity.

Etanercept has been demonstrated to be less strongly associated with liver enzyme elevation in patients with RA than either infliximab or adalimumab (4). Moreover, only a few cases of etanercept-related hepatotoxicity have been reported (1,3,5-7).
The precise incidence rate remains unknown. Van Denderen et al. (3) reported that nine out of 105 patients with ankylosing spondylitis developed liver dysfunction after etanercept treatment; this incidence of 9% is significantly higher than the incidence rates reported in the general population (1.0%-1.1%) (4).

We recommend periodic monitoring of liver enzymes for patients treated with etanercept. Etanercept therapy should be temporary or discontinued in patients with serious liver dysfunction (3,5). Etanercept-induced hepatotoxicity abated after switching to infliximab therapy in one case (1), while in another two patients (6,7), as in our case, reducing the dose of etanercept was a successful strategy to balance the effectiveness against hepatotoxicity.

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References