

Case Report

Successful Treatment with Adalimumab in a Patient with Psoriasis vulgaris after Infliximab-Related Liver Injury

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Abstract

Liver injury caused by infliximab is rare. Only 2 cases have been reported, and both of them were successfully treated with etanercept after cessation of infliximab. No recurrence of liver injury during the treatment of etanercept was considered to be due to no cross reactivity with infliximab. We present a 36-year-old male with psoriasis developing liver injury with infliximab. Adalimumab has been suspected to recur liver injury because of similar mechanism of action to that of infliximab. However, our case was successfully treated with adalimumab without liver-function abnormalities. Adalimumab is a useful substitute for infliximab, suggesting toxicity or antigenicity of mouse/human chimera monoclonal antibody against TNF- α .

Introduction

Infliximab and adalimumab are anti-tumor necrosis factor (TNF)- α antibodies used in the treatment of moderate to severe psoriasis vulgaris in Japan. Etanercept use is not allowed in Japanese patients with this disease. A remaining option for psoriasis vulgaris treatment in Japan before March 2015 was ustekinumab. We present a patient with psoriasis vulgaris successfully treated with adalimumab after infliximab-related liver injury. When the patient was treated, biological agents available for psoriasis were only infliximab, adalimumab, and ustekinumab.

Case Report

A 36-year-old male presented with a 12-year history of psoriasis vulgaris seeking treatment with biological agents. The patient was otherwise healthy, but obese (body mass index, 30.8 kg/m²). Physical examination revealed multiple keratotic red plaques all over the body and a Psoriasis Area and Severity Index (PASI) of 21.6 (Figure 1). Laboratory tests

revealed positive anti-hepatitis B surface (HBs) and anti-hepatitis B core (HBc) antibodies, but negative HBs antigen and HB virus (HBV) DNA. Although the aspartate transferase (AST) and gamma-glutamyl transferase (γ -GT) levels were within the normal ranges, alanine transferase (ALT) level was 43 U/L (normal 6–30 U/L), which was attributed to fatty liver revealed on echogram. Ustekinumab was first administered, following the patient's request, resulting in a poor response. Infliximab was then administered and remarkably improved psoriasis, reducing PASI to 4.4 after 3 infusions at a dose of 5 mg/kg (weeks 0, 2, and 6) (Figure 2). However, at week 14, AST (normal, 13–33; 29 U/L at week 0), ALT (67 U/L at week 0), and γ -GT (normal, 10–47; 75 U/L at week 0) increased to 193, 488, and 194 U/L, respectively. At this point, we referred the patient to a hepatologist. Along with the absence of detection of HBs antigen and HBV-DNA, results of anti-nuclear antibody (ANA), hepatitis A and C, Epstein-Barr virus, herpes simplex virus, and cytomegalovirus blood screening and immunoglobulin G were negative or within normal ranges. Physical examination was otherwise unremarkable, and no sign of hepatic failure were observed.



Figure 1a



Figure 2a



Figure 1b
Figure 1. Clinical manifestation before treatment.

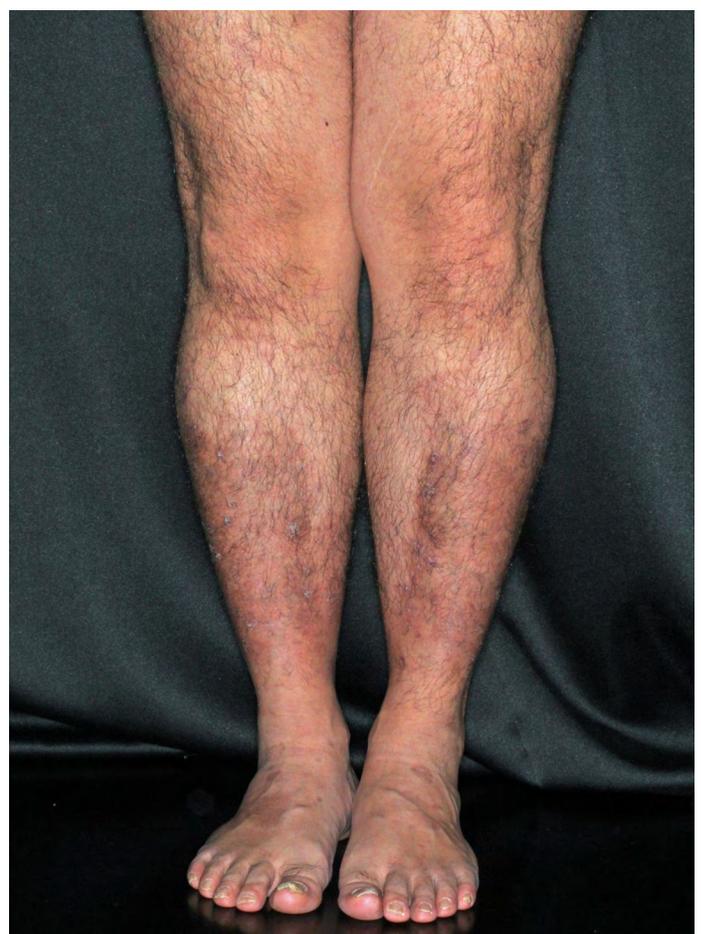


Figure 2b
Figure 2. Clinical manifestation after 3 infusions of infliximab. Post-inflammatory pigmentation is seen.

The patient denied any history of recent alcohol intake or use of new medication, and body weight was reasonably stable. A diagnosis of liver injury due to infliximab was established. Liver function tests normalized 3 months after cessation of infliximab, along with administration of mono-ammonium glycyrrhizinate and ursodeoxycholic acid. Liver biopsy was not performed. Despite a possible recurrence of liver injury with anti-TNF- α antibodies treatment, which may result in hepatic failure, the patient was eager to receive the treatment. Hepatologist prohibited the use of infliximab, but reluctantly allowed the use of adalimumab with careful monitoring. Adalimumab (45 mg) was subsequently started and PASI was 9 at that time. Three months later, the dose of adalimumab was increased to 90 mg because of inadequate efficacy, resulting in a decrease in PASI to 5.0 in 2 months. Liver injury did not recur during adalimumab treatment.

Discussion

Infliximab rarely reactivates HBV. Only 3 patients with positive HBC antibody and negative HBs antigen underwent HBV reactivation during treatment with infliximab, and these patients suffered from inflammatory bowel disease or rheumatoid arthritis [1]. Infliximab occasionally induces autoimmune hepatitis or immunomediated hepatitis, in which ANA becomes positive [2]. Since ANA was negative in our case, this type of hepatitis was excluded. Infliximab-related liver injury was diagnosed based on the absence of infectious disease or external intervention. Only 2 similar patients with psoriasis have been reported [3,4]. In both cases, psoriasis was successfully treated with etanercept without inducing liver-function abnormalities, and after <6 weeks of cessation of infliximab, liver function normalized. Since etanercept, a soluble TNF- α -receptor fusion protein, does not cross-react with infliximab, it was used as an alternative [3,4]. Adalimumab, a humanized monoclonal antibody against TNF- α , is suspected to have a similar

mechanism of action to that of infliximab on liver function. Our case shows that adalimumab is a useful substitute for infliximab, suggesting toxicity or antigenicity of mouse/human chimera monoclonal antibody against TNF- α .

Considering a possible recurrence of liver injury with adalimumab, it may not have been appropriate to treat this patient with adalimumab even though the patient was eager to receive the treatment. However, the patient did not want any treatment other than biological agents. We carefully monitored liver function every week for the initial 1 month after initiation of adalimumab to find liver-function abnormalities as quickly as possible. The patient was satisfied with our treatment.

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Conflict of interest

None.

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