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CASE REPORT

Treatment of Atopic Dermatitis with Upadacitinib in a Patient During Hepatitis C Activity Period

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Abstract: This case report aims to explore the efficacy and safety of upadacitinib in patients with severe atopic dermatitis during hepatitis C activity period, providing reference for the treatment of severe atopic dermatitis patients in clinical hepatitis C activity period. We reviewed the treatment history of a patient with severe atopic dermatitis with hepatitis C in our hospital and analysed the safety of applying upadacitinib for the treatment of severe atopic dermatitis in conjunction with the review of relevant literature. During the 1-year follow-up, the patient's peripheral rash gradually improved, and the hepatitis C viral RNA load was normalised at the 6-month follow-up, reaching the clinical criteria for hepatitis C cure. The patient took only oral triamcinolone and upadacitinib for half a year after hepatitis C cure, and no recurrence of hepatitis C or liver function abnormality was found. Upadacitinib can be considered as a treatment option for patients with severe atopic dermatitis during hepatitis C activity period, but more clinical cases and drug research are needed to assess its safety during hepatitis C activity period.

Keywords: upadacitinib, atopic dermatitis, hepatitis C, case report

Introduction

Atopic dermatitis (AD), also known as atopic eczema, is a chronic inflammatory skin condition characterized by itching, redness, and the formation of dry, scaly patches on the skin. In addition, severe patients may experience conditions such as oozing and crusting. Patients with AD often have a compromised skin barrier function, allowing allergens and irritants to penetrate the skin more easily, triggering an immune response and inflammation.[1] For patients with severe atopic dermatitis, traditional treatments have limited efficacy and are associated with increased adverse reactions. Biologics and JAK inhibitors have emerged as new options in the treatment regimen.[2] However, for patients with hepatitis, it is of importance to choose new therapies cautiously. A 9-year cohort study found that the use of biologics in patients with psoriasis carries a risk of reactivation of hepatitis B virus (HBV) and hepatitis C virus (HCV), with seropositivity for hepatitis B surface antigen and e-antigen and treatment with a tumour necrosis factor-alpha inhibitor as risk factors for reactivation of HBV, although no predictors of reactivation were found in relation to HCV.[3] The safety of upadacitinib is controversial, in patients with AD, the meta-analysis[4] has shown that the risk of cardiovascular adverse events and thrombosis with JAK inhibitors is small with both long-term and short-term use and is generally within the safe range. However, the limited clinical data related to chronic infections such as viral hepatitis, there is currently a lack of reference basis for the safety issues of JAK inhibitors in this group of patients.[5] Liver function needs to be monitored when using JAK inhibitors in the treatment of patients with atopic dermatitis, it is not recommended for patients with AD with comorbid active hepatitis B or hepatitis C.[6] The study[7] has reported a case of a patient with active hepatitis C who effectively and safely treated AD with dupilumab. Currently, there are no reports in the literature on the treatment of severe AD with active hepatitis C combined with cirrhosis with upadacitinib. This article describes the case of a patient

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with AD who was infected with HCV and treated with upadacitinib and reviews the relevant literatures. It aims to provide new treatment ideas for patients with severe atopic dermatitis complicated by HCV infection.

Case Presentation

A 59-year-old male, presented with diffuse erythematous plaques and nodules accompanied by itching for over 7 months, worsening over the past month. The patient reports that he was diagnosed with hepatitis C with cirrhosis 2 weeks ago. After taking the liver-protecting drugs, he felt that the itching had worsened, so the liver-protecting drugs were discontinued.

Clinical and Histopathologic Findings

The physical examination reveals diffuse dark red patches and indurations covering the body, with some coalescing into plaques. Additionally, scattered skin lesions are observed to be oozing and crusting (Figure 1). Perivascular lymphocytic infiltration with scattered eosinophils in the superficial dermis, psoriasiform epidermal hyperplasia, irregular elongation of rete ridges, spongiosis with exocytosis of inflammatory cells, and superficial crust formation (Figure 2). During hospitalisation, methylprednisolone 40mg/d and topical hydrocortisone butyrate cream were given to the patient, but the itching was not relieved. After excluding abnormalities of the blood and liver functions, the patient began to take oral upadacitinib sustained-release tablets 15mg/d; on the day of the patient's administration of the drug, the itching of the peripheral body decreased significantly, and the Pruritus Numeric Rating Scale (Pruritus-NRS) was relieved by 50%, after 5 days the nodules flattened, and some of the erythema was pale, and the methylprednisolone was adjusted to 20mg/d. Figure 1 shows the patient's skin on the 10th day after taking the

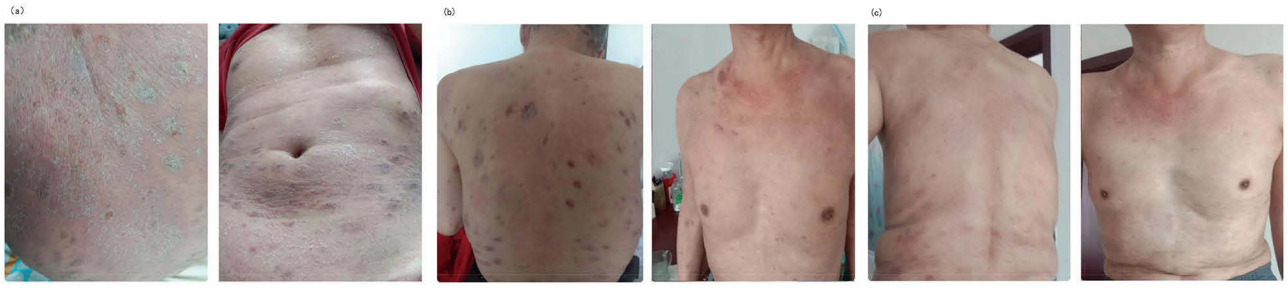

Figure 1 Changes in skin lesions before and after the patient's use of upadacitinib. (**a**) Before medication; (**b**) After medication for 10 days; (**c**) After medication for 55 weeks.

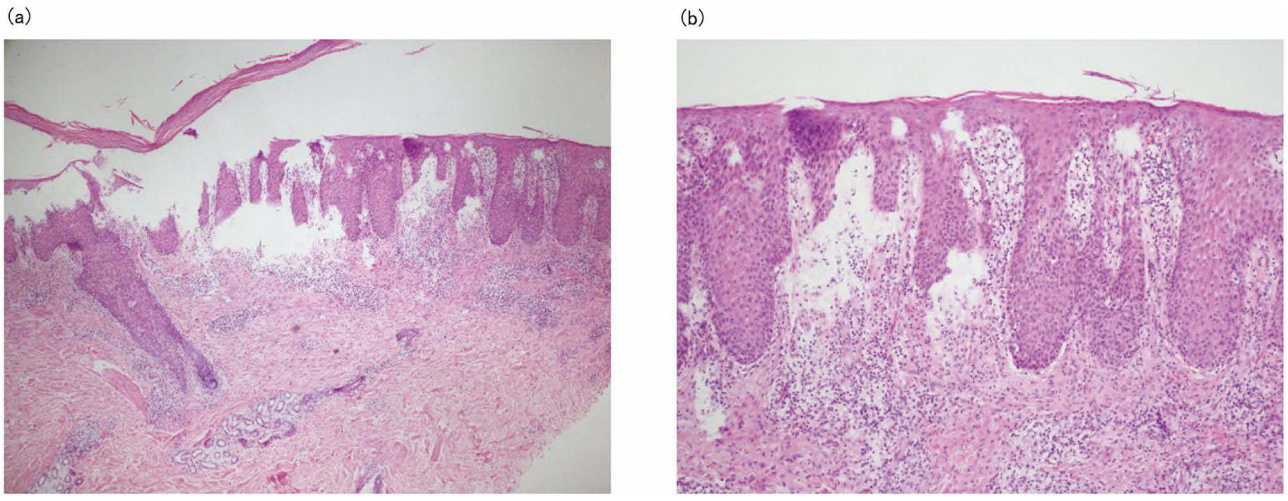

Figure 2 Pathological results of patient. (**a**) HE staining at 40x magnification; (**b**) HE staining at 100x magnification.

medicine. After discharge, the patient was started to have 6 months of continuous oral direct-acting antiviral agents (DAAs) after 10 weeks of treatment. After 22 months of treatment with upadacitinib, his disease remains well controlled (Figure 1), with no observed adverse drug reactions. Furthermore, there has been no recurrence of hepatitis C, and follow-up testing has shown an almost undetectable HCV viral load.

Discussion

Upadacitinib, an oral JAK inhibitor engineered for increased selectivity toward JAK1 over other JAKs, selectively inhibits JAK1, thereby disrupting the signaling of numerous proinflammatory mediators. It also modulates CD4 regulatory T cells (Tregs) to suppress immune system overactivation.[8] Previous meta-analyses have shown that hepatitis B virus carriers and patients with cured hepatitis B virus infection are at risk of hepatitis B reactivation with corticosteroid use.[9] We hypothesize that the use of JAK inhibitors and corticosteroids may be a suitable therapeutic regimen for patients with atopic dermatitis combined with hepatitis C. The use of JAK inhibitors will help to assist in the reduction of corticosteroid dosage and in the control of the disease progression JAK inhibitors will help to assist in corticosteroid tapering, in controlling disease progression while mitigating the risk of reactivation of HCV associated with high-dose corticosteroids, and enabling patients to transition to moderate or low-dose corticosteroid therapy as soon as possible. In addition, a 24-week head-to-head comparative study between upadacitinib and dupilumab found that, compared with dupilumab, upadacitinib can more rapidly relieve patients' itching and skin lesions, and it also has good safety.[10] Considering this characteristic comprehensively, upadacitinib is suitable for this patient to relieve itching. The patient in this case met the clinical cure criteria for hepatitis C after six months of regular use of DAAs. During the six months of follow-up, the patient was taking only 20 mg corticosteroids and 15 mg upadacitinib, and no risk of reactivation of hepatitis C was observed. However, it is worth noting that aberrant activation of Tregs in the peripheral blood and liver suppresses the body's antiviral immune response and promotes liver fibrosis during the natural course of chronic HCV infection. Although previous studies have shown that DAAs can achieve a high cure rate, DAAs cannot reverse the over-activation of Tregs long after HCV elimination, and an increased risk of HCV re-infection, continued progression of cirrhosis, and even the development of hepatocellular carcinoma are possible complications after HCV elimination with DAAs.[11] While it is of concern whether the feature of upadacitinib to increase the number and function of Tregs and thus modulate the excessive autoimmune response would exacerbate the progression of liver fibrosis and induce HCV reactivation in cirrhotic patients, during our follow-up, we found that there was no further progression of hepatic fibrosis on magnetic resonance imaging (MRI) and the RNA load of HCV was not found to be abnormal in our patient. In conclusion, upadacitinib emerges as an effective and relatively safe therapeutic option for patients grappling with immune-mediated disorders. However, clinicians typically exhibit hesitancy when considering its prescription for individuals with chronic HCV infection, given its immunomodulatory properties and potential association with severe infections. This apprehension includes concerns over the reactivation of latent hepatitis C virus and the heightened risk of morbidity and mortality associated with active HCV.[12]

Conclusion

This case has revealed that the long-term use of upadacitinib in the treatment of patients with severe AD who have both hepatitis C and liver cirrhosis demonstrates good efficacy and safety. After the patient stopped using anti-hepatitis C drugs, there was no occurrence of HCV reactivation. However, currently, patients with AD complicated by hepatitis C still account for a small proportion in real-world studies. The mechanism regarding whether upadacitinib will increase the potential activation risk of past hepatitis C virus infection in patients with AD still requires further exploration and research.

Consent to Publish Statement

The patient consents to the publication of relevant materials in this journal and related publishing media. This case report does not involve any identifiable patient information, poses no potential risks to the patient, and is not subject to review by an ethics institution.

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Disclosure

Junke Huang, Mingyue Wang are co-first authors for this study. All authors declare that they have no competing interests for this work.

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