Epidermolysis Bullosa Pruriginosa Treated with Baricitinib

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Epidermolysis Bullosa Pruriginosa Treated with Baricitinib:A Case Report

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EBP: Epidermolysis Bullosa Pruriginosa

JAK-STAT: Janus kinase-signal transducer and activator of transcription

JAK: Janus kinase

DEB: Dystrophic Epidermolysis Bullosa

VAS: The Visual Analogue Scal

Abstract : **Introduction:** Fewer than 100 cases of Epidermolysis Bullosa Pruriginosa(EBP) have been reported to date. Numerous inflammatory dermatoses are driven by soluble inflammatory mediators, which rely on Janus kinase-signal transducer and activator of transcription (JAK-STAT) signaling, and inhibition of this pathway using Janus kinase (JAK) inhibitors might be a useful therapeutic strategy for these diseases. Chronic inflammation is a hallmark of Dystrophic Epidermolysis Bullosa (DEB), thus upregulation of inflammatory cytokines and JAK signaling may play a role in DEB-related pruritus. EBP is a persistent, recurring disease that seriously affects quality of life. **Patient concerns:** A male patient, 28 years of age, was admitted to our hospital because of recurrent papules, nodules, and intense itching on the trunk and extremities for 12 years. Repeated large and intense itching for 12 years has seriously affected the patient's normal life.**Diagnosis:** The patient was diagnosed with Epidermolysis Bullosa Pruriginosa based on examination results. **interventions:** Oral baricitinib tablets (2 mg, once a day) + Oral desloratadine citrate disodium tablets (8.8 mg, once a day) combined with topical compound flumethasone ointment and Fucidin cream. **outcomes:** The patient's skin rashes had subsided and flattened significantly, and his itching was markedly relieved. The Visual Analogue Scal (VAS) itching score of the patient had gradually declined from

8–9 points to 2–3 points. **Conclusion** : this study confirms that baricitinib is effective and feasible in treating EBP, especially in significantly relieving itching, which rendered new ideas for therapeutic approaches for EBP in the future.

Keywords: Epidermolysis Bullosa, kinase inhibitors, Baricitinib Treatment

INTRODUCTION

EBP is characterized by recurrent itching and pruritic nodules. In the case of intense itching, skin becomes fragile, resulting in thickening and lichenification. In most cases, skin rashes are distributed over lower extremities, forearms, elbows, dorsum of hands, shoulders, and lower back, especially the extensor aspect of the extremities. Baricitinib is a reversible, selective inhibitor of tyrosine protein kinase, which is capable of modulating the signal transduction of helper T-cells (Th1, Th2, Th17, and Th22) and might cause many immune-mediated disorders. EBP is characterized by nodular prurigo-like lichenoid lesions with intense itching, in addition to the features of DEB, such as blisters and onychodystrophy.[1] Currently, EBP is treated with topical corticosteroids, tacrolimus, and oral thalidomide, but the outcomes are often unsatisfactory.[2-3]Baricitinib is a reversible selective inhibitor of tyrosine protein kinase, which is capable of modulating the signal transduction of helper T-cells (Th1, Th2, Th17, and Th22) and participates in many immune-mediated disorders. Here, one case of baricitinib in the treatment of EBP is discussed.

CASE PRESENTATION

A male patient, 28 years of age, was admitted to our hospital because of recurrent papules, nodules, and intense itching on the trunk and extremities for 12 years. The patient had visited another hospital 12 years ago (in 2010). He was diagnosed with EBP based on examination results from other hospitals (Figure1A) and herpetic autoantibody test results.

The patient had visited other hospitals several times due to disease relapse, but the outcomes were often unsatisfactory (Figure2). The patient came to our hospital on August 2,2021. The physical examinations revealed multiple reddish-brown hemispherical mung bean-to-soybean-sized nodules were symmetrically distributed on the trunk and extremities, densely packed in patches, some of which were anabrotic and crustosus due to scratching (Figure 1C and 1D). Laboratory test results indicated routine blood and urine test with normal liver and kidney function, blood function, blood electrolytes, and blood sedimentation were normal.

METHODS

We did a pathology biopsy on him again (Figure1B). He underwent symptomatic treatment with oral baricitinib tablets (2 mg, once a day) + oral desloratadine citrate disodium tablets (8.8 mg, once a day) combined with topical compound flumethasone ointment and Fucidin cream since August 2, 2021. The Visual Analogue Scale (VAS) scale for the degree of itching was adopted to assess the severity and control of the disease. The VAS score of the patient was 7–8 points at the initial diagnosis.

CONCLUSION AND RESULTS

During the 2 years of treatment with baricitinib, the VAS itching score had steadily decreased (Figure 2), and the patient reported significant improvement in itching and sleep quality after treatment, without any adverse effects. After discontinuation of baricitinib for 2 weeks, in July 2022, the patient returned to the clinic for reexamination, and the results indicated that the number of skin rashes on the outer side of both

thighs had decreased by half, and the color had become dull, although some dark brown hyperpigmentation and scars remained on the extensor aspect of both lower legs. (Figure 1E and 1F). The results of regular reexaminations showed routine blood and urine with normal liver and kidney function and electrolytes. Currently, the patient is still under follow-up.

DISCUSSION

DEB is an autosomal dominant or recessive genodermatosis caused by variations in COL7A1. Its pathogenesis is not completely understood. EBP is characterized by nodular prurigo-like lichenoid lesions with intense itching, in addition to the features of DEB, such as blisters and onychodystrophy. [1] Currently, EBP is treated with topical corticosteroids, tacrolimus, and oral thalidomide, but the outcomes are often unsatisfactory.[2-3] Baricitinib is a reversible selective inhibitor of tyrosine protein kinase, which is capable of modulating the signal transduction of helper T-cells (Th1, Th2, Th17, and Th22) and participates in many immune-mediated disorders. Here, one case of baricitinib in the treatment of EBP was discussed.

This case clinically presented with dense nodular, keratotic papules, mainly on the extensor side of both lower limbs, which were brownish in color, with umbilical concavity at the center of some of them, and subepidermal blisters could be seen by the results of the examination, while there were no obvious eosinophils in the blisters, and there was mixed inflammatory cell infiltration in the dermis, so we considered this to be a case of a specific type, Epidermolysis Bullosa Pruriginosa. Janus kinase-signal transducer and activator of transcription (JAK-STAT) is an intracellular signaling pathway upon which many different proinflammatory signaling pathways converge. Numerous inflammatory dermatoses are driven by soluble inflammatory mediators, which rely on JAK-STAT signaling, and inhibition of this pathway using JAK inhibitors might be a useful therapeutic strategy for these diseases. Evidence suggests that the dysregulation of helper T-cell (Th1, Th2, and Th17) signal transduction is implicated in epidermolysis bullosa. Chronic inflammation is a hallmark of DEB, thus upregulation of inflammatory cytokines and JAK signaling may play a role in DEB-related pruritus. Caroppo reported one case of EBP who was successfully treated with dupilumab. Dupilumab can dually block and inhibit both IL-4 and IL-13 and suppress Th2-mediated inflammatory responses, thus significantly improving skin lesions and relieving itching.[4] This suggests that EBP may be triggered by Th2 immune mechanisms. In addition, it was reported that baricitinib could alleviate itching associated with AD, and the significant relief of itching proves the effectiveness of this strategy, which is the rationale behind the application of baricitinib in our hospital for targeted treatment through its downstream JAK-STAT signal. JAK may be a favored target for EBP-associated symptoms. Moreover, considering the affordability and durability of the treatment regimen for patients, baricitinib has become the preferred treatment choice in our clinic instead of dupilumab. Jiang XY et al. reported one case of EBP in a 40-year-old man without a family history of DEB and with severe skin lesions and intense itching, which is significantly improved after treatment with baricitinib. [5] He was followed up once every 2 weeks until 16 weeks, and then every 8 weeks. The scores of all three indicators decreased over time. Joo Kwon retrospectively reviewed the medical records of DEB patients with refractory pruritus who were treated with either baricitinib, a JAK1/2 inhibitor, or upadacitinib, a selective JAK1 inhibitor. A total of 12 DEB patients (six recessive DEB and six dominant DEB) were included in this study. The mean±SD baseline pruritus visual analog scale score was 7.5 ± 1.7. Upadacitinib or baricitinib treatment resulted in a rapid and sustained decrease in itch.[6]

In this paper, one case of EBP was discussed. The patient had a long history of EBP and a relevant family history of the disease. The typical skin lesions initially manifested as multiple lichenoid papules and nodules on both lower extremities, especially their extensor aspect, with scars forming in the center of the larger nodules, accompanied by mild scale. Combined with the fact that the results of previous examinations, the herpetic autoantibody test, and other examinations were all negative, prurigo nodularis and herpes could be excluded. The patient had intense itching, which is one of the important manifestations of EBP. The patient had received traditional treatment for more than 10 years, and while the progression of the disease had been controlled to a certain extent, the outcome of itching relief was unsatisfactory. The patient was treated

with baricitinib in our hospital with the hope of relieving the itching. During the 2 years of treatment with baricitinib, the patient's skin rashes had subsided and flattened significantly, and his itching was markedly relieved. The VAS itching score of the patient was assessed at follow-up, and the point plot showed that the score had gradually declined from 8–9 points to 2–3 points, indicating a greatly improved quality of life.

EBP is a persistent, recurring disease that seriously affects quality of life. this study confirms that baricitinib is effective and feasible in treating EBP, especially in significantly relieving itching, which rendered new ideas for therapeutic approaches for EBP in the future. Particularly important for patients suffering from severe itchiness.

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AUTHOR CONTRIBUTIONS

Zhe He: Conceptualization; writing – original draft; writing – review and editing. **Rui Zheng:** Writing – original draft; writing – review and editing. **Qian Dong:** Writing – original draft; writing – review and editing. **Yue Xi:** Writing – original draft; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

There are no conflicts of interest to declare.

ETHICS STATEMENT

None.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

DATA AVAILABILITY STATEMENT

All the required information is in the manuscript itself.

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Figure 1 Hyperkeratosis, epidermal hyperplasia, and fissures can be seen at the junction of the true epidermis, inflammatory cells, mainly lymphocytes, were seen around the vessels in the superficial dermis (A, scale bar: 50μm). Epidermis showed subepidermal bulla. Dermis shows mixed inflammatory infiltrate (B, HE×40). multiple reddish-brown hemispherical mung bean-to-soybean-sized nodules were symmetrically distributed on the bilateral calves and right thigh, densely packed in patches, some of which were anabrotic and crustosus due to the intense itching (C and D). After 2 years of baricitinib treatment, the results uncovered that the number of skin rashes on the outer side of both thighs had decreased by half, and the color had become dull, although some dark brown hyperpigmentation and scars remained on the extensor aspect of both lower legs (E and F).

Figure 2 Change in VAS after oral baricitinib treatment showed a gradual downward trend, Patient's past and current treatment plan.