Case Report

Refractory Epidermolysis Bullosa Pruriginosa with Rapid Clinical Response to Upadacitinib Treatment

Zeynep Utlu, Zeynep Arslan, Zeynep Karaca Ural
Department of Dermatology and Venereology, Atatürk University Faculty of Medicine, Erzurum, Türkiye

Abstract

Epidermolysis bullosa pruriginosa (EBP) is a rare subtype of dystrophic EB. Topical corticosteroids, tacrolimus, oral thalidomide, and immunosuppressants are among the treatment options that can be given, but there is no consistently effective treatment. Some case reports have shown positive results in treatment with omalizumab, dupilumab, and Janus kinase inhibitors. We present a 37-year-old female EBP patient who had not responded to multiple previous treatments (systemic steroids, hydroxychloroquine, dapsone, omalizumab, and cyclosporine) but achieved a rapid clinical response to upadacitinib treatment. We are sharing our case to encourage the consideration of upadacitinib as an alternative treatment for refractory EBP cases.

Keywords: Epidermolysis bullosa pruriginosa, JAK inhibitors, upadacitinib

Introduction

Epidermolysis bullosa pruriginosa (EBP) is a rare subtype of dystrophic EB (DEB), a group of autosomal dominant or recessive genodermatoses caused by mutations in the *COL7A1* gene.[1] There is no definitive cure, but topical corticosteroids, tacrolimus, oral thalidomide, and immunosuppressants are among the treatment options that can be given to EBP cases.[1]

Mutations in the *COL7A1* gene result in deficient or dysfunctional collagen VII, which leads to dysfunction of the anchoring fibrils beneath the basal lamina.[2] In addition to the features of DEB, such as vesiculobullous lesions and nail dystrophy, EBP also presents with intensely pruritic, nodular, prurigo-like lichenified lesions.

We present a rapid clinical response to upadacitinib therapy in a patient with EBP who had previously tried treatments without response.

Case Report

Our 37-year-old female patient presented to our dermatology clinic with complaints of rash and itching that had persisted for 1.5 years. She had previously undergone five different biopsies at external centers, none of which could provide a definitive diagnosis. The genetic test diagnosed EBP due to the Col7a1 mutation. She had no known skin disease or other chronic disease. The patient has 3 living healthy children after one miscarriage. Her children do not exhibit any signs of EB. There isn't known history of skin, autoimmune, or hereditary disease in the patient's first-degree relatives, except for rheumatoid arthritis (RA) in the mother.

Dermatological examination revealed vesiculobullous lesions on the back, predominantly in the sacral and bilateral lumbar regions; along the bilateral upper extremities, predominantly on the extensor face; concentrated in the bilateral pretibial areas; along the entire crus and thighs, thoracic and abdominal regions; and on the scalp. These bullous lesions had opened, resulting in widespread eroded lesions with an erythematous

Adress for correspondence: Zeynep Utlu, Assoc. Prof., MD, Department of Dermatology and Venereology, Atatürk University Faculty of Medicine, Erzurum, Türkiye
Email: dr.zeynep.utlu@gmail.com
ORCID ID: 0000-0002-0178-2871

Submission: 22-Oct-2024 **Web Publication:** 04-Jun-2025
Acceptance: 27-Dec-2024

Access this article online

Quick Response Code:

Website: www.turkjdermatol.com

DOI: 10.4274/tjd.galenos.2024.83803

How to cite this article: Utlu Z, Arslan Z, Karaca Ural Z. Refractory epidermolysis bullosa pruriginosa with rapid clinical response to upadacitinib treatment. Turk J Dermatol. 2025;19(2):111-114.

base and crusting in some areas. These lesions collectively formed foci of bleeding and infection. In addition, there were scattered milia all over the body (Figure 1). The skin lesions were accompanied by severe pruritus. There was a complaint of stricture in the proximal oesophagus due to EBP involvement.

The patient was given systemic steroids, hydroxychloroquine, dapsone, omalizumab, and cyclosporine treatments in other clinics, but no treatment elicited a response.

When she applied to our service, the patient had not received any systemic treatment for 15 days, and her laboratory tests were as follows: hemoglobin: 6.3, erythrocyte sedimentation rate: 111 (reference range 0-25), and C-reactive protein: 147 (reference range 0-5). During his hospitalization, his numerical rating scale (NRS) score was ten, and pruritus control was attempted with a combination of antihistamines. After one month of symptomatic treatment, including intravenous antibiotics, systemic antihistamines, topical steroids, epithelializers, there was no improvement in pruritus and new lesions continued to appear.

The 40 kg patient was started on upadacitinib at a dose of 15 mg/day. On the second day of treatment, pruritus decreased. On the 10th day, the patient's NRS score was 2. No new lesions were observed, and existing lesions regressed rapidly (Figure 2).

Discussion

EBP is a rare subtype of DEB, characterized by hallmark DEB features, including vesiculobullous lesions and nail dystrophy. Additionally, hypertrophic, lichenified, and pruritic plaques or nodules, which typically emerge during adolescence but may be present at birth, are frequently observed. Over time, these lesions can lead to purplish linear scarring and milia formation.[3] Our patient presented with nail dystrophy and vesiculobullous lesions on an erythematous base, which were predominantly distributed in trauma-prone regions, such as the sacral area and extensor surfaces of the extremities. These lesions were associated with crusting and erosion, and their chronicity or healing resulted in the development of papules, plaques, scarring, and milia. The disease involved nearly 75% of the patient's body surface, sparing only the face and palmar

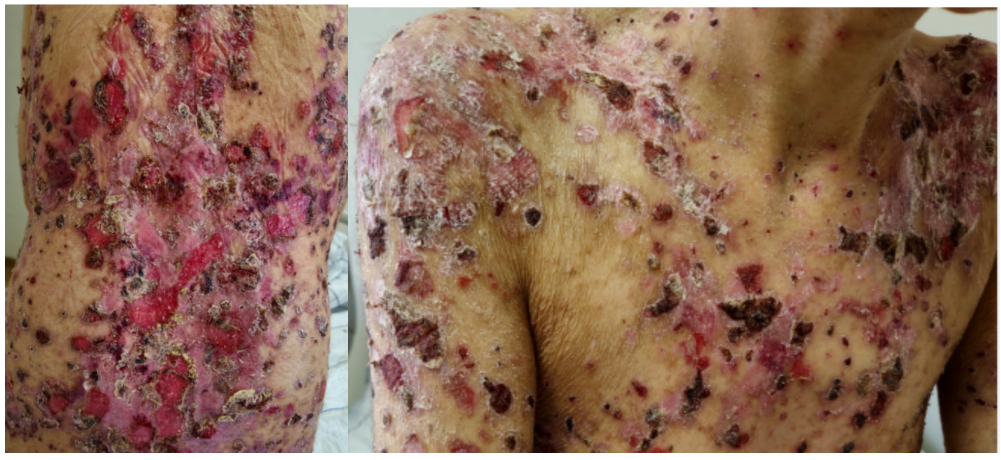

Figure 1. Skin lesions at the time of patient's admission to our service

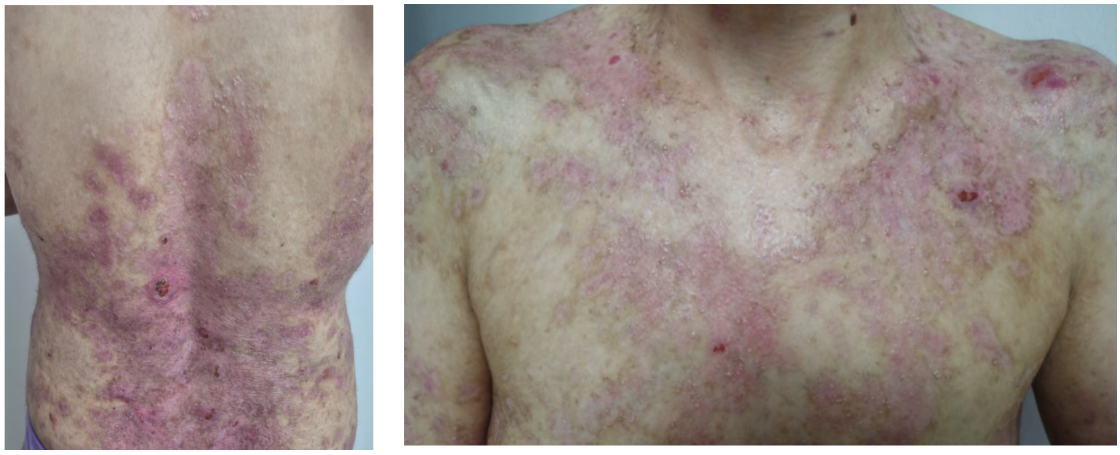

Figure 2. Skin lesions on day 10 of the patient's upadacitinib therapy

regions. Mucosal involvement was also noted with a proximal esophageal stricture.

The diagnosis of EBP relies on a combination of clinical features, histopathological findings, and genetic testing. Characteristic trauma-induced lesions, family history, and molecular analysis are key diagnostic pillars.[3] In this case, no family history of similar symptoms was reported, and the patient's complaints had begun 1.5 years before presentation. During this period, six skin biopsies were performed, which revealed findings consistent with DEB, including subepidermal cleavage, fibrin deposition, milia, hyperkeratosis, vascular proliferation, and perivascular lymphohistiocytic infiltration. However, a definitive diagnosis could not be established until genetic testing identified a pathogenic mutation in the *COL7A1* gene, confirming the diagnosis of EBP.[4]

The exact pathogenesis of pruritus in EBP remains unclear, and our treatment goals are to eliminate pruritus and prevent new lesions. Recently, EBP has been shown to have a Th2 cell-driven immune response, resulting in elevated serum levels of interleukin (IL)-4, IL-5, IL-13, and IgE.[5] Furthermore, some case reports have demonstrated favourable responses to omalizumab[6] and dupilumab[2] in EBP patients, supporting this notion regarding the underlying pathogenesis of pruritus in EBP. Our patient had previously received omalizumab treatment at an outside centre, which initially reduced pruritus but did not provide long-term success.

Janus kinases (JAKs) are intracellular enzymes that play a role in the signalling of cytokines and growth factors in various cellular processes such as inflammatory response, haematopoiesis, and immune system function. The JAK family of enzymes modulates gene expression and cellular function by phosphorylating signal transducers and activators of transcription. The JAK family consists of four members (JAK1, JAK2, JAK3 and TYK2). Upadacitinib is a selective and reversible JAK inhibitor. It inhibits JAK1 or JAK1/JAK3 signalling via cytokine receptors that involve JAK2. JAK1 inhibition blocks multiple signalling pathways, contributing to symptoms such as skin lesions and pruritus in atopic dermatitis.[7] Two previous cases of EBP have been reported with good treatment outcomes using JAK inhibitors, baricitinib (a JAK1/2 inhibitor)[1] and tofacitinib (a JAK1/3 inhibitor).[8] Upadacitinib, which is indicated for the treatment of RA, psoriatic arthritis, ankylosing spondylitis, atopic dermatitis, and ulcerative colitis[7], has been successfully used off-label in two EBP cases reported in the literature.[2,7] In one case, Kim et al.[5] reported in August 2022 that a significant reduction in pruritus and new lesions wasn't reported after ten weeks of upadacitinib use.

Our patient's clinical response to upadacitinib was much faster, similar to the duration of effect seen in atopic dermatitis, which is also rapid. By the 10th day, the patient's pruritus had nearly entirely resolved. New lesions were not observed, and existing lesions regressed rapidly.

Furthermore, the patient's rapid response highlights the importance of addressing the psychosocial burden associated with EBP. Chronic pruritus and erosive lesions significantly impair quality of life, leading to sleep disturbances, anxiety, and depression.[9] The prompt alleviation of symptoms improved the patient's physical condition and positively impacted her mental well-being, as noted during follow-up visits.

In conclusion, our case highlights the potential role of upadacitinib as a novel and effective treatment for refractory EBP. This therapeutic approach addresses both the inflammatory and pruritic components of the disease, offering a promising alternative for patients who fail to respond to conventional therapies. We are sharing our case to encourage the consideration of upadacitinib as an alternative treatment option for refractory EBP cases.

Ethics

Informed Consent: The authors certify that they have obtained all appropriate patient consent forms. In the forms, the patient has given his/her/their consent for his/her/their images and other clinical information to be reported in the journal.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Z.U., Z.A., Concept: Z.U., Design: Z.K.U., Data Collection or Processing: Z.A., Literature Search: Z.U., Z.A., Writing: Z.A., Z.K.U.

Conflict of Interest: The authors declared that they have no conflict of interest.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Jiang X, Wang H, Lee M, Lin Z. Epidermolysis bullosa pruriginosa treated with baricitinib. JAMA Dermatol. 2021;157(10):1243-1244.
2. Clawson RC, Duran SF, Pariser RJ. Epidermolysis bullosa pruriginosa responding to dupilumab. JAAD Case Rep. 2021;16:69-71.
3. Kim WB, Alavi A, Pope E, Walsh S. Epidermolysis bullosa pruriginosa: case series and review of the literature. Int J Low Extrem Wounds. 2015;14(2):196-199.

4. Issa CJ, Hong AC, Lio PA. Treatment of dystrophic epidermolysis bullosa pruriginosa: a systematic review of clinical outcomes after initiation of dupilumab therapy. Dermatologic Therapy. 2023;1:e3863357.
5. Kim N, Jue MS, Huh YJ, Sung KJ, Kim H, Kim JE, Ko JY. Epidermolysis bullosa pruriginosa with extensive truncal involvement treated with upadacitinib. J Eur Acad Dermatol Venereol. 2022;37(2):e215-e217.
6. Taha SA, Al-Nesf MA, Al-Obaidli AM. Successful treatment of epidermolysis bullosa pruriginosa with anti-IgE therapy (omalizumab): a case report and four years follow up. J Clin Exp Dermatol Res. 2020;11(3):1-3.
7. Zhang Z, Lin Z. Epidermolysis bullosa pruriginosa treated with upadacitinib. JAMA Dermatol. 2024;160(10):1124-1125.
8. Chen KJ, Fang S, Ye Q, Jia M. Successful use of tofacitinib in epidermolysis bullosa pruriginosa. Clin Exp Dermatol. 2022;47(3):598-600.
9. Erturk IE, Arican O, Omurlu IK, Sut N. Effect of the pruritus on the quality of life: a preliminary study. Ann Dermatol. 2012;24(4):406-412.