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A Case of Refractory Facial Erythema in a Patient with Atopic Dermatitis

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Abstract

A 22-year-old female patient had recurrent red rashes on the peripheral skin with itching for more than 10 years. Specialized examination revealed dry and rough skin on the head, face, limbs, and trunk. Multiple hypertrophic plaques of varying sizes, covered with a few scales, were observed on the dorsa of hands, palms, extremities (elbow fossae, popliteal fossae) and dorsa of both feet. **Diagnosis**: Atopic Dermatitis (moderate to severe). **Treatment**: The patient showed a poor response to conventional therapy. After treatment with dupilumab, Atopic Dermatitis symptoms improved significantly. However, facial erythema and swelling were aggravated after six months of this regimen. Upon re-evaluation, dupilumab was discontinued. Oral cyclosporine was administered to alleviate facial erythema, followed by maintenance therapy with upadacitinib sustained-release tablets (15 mg/d), which has not recurred.

Keywords

Atopic Dermatitist, Facial Erythema, Dupilumab, Upadacitinib Sustained-Release Tablets, Cyclosporine

1. Introduction

Dupilumab, a fully humanized IgG4 monoclonal antibody, disrupts interleukin (IL)-4 and IL-13 signaling by binding to the IL-4 receptor alpha (IL-4Rα) subunit [1] [2]. As IL-4 and IL-13 are key factors in Th2-mediated inflammatory responses, dupilumab effectively inhibits type 2 inflammation through this pathway, thereby reducing disease incidence. Dupilumab-associated facial redness (DFR) typically occurs approximately two months after treatment initiation and may be associated with impaired skin barrier function in atopic dermatitis (AD) patients, which allows for fungal colonization and exacerbates the inflammatory response.

In this case, the problem of aggravated facial erythema appeared after six months of treatment. It is worth discussing what caused the facial erythema to occur. Are there better treatment options? The case is reported as follows.

2. Clinical Information

A 22-year-old female patient had a 10-year history of recurrent cutaneous rashes with pruritus. Starting over 10 years ago, papules, erythema and plaques appeared on her body for no apparent reason, and her skin became dry and itchy. She received topical moisturizers, emollients, glucocorticoids, pimecrolimus, and oral loratadine at another hospital. Her condition worsened one year ago. The patient was previously healthy, with a history of allergic rhinitis. Physical examination: A systemic examination showed no significant abnormalities. Dermatological examination: The skin of the entire body, including the face, is dry, dull in color, and rough to the touch. There were scattered red patches, papules, scratches and crusts present. The backs of both hands, palms, elbows, popliteal fossae and the backs of both feet showed multiple hypertrophic plaques of varying sizes covered with a few scales. Laboratory investigations: blood and urine tests, liver and kidney function tests, lipid tests and glucose tests were normal. Atopic dermatitis severity score (SCORAD) was 64.5; lesions covered 60% of the body surface area; Investigator's Global Assessment (IGA) was 4; and itch Numerical Rating Scale (NRS) was 8.

Treatment: The patient received subcutaneous injection of dupilumab: 600mg as initial dose, followed by 300mg every two weeks. After one month, the patient's rough, dull skin had nearly returned to normal and the area of hypertrophic plaques had decreased. This regimen was continued for six months. During this time, the rash gradually subsided, though new erythema occasionally appeared on the face. On May 20, 2024, the erythema on the face worsened with swelling and gradually evolved into diffuse erythema, papules, a tendency to exudate, and itching (**Figure 1**). A follow-up examination was performed on May 20, 2024. Chest CT scans, blood work, liver and kidney function tests, hepatitis B and C tests, syphilis tests, HIV chemiluminescence tests, and Mycobacterium tuberculosis γ-interferon in vitro release tests showed no obvious abnormalities. Tests for Malassezia facialis and Trichoderma reesei were negative. Dupilumab was discontinued, and Upadacitinib Sustained-release tablets (UPA) were prescribed at 15 mg per day on June 3, 2024.One month later, the patient's facial erythema was still present, with obvious oozing and yellowish crusting on the surface (**Figure 2**). On July 8, 2024, the patient was instructed to take oral UPA, combined with cyclosporine softgels (100 mg twice daily). After three days, the UPA were discontinued; the cyclosporine therapy was maintained, combined with topical treatment, and the patient was asked to discontinue all daily facial products. After two months of treatment, on September 2, 2024, the facial lesions were less symptomatic and reddish in color (**Figure 3**). Treatment was switched to 15 mg of UPA once daily to control symptoms. The disease has not recurred to date, and the patient is still being monitored.

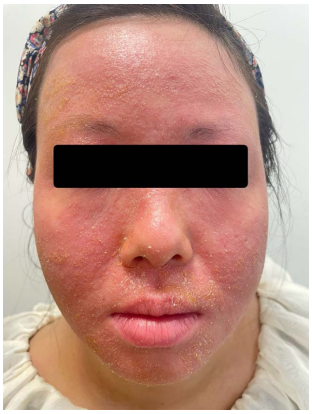

Figure 1. Diffuse erythema on the face.

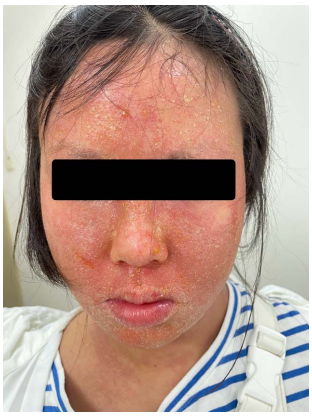

Figure 2. Facial erythema, scattered.

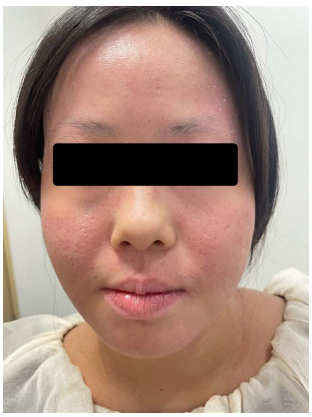

Figure 3. Pale erythema on the face in yellow crusts, slightly swollen.

3. Discussion

In this case, the patient had dry and rough facial skin at the beginning of treatment in our department, and developed recurrent facial erythema, swelling, and oozing after subcutaneous injections with dupilumab. Previous studies have found dupilumab to be safe for long-term use in AD, and its common side effects include ocular symptoms such as conjunctivitis, keratitis, and retinopathy [3] [4]. A few

patients have experienced injection-site reactions [5], as well as facial erythema, herpes infections, pemphigus, pneumonitis, and eosinophilia [6]. Dupilumab-induced facial erythema (DFR) was first reported in April 2018 and has been documented in several recent publications [7] [8]. DFR is a new rash or a worsening of a pre-existing rash on the face, neck, or other exposed areas. It occurs in approximately 4% - 44% of patients treated with dupilumab [9]. The average duration of episodes is 65.4 days. DFR usually presents as erythematous plaques on the face and neck with mild desquamation and edema. Possible mechanisms include barrier damage, an inflammatory response, Trichoderma reesei, helminth mites, and failure of site-specific therapy [10].

Determining the etiology of the disease is a prerequisite for developing a treatment plan. In the present case, the patient had severe AD. The efficacy of treating the facial lesions with dupilumab was less obvious than that of lesions on other anatomical sites. The facial lesions became acutely erythematous and oozed during the treatment period. The patient had no history of suspicious exposure. No abnormalities, such as Trichophyton rubrum or Malassezia species, were found upon examination. Therefore, it was thought that the erythema on the patient's face was due to treatment failure at a specific site or reactivation of the original contact sensitization.

Two key questions that need to be explained regarding the patient's successive course of treatment with UPA and cyclosporine: (1) The first treatment with UPA was ineffective, but why was the later maintenance treatment effective? (2) Is cyclosporine more suitable for treating this type of acute rash? Since the patient received topical glucocorticoid therapy and strict daily chemical control measures with cyclosporine after UPA treatment failed, we cannot conclude that UPA is ineffective or that cyclosporine is preferable. Perhaps a combination of systemic and topical anti-inflammatory therapy, along with the exclusion of suspected sensitizers, may be critical.

4. Conclusion

This case highlights the clinical challenges of DFR in a patient with moderate-to-severe atopic dermatitis AD. Despite significant improvement in the overall symptoms of atopic dermatitis following treatment with dupilumab, persistent facial erythema and swelling persisted after six months, highlighting the need for vigilant monitoring of facial manifestations during long-term treatment with dupilumab. The success of this case with maintenance therapy with udantinib after continuous cyclosporine to control acute inflammation provides practical insights into addressing DFR. It emphasizes the importance of aetiological assessment as a basis for tailoring interventions.

Patient Consent

Written informed consent was obtained from the patient prior to preparing this

case report.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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