Dermatology Practical & Conceptual

Dupilumab-associated Facial Erythema Successfully Treated With Oral Ivermectin

Javier Gil Liane[1], Daniel Morgado-Carrasco[1]

1 Department of Dermatology, University of Barcelona, Hospital Clinic Barcelona, Spain

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Corresponding author: Daniel Morgado-Carrasco, MD, Dermatology Department, Hospital Clínic de Barcelona, Barcelona. C/ Villarroel, 170, 08036 Barcelona, Spain. Phone: (+34) 93 227 54 00, Fax: (+34) 932275438, E-mail: morgadodaniel8@gmail.com

Introduction

Dupilumab, a monoclonal antibody which inhibits IL-4 and IL-13 signaling, has revolutionized atopic dermatitis (AD) treatment. Dupilumab-associated facial erythema (DFE) has been described in 10% of patients and can lead to dupilumab discontinuation [1]. Etiology remains unclear and treatment is challenging [1-3]. Here we present a patient with DFE successfully treated with oral ivermectin.

Case Presentation

A 20-year-old woman with severe AD, refractory to cyclosporine, started dupilumab. After 6 weeks, although AD lesions had resolved, she manifested itching and facial erythema which were not previously present. On physical examination, scaly ill-defined erythematous plaques were observed on the forehead and cheeks. Dermoscopy showed small pustules (Figure 1 A and B). DFE was diagnosed. No patch tests were performed. There was no response to topical corticosteroids or tacrolimus with local adverse effects (AE), nor to oral itraconazole and topical ketoconazole. Since small pustules were present on dermoscopy, dupilumab-associated rosacea was suspected. To avoid local AE, a single dose of oral ivermectin 200 mcg/kg (12 mg) was prescribed. The patient presented a complete resolution of facial erythema in 3 weeks, which has been maintained after 14 months of follow-up (Figure 2).

Conclusions

Face and neck dermatitis (FND) in atopic dermatitis is a diagnostic challenge in which dupilumab adds a new grade of complexity [2]. In a recent systematic review of 101 patients with DFE, 45% of patients reported different cutaneous symptoms from preexisting atopic dermatitis [3]. Diverse etiologies for DFE have been proposed, including worsening of AD, allergic contact dermatitis (ACD), rosacea, topical corticoids withdrawal (TCW), Malassezia furfur (MF) hypersensitivity and alcohol-induced facial flushing [2-4].

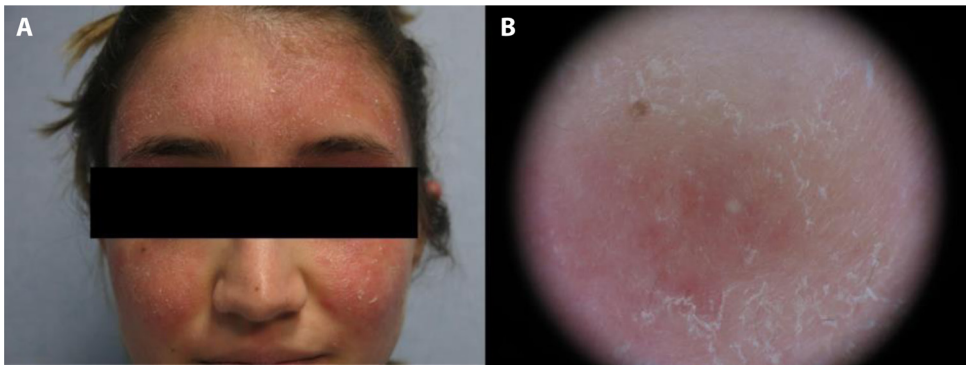

Figure 1. Dupilumab-associated facial erythema. (A) New onset of scaly erythematous plaques on the forehead and cheeks, without affecting nasolabial folds or the palpebral region, 6 weeks after initiating dupilumab therapy. (B) Dermoscopy examination shows white scaling and a central pustule.

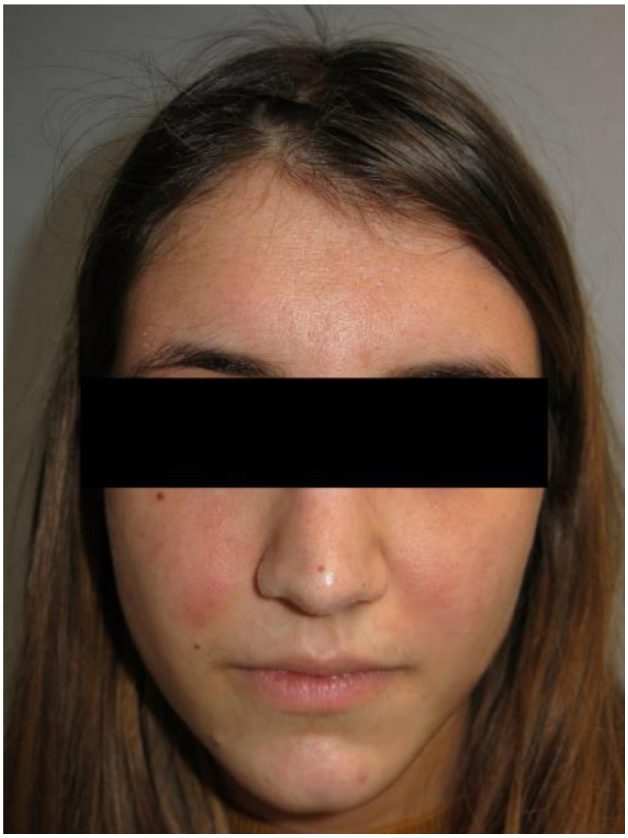

Figure 2. Almost complete resolution after a single dose of oral ivermectin (200 mcg/kg).

In a retrospective study of 94 patients with dupilumab [4], 6% presented rosacea-like folliculitis and increased demodex count in reflectance confocal microscopy [1,4].

Although DFE pathogenesis remains unclear, recent studies have hypothesized that IL-4 blockage shifts Th1/Th2 balance towards Th1/Th17-mediated dermatoses [2]. In rosacea, especially if papulopustular, the main factors are induction of *Demodex* proliferation by Th2 blockade and Th17-infllamatory response [1].

Regarding DFE treatment, topical corticosteroids and calcineurin inhibitors are the most used, although with low response rates. However, management of DFE should start with a precise differential diagnosis, since ACD, rosacea, TCW and MF-dermatitis respond to different approaches [2, 5]. Thus, most treatment failures could be explained by DFE being erroneously thought of as a unique entity. Evidence on rosacea-like dermatitis treatment remains sparse [2]. Partial or complete response to acaricidal agents such as topical and oral metronidazole, topical ivermectin or doxycycline have been reported [2]. Topical ivermectin is a first-line therapy for papulopustular rosacea, although it requires prolonged treatment (up to 12 weeks). Oral ivermectin treatment for rosacea has been reported in isolated cases with satisfactory results. It has very low systemic AE (<1%) and two main advantages: single administration schedule and avoidance of local AE.

In patients under treatment with dupilumab presenting with facial erythema, DFE should be considered. Rather than a unique entity, DFE should be considered as a compendium of differential diagnoses. If rosacea-like dermatitis is suspected, oral ivermectin could represent a good and well-tolerated alternative.

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