



## Mepolizumab induced palmoplantar psoriasis: A case report

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### Abstract

#### BACKGROUND

Atopic dermatitis and asthma are two diseases whose pathogenesis is largely attributable to the activation, at least in the initial stages, of T helper (Th)-2 Lymphocytes, the related cytokine axis, and B lymphocytes with antibody production. Psoriasis is conversely a pathology resulting from a recruitment of Th-17 and Th-1 lymphocytes, after an initial role of innate immunity. Mepolizumab is a humanized monoclonal antibody directed against interleukin (IL)-5, a central cytokine in the Th-2 axis, therefore involved in the pathogenesis of asthma. Several authors have described the appearance of psoriatic lesions in patients with asthma or atopic dermatitis following the therapy with dupilumab, a monoclonal antibody that blocks the interleukin (IL)-4, another Th-2 cytokine.

#### CASE SUMMARY

We present the case of a 59-year-old patient who developed psoriasiform lesions on the palms after mepolizumab therapy for asthma, for the activation of the parallel cytokine cascade after the blockade of IL-5. We successfully treated the patient with a topical calcipotriol and betamethasone ointment.

#### CONCLUSION

We should investigate with further attention the possible impact on the human immunological ecosystem put in place by the inhibition of the activity of individual inflammatory mediators, so as to be able to recognize the initial adverse effects early.

**Key Words:** Psoriasis; Interleukin-5; Mepolizumab; Asthma; Immunology; Case report

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**Core Tip:** We report the case of a 59-year-old patient with severe asthma who developed palmar psoriasis after 6 mo from the initiation of treatment with a humanized monoclonal antibody directed against interleukin-5 (IL-5), mepolizumab. There are several case reports of psoriasis induced by dupilumab therapy in the literature, but this phenomenon has not yet been recognized with modulating IL-5R signalling. This article reports the pathogenetic hypotheses that may underlie this phenomenon.

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## INTRODUCTION

Despite the lack of a precise overview of the cytokine ecosystem that governs human immune responses, numerous clues suggest that certain types of diseases are more associated with specific cytokine circuits[1]. Extrinsic asthma, atopic dermatitis, and chronic spontaneous urticaria are indeed based on the hyperactivation of the cytokine pathway associated with a predominantly T helper (Th)2-type or humoral response, as confirmed by the efficacy of drugs against inflammatory mediators, including interleukin (IL)-4, IL-5, IL-9, IL-13, IL-31, and thymic stromal lymphopoietin. Often, these conditions are associated with a large production of immunoglobulins E[2-5].

Psoriasis, on the other hand, is a chronic/relapsing inflammatory skin disease characterized, in an initial phase, by activation of innate immunity, followed by the subsequent involvement of the adaptive counterpart, without the involvement of humoral immunity[6]. Specifically, Th1, Th17, and Th22 lymphocytes are activated in response to the differentiation stimulus of the cytokines IL-12 and IL-23 secreted by the activated dermal dendritic cells. In this context, Th1 cells play an important role in producing interferon- $\gamma$  and tumor necrosis factor- $\alpha$ , amplifying the inflammatory cascade and supplying proliferative stimuli to the keratinocytes. Th17 cells create a positive feedback circuit to increase the production of IL-17 by themselves promoting epidermal hyperplasia and neutrophil recruitment from blood to the psoriasis-affected derma and epidermis[6,7]. Psoriasis affects 2%-5% of the population, and 2.8%-40.9% of individuals with psoriasis have palmoplantar psoriasis (PPP), which is a variant of psoriasis that affects the palms and/or soles and can start at any age[8].

In the literature, there have been several reported cases of patients with atopic dermatitis and/or asthma who, once subjected to treatment with dupilumab, a monoclonal antibody that inhibits IL-4/IL-13 signaling, developed a skin picture of psoriasis for an immunological shift from a Th2/humoral to a Th1/cell-mediated pattern[9-11].

Mepolizumab is a humanized monoclonal antibody directed against IL-5, a central cytokine in the Th-2 axis, therefore involved in the pathogenesis of asthma, is approved by the Food and Drug Administration in 2015. IL-5, secreted by Th2 lymphocytes, has numerous effects on eosinophils, promoting their maturation, activation, survival, and chemotaxis from the bloodstream to the airways[12]. IL-5 acts to increase the likelihood of differentiation of conventional B cells to antibody-secreting plasma cells (ASCs) and synergizes with IL-4[13].

We report the case of a 59-year-old patient with a family history of psoriasis that developed severe psoriasiform lesions on the palms after 6 mo of mepolizumab therapy for severe asthma. We speculate that the appearance of PPP could be explained by a switch of the immune response from the prevalent antibody-mediated immunopathogenesis to a cell-mediated pathology after IL-5 blockage by mepolizumab, in a similar manner to what has occurred in patients after the use of dupilumab.

## CASE PRESENTATION

### Chief complaints

A 59-year-old woman came to the Allergy Dermatology Unit at the Tor Vergata Polyclinic for itchy, scaly erythematous lesions on palmar and plantar skin for 6 mo (Figure 1). She denied any previous exposure to irritating substances.

### History of present illness

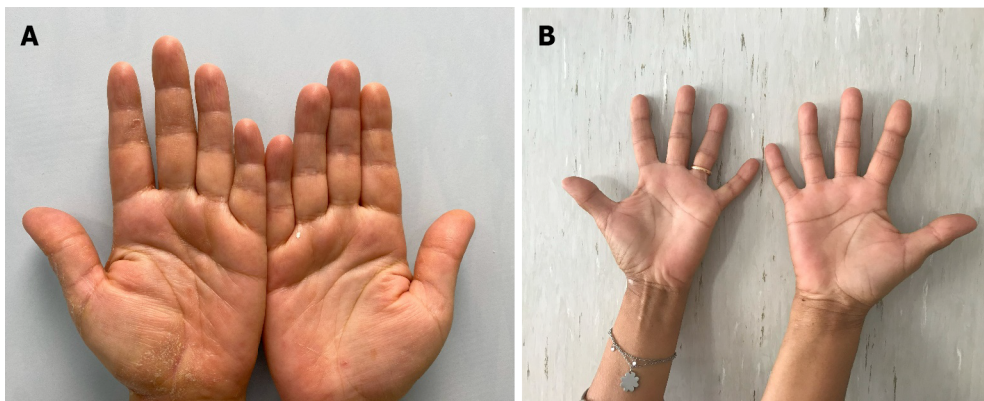
The patient had a past medical history of severe asthmatic disease, which was diagnosed at her age of 20 and treated with mepolizumab, a humanized monoclonal antibody directed against IL-5[12], for 12 mo with a good clinical response assessed by a pneumologist.

### History of past illness

The patient reported that she had no other pathologies.

### Personal and family history

The patient had a family history of psoriasis, as her father suffered from moderate-severe chronic plaque psoriasis. She



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**Figure 1** Clinical pictures of affected palms before and after treatment. A: Before treatment; B: After 12 wk.

had no family history for atopy.

### **Physical examination**

The patient presented itchy, scaly erythematous lesions on palmar and plantar skin for 6 mo; there were no associated lesions on the body, but the nail apparatus showed splinter haemorrhage and pitting. The patient complained of itching and burning, with an itch visual analogue scale (VAS) score of 6. The hand Physician's Global Assessment (PGA) score was estimated to be 3.

### **Laboratory examinations**

All other physical findings, as well as blood chemistry, urine analysis, and complete blood count, were found to be normal except for the C-reactive protein (CRP) value, slightly above the threshold limit (0.9 mg/dL; normal range: < 0.5 mg/dL).

### **Imaging examinations**

There was no need for imaging examinations for the dermatologic issue. On dermoscopy, characteristic features of psoriasis lesions were diffuse scaling, white scales, and dotted vessels along with a regular distribution of vessels as shown in [Figure 2](#)[14].

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## **FINAL DIAGNOSIS**

By clinical evaluation, a diagnosis of PPP was made.

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## **TREATMENT**

A topical calcipotriol and betamethasone ointment was prescribed to the affected areas once daily for 8 wk.

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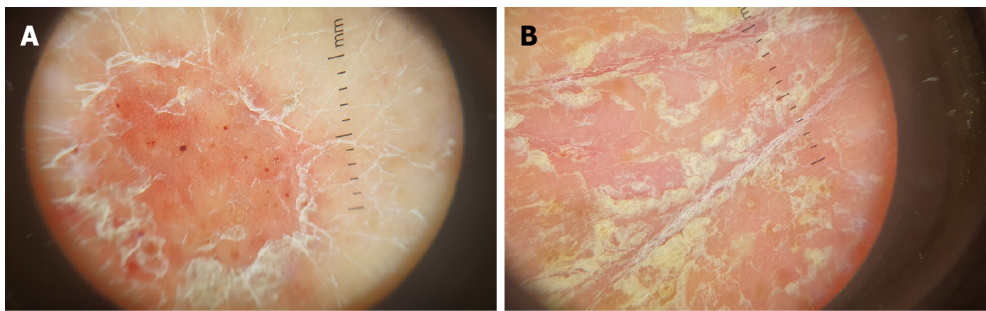
## **OUTCOME AND FOLLOW-UP**

We prescribed control blood tests and set a date for a new dermatological visit after 12 wk. During the control visit, the patient presented almost complete resolution of the skin features and the symptoms of itch and burning. Itch VAS was assessed and the result was 0. The hand PGA score estimated by the clinician was 0.5. The patient showed us the results of the blood analysis which roughly overlapped with the results shown in the first visit, with a slight increase in CRP (0.8 mg/dL) and a slightly increased cholesterol value (205.0 mg/dL). The patient has continued the treatment with mepolizumab. We prescribed a maintenance treatment with calcipotriol alone three times per week for 8 wk and a new date for a control visit after 12 wk.

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## **DISCUSSION**

IL-4 is a cytokine secreted by Th2 lymphocytes and may serve as an excellent paradigm to shed light on the modulation of the balance that governs the immune response, being fundamental not only for the differentiation of naïve Th



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**Figure 2 Dermoscopic images.** A: Dermoscopic pattern of regularly distributed dotted vessels and white scales; B: Yellow white scales in a thickened hand skin area.

lymphocytes to Th2 lymphocytes, but also for stimulating the production of immunoglobulins by B lymphocytes[1,5,15].

IL-4 is also implicated in suppressing the effector functions of Th1 lymphocytes in the context of pathologies connected to a de-regulation of the latter, such as delayed hypersensitivity, certainly inducing a transient cessation of Th1-type pro-inflammatory activity[1]. In this regard, there is some evidence that psoriasis can improve in laboratory animals subjected to the administration of human IL-4 at a precise therapeutic range[16].

In atopic subjects, it is believed that there is an upregulation of the genes that control the release of IL-4 by Th2 Lymphocytes in response to environmental allergens and clinicians have been interfering for years in this altered Th1-Th2 balance through immunotherapy for atopy[17,18]. This therapeutic strategy, consisting in the injection of purified allergens in patients with atopy, can reduce the production of IL-4 by Th-2 Lymphocytes, reducing the reactivity of the memory Th-2 Lymphocytes to these allergens. By the reduction of IL-4 levels, it was possible to find an increase in the mRNA encoding IL-12, secreted by Th1 and antigen-presenting cells. IL-12, *in vivo*, has been shown to be able to prevent Th2-mediated immune responses and, sometimes, also to convert them into Th1 ones[1,18-20].

To date, the role that IL-5 can play in regulating the Th1/Th2 or humoral-cellular immunity balance is unknown; however, in the light of the different evidence observed with IL-4 inhibitory antibodies, it is possible to hypothesize that a similar link may also exist in the blockade of IL-5, although it must be recognized that different functions are attributable to IL-4 and IL-5 cytokines, both however involved in the first moments of activation of the Th2 axis[21].

Indeed, IL-5 is implicated in activating ASC differentiation and is a co-activator for B cell proliferation, enabling humoral immune responses mostly following the activation of Th2 cells[13], and there is evidence in rats and *in vitro* studies that IL-5 therapies can treat graft rejection phenomena by reversing autoimmune mechanisms based on Th1 and Th17 activation[22].

At the same time, we think that in our specific case, there was a similar conversion of the immune response from a predominantly antibody-based one, responsible for the patient's asthma, to one with a strong cell-mediated component, responsible for the patient's PPP.

## CONCLUSION

Nowadays, given the increasing use of IL inhibitory monoclonal antibodies in numerous pathologies, we should investigate with further attention the possible impact on the human immunological ecosystem put in place by the inhibition of the activity of individual inflammatory mediators, so as to be able to be increasingly aware of the manifestations of pathologies that could arise or be revealed by the treatment itself and therefore recognize the initial lesions early.

## FOOTNOTES

**Author contributions:** Artosi F and Diluvio L contributed to conceptualization; Campione E contributed to methodology; Artosi F and Diluvio L contributed to investigation; Artosi F, Diluvio L, and Vultaggio M contributed to data curation; Artosi F contributed to writing and original draft preparation; Diluvio L and Bianchi L contributed to writing review and editing.

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