# Generalized hypertrichosis associated with the use of interleukin 17 blockers in 2 patients with psoriasis

Luis E. Sánchez-Dueñas, MD,[a] Lizet K. Rojano-Fritz, MD,[a] and Juan C. García-Rodríguez, MD[b]
*Guadalajara and Mexico City, Mexico*

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## INTRODUCTION

Hypertrichosis is excessive hair growth on the non–androgen-dependent areas. It can be congenital or acquired and localized or generalized.[1] Hypertrichosis has been associated with various prescription drugs such as corticosteroids, cyclosporine, retinoids, antibiotics, antihypertensive drugs, psoralen, phenytoin, diazoxide, minoxidil, and latanoprost.[2,3] In recent years, biological therapy seems to be associated with hypertrichosis.[1,4,5] Here we present 2 patients with plaque psoriasis who experienced noticeable increase in hair growth on all of their body surface during the time they were receiving interleukin (IL)-17A inhibitor therapy for plaque psoriasis.

## CASE REPORT

A 62-year-old man presented with a 1-year history of plaque psoriasis that was unresponsive to topical calcipotriol/betamethasone and to systemic methotrexate for the last 3 months. The patient has a medical history of arterial hypertension, hyperuricemia, and insulin resistance for which he was treated with candesartan, clopidogrel, allopurinol, and metformin for the last 15 years. Severe plaque psoriasis was diagnosed according to severity assessments: Psoriasis Severity Index (PASI) area, body surface affected, and Dermatology Life Quality Index, all of them measured more than 10. The patient was a candidate for 300 mg of secukinumab once a week for 4 weeks (5 doses) as an induction therapy then 300 mg once a month as maintenance therapy. Complete clinical resolution was achieved with a PASI 100 response at week 16. After 20 months of therapy with secukinumab, the patient noticed thicker hair growth on the scalp, torso, and extremities (Fig 1, *A* and *B*).

*Abbreviations used:*

IL: interleukin
PASI: Psoriasis Severity Index

A 39-year-old man with no comorbidities had a 15-year medical history of severe stable chronic plaque psoriasis. He was treated previously with topical high-potency steroids, calcipotriol/betamethasone, full-body phototherapy, and systemic therapy with oral methotrexate. The treatment was suspended 6 months prior due to lack of efficacy. According to the result of severity assessments (PASI, 19; body surface affected, 20%; and Dermatology Life Quality Index, 13) this patient was a candidate for biological therapy. He was administered a single dose of 160 mg of ixekizumab followed by 6 doses of 80 mg every 2 weeks. The maintenance dose was 80 mg every 4 weeks achieving a PASI 100 response at week 16. After 1 month of therapy, the patient noticed more pigmented hair and increased density of growth on his back and extremities; this process continued until week 20 (Fig 2, *A* and *B*).

## DISCUSSION

The discovery of the role of the TH17 lymphocyte pathway led us to a substantial change in our understanding of the pathogenic immune events in

From the Dermatology Department, Dermika Centro Dermatológico Láser[a] and the Dermatology Department, DermaAdvance, Mexico City.[b]

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Correspondence to: Luis E. Sánchez-Dueñas, MD, Department Dermatology, Dermika Centro Dermatológico Láser, Golfo de Cortés 3002, Col. Vallarta Norte Guadalajara, Jalisco, 44280, Mexico. E-mail: drlapeau@hotmail.com.

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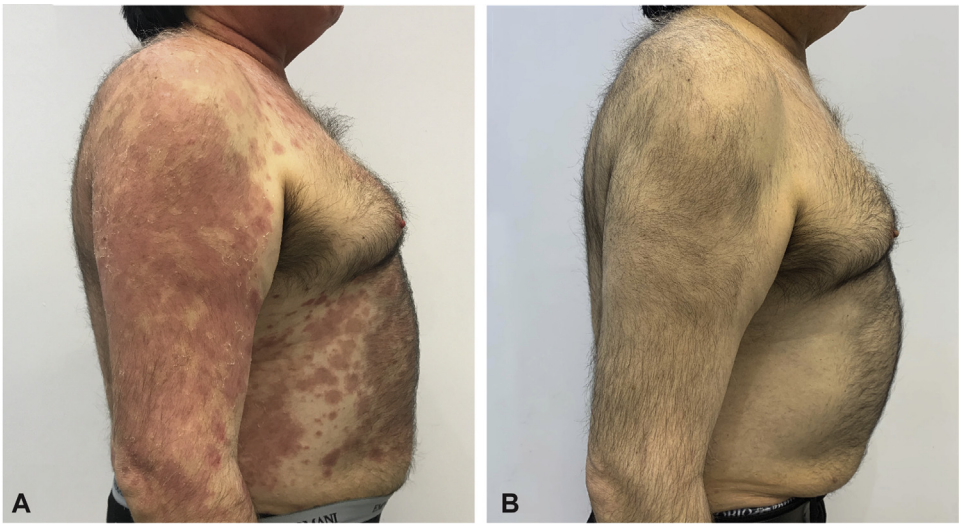


**Fig 1.** A 62-year-old man with severe plaque psoriasis before secukinumab. **A**, Scarce hair on upper extremities and trunk. **B**, At 20-month follow-up, thicker and more pigmented hairs seen on previously affected areas.

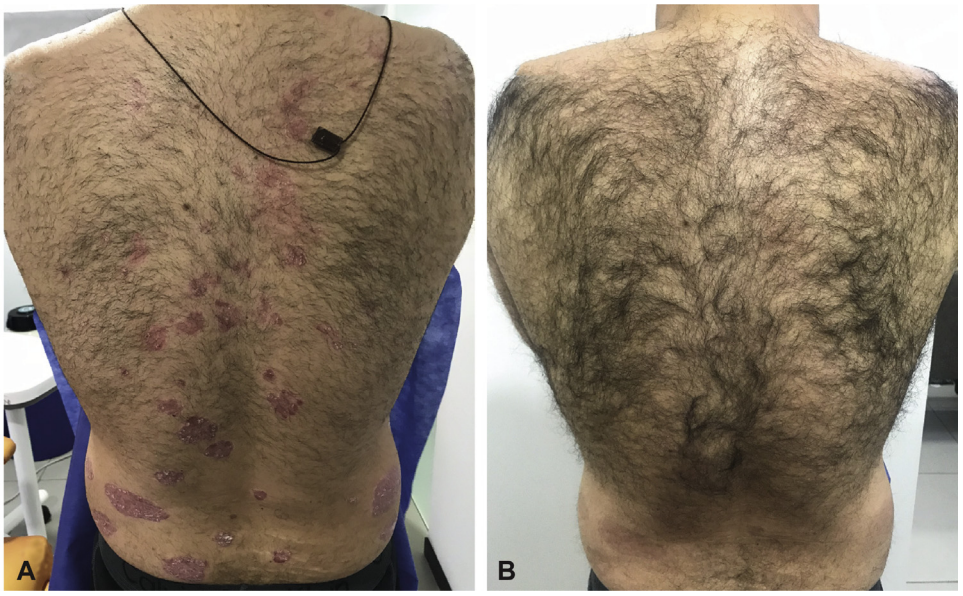


**Fig 2.** A 39-year-old man before ixekizumab. **A**, Back with plaque psoriasis and basal hair growth condition. **B**, At 6-month follow-up, excessive hair growth was remarkable.

psoriasis. It has led to a paradigm change in the treatment of this condition.[6] IL-17A participates in the cascade of inflammatory transformations in the etiopathogenesis of immunologic and inflammatory diseases.[7]

The effect IL-17A blockade has on inflammatory circuits in skin lesions was evaluated in the studies of patients with psoriasis who received anti—IL-17A monoclonal antibodies, either secukinumab (fully human monoclonal IgG1k) or ixekizumab (humanized recombined monoclonal IgG4k).[8]

The use of biological IL-17A inhibitors can result in the appearance of some side effects such as infection, nasopharyngitis, upper respiratory tract infections, inflammation on the nasal mucosa, headaches, and candida infections.[9] In recent years, hypertrichosis has been reported in anecdotal cases or series cases.[1,2,10]

Rongioletti et al,[2] reported on a patient with erythrodermic psoriasis who was treated with secukinumab. After 6 months of therapy, the patient noticed that his scalp hair was becoming darker over

the entire scalp with a diffuse increase in hair density. Hair thickening and pigmentation were attributed to a change immune control after secukinumab was administrated. IL-17 may increase the synthesis of antimelanogenic cytokines and can synergize with tumor necrosis factor-$\alpha$ inducing pigmentation-related signaling and melanin production inhibition.

Secukinumab was deemed responsible for hair growth in androgenetic alopecia-like hair loss in an 85-year-old man with psoriatic erythroderma. This condition quickly developed within the second month of therapy.[10] This patient also noticed an increased proportion of black hair on the top of his scalp. Six months after the treatment, the hair growth continued to develop. The investigators speculated that IL-17A blockade might cancel the depigmentation effect of IL-17A over the pigment cells in hair follicles, resulting in repigmentation of hair. The case also suggested that recovery of hair growth in patients with psoriatic alopecia after a secukinumab treatment could be expected, as happened in our case, as the patients also had thicker and more pigmented hair when their hair regrew.

According to Sacchelli et al,[1] a 67-year-old man with moderate recalcitrant psoriasis started treatment with secukinumab for cutaneous psoriasis. Four months later, the patient reported a generalized increase in body hair, especially on his torso and lower back. Our patients also experienced this effect. In previous reports, investigators consider that thicker hair growth should not affect therapeutic choices, as this effect stabilizes if treatment is not discontinued.

Hypertrichosis is a cosmetic disorder that involves a switch from vellus to terminal hair in body regions that do not usually bear terminal hair. Although its mechanisms are poorly understood, hair growth usually reverts to regular hair after discontinuation of the drug.[3] The reaction/effect starts on the upper limbs or the face and spreads down to the back and lower limbs. Once the effect has developed, it seems to persist and progressively stabilize if the therapy is not discontinued. As in our first case, the patient noticed the hair growth; however, he was not concerned about hypertrichosis; therefore, this phenomenon was identified in a follow-up visit 20 months after treatment with secukinumab had been initiated. At that moment, psoriasis was under remission, and excessive hair growth was remarkably visible in areas previously affected by psoriasis. This patient had concomitant treatment for the last 15 years with candesartan, clopidogrel, allopurinol, and metformin; nevertheless, the patient had never experienced excessive hair growth before. To our knowledge, this is the second case of secukinumab associated with generalized hypertrichosis reported in the English-language medical literature.

In the second case, the patient had an acute hypertrichosis during ixekizumab therapy after just 1 month of treatment. To our knowledge, this is the first reported case of hypertrichosis associated with ixekizumab in the medical literature. Even though we expect to see hair re-growing after clinical improvement of psoriasis, the variation from vellus to terminal hair appears to be associated with the use of biological therapies.

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