Successful treatment of type II pityriasis rubra pilaris with secukinumab

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INTRODUCTION

Pityriasis rubra pilaris (PRP) is a heterogeneous inflammatory skin disease characterized by follicular papules, orange palmoplantar keratoderma, and erythematous scaly patches with islands of skin sparing. Type II PRP is a rare, severe, chronic form of PRP presenting atypical features including long disease duration, palmoplantar keratoderma, ichthyosiform scaling, eczematous areas, and resistance to therapy. Here we propose a new alternative therapy for type II PRP with secukinumab, an anti-interleukin (IL)-17A monoclonal antibody.

Abbreviations used:

IL: interleukin
PRP: pityriasis rubra pilaris
TNF: tumor necrosis factor

CASE REPORT

A 33-year-old woman with a childhood history of hydronephrosis secondary to vesicoureteral reflux had a 9-year history of erythroderma with confluent folliculocentric erythematous scaly plaques, islands of sparing, orange palmoplantar hyperkeratosis (Fig 1), and eczematous lesions. Differential diagnoses included PRP (atypical because of its severity and eczematous lesions), psoriasis, atopic dermatitis, and epidermotropic cutaneous T-cell lymphoma. Search for skin and blood T-cell clone was negative. Blood screening did not show Sezary cells or phenotypically atypical lymphocytes. Whole genome sequencing including CARD14 sequencing did not find any possible causal mutation. Several skin biopsy specimens showed epidermal acanthosis, alternating orthokeratosis and parakeratosis, and dermal lymphohistiocytic infiltrate with few neutrophils. Finally, type II PRP was diagnosed. Clinical course was particularly severe, including intense erythroderma, *Staphylococcus aureus* septicemia requiring 2 admissions in the intensive care unit, severe depression, and anorexia with loss of 30 kg. Previous unsuccessful treatments, given more than 3 months, included topical corticosteroids, acitretin, photochemotherapy, cyclosporine, methotrexate, infliximab, ustekinumab, intravenous immunoglobulin, and omalizumab. Prednisone was efficient, but the patient experienced relapse with less than 0.5 mg/kg/d. The condition partially improved using cyclosporine (5 mg/kg/d) in association with 10 mg prednisone. After informed consent, secukinumab was initiated in association with cyclosporine and 10 mg of prednisone. The patient received 5 subcutaneous 300-mg weekly injections followed by once-a-month injections. After 4 weeks, secukinumab allowed a significant and prompt

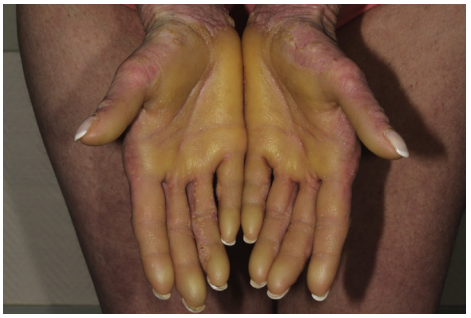

Fig 1. Orange palmoplantar hyperkeratosis.

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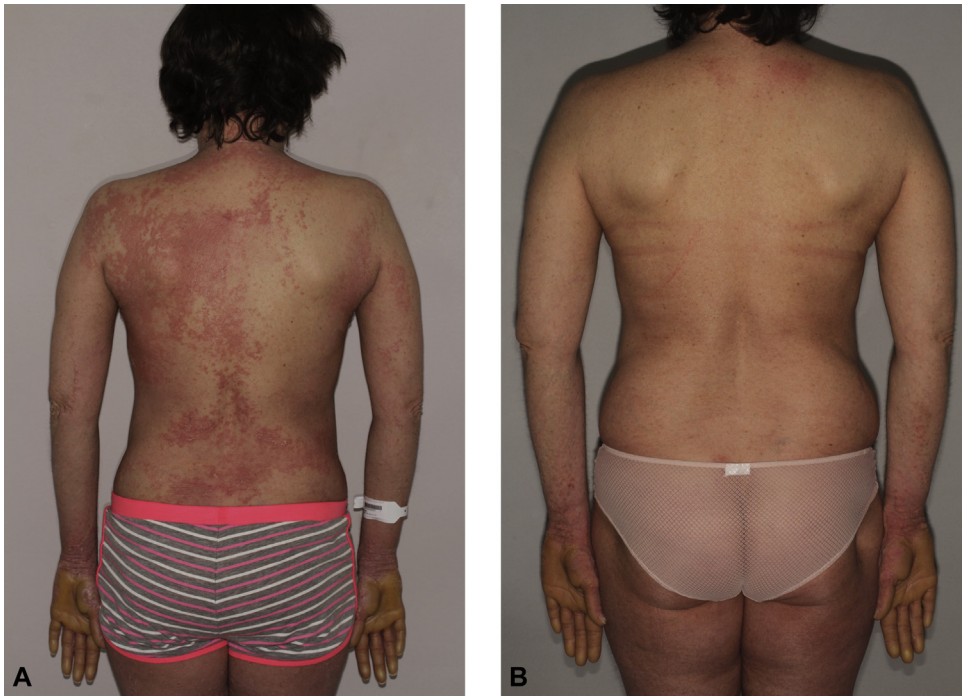

Fig 2. A, Pityriasis rubra pilaris before secukinumab treatment. **B**, Pityriasis rubra pilaris 4 weeks after secukinumab treatment.

clinical response and quality-of-life improvement. Psoriasis area and severity index and dermatologic life quality index score, respectively, decreased from 27.6 to 5.6 and from 30 to 15 after 4 injections (Fig 2). Secukinumab was well tolerated except an oral and esophageal candidiasis (treated with fluconazole for 14 days). Secukinumab was highly effective on clinical symptoms and quality of life, without recurrence of PRP lesions with a 6-month follow-up.

DISCUSSION

PRP is a rare skin disease, and a standard therapeutic protocol does not exist.[1] Treatment options include topical corticosteroids, acitretin, methotrexate, cyclosporine, phototherapy, and tumor necrosis factor (TNF)-α blockers. Secukinumab (Cosentyx, Novartis, Basel, Switzerland) is a recombinant, high-affinity, fully human IgGκ monoclonal antibody that directly binds and neutralizes IL-17A and specifically downregulates T helper cell 17, T helper cell 1, and other immune-related genes.[2] Secukinumab has been approved since January 2015 for the treatment of moderate-to-severe plaque psoriasis in adult patients. PRP and psoriasis share many clinical and histologic similarities. Treatments used for psoriasis have been effective for the treatment of PRP: TNF-α blockers, ustekinumab (anti—IL-12/IL-23 antibody), and efalizumab (anti-CD11a antibody).[3-5] The clinical response to secukinumab in our patient suggests the involvement of IL-17A in the aberrant proliferation and differentiation of keratinocytes in PRP lesions.[6] In psoriasis, blocking IL-17A using secukinumab was more effective than etanercept (a recombinant TNF-α receptor protein)[7] and ustekinumab (a monoclonal antibody targeting the p40 protein subunit of IL-12 and IL-23).[6] Serum level of IL-17 was not evaluated in our patient at the time of secukinumab start, but very high levels of IL-17 have been found in a previous PRP patient providing a rationale for targeting IL-17 in some PRP patients.[8] Two to five percent of patients receiving secukinumab for psoriasis subsequently have superficial candidiasis, usually self-limited or resolving with standard therapy. Given the key role of IL-17 in host defense, more data will be required to address the long-term safety profile of secukinumab.[7] We describe secukinumab as a new alternative therapy for type II PRP. Secukinumab induced pruritus relief after 1 week of treatment and improvement of erythematous plaques and palmoplantar keratoderma after 2 weeks of treatment. Secukinumab could be considered an alternative therapeutic option for refractory type II PRP. Further studies are required to clarify the pathogenic role of IL-17 axis in PRP.

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REFERENCES

1. Ross NA, Chung H-J, Li Q, Andrews JP, Keller MS, Uitto J. Epidemiologic, Clinicopathologic, Diagnostic, and Management Challenges of Pityriasis Rubra Pilaris: A Case Series of 100 Patients. *JAMA Dermatol*. 2016;152(6):670-675.
2. McInnes IB, Mease PJ, Kirkham B, et al. Secukinumab, a human anti-interleukin-17A monoclonal antibody, in patients with psoriatic arthritis (FUTURE 2): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Lond Engl*. 2015; 386(9999):1137-1146.
3. Petrof G, Almaani N, Archer CB, Griffiths WA, Smith CH. A systematic review of the literature on the treatment of pityriasis rubra pilaris type 1 with TNF-antagonists. *J Eur Acad Dermatol Venereol*. 2013;27(1):e131-e135.
4. Krase IZ, Cavanaugh K, Curiel-Lewandrowski C. Treatment of Refractory Pityriasis Rubra Pilaris With Novel Phosphodiesterase 4 (PDE4) Inhibitor Apremilast. *JAMA Dermatol*. 2016;152(3): 348-350.
5. Wohlrab J, Kreft B. Treatment of pityriasis rubra pilaris with ustekinumab. *Br J Dermatol*. 2010;163(3):655-656.
6. Thaçi D, Blauvelt A, Reich K, et al. Secukinumab is superior to ustekinumab in clearing skin of subjects with moderate to severe plaque psoriasis: CLEAR, a randomized controlled trial. *J Am Acad Dermatol*. 2015;73(3): 400-409.
7. Langley RG, Elewski BE, Lebwohl M, et al. Secukinumab in plaque psoriasis—results of two phase 3 trials. *N Engl J Med*. 2014;371(4):326-338.
8. Adnot-Desanlis L, Antonicelli F, Tabary T, Bernard P, Reguiaï Z. Effectiveness of infliximab in pityriasis rubra pilaris is associated with pro-inflammatory cytokine inhibition. *Dermatol Basel Switz*. 2013;226(1):41-46.