Dermatology Reports

https://www.pagepress.org/journals/index.php/dr/index

eISSN 2036-7406

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Please cite this article as: Lora V, Graceffa D, Di Prete M, Cota C. Tildrakizumab in the treatment of plaque psoriasis in an HIV+ patient: a case report and literature review of anti-interleukin drugs. *Dermatol Rep 2024 [Epub Ahead of Print] doi: 10.4081/dr.2024.10140*

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Submitted 13/09/24 - Accepted 22/10/24

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Tildrakizumab in the treatment of plaque psoriasis in an HIV+ patient: a case report and literature review of anti-interleukin drugs

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Key words: biological therapy; HIV infection; psoriasis; special populations; tildrakizumab

Authors' contributions: VL, CC, study conception and design; VL, MDP, DG, CC, collection and interpretation of data; VL, statistical analysis; VL, CC, manuscript drafting; VL, MDP, DG, CC, manuscript editing; VL, MDP, DG, CC, approval to submit.

Conflicts of interest: The authors have no conflict of interest related to this article.

Availability of data and materials: All data concerning this case report are available from the corresponding author upon reasonable request and within limits of privacy regulations.

Ethics approval and consent to participate: The approval of an ethics committee was not required according to current regulations. The patient gave informed consent to the publication of anonymous clinical data.

Acknowledgements: Editorial assistance was provided by Laura Brogelli, MD, PhD, and Aashni Shah (Polistudium SRL, Milan, Italy). This assistance was supported by internal funds.

Abstract

Treatment of psoriasis associated with human immunodeficiency virus (HIV) infection is challenging due to the high incidence of comorbidities and polypharmacy and the lack of evidence on the efficacy and safety of available drugs in these patients. Therefore, clinical or anecdotal reports provide useful indications for therapy decision-making. A 64-year male with plaque psoriasis (Psoriasis Area and Severity Index=14.3) infected with HIV for 4 years, with hypercholesterolemia, hypertension, and impaired quality of life (Dermatology Life Quality Index=14) was resistant to topical therapy and acitretin. Tildrakizumab 200 mg was started, obtaining Psoriasis Area and Severity Index=0 at week 16 which was maintained after 13 months of follow-up. No adverse event was reported, and immune cell levels were unchanged. This is the first report on the treatment of psoriasis with tildrakizumab in an HIV+ patient. A literature search showed that prior to this patient, 38 HIV+ subjects had been treated with anti-cytokine agents for psoriasis.

Introduction

Patients infected with human immunodeficiency virus (HIV) carry a higher risk of developing chronic plaque psoriasis, with an overall prevalence ranging from 4% to 8%.[1,2] Psoriasis in HIV patients is more serious and has a longer duration of exacerbations compared to otherwise healthy subjects.[2] Psoriasis may also be considered a revealing sign of HIV infection.[3]

Treatment of psoriasis associated with HIV is challenging due to the high incidence of comorbidities and polypharmacy in these patients.[2] Over the past 25 years, highly active antiretroviral therapy (HAART) has allowed long survival with good general conditions and control of CD4 lymphocyte counts, allowing the use of immunomodulatory drugs in these patients for the treatment of chronic inflammatory comorbidities.[4] Additionally, patients with chronic infections such as HIV are not included in clinical trials.[5,6] This exclusion limits evidence on the efficacy and safety of available

treatments, which represents a barrier to correct management, especially if newer agents such as biological therapies are considered.[4,7] Therefore, clinical or anecdotal reports do have a role in providing indications for therapy decision-making of psoriasis in HIV patients in clinical practice.[3,5,8,9]

Among the interleukin(IL)-23 inhibitors, a class of biologics with a good safety profile, tildrakizumab is particularly suitable for the treatment of 'special populations' of patients with psoriasis, given its flexibility of dosage.[10,11]Indeed, it is the only anti-IL-23 drug to have been approved in the two dosages of 100 mg and 200 mg that can be chosen based on clinical features, comorbidities, and psoriasis response.[10] However, to our knowledge, treatment of psoriasis with tildrakizumab in HIV patients has never been documented to date.

Here, we report the first case of a patient with psoriasis and HIV infection, successfully treated with tildrakizumab.

Case Report

A 64-year-old male came to our center (Istituto Dermatologico San Gallicano, Rome, Italy; a referral Center for the treatment of dermatological diseases in central Italy) in June 2023. He presented with localized plaque psoriasis of the trunk and limbs (Figure 1). He had skin lesions also at challenging sites, such as the back of the hand, scalp, nails, and genitals. His Psoriasis Area and Severity Index (PASI) score was 14.3, his Static Physician's Global Assessment (PGA) was 3, the Static PGA of Genitalia was 3, fingernail-PGA was 2 with involvement of thumbnails of both hands, and scalp-specific PGA was 3. His body weight was 75 kg, height 164 cm, and BMI was 27.8 kg/m^2, overweight. He had had psoriasis for 10 years and had worsened in the last 2 years. High strength topical corticosteroids and topical vitamin D derivatives had been prescribed by the general

practitioner with partial resolution. A previous dermatologist prescribed a low dose of oral acitretin (10 mg/day) that was discontinued after a few months due to worsening of hypercholesterolemia.

He reported a previous HBV infection (HBV DNA was negative at our first visit), hypercholesterolemia in treatment with ezetimibe 10 mg/day since 2020, and hypertension treated with lisinopril 20 mg/day and cardio-aspirin 100 mg/day since 2019. He was a current smoker (10 cigarettes/day).

The patient had been infected with HIV for 4 years and treated with dolutegravir/lamivudine50/300mg/day. Viral load at the time of our first visit was below 30 copies/mL, and CD4 cell count was 991 cells/mm^3, both within the normal range. The patient did not report further information about his HIV infection management, and indeed, he told us that he had never accepted HIV seropositivity and that he was scared that this infection could have been disclosed. He also reported psoriasis as an additional stigma. The quality of life was very impaired, and the Dermatology Life Quality Index (DLQI) score was 14.

Given the extension of psoriasis, the involvement of challenging sites and the marked impact on QoL, we decided to start a systemic treatment. Phototherapy was not feasible since the patient could not attend hospital visits two or three times a week. Acitretin was contra-indicated due to dyslipidemia, and ciclosporin was contraindicated due to hypertension. The prior HBV infection, although cured, also made treatment with methotrexate unsuitable.

After consultation with the treating infectious disease specialist, we decided to prescribe a biological agent. However, we excluded TNF agents due to the suboptimal safety profile reported by a retrospective multicenter study in patients with HIV infection and the controversial association with an increased risk of infection.[12–14] Anti-IL-17 antibodies were not chosen because they may increase the risk of fungal infections.[15]

Therefore, among the IL-23 inhibitors, we proposed treatment with tildrakizumab, given its favorable safety profile, the possibility of flexible dosage and its efficacy in difficult-to-treat areas.[10]

The starting dose was the highest possible – 200 mg – at weeks 0 and 4 and then every 12 weeks. PASI 0 and DLQI3 were reached at week 16 and maintained till week 28 when we reduced tildrakizumab dosage to 100 mg every 12 weeks (Figure 2). After 13 months of follow-up, the patient is still in remission. No adverse events were reported, and HIV viral load and CD4 count remained unchanged.

Discussion

To our knowledge, this is the first report on the treatment of psoriasis with tildrakizumab in a patient with HIV. We obtained a rapid and sustained remission of skin lesions, even in difficult-to-treat areas, without adverse events or changes in the immune cell levels, with a follow-up of 12months. We decided to use the higher dosage that is suitable for patients with high disease burden due to the severity of psoriasis and the impaired quality of life that our patient had reported.[10] The dosing flexibility of the drug fostered its use in a patient at risk of infections and adverse events. Indeed, this pharmacologic characteristic allows the dosage of tildrakizumab to be reduced to the lowest possible one when psoriatic disease is in remission in particularly fragile patients.

We searched the literature (search strategy in Supplementary Table 1) and realized that only 112 psoriasis patients living with HIV were described as having been treated with biological drugs before our patient and that only 38 had received drugs different from anti-TNF-α agents, before the patient described here.[16,17] Patients reported in publications have a mean age of 47.7 years and are mainly males (33/38). Reported comorbidities include HCV (n=5), HBV (n=3), psoriatic arthritis (n=4), depression (n=3), hypertension (n=2), type 2 diabetes (n=2), and porphyria cutanea tarda, thrombocytopenic purpura, acute myocardial ischemia; obesity, dyslipidemia, hepatocellular

carcinoma, alcohol abuse, Kaposi sarcoma, each one in one case. Most patients suffered from plaque psoriasis (33/38, 86.8%), four from erythroderma (10.5%), and one guttate psoriasis (2.6%). Thirty-four patients were receiving HAART and had stable viral loads during treatment; one patient was not treated for HIV, and treatment for HIV was not reported for three patients. One patient described by Myers was treated with ustekinumab 45 mg for 11 months without HAART, had an alcohol abuse disorder, and also reported a stable viral load of 51/76, CD4 cell count = 997/1063 and no adverse events.[18] Notably, treatment-related death was observed only in patients receiving anti-TNF-α agents.[16]

The biologics used in the 38 patients receiving anti-cytokine agents were ustekinumab (n=16), risankizumab (n=10), secukinumab (n=7), ixekizumab (n=3), brodalumab (n=1), and guselkumab (n=1) (Supplementary Table 2). All these subjects reached either complete or partial clearance of psoriasis, and only seven were reported not to obtain PASI90. Only three adverse events occurred; one patient receiving ixekinumab had grade 1/2 herpes zoster, one receiving secukinumab had grade 3/4 candida esophagitis, and one receiving secukinumab had grade 3/4 genital candidiasis. The mean treatment duration with specific biologic was 274.8 days (n=32, range 14–2,134 days), and with anti-TNF-α agents 658.4 days (n=39, range 2–4,894).[16,17]

The patient described in this article was a male, as most of those previously described, was 64 years old, was treated with HAART, and had a follow-up comparable to other patients. In the 13 months of follow-up, we obtained PASI100, and the response was satisfactory and tolerability very good.

These data suggest that biologics targeting IL-17, -12, and-23 may be safer than first-generation biologics, in agreement with the conclusions of the systematic review published by Sood et al.[16] Cases treated with anti-IL-23 agents had a short follow-up, except two cases observed up to 40 months. Our observation of 13 months suggests that tildrakizumab may be a safe intervention for subjects with HIV.

Conclusions

To our knowledge, this is the first report on the treatment of psoriasis with tildrakizumab in a patient with HIV. We obtained a rapid and sustained remission of skin lesions, even in difficult-to-treat areas, without adverse events or changes in the immune cell levels.

Clinical trials and observational studies in real life showed that tildrakizumab has rapid activity and is effective for long periods.[18–20] The option of two different schedules may be very convenient for difficult patients, such as immunosuppressed ones, as therapy may be modulated to the changing conditions of patients. Additionally, adherence to tildrakizumab by patients in polypharmacy may be favored by the administration only every 12 weeks.[10]

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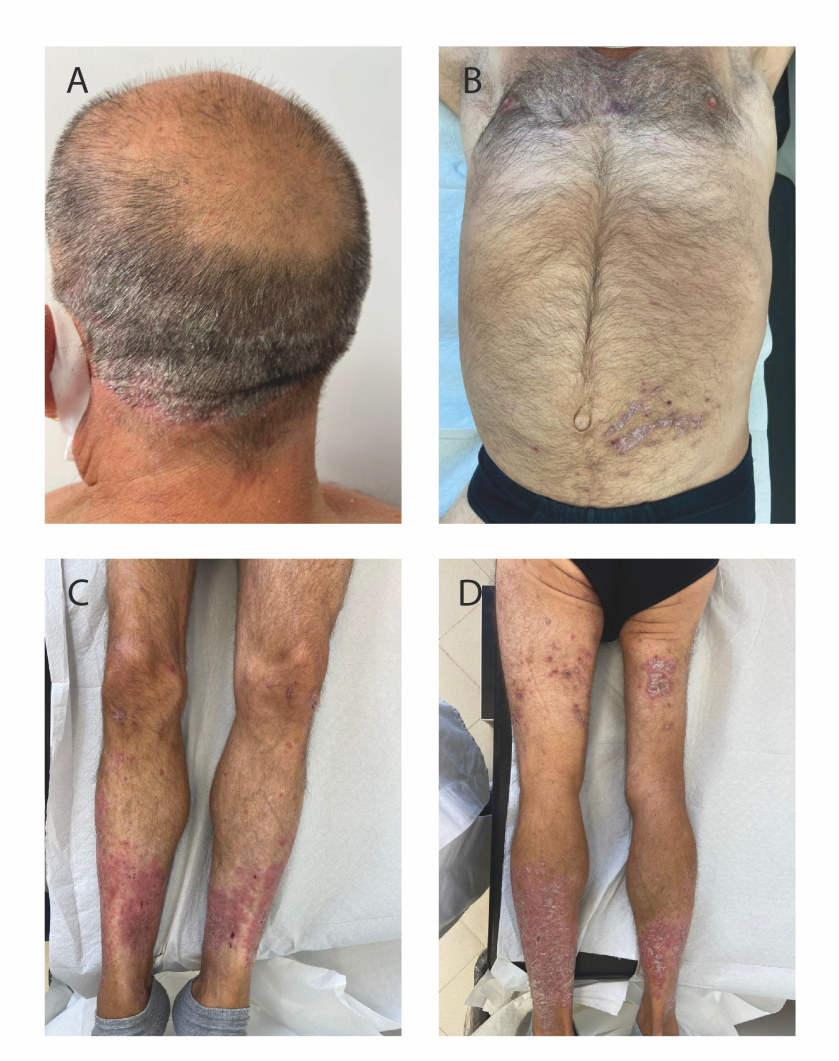

Figure 1. **Baseline status of plaque psoriasis.** (A) Scalp; (B) anterior trunk; (C) anterior side of lower limbs; and (D) posterior side of lower limbs.

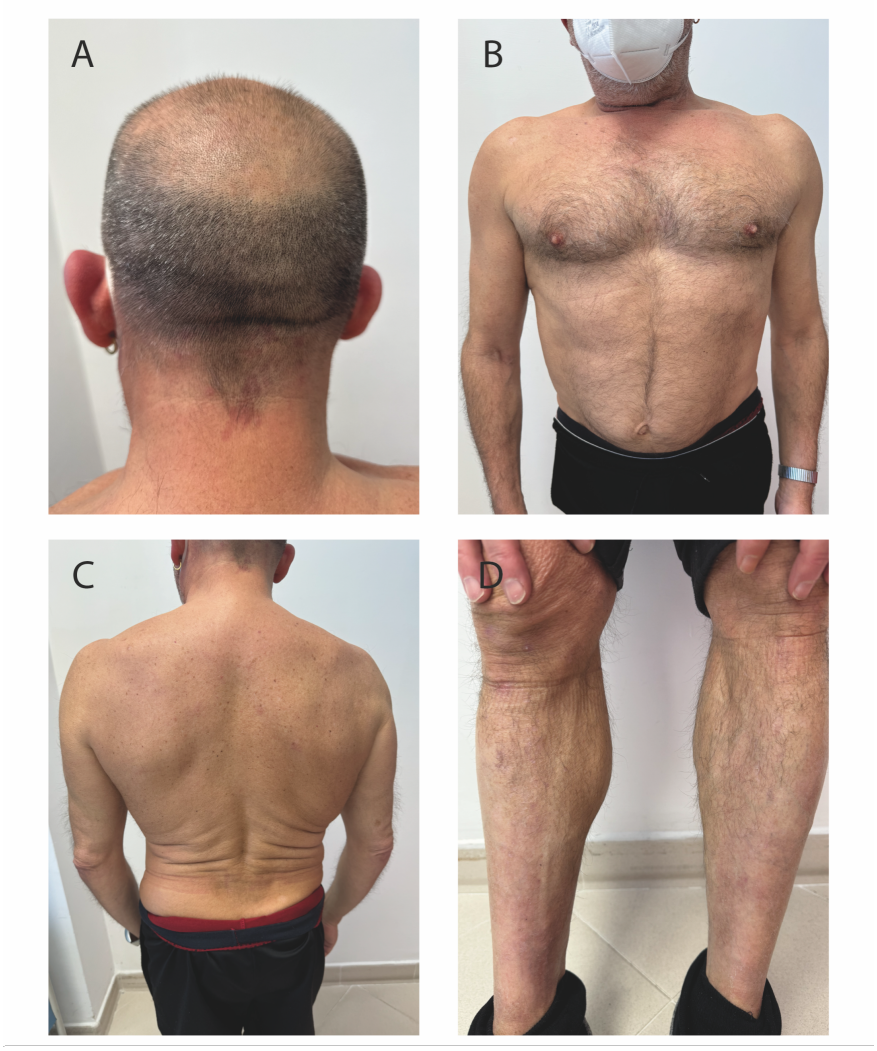

Figure 2. Remission of plaque psoriasis (PASI100) after a follow-up of 16 weeks with tildrakizumab. (A) Scalp; (B) anterior trunk; (C) back; and (D) anterior side of lower limbs.

Supplementary materials online:

Supplementary Table 1. Search strategy used for literature screening.

Supplementary Table 2. Individual features of 39 patients with psoriasis and HIV infection treated with anti-interleukin drugs.