OXFORD

Oxford Medical Case Reports, 2023, **7**, 251–253
https://doi.org/10.1093/omcr/omad066
Case Report

Control of porphyria cutanea tarda with anti-IL-17 secukinumab in a person with psoriasis living with HIV

Helbies Bedier[1,2], Stéphane Isnard[2,3], Réjean Thomas[4] and Jean-Pierre Routy[1,2,3,*]

[1]Department of Medicine, Division of Hematology, McGill University Health Centre, Montreal, QC, Canada
[2]Department of Infectious Diseases and Immunity in Global Health, Research Institute of the McGill University Health Centre, Montreal, QC, Canada
[3]Department of Medicine, Chronic Viral Illness Service, McGill University Health Centre, Montreal, QC, Canada
[4]Clinique l'Actuel, Montreal, QC, Canada

*Correspondence address. McGill University Health Centre, 1001 Boulevard Decarie, Suite E.M3.3232, Montreal, QC H4A 3J1, Canada. Tel: 514-843-1558; Fax: 514-843-1418; E-mail: Jean-pierre.routy@mcgill.ca

Abstract

A 65-year-old woman successfully treated for human immunodeficiency virus (HIV) and Hepatitis C virus was diagnosed with porphyria cutanea tarda (PCT) and treated by phlebotomies. She developed extensive psoriatic skin lesions resistant to topical treatments and methotrexate. She then received the anti-interleukin-17 (IL-17) secukinumab (Cosentyx) which improved her psoriatic skin lesions. Unexpectedly, her PCT skin lesions healed, allowing phlebotomy discontinuation over 2 years. Without lesions, the patient decided to discontinue secukinumab, leading to the recurrence of psoriatic and PCT skin lesions, which were controlled upon therapeutical rechallenge. No AIDS-related manifestations or infections developed, her CD4 count remained elevated and her HIV viral load was controlled under antiretroviral therapy. Both skin conditions and consequently the patient's quality of life have improved with secukinumab, allowing exposure to sunlight and phlebotomy discontinuation for >4 years. Likely, the IL-17 pathway is involved in the clinical manifestations of PCT, opening new avenues for therapeutical interventions.

INTRODUCTION

The term porphyria refers to a group of heterogenous disorders involving a defect in one of the eight steps of heme synthesis, with different clinical presentations depending on the defect [1]. Porphyria cutanea tarda (PCT) is the most frequent type of porphyria, presenting with blistering of sunlight-exposed skin. The hepatic deficiency of uroporphyrinogen decarboxylase results in excess circulating porphyrins excited by sunlight [2]. Photo-activation of the complement system in the presence of uroporphyrin activates dermal mast cells to release proteases and various inflammatory cytokines, leading to fibroblast damage and separation of the dermis and epidermis, resulting in skin fragility and vesicles. PCT manifestations onset and severity can be triggered by alcohol consumption, estrogen, hemochromatosis, and hepatitis C virus (HCV) and human immunodeficiency virus (HIV) infections with iron accumulation in the liver easily measured by plasma ferritin [3]. Phlebotomy is the standard treatment to rapidly decrease ferritin levels [2].

Psoriasis is an autoimmune skin disease that presents with patches caused by excessive growth of the epidermis [4].The skin of a psoriatic patient is enriched with Th17 cells and interleukin (IL)-17+ CD8+ T-cells that induce skin inflammation upon recognition of the skin lipid self-antigens presented by CD1 [5]. Local inflammation with IL-36, tumour necrosis factor-alpha, IL-1β, IL-6 and IL-17 is thought to induce premature keratinocyte maturation. Standard treatment includes topical corticoids or systemic anti-inflammatory drugs such as methotrexate [4].

Recently, clinical trials with anti-IL-17 monoclonal antibodies have reported growing evidence of IL-17 involvement in other autoimmune diseases, such as systemic lupus erythematosus, and various other chronic diseases with inflammatory pathology [5]. Secukinumab (Cosentyx) is a human IgG1 monoclonal antibody binding to IL-17A. Since 2017, it has been indicated to treat moderate-to-severe psoriasis plaques and/or arthritis as well as ankylosing spondylitis arthritis in adults [6, 7].

Our case reports a female patient receiving HIV antiretroviral treatment (ART) who developed extensive psoriatic skin lesions while being treated by phlebotomies for PCT. Her psoriasis skin lesions, refractory to topical treatments and methotrexate, improved remarkably with anti-IL-17 secukinumab, which also improved her PCT skin lesions. After discontinuing secukinumab, both psoriatic and PCT skin lesions recurred after 2 months and were controlled upon therapeutic re-initiation.

CASE REPORT

A 65-year-old female patient, non-smoker and not alcoholic, living with HIV and HCV, was referred in 2014 to be treated by phlebotomies for her PCT. In 1992, she was diagnosed with HIV after receiving a blood transfusion for thrombocytopenic

Received: February 3, 2023. **Revised:** April 13, 2023. **Accepted:** May 29, 2023

purpura. She received ART only in February 2007 when her CD4 T-cell count slowly declined to 299/mm^3, and her plasma HIV load reached 81 621 copies/ml. She received raltegravir (Isentress) and emtricitabine/tenofovir (Truvada). Over time, her CD4 T-cell counts improved as well as her CD4/CD8 and remained with an undetectable viral load. In June 2007, she was diagnosed with HCV infection, probably acquired from the same initial blood transfusion and was successfully treated four years later.

In December 2010, she suffered from severe extensive blistering and peeling of skin upon minimal sun exposure that forced her to wear gloves and a hat in her daily activities. She was diagnosed with PCT by a dermatologist, confirmed by elevated uroporphyrins in urine and negative testing for systemic lupus erythematosus. She was being treated with phlebotomies first weekly then every 2–3 months to maintain a target ferritin of 10–20 μg/L. Following HCV treatment with interferon-α and ribavirin in May 2012, PCT lesions healed, and she was able to hold phlebotomy for a year, with ferritin values above 10 μg/L.

In May 2013, she was diagnosed by a dermatologist with severe psoriasis, which, over 5 years, became refractory to topical treatment and oral methotrexate (20 mg weekly). In January 2018, she presented to our clinic with worsening psoriatic plaques covering her arms, thighs, abdomen and buttocks.

Due to her HIV status and elevated CD4 count, after a discussion between her dermatologist, treating physician and our team, we decided to use the anti-IL-17 antibody secukinumab to treat her severe psoriasis, under strict immune monitoring.

In August 2018, after a complete update of vaccinations and having a persistent HCV negative PCR, the patient received secukinumab 300 mg subcutaneously weekly for 4 weeks, then 300 mg monthly for 6 months as recommended, then followed by 150 mg monthly as requested by the patient [6–8]. After 2 months of treatment, psoriasis lesions dramatically improved. Unexpectedly, her sunlight-induced forearm blisters also reduced in number and intensity. As sun exposure was no more a trigger for her PCT lesions, phlebotomies were halted without any skin changes, despite the increase in her ferritin levels. Due to the persistent resolution of her two skin conditions, she decided to go on vacation to Florida in February 2020, she was able to tolerate sun exposure in a swimming suit on the beach without sunscreen. As such, she decided to hold her secukinumab treatment. However, 3 months after treatment discontinuation, new psoriasis skin lesions reappeared along with blisters on the sun-exposed forearm.

Two months after resuming secukinumab treatment, a marked improvement in her psoriasis and PCT skin lesions occurred. To this day, under the secukinumab maintenance dose, the patient has not developed any more skin lesions, only a few dyschromic skin changes (Fig. 1). She does not undergo phlebotomies and her last ferritin levels were at 78 μg/L (Fig. 2, Table 1).

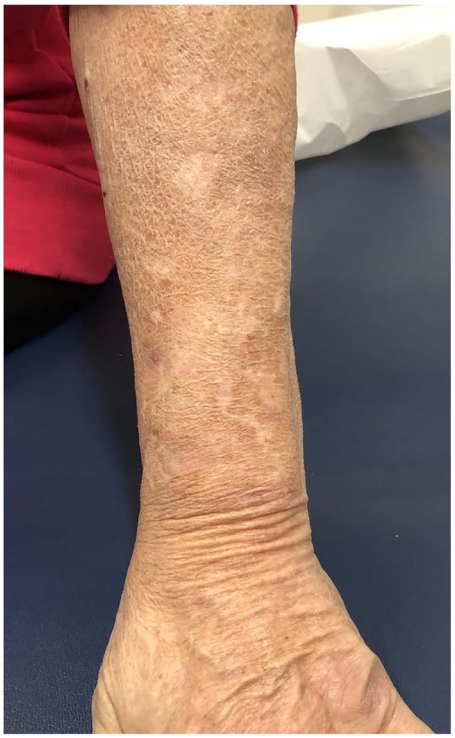

Figure 1. Healed PCT lesion with persistent skin dyschromia.

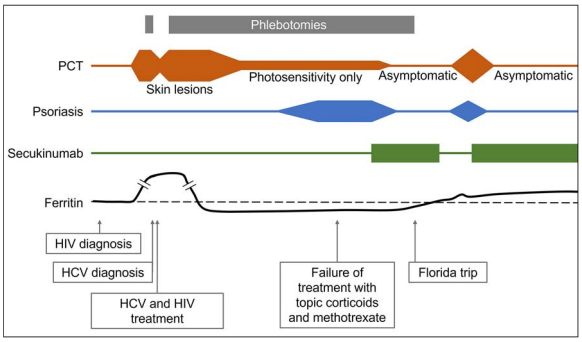

Figure 2. Scheme of the patient's case development. (Line thickness indicates disease symptom intensity).

DISCUSSION

IL-17A is a naturally occurring cytokine produced in response to several immune and inflammatory processes. Cytokines and other inflammatory mediators contribute to skin lesions in PCT. Storjord *et al.* reported that in acute intermittent porphyria,

Table 1. Key biologic markers in relation to the patient's PCT manifestation.

Date (mmm/yyyy)	Feb 2007[a]	Jun 2008[b]	Dec 2009[c]	Dec 2012[d]	Mar 2018[e]	Oct 2018[f]	Aug 2019	May 2020[g]	Sep 2020[h]	Oct 2021	Aug 2022	Mar 2023
Biologic Marker												
HIV viral Load (copies/ml)	81 621	258	<40	< 40	<20	<20	<20	28	<20	<20	<20	<20
CD4 (/mm^3)	299	477	286	1030	1535	1098	1100	1490	1234	1394	1447	1461
CD4/CD8 Ratio	0.6	0.7	1.2	1.02	1.8	1.5	1.4	1.7	1.6	1.7	1.7	1.8
Ferritin (μg/L)	NA	NA	759	88.5	7.3	28.9	17.4	40.8	39	89.7	104.1	78

[a]Start of CD4 decline leading to the initiation of ART [b]Diagnosis of HCV [c]Diagnosis of PCT, start of its severe skin symptoms and initiation of phlebotomies [d]Few months after the start of HCV treatment [e]Diagnosis of psoriasis [f]Two months after the start of secukinumab treatment for psoriasis [g]Two months after the patient stopped her secukinumab and before she was rechallenged with it again. [h]Few months after resuming secukinumab treatment.

the porphyrin-induced release of free radicals stimulated inflammation through direct activation of the transcription factor nuclear factor kappa B, leading to the release of IL-6, IL-8, and IL-17. This report highlighted the role of IL-17 on skin inflammation [9].

In summary, our case report suggests that secukinumab was effective and well-tolerated in treating both psoriasis and PCT skin lesions without inducing AIDS-related comorbidity or infections. The recurrence of PCT and psoriasis skin lesions upon discontinuation of secukinumab and control upon rechallenging with this drug, combined with a possible biological mechanism (inhibition of IL-17 pathway), indicates a plausible causal link as per WHO criteria [10]. This well-documented observation supports the role of anti-IL-17 in controlling the clinical manifestations of certain patients with PCT, compelling further studies.

CONFLICT OF INTEREST STATEMENT

None declared.

FUNDING

Our group is supported by grants from the Fonds de la Recherche Québec-Santé (FRQ-S): Réseau SIDA/Maladies Infectieuses and Thérapie cellulaire; the Canadian Institutes of Health Research (CIHR; Grants HOP 103230 and PTJ 166049); the Vaccines & Immunotherapies Core of the CIHR Canadian HIV Trials Network (CTN; Grant CTN 247); the Canadian Foundation for AIDS Research (CANFAR; Grant 02–512); CIHR- funded Canadian HIV Cure Enterprise (CanCURE 2.0) Team Grant HB2–164064.

ETHICAL APPROVAL

Not required.

CONSENT

Patient written informed consent was obtained.

GUARANTOR

Dr Jean-Pierre Routy.

REFERENCES

1. Bissell DM, Anderson KE, Bonkovsky HL. Porphyria. *N Engl J Med* 2017;**377**:862–72.
2. Stolzel U, Doss MO, Schuppan D. Clinical guide and update on porphyrias. *Gastroenterology* 2019;**157**:365–381.e4.
3. Ricci A, Di Betto G, Bergamini E, Buzzetti E, Corradini E, Ventura P. Iron metabolism in the disorders of heme biosynthesis. *Metabolites* 2022;**12**.
4. Griffiths CE, Barker JN. Pathogenesis and clinical features of psoriasis. *Lancet* 2007;**370**:263–71.
5. Mills KHG. IL-17 and IL-17-producing cells in protection versus pathology. *Nat Rev Immunol* 2023;**23**:38–54.
6. Eshwar V, Kamath A, Shastry R, Shenoy AK, Kamath P. A review of the safety of interleukin-17A inhibitor Secukinumab. *Pharmaceuticals* 2022;**15**. https://doi.org/10.3390/ph15111365.
7. Fala L. Cosentyx (Secukinumab): first IL-17A antagonist receives FDA approval for moderate-to-severe plaque psoriasis. *Am Health Drug Benefits* 2016;**9**:60–3.
8. Novartis N. *Cosentyx (Secukinumab) Injection [Prescribing Information]*. East Hanover, NJ: Novartis, 2016 Internet2016 [Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/125504s001s002lbl.pdf.
9. Storjord E, Dahl JA, Landsem A, Fure H, Ludviksen JK, Goldbeck-Wood S *et al.* Systemic inflammation in acute intermittent porphyria: a case-control study. *Clin Exp Immunol* 2017;**187**:466–79.
10. W.H.O. *The Use of the WHO-UMC System for Standardised Case Causality Assessment*. USA: WHO, 2013 Internet 2013 [Available from: https://www.who.int/publications/m/item/WHO-causality-assessment.