Dermatology Reports

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

eISSN 2036-7406

Please cite this article as:

Alibrahim L, Alrashid S, Aleissa M. Papillon-Lefèvre syndrome with excellent response to risankizumab. *Dermatol Rep 2026 [Epub Ahead of Print] doi: 10.4081/dr.2026.10309*

Received 20/02/25 - Accepted 08/02/26

Papillon-Lefèvre syndrome with excellent response to risankizumab

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Key words: Papillon-Lefèvre syndrome; palmoplantar keratoderma; risankizumab.

Contributions: Latifah Alibrahim: literature search, writing – original draft; Sarah Alrashid: writing review & editing; Majed Aleissa: revision with consistent integrations. All the authors read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Conflict of interest: the authors have no conflict of interest to declare.

Ethics approval and consent to participate: no ethical committee approval was required for this case report by the Department, because this article does not contain any studies with human participants or animals. Informed consent was obtained from the patient included in this study.

Consent for publication: written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

Availability of data and materials: not applicable.

Abstract

Papillon-Lefèvre syndrome (PLS) is a rare autosomal recessive genodermatosis. It is clinically characterized by diffuse palmoplantar keratoderma (PPK), psoriasiform skin lesions, and rapidly progressive periodontopathy. Management of PLS can be challenging. Herein, we present the case of a 27-year-old female who experienced poor response to multiple therapies, including topical keratolytic creams, oral isotretinoin and acitretin, and the tumor necrosis factor (TNF) inhibitor adalimumab. Notably, she achieved complete resolution of her cutaneous manifestations following treatment with the interleukin (IL)-23 inhibitor risankizumab.

Introduction

Papillon-Lefèvre syndrome (PLS) is an autosomal recessive genodermatosis, caused by a homozygous mutation of the *Cathepsin C* (*CTSC*) gene encoding for cathepsin C or dipeptidyl peptidase.[1,2]

PLS is clinically characterized by diffuse palmoplantar keratoderma (PPK), psoriasiform skin lesions, and rapidly progressive periodontopathy involving primary and permanent dentition. Herein, we present the case of a 27-year-old female who tried multiple management modalities for the cutaneous manifestations with sub-optimal response, including topical steroid, salicylic acid, and emollients. She also tried systemic therapies, such as isotretinoin, acitretin, and the tumor necrosis factor (TNF) inhibitor adalimumab.[3] Complete resolution of the cutaneous manifestation was achieved by managing through the use of interleukin (IL)-23 inhibitor risankizumab.

Case Report

A 27-year-old female presented with multiple scaly erythematous plaques mainly over the bilateral elbows, knees, knuckles, and neck (Figure 1). The lesions were first noted at the age of 2 years. Examination of the palms and soles showed hyperkeratotic yellowish diffuse plaques with gradient erythema. The diagnosis of PLS was proposed and confirmed genetically with a homozygous mutation in exon 6 of the *CTSC* gene at 4 years of age.

Multiple management modalities were attempted. Topical treatments with retinoids and urea 20% cream were tried, with minimal improvement. Systemic therapies were also administered, including acitretin at a dose of 10 mg and isotretinoin at 40 mg daily, which resulted in mild to moderate improvement.

Among TNF inhibitors, adalimumab was initiated at a dose of 80 mg at week 0, followed by 40 mg at week 1 and then 40 mg every 2 weeks, with only mild improvement.

The disease had a significant psychological impact on the patient's life. Therefore, the IL-23 inhibitor risankizumab was initiated at a dose of 150 mg at week 0 in January 2023, followed by 150 mg at week 4 and then 150 mg every 3 months. This treatment led to complete resolution of her skin manifestations, with no relapse at a two-year follow-up (Figure 2).

Discussion

PLS (OMIM 245000) is classified as ectodermal dysplasia with an autosomal recessive mode of inheritance caused by mutations in the alleles of the *CTSC* gene on chromosome 11q14.2, encoding for lysosomal protease cathepsin C. Deficiency or absence of cathepsin C protein activity is associated with the severity of symptoms.[1,2] The estimated incidence of PLS is one to four cases per million, with approximately 40% of the cases observed having a familial occurrence. The disease mainly occurs between the ages of 6 months and 4 years, affecting both sexes equally with no racial predilection.[4,5] PLS is a disorder of keratinization that is characterized mainly by severe, progressively destructive periodontal disease and precocious loss of dentition. The cutaneous form of PLS presents as symmetrical trans gradient PPK, followed by the development of psoriatic lesions over the dorsal surfaces. Other features of PLS include frequent pyogenic infections, pseudo-ainhum, and calcification of the dura.[2]

A multidisciplinary approach, mainly by dermatologists and dentists, and early diagnosis of PLS is crucial and can improve the prognosis of this syndrome. Multiple management modalities have been used in the management of cutaneous lesions of PLS, including topical therapies such as keratolytic salicylic acid, urea, and topical steroid emollients. Systemic acitretin, etretinate, and isotretinoin has shown to be effective in managing both cutaneous and dental symptoms. Retinoids are found to be the most widely used systemic category in the management of PLS.[6] To our knowledge, only two studies reported in the literature have investigated the management of biological therapy.

The IL-23/T helper (Th)17 pathway plays a central role in the onset and progression of hyperkeratotic and psoriasiform skin disorders. This pathway is driven by the interaction between IL-23 and Th17 cells, resulting in the release of pro-inflammatory cytokines such as IL-17, which promote excessive keratinocyte proliferation and inflammation. Th17 cells, a subset of T helper cells, are the primary producers of IL-17, a critical mediator in the pathogenesis of psoriasis. Elevated activity of the IL-23/Th17 pathway has been observed in psoriatic skin, highlighting its role in disease development. Therapies targeting this pathway, particularly biologic agents, have shown strong clinical effectiveness, underscoring its therapeutic relevance.[7]

A case report by Almukhadeb *et al.* described the use of adalimumab 80 mg subcutaneously at week 0, followed by 40 mg at week 1 and 40 mg every 2 weeks after failure of topical options such as

isotretinoin and urea cream. Treatment with a biologic agent such as adalimumab was associated with an excellent response in their case after three months, with marked improvement of the skin lesions. In contrast, our case showed minimal to no improvement and was characterized by multiple relapses.[8]

Latour-Álvarez *et al.* discussed the use of IL-12/23 p40 inhibitor (ustekinumab). In their case, after the failure of multiple management options, such as acitretin and isotretinoin, ustekinumab was initiated at 45 mg at week 0 and 4, followed by 45 mg every 8 weeks until response was maintained.[9]

A recent analysis of cytokine expression in affected skin from PLS patients revealed elevated levels of IL-1A, IL-1B, IL-12B, IL-36, TNF, IL-17, IL-26, interferon (IFN)-γ, and IL-13. These results suggest an immune response characterized by increased Th1/Th17 cytokine activity and heightened expression of the IL-1/IL-36 cytokine family. In our patient, treatment with risankizumab led to complete relief from itching, marked improvement of psoriasiform skin lesions, and moderate improvement in PPK.[9]

Yoshida *et al.* and Li *et al.* described the use of secukinumab, a biologic agent targeting IL-17, which has been reported in three patients with marked improvement.[10,11]

To our knowledge, this is the first case report to have described the use of the IL-23 inhibitor risankizumab to treat the cutaneous manifestations of PLS. Treatment with biological drugs have shown to be dramatically effective and should be considered in refractory cases.

Conclusions

PLS is a genetic disease with significant psychological impact on patients' life. Treatment is usually unsatisfactory with limited data on treatment in literature. IL23 inhibitors showed impressive results and could be a potential therapeutic option.

References

1. Wani AA, Devkar N, Patole MS, Shouche YS. Description of two new cathepsin C gene mutations in patients with Papillon-Lefèvre syndrome. J Periodontol 2006;77:233-7.
2. James WD, Berger T, Elston D. Andrews' Diseases of the Skin: Clinical Dermatology. 10th ed. Philadelphia: Saunders; 2006.
3. Al-Khenaizan S. Papillon-Lefévre syndrome: the response to acitretin. Int J Dermatol 2002;41:938-41.
4. Drucker DB, Marshall R, Bird PS. Aetiology of Papillon LeFèvre syndrome. Anaerobe 2001;7:151-8.
5. Cagli NA, Hakki SS, Dursun R, et al. Clinical, genetic, and biochemical findings in two siblings with Papillon-Lefèvre syndrome. J Periodontol 2005;76:2322-9.
6. Sreeramulu B, Shyam ND, Ajay P, Suman P. Papillon-Lefèvre syndrome: clinical presentation and management options. Clin Cosmet Investig Dent 2015;7:75-81.
7. Potestio L, Martora F, Lauletta G, et al. The Role of Interleukin 23/17 Axis in Psoriasis Management: A Comprehensive Review of Clinical Trials. Clin Cosmet Investig Dermatol 2024;17:829-42.
8. Almukhadeb E, Alanazi W, Alshareef R, et al. Excellent response to adalimumab in a patient with Papillon–Lefèvre syndrome: a case report. JEADV Clin Pract 2023;2:621-4.
9. Latour-Álvarez I, Ortega-Ramírez J, Alonso-Serrano E, Torrelo A. Novel compound heterozygous mutation in *CTSC* gene with response to ustekinumab. J Eur Acad Dermatol Venereol 2023;37:e798-800.
10. Yoshida I, Lommel K, Oji V, et al. Use of Retinoids and Secukinumab in a Patient with Papillon-Lefèvre Syndrome. J Investig Dermatol 2024;144:S272.
11. Li J, Wang Z, Xu Z. Secukinumab and Upadacitinib Treatment for Papillon-Lefèvre Syndrome in 2 Cases. JAMA Dermatol 2025;161:887-90.

Figure 1. a, **b**) Hyperkeratotic plaques over the palms and knuckles; **c**) scaly erythematous plaques over the lower limb.

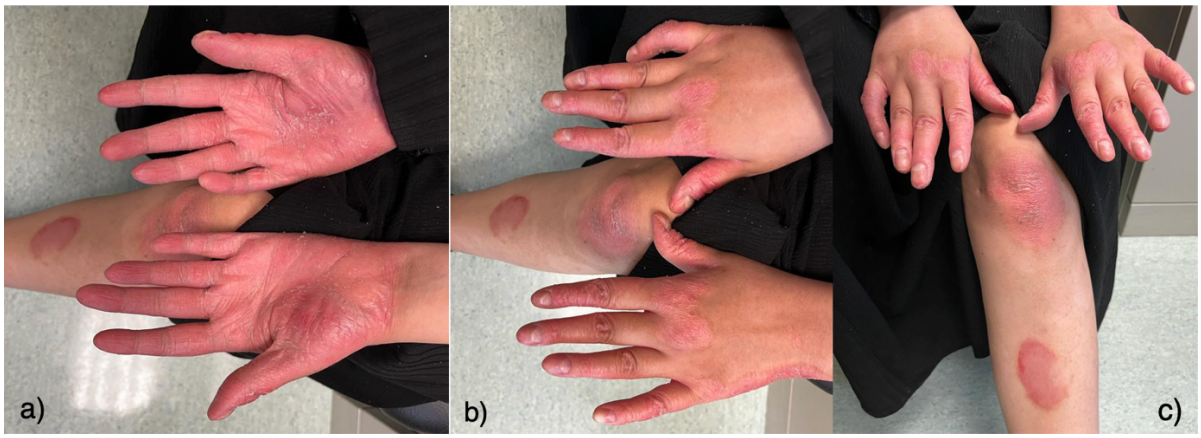

Figure 2. Patient response to treatment with risankizumab after 6 months.