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Case Report

Successful Treatment of Nail Lichen Planus with Roflumilast 0.3% Cream: A Case Report

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Abstract

Nail lichen planus is considered a true nail emergency resulting in destruction of the nails. Nail lichen planus is frequently resistant to treatments and has a high recurrence rate. This is a case report of a patient with lichen planus involving all of her fingernails, which exhibited 100% improvement following the daily application of the PDE4 inhibitor, topical roflumilast 0.3% cream, once daily.

Keywords: Nails; Lichen Planus; Topical Roflumilast 0.3% Cream; PDE4 Inhibitor

Introduction

Cutaneous Lichen Planus (LP) is a rare condition which occurs in approximately 0.2-1% of the population, with most cases developing in middle age between the ages of 30-60 years old [1]. Cutaneous lichen planus is characterized by pruritic, erythematous and violaceous papules and plaques, with a predilection for the wrists, lower back and ankles. Lacy, white lines, called Wickham striae, are seen overlying the lesions. Wickham striae are also seen in the mucosal lichen planus variant. Lichen planus can be worsened due to friction, trauma or scratching which is known as the Koebner phenomenon [1].

There are multiple variants of lichen planus including: scalp, inverse, bullous, hypertrophic, atrophic, mucosal, drug-induced and nail. A meta-analysis of over 12,000 oral LP patients using strict diagnostic criteria showed a risk of 0.5% for malignant transformation [2]. Other studies with less stringent criteria suggest a risk of 1-4% [3]. The incidence of nail lichen planus amongst patients with LP is approximately 10-15% [1,4]. Lichen planus of the nails can appear as nail dystrophy, onycholysis, longitudinal ridging, and/or pterygium formation. Lichen planus is extremely resistant to therapy of the nails and can require intralesional steroid injections, topical steroid and retinoid treatment to the nail matrix, oral hydroxychloroquine, oral prednisone and phototherapy including narrowband UVB and PUVA [5].

Here we present a resistant case of nail lichen planus impacting all of the fingernails which was successfully treated with topical roflumilast 0.3% cream once daily.

Case Report

We describe an 82-year-old female patient who presented with lichen planus of all ten fingernails, characterized by onychorrhexis, nail dystrophy, onycholysis and longitudinal ridging (Fig. 1). She also has oral lichen planus of the buccal mucosa. In 2021, she developed violaceous macules and papules on her forearms and hands, which was classic for cutaneous lichen planus. Her oral condition on the tongue responded well to clobetasol 0.05% ointment 1x a night for 1 week, then 1x a week as needed for a few weeks. After two months of treatment, her oral mucosa and tongue were clear of lichen planus. Her nail condition was not responding to multiple conventional therapies, including topical steroids such as clobetasol 0.05% ointment, hydrocortisone 1% ointment, triamcinolone 0.1% ointment and betamethasone 0.05% ointment; topical retinoids such as tazarotene 0.05% gel and cream and adapalene 0.1% gel; the topical steroid/retinoid halobetasol/tazarotene 0.01%/0.045% lotion; the topical vitamin D3 analog calcipotriene 0.005% solution; and the topical calcineurin inhibitor tacrolimus 0.1% ointment - all

applied to the nails and nail matrices; narrowband UVB light treatment; short pulses of oral prednisone; and oral hydroxychloroquine 200 mg daily, which yielded some improvement for the nails but did not clear them. All topicals were used for a minimum of 24 weeks without improvement. The patient had to discontinue use of hydroxychloroquine as the medication was, by history, affecting her eyesight. Fingernail clippings were sent to Bethesda Dermatopathology Lab, Bethesda, MD for fungal staining and returned negative for fungus. The patient responded rapidly to topical application of roflumilast 0.3% cream to the nail matrices daily after only a few months of treatment, following which the patient's nails reverted to normal (Fig. 2). We believe this is one of the first cases that have demonstrated a curative response of nail lichen planus to a PDE4 (phosphodiesterase-4) inhibitor, as well as long-term efficacy demonstrated with 1x a week application to the nail matrix for maintenance.

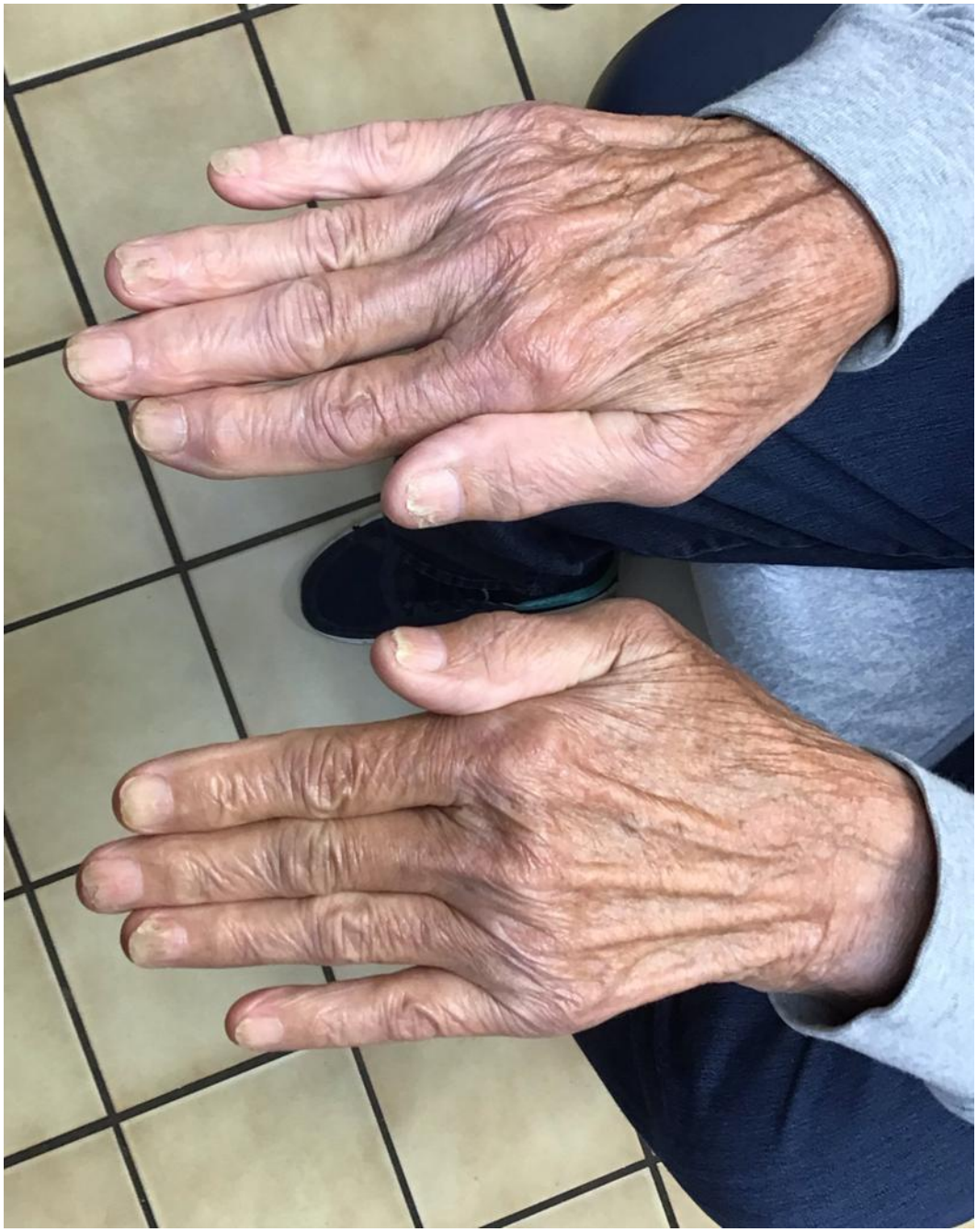

Figure 1: Prior to daily application of topical roflumilast 0.3% cream. Fingernails showed onychorrhexis, nail dystrophy, onycholysis and longitudinal ridging.

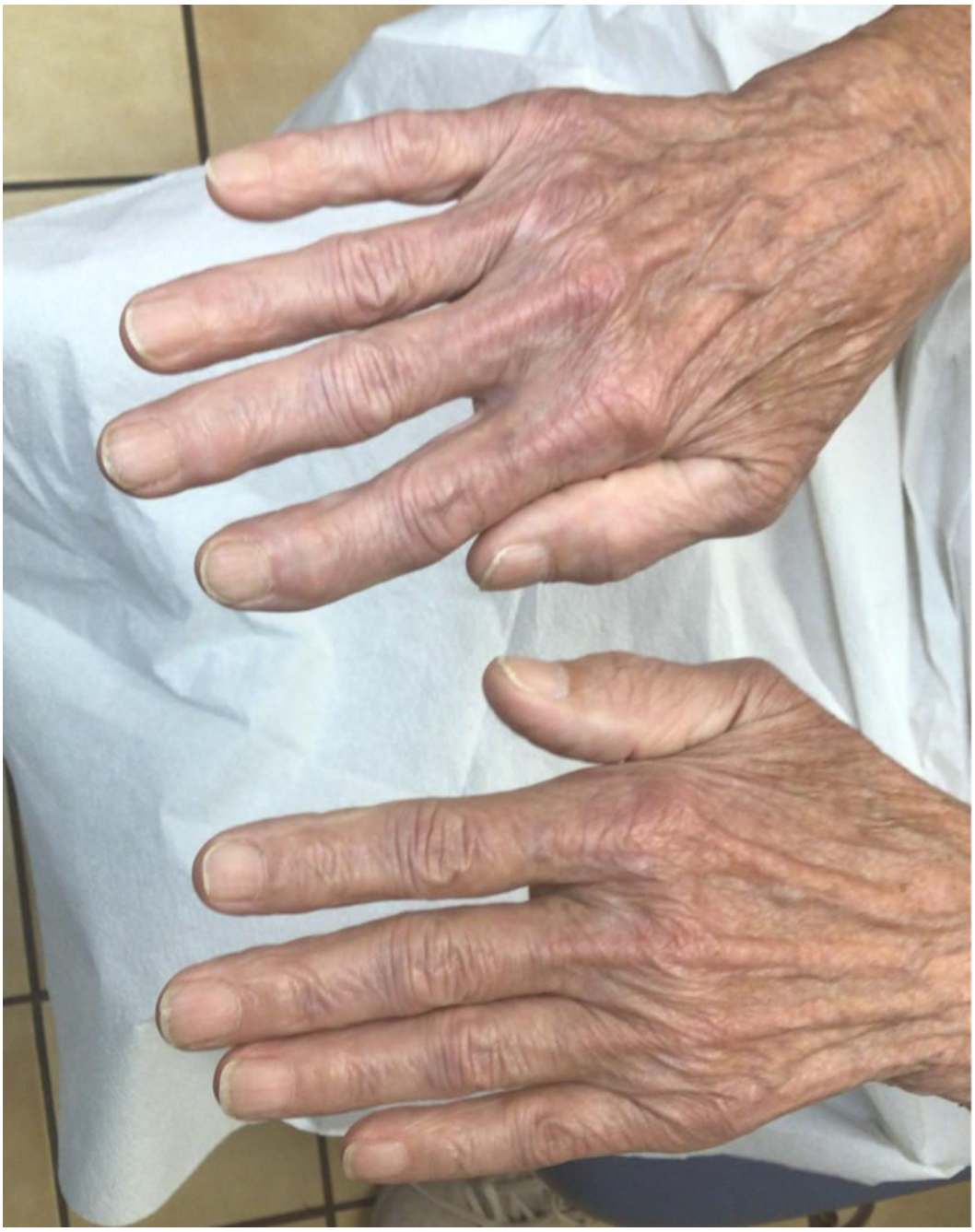

Figure 2: 7 months after daily application of topical roflumilast 0.3% cream.

Discussion

Although the full pathophysiology of lichen planus has not yet been fully elucidated, we do know that the predominant infiltrates are CD8+ cytotoxic T lymphocytes that appear to be epidermotropic and cause a band-like sawtooth lymphocytic infiltrate at the Dermal-Epidermal Junction (DEJ) [1,6]. The activated T lymphocytes lead to apoptosis of basal layer keratinocytes [1].

Histologically, orthokeratosis, acanthosis, pointed rete ridges and dome shaped papillae, hypergranulosis and basal layer vacuolization can be seen. The hypertrophic variety shows more orthokeratosis and hypergranulosis and the atrophic variety shows less [7]. Mucosal lichen planus is often accompanied by Wickham striae which appears histologically as hypergranulosis of the epidermis [8]. The atrophic variant shows epidermal atrophy and reduced elastin fibers in the upper dermis in addition to the above [9]. Eosinophils can be found when it is drug-induced [1]. Direct Immunofluorescence (DIF) can show irregular deposits of immunoglobulin A (IgA), IgG, IgM or C3 at the DEJ. With DIF, necrotic keratinocytes can also be seen at the basal layer due to apoptosis, which are called colloid, Civatte or cytoid bodies [1].

Lichen planus of the nail matrix shows the histological findings of lichen planus of the skin in addition to parakeratosis and serous exudates [10].

The suspected mechanism of action for the effectiveness of PDE4 inhibition in the treatment of lichen planus is thought to be due to the increase in cAMP levels within cytotoxic T lymphocytes. This resultant increase in cAMP would lead to suppression of cytotoxic T lymphocyte activation, proliferation and cytokine production [11].

The cytotoxic T-cells and recruitment of Th1/Th17 cells are driven by inflammatory mediators, interleukin-17 and interleukin-23 [1,6]. This pathway is well known in psoriasis and is why roflumilast 0.3% cream is efficacious for psoriasis. PDE4 inhibition has been shown to reduce tumor necrosis factor α, interleukin-17 and interleukin-23 [12].

One may be able to extrapolate that roflumilast may be effective based on the documented use of oral roflumilast as well as oral apremilast, another PDE4 inhibitor, for the effective treatment of oral and cutaneous lichen planus [13,14]. There have been no known reports of systemic PDE4 inhibitors and their effectiveness in treatment of nail lichen planus.

Lichen planus can be due to a multitude of drugs including ACE inhibitors, beta blockers, thiazide, potassium and loop diuretics, NSAIDs, phenothiazines, antiepileptics, antituberculars, antifungals and sulfa drugs [15-24]. Paradoxically, hydroxychloroquine can induce lichen planus as well as treat it [25].

There is also evidence suggesting a strong association between hepatitis C viral infections and lichen planus [26]. Furthermore, it is interesting to note that metal allergies to the metals used in dental implants can not only contribute to oral lichen planus but can also contribute to the onychodystrophy found in nail lichen planus [27].

Conclusion

Additional studies will be needed to determine the long-term efficacy of PDE4 inhibitors specifically, topical roflumilast for the treatment of nail lichen planus as relapse is very common with lichen planus.4 Further studies are also needed to elucidate the pathophysiology involved with nail lichen planus. Limitations include small sample size and the possibility of spontaneous remittance.

Conflicts of Interest

The authors declare no conflict of interest for this paper.

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