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# Therapeutic challenges in a case of psoriasis with nail onset

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## *Case report*

# **Therapeutic challenges in a case of psoriasis with nail onset**

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### **Abstract**

Nail psoriasis affects a large number of patients with psoriasis and has a major psychosocial impact. Furthermore, it may be regarded as a predictor of more severe forms of psoriasis and early sign of psoriatic arthritis. The clinical presentations vary depending on the structure affected (nail matrix or nail bed), the nail lesions may range from minor to severe, but they are not specific. Treatment is a challenge, in most cases the lesions being resistant to therapy.

We present a rare case of psoriasis with nail onset in a 59-year-old woman. The nail involvement confined to the fingernails was severe, with significant impairment of the patient's quality of life. Conventional therapies failed to improve the nail lesions, but a marked improvement was achieved under etanercept therapy.

**Keywords:** nail psoriasis, treatment, quality of life



## Introduction

Psoriasis is a chronic immune-mediated disorder affecting about 2% of the general population. The pathogenic mechanisms involved in the development of psoriasis lesions are related to the activation of the immune system, which leads to the release of proinflammatory cytokines, such as TNF alpha, IL17, 12, 23, etc. These mediators of inflammation stimulate processes such as excessive keratinocyte proliferation and angiogenesis, promoting the occurrence of psoriasis lesions (1, 2).

Most patients with psoriasis develop nail lesions during the course of the disease, the prevalence of nail psoriasis among patients with psoriasis ranging between 10 and 78%, with a mild male predominance (3). Approximately 1-5% of patients present nail lesions without skin manifestations (4). However, studies have shown that many patients who initially had only nail involvement developed skin or joint lesions later (5).

Nail psoriasis involves the fingernails more frequently than the toenails (3). Clinical signs vary depending on the structure affected. If the lesions are confined to the nail matrix, pitting (cupuliform depressions), leukonychia, red spots in the lunula, or nail crumbling may occur. Nail bed lesions lead to onycholysis, subungual hyperkeratosis, splinter hemorrhages, oil drop discoloration, and nail thickening. Nail pitting is the most common sign encountered in nail psoriasis (6-8). These changes are not specific and may also occur in other disorders (9).

NAPSI (spell out the first time?) is the most commonly used index for assessing the severity of nail psoriasis. The method involves the division of the nail into four quadrants by drawing imaginary lines (a vertical and a horizontal line) and the evaluation of the matrix and nail bed lesions in each quadrant (3, 9).

Treatment is difficult due to the low penetration of topical treatments in the nail, the pathologic changes

further contributing to this problem. As a result, systemic therapy is often necessary (10).

## Case Report

A 59-year-old woman was admitted to our clinic for nail changes and erythematous-squamous lesions located on the tips of her fingers. She stated that the first nail changes had started six months earlier and shortly afterwards, the skin lesions appeared on her fingers. The patient addressed a dermatologist who performed a mycological examination that was negative and a skin biopsy that established the diagnosis of dyshidrotic eczema. Keratolytics and topical corticoids were prescribed. The anamnesis revealed that her father had psoriasis vulgaris. The patient had no relevant history of medical or surgical conditions.

At the time of presentation to our clinic, the physical examination revealed hyperkeratotic nails, with a brown-yellow appearance and subungual deposit, erythematous-squamous lesions, moderately pruritic, localized especially on the tips of her fingers, were also observed (Figure 1).



**Figure 1.** Hyperkeratotic nails, with a brown-yellow appearance and subungual deposit, erythematous-squamous lesions, localized especially on the tips of her fingers

The toenails were not involved. Otherwise the clinical examination was normal. Laboratory investigations did not show any significant abnormality.

The main differential diagnoses included skin conditions associated with nail involvement such as palmar eczema, psoriasis vulgaris, lichen planus, and alopecia areata. We established the presumptive diagnosis of psoriasis vulgaris, given her positive family history and clinical examination. We decided to perform another biopsy, but the result was inconclusive. We initiated treatment with acitretin, as many studies have demonstrated a beneficial effect on subungual hyperkeratosis and multiple nail involvement.

After 2 months, well defined erythematous-squamous, slightly pruritic lesions occurred predominantly on her lower limbs. A biopsy from her left calf was taken, confirming the diagnosis of psoriasis vulgaris. The histopathologic examination showed parakeratosis, epidermal micro-abscesses with neutrophils, acanthosis and papillomatosis; in the papillary dermis a dense lymphocytic infiltrate predominantly disposed perivascularly was noticed. Regarding the nails' appearance, no satisfactory results were observed after the treatment with acitretin (Figure 2).



**Figure 2.** The clinical aspect after 8 weeks of treatment with acitretin

Therefore we decided to stop acitretin and start methotrexate. After 6 months, the clinical evaluation revealed extensive erythematous-squamous lesions and a modest relief of nail lesions. We considered the initiation of the biological therapy. PASI score was 24.8, DLQI score 24, and NAPS I score 72. Meeting the

required criteria, the patient was started on etanercept. The evolution was rapid and favorable, a 75% improvement in PASI score was observed after six months of treatment. After 8 months of treatment, PASI score was 5, DLQI score 5, and NAPS I score 32 (Figure 3).



**Figure 3.** The clinical aspect after 8 months of etanercept therapy

## Discussion

It seems that nail involvement in psoriasis is much more common than previously thought. Studies have shown that nail psoriasis is positively associated with both duration and severity of the disease (4, 11). Furthermore numerous studies have revealed a strong correlation between nail psoriasis and psoriatic arthritis; 63-83% of the patients with psoriatic arthritis present nail changes (12). Some authors have suggested that nail psoriasis could be considered a predictor of the development of psoriatic arthritis (13). In the presented case, the patient had not developed joint lesions yet.

Nail psoriasis has a significant impact on the patient's quality of life, in some cases interfering even with the simplest daily activities (10). In a large study, a

questionnaire was applied to 1,728 subjects with psoriasis; 1,379 of them had nail lesions, with involvement of both finger and toenails. Regarding patients with nail lesions, 93% felt a significant cosmetic handicap, 60% reported interferences with their daily and professional activities, and 51.8% complained of pain (14). In the study by Klaasen (15), the impact on the quality of life of patients with nail psoriasis was assessed using DLQI and NPQ10, with higher scores among women obtained. Psoriasis had a significant impact on the quality of life, with results similar to those obtained in patients with cardiovascular disease, diabetes, or depression (15). In our case, the patient's quality of life was dramatically reduced, the disease interfering with the simplest daily activities. In addition, the patient had a tendency toward social isolation.

In a recent study, a positive family history of psoriasis was more common in the case of those with nail lesions compared to those without nail lesions (53.7% vs. 42.8%). Furthermore, a significant percentage of those with nail lesions had an early onset of psoriasis (under the age of 40 years) (4). Regana et al. have revealed a positive relationship between the severity of nail lesions and being 65 years or older, as well as a positive family history of psoriasis or type of psoriasis, most of whom suffered from moderate-severe psoriasis (16). Our patient had a positive family history, her father suffering from psoriasis.

Our case illustrates the difficulty in treating nail psoriasis, multiple therapies being often necessary until a satisfactory response is achieved. In mild and moderate forms of nail psoriasis, local therapy is the first choice. Systemic therapy is recommended when nail psoriasis is associated with extensive cutaneous psoriasis lesions, if the lesions are severe or involve several nails (5 out of 10 or more), and if the disease has a significant impact

on the patient's quality of life, interfering with the daily activities (6, 17).

In our case, we opted for acitretin given the extensive nail lesions, characterized by an important hyperkeratosis, associated with skin lesions on the tip of the fingers. Riccerri reported a case of psoriasis in a 73-year-old patient with severe nail psoriasis involving all fingernails and toenails successfully treated with acitretin (0.5 mg/kg). He associated urea-based lacquer as adjuvant treatment (18). Tosti reported a 41% reduction in the NAPSI score among patients treated with acitretin, the first improvement in the clinical appearance being observed after 4-8 weeks of treatment (19). However, acitretin may lead to onycholysis and nail fragility, so doses should be as low as possible (20). In our case after 8 weeks of treatment, no satisfactory results were observed and further skin lesions developed. Thus we cease acitretin treatment and began methotrexate treatment.

Several studies have demonstrated the efficacy of methotrexate on nail psoriasis; the favorable results are probably based on the drug action on T-lymphocytes (8). For example, patients with nail psoriasis who received 15mg/weekly of methotrexate showed a reduction in the NAPSI score of 43.3% after 24 weeks of treatment. In the same study, patients treated with cyclosporine showed a 37% mean improvement in the NAPSI score (21). However, in other studies cyclosporine was superior to methotrexate (16). In our case, six months after starting treatment with methotrexate, results were not satisfactory and we decided to initiate therapy with a biological agent. Biological agents have proven their efficacy in both cutaneous and nail lesions. Infliximab, adalimumab and etanercept are the most studied treatments; we decided to give our patient etanercept.

Regana et al. have shown that classical treatments (methotrexate, cyclosporine) lead to results comparable to those obtained using biological therapy (16). However, it should be noted that classical therapies must be administered over longer periods of time to achieve good results (16, 22).

Etanercept is a genetically engineered fusion protein that combines the constant portion of IgG, the Fc fragment containing the CH2 and CH3 constant regions, with two p75 receptors of TNFR-2 (23). Etanercept binds soluble TNF $\alpha$  and TNF $\beta$  (24). A randomized study (CRYSTAL) of 564 patients with moderate-severe psoriasis associated with nail lesions receiving etanercept showed a decrease in the NAPSI score of 28.9% at 12 weeks and 51% at 54 weeks of treatment (25). The efficacy of etanercept in nail psoriasis has also been supported by other studies (7, 26, 27). In our case, there was a rapid response to etanercept with a significant reduction in the NAPSI score.

Bardazzi et al. concluded that adalimumab, infliximab, ustekinumab and etanercept exhibit similar efficacy in the treatment of nail psoriasis. They also postulated that patients with nail lesions reach PASI 75 slower than those without nail involvement (28).

## Conclusions

We present a case of psoriasis vulgaris with nail onset, characterized by severe nail lesions and a significant impact on the patient's quality of life, with a marked improvement following the treatment with etanercept and poor response to classical therapies with acitretin and methotrexate. Nail lesions are common among psoriasis patients and are associated with a significant psychosocial impact. Treatment often remains a significant challenge.

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