# **PRACTICAL DERMATOLOGY**

# **Diagnosis and Management of Nail Psoriasis**

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Abstract. Nail psoriasis has traditionally been considered as one of the most difficult forms of psoriasis to treat. The most recent studies have found a higher prevalence of fungal infections in psoriatic nails and therefore cultures before and during treatment are necessary. Over the last few years, novel psoriatic therapies have been developed, some of which are effective for both skin and nail lesions (cyclosporine and biologic agents). Of the topical agents, vitamin D and A derivatives as well as nail lacquer containing 8% clobetasol propionate can help improve lesions of both the nail bed and matrix.

Key words: psoriasis, nails, diagnosis, management.

### ASPECTOS DIAGNÓSTICOS Y TERAPÉUTICOS DE LA PSORIASIS UNGUEAL

Resumen. La psoriasis ungueal ha sido considerada clásicamente una de las manifestaciones más difíciles de tratar de la enfermedad. Los últimos estudios han evidenciado una mayor prevalencia de infecciones fúngicas en las uñas psoriásicas, por lo que debemos practicar cultivos al inicio y durante el tratamiento. En los últimos años han aparecido numerosas novedades terapéuticas en la psoriasis; algunas son eficaces tanto para las lesiones cutáneas como para las ungueales (ciclosporina y biológicos). A nivel tópico, los derivados de la vitamina D y A, así como la laca de clobetasol propionato al 8% pueden conseguir mejorar tanto las lesiones del lecho como las de la matriz ungueal.

Palabras clave: psoriasis, uñas, diagnóstico, tratamiento.

# Introduction

For many years, the nails have been one of the most frustrating anatomical locations for the treatment of psoriasis, both for patients and dermatologists. While, unsurprisingly, many patients with psoriasis have made use of specific novel and not-so-novel treatments for the rest of the body, the nails have been neglected, since, except for painful infiltrations of corticosteroids, no new treatments had been developed. Furthermore, patients often report associated pain and for many it is yet another change in their physical appearance that is often very noticeable. Thus, it is clearly a health care problem that has not received the attention it deserves.

Currently, the development of new drugs and vehicles that allow nail penetration mean that the situation has changed substantially. For diagnosis, quantitative methods similar to the psoriasis area and severity index (PASI) have been developed to allow assessment of the severity of the lesions and thereby facilitate greater reproducibility of studies.

### **Epidemiologic Features**

Nail involvement is very common in the course of psoriasis, with between 10% and 78% of patients affected.<sup>1</sup> In our own experience, we have observed nail involvement in 53% of our patients (n=164).<sup>2</sup> The fingernails are affected more often than the toenails, and more than 1 nail is usually involved. In fact, psoriasis is one of the diseases that most often involves the nails. It is also well know that there is an association between psoriatic arthritis and nail psoriasis (70% of patients have nail lesions)<sup>3</sup> (Figure 1), which often precedes the disease rather than just accompanying it. Patients are sometimes referred by rheumatology departments during assessment of arthritis, and it is not surprising for a patient with psoriatic arthritis to only have lesions of the nails, or at most, in the gluteal cleft (Figure 2) or scalp (Figure 3).

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Figure 1. Patient with psoriatic arthritis (presenting as dactylitis) and nail psoriasis (onycholysis and oil spots).



Figure 2. Psoriasis of the gluteal cleft, which usually accompanies nail psoriasis and psoriatic arthritis, especially in men.

Nail psoriasis in young children is rare,<sup>3</sup> and on occasions, when it occurs, it may form part of the syndrome known as 20-nail dystrophy, which can itself have various causes.

It has recently been shown that patients with nail psoriasis are negative for the HLA-Cw\*0602 allele on chromosome 6, as well as being late-onset cases of psoriasis that display a severe course.<sup>4</sup>

In recent years, numerous studies have addressed the psychosocial impact of psoriasis and the effect of the disease on patients' quality of life. In a study published by our group in 2003, we reported that 38.8% of our patients had not been to public swimming pools in the last month and stress was the triggering factor for outbreaks in 43% of those surveyed (n=1500).<sup>5</sup> Clearly, those lesions that affect the appearance of the hands and nails have a major psychosocial impact. In addition, we should not forget that many patients also report painful nails, as indicated in a study undertaken in 1728 patients, of whom 51.8% reported pain in the affected nails and 58.9% were restricted in their daily activities.<sup>1</sup>

There is an association between the duration of cutaneous lesions and the frequency of nail involvement.<sup>6</sup>

As in other anatomical sites, when the patient has an outbreak we must evaluate the presence of one or more triggering factors. In addition to stress, which tends to be the most important, we should not forget repeated trauma (Koebner phenomenon), which accounts for the more frequent involvement of the fingernails than the toenails, particularly in manual workers.<sup>4</sup> The appearance of nail psoriasis has also been described in response to lithium,<sup>7</sup>  $\beta$ -blockers, and interferon.<sup>4</sup>

It was traditionally thought that onychomycosis was very rare in psoriatic nails<sup>8</sup>; however, this view has changed since the recent study published by Gupta et al, <sup>9</sup> who analyzed a series of 561 patients with psoriasis and found that when there were psoriatic lesions of the toenails the frequency of



Figure 3. Psoriasis of the scalp, particularly associated with nail psoriasis.

onychomycosis increased by up to 27%, the risk increased with age, and the fungi responsible were the same as in the healthy population. In our experience, in a series of 20 patients with nail psoriasis, 6 (30%) had positive cultures for dermatophytes, yeasts, and moulds, and interestingly, 2 of those patients had positive cultures for Epidermophyton floccosum, a rare pathogen in tinea unguium.<sup>10</sup> Finally, an important factor to take into account is that the use of artificial nails can increase the risk of bacterial and fungal secondary infection of psoriatic nails. We should recommend that patients do not manipulate or chew their nails, and that they avoid excessive manicure. An important conclusion to draw from the study is that we should always perform a direct examination (potassium hydroxide) and fungal culture prior to initiation of treatment, particularly if we plan to use corticosteroids, and of course, if the patient reports pain in the nail at the beginning or during treatment. A practical

#### Table 1. Epidemiology of Nail Psoriasis

- Affects between 10% and 78% of patients with psoriasis. In our experience (n=164), the rate is 53%.
- The fingernails are more often affected than the toenails.
- Lesions are usually present in various nails.
- It is usually associated with psoriasis affecting the scalp and gluteal cleft, and is sometimes the only manifestation of the disease.
- It is often associated with psoriatic arthritis.
- It is more common in adults.
- Triggers: trauma (Koebner), stress, infection (mycosis), and drug treatments.
- Concomitant mycosis must always be ruled out.
- It has a serious psychosocial impact, in addition to pain (51.8%) and limitation of day-to-day activities (58.9%).

#### Table 2. Clinical Forms of Nail Psoriasis

- 1. Psoriasis of the Nail Matrix
- Pits or pitting, or dimples
- Trachyonychia
- Leukonychia
- Beau Lines
- Red lunulae
- 2. Psoriasis of the Nail Bed
  - Onycholysis
  - Subungual hyperkeratosis
  - Oil spots or salmon patches
  - Splinter hemorrhages
- 3. Paronychia
- 4. Acropustulosis



**Figure 4.** Oil spots. Always considered characteristic of psoriasis, they tend to be rounded and in this case isolated. They usually coexist with other lesions; in this patient, splinter hemorrhages are visible.

consideration to bear in mind is that similar lesions occur in nail psoriasis and onychomycosis and they can be confused; this is another reason why additional tests should be done prior to commencing treatment. Given that psoriasis is an immunologic disease triggered by superantigens, it is not surprising that fungal infections can lead to outbreaks, and such infections should therefore be appropriately managed (Table 1).

# **Clinical Forms of Nail Psoriasis**

As for other anatomical sites, nail psoriasis occurs in outbreaks with remissions that may be spontaneous or a result of treatment. In general, patients present with lesions in other areas and there is usually a correlation between the severity of those lesions and the extent of nail involvement.<sup>6</sup>

Psoriasis can affect any element of the nail apparatus nail bed or matrix, or both—and as a result will have different clinical manifestations according to the affected element. In clinical practice, it is most common to find lesions of the nail bed in isolation or combined to a greater or lesser extent with lesions of the matrix (pitting). In contrast, matrix lesions rarely occur in isolation. Furthermore, patients always consult for nail bed lesions, such as onycholysis or hyperkeratosis, which can cause pain as well as being unsightly (Table 2).

### Psoriasis of the Nail Matrix

### Pits or Dimples in the Nails

Pits or dimples in the nails are punctate depressions that are generally multiple and irregular, and rougher and deeper than those observed in other diseases such as alopecia areata or eczema. They are due to focal and transient disease of the proximal matrix and correspond to islands of parakeratosis that are eliminated when the nail appears, leaving behind a depression in the nail plate (Figure 4).

### Trachyonychia

Trachyonychia occurs as a result of a permanent alteration of the proximal matrix; the surface of the nail is rough and dull.

### Leukonychia

Leukonychia is a partial whitish coloration of the nail plate as a consequence of disease of the intermediate matrix.

### Beau Lines

Beau lines appear when the proximal or intermediate matrix is affected along its length.

### Red Lunulae

Red lunulae occur as a result of disease of the distal matrix.

# Psoriasis of the Nail Bed

### Onycholysis

Onycholysis is one of the most common and characteristic conditions of nail psoriasis. In addition, psoriasis is one of the main causes of onycholysis. It causes the distal nail plate to lift away from the nail bed and produces a whitish area of varying size that is surrounded by an erythematous collar or an "oil spot," a sign that is highly suggestive of psoriasis and helps to rule out other causes of onycholysis (Figure 5). Occasionally, the whitish color becomes green or brownish due to accumulation of bacteria or fungi.

### Subungual Hyperkeratosis

Along with onycholysis, subungual hyperkeratosis is a very common manifestation of nail psoriasis (Figure 6), and both may often be present in the same patient. It occurs as a result of excessive proliferation of parakeratotic cells that form a dense, pulverulent, whitish mass that causes distal lifting of the nail plate. It is the clinical entity that is most often confused with onychomycosis.

### Oil Spots or Salmon Patches

Oil spots and salmon patches are the only lesions that are exclusive to nail psoriasis; they appear as round or oval orange-colored areas in the center of the nail plate (Figure 7).

### Splinter Hemorrhages

Splinter hemorrhages are linear and distal with a threadlike appearance. They are usually only observed in the fingernails.

### Paronychia

Paronychia is a relatively common manifestation of psoriasis. It is associated with erythematous scaly lesions that affect the proximal and/or lateral edges of the nail, generally alongside lesions of the matrix or nail plate (Figure 8).

### Acropustulosis

Acropustulosis presents with periungual or subungual pustules in the context of acrodermatitis continua of Hallopeau (Figure 9) or, less often, localized or generalized pustular psoriasis.



Figure 5. Psoriatic onycholysis. A border in the form of an oil spot is characteristic and helps to differentiate it from other causes of onycholysis



Figure 6. Subungual hyperkeratosis alongside other psoriasis lesions.



Figure 7. Patient with nail psoriasis predominantly affecting the matrix (pitting) and mild subungual hyperkeratosis.



Figure 8. Psoriatic paronychia.

#### Table 3. Clinical Diagnosis of Nail Psoriasis

- Assess other areas affected by psoriasis.
- In cases of isolated nail psoriasis, examine the scalp and gluteal cleft.
- Dimples or pits caused by psoriasis are deep and irregular.
- Oil spots are characteristic of psoriasis.
- Psoriatic onycholysis is surrounded by a salmon stain.
- Perform potassium hydroxide staining and fungal culture.
- Nail biopsy is sometimes necessary.



Figure 9. Acrodermatitis continua of Hallopeau.

# **Diagnosis of Nail Psoriasis**

In most cases, a diagnosis of nail psoriasis is established according to clinical criteria, and as such it is important to examine the rest of the skin in order to identify psoriatic plaques. Although it should be remembered that sometimes the only phenotypic manifestation of psoriasis is found in the nails, it is nevertheless relatively common for nail psoriasis to coexist with psoriatic arthritis and lesions on the scalp and gluteal cleft. From a clinical point of view, the presence of deep, irregular pits or dimples, or of oil spots and onycholysis surrounded by a salmon stain is highly suggestive of psoriasis (Table 3). It is advisable to complement the examination with digital photographs, allowing the lesions to be assessed more objectively and to assess the therapeutic progress.

Clinical diagnosis should be completed with tests such as direct examination and potassium hydroxide staining of the scales obtained from nail lesions, as well as subsequent fungal cultures. Sometimes it is also recommendable to obtain bacterial cultures (nails with green discoloration). Biopsy of the matrix or nail bed, which allows observation of the histologic characteristics of psoriasis, is not often performed to confirm diagnosis.<sup>6</sup>

In the same way that cutaneous psoriasis can be quantified with a numerical parameter, the PASI score, a similar scale has recently been developed for the nails, known as the nail psoriasis severity index (NAPSI).<sup>11</sup> This allows an objective evaluation of the severity of nail psoriasis and facilitates more reliable clinical studies. Instructions for calculating the NAPSI score are provided in Table 4. As occurred with the PASI score, and despite the NAPSI having been described in 2003, it has been criticized for a lack of objectivity and a modification has been proposed.<sup>12</sup> The main advantage of the modified NAPSI is that it allows a more detailed assessment of the target nail for each specific parameter, and as such provides a better reflection of the course of the disease following treatment.

# **Treatment of Nail Psoriasis**

Patients with nail psoriasis often improve with standard systemic or biologic treatment of the skin lesions or arthritis, since it most often coexists with those conditions.

Nevertheless, there is a subgroup of patients who consult dermatologists and present isolated nail psoriasis or nail lesions that predominate over other cutaneous lesions; there are also patients in whom nail psoriasis simply has a strong psychosocial impact. In such cases, we need to be aware of which treatments are currently available (Table 5). Table 6 shows the protocol we use for patients with nail psoriasis, presented in the form of an algorithm. 
 Table 4. Instructions for Calculation of the Nail Psoriasis

 Severity Index (NAPSI)

The nail is divided into 4 imaginary quadrants via horizontal and vertical lines. Each nail is examined for signs of disease in the matrix or nail bed.

- Nail matrix: pitting, leukonychia, red lunulae, trachyonychia. Each quadrant of the nail is examined for the presence of these parameters: 0, none; 1, in a single quadrant; 2, in 2 quadrants; 3, in 3 quadrants; and 4, if present in all quadrants of the nail.
- 2. Nail bed: onycholysis, subungual hyperkeratosis, oil spots, splinter hemorrhages; from 0 to 4.
- 3. Each nail receives a score from 0 to 8. The scores for all the nails are added together to obtain the NAPSI score, which ranges from 0 to 80 for the fingernails and 0 to 160 if the toenails are included.
- 4. Modified NAPSI. The modified NAPSI involves assessment of a target nail. It is also divided into 4 quadrants and for each quadrant the nail parameters are each assessed separately: 0 = unaffected, 1 = mild, 2 = moderate, and 3 = severe. In this case the score ranges from 0 to 96.

#### Table 5. Treatment of Nail Psoriasis

1. Topical Treatments
<ul> <li>Potent corticosteroids</li> <li>In nail lacquer</li> <li>Intralesional</li> <li>Under occlusion</li> </ul>
<ul> <li>Vitamin D derivatives</li> <li>Calcipotriol</li> <li>Tacalcitol</li> </ul>
– Vitamin A derivatives Tazarotene
– 5-Fluorouracil
– Dithranol
– Cyclosporin
– Topical psoralen UV-A therapy
2. Systemic Treatment – Retinoids Acitretin
- Methotrexate
– Cyclosporin
– Biologic agents Efalizumab Etanercept Infliximab

# **Topical Treatments**

### Topical Corticosteroids

Class I topical corticosteroids are used under occlusion in disease affecting the nail matrix or periungual tissue.<sup>6,13</sup> However, since there is minimal absorption of the drug, the treatment is ineffective. Association with keratolytics (high-concentration urea, salicylic acid) or retinoic acid was recommended for a while in order to promote penetration, but the results tend to be poor, particularly if the goal is to treat the nail matrix. We have obtained good results for paronychia.

In contrast, a relatively popular treatment option for nail psoriasis for a few years was the use of corticosteroids by infiltration.<sup>13</sup> Triamcinolone acetonide was injected into the matrix or nail border using insulin needles or Dermojet. In addition to the pain caused, notable among

Table 6. Diagnostic and Therapeutic Algorithm for Patients With Nail Psoriasis

- 1. Perform potassium hydroxide staining and bacterial culture before and during treatment.
- 2. In case of diagnostic uncertainty, look for psoriasis lesions at other sites (scalp, gluteal cleft) and/or perform a nail biopsy.
- 3. Describe the type of nail lesion (bed or matrix) and, if possible, calculate the NAPSI.
- 4. Provide patients with advice on nail care: avoid repeated trauma, keep the nails dry, and cut nails after bathing. Attend follow-up appointments if the nails change color (secondary infection).
- 5. Does the patient have psoriatic arthritis? If the answer is yes, the patient should be assessed by a rheumatologist and combined treatment instigated. If the answer is no, dermatologic treatment is indicated. This can be systemic or biologic treatment of the psoriasis or a specific treatment of nail psoriasis, depending on the response to point 6 (both points should be considered together).

6. Does the patient have lesions on other parts of the skin? Calculate the PASI score, BSA, and assess quality of life (DLQI).

7. Does the patient receive systemic or biologic treatment for psoriasis? If the answer is yes, the nail lesions may improve or disappear. If the answer is no, specific treatment of nail psoriasis is indicated. If the lesions predominantly affect the nail bed, apply vitamin D derivatives (calcipotriol, tacalcitol) under occlusion; in isolated lesions of the matrix and with few nails involved, infiltration of corticosteroids can be used, while if various nails are affected, 8% clobetasol lacquer should be applied; in the case of mixed lesions, vitamin D should be applied during the week and 8% clobestasol lacquer at the weekend; and if no improvement is observed, 0.1% tazarotene gel or topical PUVA should be used.

Abbreviations: BSA, body surface area; NAPSI, Nail Psoriasis Severity Index; PASI, Psoriasis Area and Severity Index; PUVA, psoralen UV-A.

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the side effects are atrophy, hypochromia, secondary infections, inclusion cysts, and tendon rupture. In our opinion, more effective alternatives are currently available that also do not lead to the pain and side effects associated with corticosteroids, so that injection should be limited to use in very severe trachyonychia affecting only a few fingers.

In 1999, Baran and Tosti<sup>14</sup> published an interesting study in which they treated 45 patients with nail psoriasis using a nail lacquer containing 8% clobetasol-17-propionate. It is well known that lacquers allow greater penetration of the nail than other excipients, as is apparent for the treatment of onychomycosis. However, the novel aspect of that study was the very high concentration of clobetasol propionate used (8% rather than the usual 0.05%). The authors did not observe secondary infections or atrophy during follow-up. The results were very encouraging and improvement was observed both in pitting and in parameters associated with the nail bed (especially onycholysis). We have subsequently reported our own positive experience with that treatment in 10 patients.<sup>15</sup> In our study, clear lacquer containing 8% clobetasol propionate was applied daily for 21 days and then twice a week for 9 months. After 4 weeks we could observe a marked improvement in nail parameters, especially pitting, onycholysis, and oil spots, and the patients who had painful nails (3 out of 10) reported complete disappearance of pain within that time. The improvement of the nail lesions was progressive, with application of the product, and sustained. We did not observe any side effects, not even atrophy of the periungual skin. Bacterial and fungal cultures were repeatedly negative during treatment, and analysis of cortisol and corticotropin in the blood and cortisol in 24-hour urine did not reveal abnormalities. Consequently, despite the limited number of patients included in our case series, we believe that 8% clobestasol in nail lacquer is a safe and effective treatment for nail psoriasis. Since this formulation is not currently marketed, we must resort to the extemporaneous preparations that our specialty was once famous for. A case has recently been described of a patient with secondary candida infection due to application of this lacquer.<sup>16</sup> In order to avoid these types of complications and optimize the treatment, it is necessary to carefully monitor the patient, and bacterial and fungal cultures must be obtained prior to and during the treatment. In patients at risk of contracting onychomycosis, 1% clotrimazole can be added to the preparation.

#### Vitamin D Derivatives

The introduction of vitamin D derivatives in the therapeutic arsenal for treatment of psoriasis has represented an important step forward by offering a topical drug without the risk of atrophy and tachyphylaxis associated with corticosteroids. Vitamin D derivatives have been reported to be useful both as monotherapy and in combination with other topical or systemic treatments and at any anatomic site in which psoriasis appears-skin, scalp, or nails. Of the 3 derivatives that are marketed in Spain (calcipotriol, tacalcitol, and calcitriol), the most extensively studied in nail psoriasis is calcipotriol, possibly as a result of it being the first to be synthesized. We published a series of 15 patients with psoriasis affecting the fingernails who were treated with calcipotriol ointment (50 mg/g) twice daily.<sup>17</sup> We observed good results in relation to psoriasis affecting the nail bed (especially subungual hyperkeratosis) but not the matrix. Tolerance was excellent. In a controlled study, calcipotriol ointment (50 mg/g) was compared with the application of betamethasone dipropionate (64 mg/g) and salicylic acid (0.03 mg/g), and it was concluded that calcipotriol was as effective as the combination of corticosteroids and salicylic acid, indicating that calcipotriol is a safe and effective treatment for nail psoriasis. As in psoriasis plaques, calcipotriol acts on hyperkeratosis but not erythema, and it is therefore not surprising that in the nails it improves the hyperkeratotic component but not that of the matrix, since it fails to penetrate. To optimize its use, as we do in the skin, we should combine it with a corticosteroid, as reported by Rigopoulos et al,<sup>18</sup> who treated 62 patients with nail psoriasis using calcipotriol each night from Monday to Friday and 0.05% clobetasol propionate each night at the weekend for 12 months. They obtained a mean improvement in subungual hyperkeratosis of 77%. Other parameters were not mentioned.

Since tacalcitol is more potent than calcipotriol in vitro and is only applied once a day, we undertook a study in our department in which we used it in combination with 8% clobetasol propionate.<sup>19</sup> The regimen consisted of application of tacalcitol every night from Monday to Friday and clobetasol lacquer at night during the weekend over a period of 6 months. We observed no side effects and obtained excellent results in the 15 patients treated, with improvements in both matrix and nail bed parameters assessed according to the NAPSI. Logically, tacalcitol must act in the same way as calcipotriol, reducing subungual hyperkeratosis, but the provision of a potent corticosteroid in a lacquer markedly improves penetration and as a result we were able to achieve improvements in pitting.

The combination of vitamin D and corticosteroids is, as we have seen, very useful to improve the treatment efficacy and safety.

### Tazarotene

In recent years, various articles have appeared reporting the usefulness of tazarotene for the treatment of nail psoriasis.<sup>20,21</sup> Recently, Rigopoulos et al<sup>22</sup> undertook a study in which 46

patients with nail psoriasis were randomly assigned to 2 groups, one treated with 0.1% tazarotene cream under occlusion each night for 12 weeks and the other treated with 0.05% clobetasol propionate cream under the same conditions. They observed a significant improvement in subungual hyperkeratosis, onycholysis, oil spots, and pitting to a similar extent in both groups after 12 weeks of treatment. There were almost no side effects in either group. Following discontinuation of treatment, there was a sustained improvement in the group treated with tazarotene, especially in relation to hyperkeratosis. Based on those results, we can intuit that, as in the case of cutaneous plaques, tazarotene is a useful drug that leads to prolonged remission.

### 5-Fluorouracil

5-Fluorouracil at a concentration of 1% in propylene glycol<sup>23</sup> or in a cream containing 20% urea<sup>24</sup> has been used sporadically for the treatment of nail psoriasis. In the few cases that have been published it appears to improve pitting and dystrophy arising in the matrix; in contrast, there is clear deterioration of onycholysis and irritation and hyperpigmentation can occur as side effects.

#### Dithranol

A study has been published describing the use of short contact therapy with dithranol ointment (0.4%-2%) applied for 30 minutes to the nail bed.<sup>25</sup> The authors observed an improvement in 60% of the patients.

### Topical Cyclosporin

Despite the poor epidermal penetration of cyclosporin, when it was first employed in dermatology it was used topically in a variety of conditions, including nail psoriasis. In an effort to optimize its effects, Tosti et al<sup>26</sup> employed a concentration of 10% in an oil-based vehicle that the patients applied over a period of months. Avulsion of the nail plate was performed prior to treatment. The authors reported good results in the nail bed.

#### Topical Psoralen UV-A

Topical psoralen UV-A (PUVA) involves application of a psoralen, usually 8-methoxypsoralen (8-MOP), to the affected nails followed by exposure to UV-A rays (320-400 nm). In our psoriasis and phototherapy unit, this was the most extensively used treatment for severe nail psoriasis until the advent of vitamin D derivatives and clobetasol propionate lacquer.

In our protocol, we bathe the affected nails with a 1% solution of 8-MOP in ethanol (0.5 mL diluted in 2 L of water) for 20 minutes. The patient then dries the surrounding

skin well and photoprotection is applied before exposure to UV-A. The results are excellent, particularly when combined with acitretin in the case of very severe hyperkeratosis or pustulosis. Notable side effects are burns and photoonycholysis. As a result, prior to use of PUVA, it is important to determine which drugs are being taken by the patient. However, onycholysis is the nail condition that shows the least improvement, or may even worsen. In order to avoid possible burns it is preferable to undertake the treatment in hospital, meaning that there may be logistic considerations for the patient.

### Nail Avulsion

Chemical avulsion of the nail with 40% urea is only considered in very severe cases of subungual hyperkeratosis and in the toenails. Surgical avulsion should be avoided.

## Systemic Treatment

Systemic treatment of nail psoriasis is very rarely indicated. Nevertheless, it is important to know how the condition responds to the therapies that are currently available, since if the patient has significant nail involvement, the modality we choose must also be effective at this anatomical site.

### Systemic Retinoids

Acitretin is used at a dose of 0.5 mg/kg. Although use of this drug has declined considerably in recent years, it continues to be a first-line treatment for pustular psoriasis.<sup>6</sup>

When used at low doses, for instance 10 to 25 mg/d in combination with PUVA (REPUVA), it continues to be an excellent alternative and an effective treatment in cases of palmoplantar psoriasis with significant nail involvement.

Acitretin is effective for reducing subungual hyperkeratosis. However, it should be remembered that many of its side effects involve the nails: onycholysis, severe nail fragility, and pyogenic granuloma. In order to reduce these effects to a minimum, the lowest possible dose should be used.

#### Methotrexate

Despite methotrexate causing a reduction in nail growth, patients treated with the drug systemically can show improvement of nail psoriasis,<sup>13</sup> without the side effects associated with acitretin. It is also effective in pustular psoriasis (including Hallopeau acrodermatitis).

### Cyclosporin

Patients with psoriasis treated with cyclosporin at standard dose (5 mg/kg/d) generally experience a marked

improvement of their nail lesions. This was demonstrated in our study of 70 patients with different types of psoriasis, of which 60% had mixed nail psoriasis at the beginning of the study. Following treatment with cyclosporin we observed a persistent improvement in lesions affecting both the matrix and the nail bed.<sup>27</sup> Despite its efficacy, the toxicity profile of cyclosporin is such that its use is not justified in cases of isolated nail psoriasis. It is also effective for the treatment of pustular psoriasis and acrodermatitis continua of Hallopeau.

In another interesting study, low doses of cyclosporin (2.5 mg/kg/d) were compared with etretinate (0.5-0.75 mg/kg/d) in relation to the efficacy for treatment of skin, nail, and joint lesions, and cyclosporin was found to be superior.<sup>28</sup>

### **Biologic Agents**

Recent years have seen the appearance of numerous biologic agents within the therapeutic arsenal for the treatment of psoriasis. Three are currently available in Spain for the treatment of plaque psoriasis (efalizumab, etanercept, and infliximab). Favorable results have also been reported with alefacept,<sup>4</sup> a drug which is not authorized in Spain. To date, there have been no studies specifically addressing the usefulness in nail psoriasis of adalimumab, a biologic agent that is not as yet indicated for use in plaque psoriasis. Clearly, none of these drugs are indicated in nail psoriasis, as is also true for systemic treatment; however, they are all clearly effective at that site.

Efalizumab. There is currently little information available on the effectiveness of efalizumab in nail psoriasis. In our study of 30 patients treated with efalizumab, we assessed the clinical response based on PASI and modified NAPSI scores, course of pruritus, and lesions on the scalp, palms, and soles.<sup>29</sup> After 24 weeks, we observed a significant reduction in the NAPSI score, thereby demonstrating the effectiveness of the drug for the treatment of nail psoriasis.

**Etanercept.** There are isolated cases in which etanercept has been reported to be effective for the treatment of nail psoriasis. In a series of 40 cases recently reported by our group, we found that most of the patients who had nail lesions at the beginning of treatment showed marked improvement of those lesions.<sup>30</sup>

**Infliximab.** For the moment, along with alefacept, infliximab is the biologic agent for which the most information is available regarding its efficacy in nail psoriasis. Just as it leads to rapid improvement of cutaneous lesions, significant improvement was observed by the tenth week, up to a 56%

reduction in the NAPSI score was observed at week 24, and the effect was sustained until week 50.<sup>4</sup>

#### **Conflicts of Interest**

The authors declare no conflicts of interest.

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