

## Review Article

# Review of nail psoriasis

## 甲銀屑病的回顧

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Nail psoriasis is often an overlooked feature in the management of psoriasis. This review article explores the impact of nail psoriasis on patients, the relationship between nail psoriasis and psoriatic arthritis, common clinical signs of nail psoriasis, the tool to assess the severity of nail psoriasis and management including specific treatments available for nail psoriasis.

甲銀屑病往往是在銀屑病治療中被忽略的一環。此綜論文章會探討甲銀屑病對患者的影響，與銀屑病關節炎的關係，其常見的臨床症狀及嚴重程度評估，最後是甲銀屑病的治理包括一些現行的特定治療。

**Keywords:** Nail psoriasis, psoriatic arthritis, treatment

**關鍵詞：**甲銀屑病、銀屑病關節炎、治療

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## Introduction

Psoriasis is a common chronic immune-mediated, inflammatory skin disease that affects approximately 2% of the Western population,<sup>1</sup> and 0.47% of the Chinese population.<sup>2</sup> Psoriasis most frequently affects the skin over the scalp, elbows, knees and genitalia. Nail involvement is seen in about 40-70% of patients with psoriasis.<sup>3-6</sup> On the other hand, around 5% of patients have isolated nail psoriasis without cutaneous psoriasis.<sup>7</sup>

Nail psoriasis is often asymptomatic or associated with minimal symptoms in the early stage. Patients often have no idea that the nail problem is caused by psoriasis and thus just focus on their skin or joint problems. Nail involvement is also regarded by many doctors only as a diagnostic sign of psoriasis or merely as a cosmetic problem without paying attention on its treatment.

## Impact of nail psoriasis

In a prospective case-control study involving 661 patients with psoriasis in Spain, around 47% patients were diagnosed with nail psoriasis. This group of patients had more severe psoriasis, longer disease duration and a higher proportion of patients with psoriatic arthritis (PsA).<sup>5</sup> In another cross-sectional study involving 3531 patients with psoriasis in Germany, around 40% were found to

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have nail psoriasis. Similarly, patients with nail involvement were found to have greater severity of psoriasis, longer disease duration, higher frequency of PsA, more days off work due to psoriasis and greater impairment in their quality of life.<sup>6</sup>

Nail psoriasis can affect the quality of life of patients due to the pain caused by the diseased nails and periungual tissue, difficulty in performing fine manual tasks and the embarrassment or stigmatisation experienced by patients as nail conditions are highly visible. Therefore, management of psoriasis should include treatment of the nail disease as well.

### Relationship with psoriatic arthritis

Nail psoriasis was especially associated with PsA affecting the distal interphalangeal (DIP) joint.<sup>8</sup> This can be explained by a study using high resolution magnetic resonance imaging which showed that the extensor tendons, which cross the DIP joint, are connected with the nail matrix via tendinous fibres. In the early phase of PsA, there is nearly always enthesitis of the DIP joint. This inflammatory process could easily affect the nail matrix due to their close anatomical relationship.<sup>9</sup> Therefore, routine assessment of a patient with nail psoriasis should include an enquiry about symptoms of inflammatory joint pain and a brief examination for any signs of PsA.

### Clinical signs of nail psoriasis

The nail unit is made up of several parts; nail plate, nail bed, hyponychium, nail matrix, nail folds, cuticle and distal phalangeal bones. The nail plate is formed primarily from the nail matrix, with secondary contribution from the nail bed.<sup>10</sup> Most of the lesions in nail psoriasis are the result of inflammation in the nail matrix and/or nail bed (Table 1).

The most common sign in nail psoriasis is pitting, occurring in almost 70% of patients.<sup>11</sup> Nail pitting is due to psoriatic lesions within the nail matrix, resulting in columns of parakeratotic cells in the stratum corneum that interfere with normal keratinisation. These columns are weaker than the surrounding area and shed off easily to leave pits in the nail plate as it grows out distally. Nail pitting is not specific to nail psoriasis and may be seen in other dermatoses such as alopecia areata and lichen planus. Other signs of nail psoriasis due to nail matrix inflammation include lunula erythema, leukonychia and nail plate crumbling.

For nail psoriasis signs due to nail bed disorders, onycholysis is the most common one.<sup>11</sup> Onycholysis in psoriasis is due to psoriatic lesions of the nail bed extending to the hyponychium and subsequently leading to shedding of weak parakeratotic cells from the stratum corneum. It usually starts distally and progresses proximally, causing a traumatic uplifting of the distal nail plate. Secondary microbial colonisation may occur. Onycholysis may be seen in many other conditions such as trauma, chronic paronychia and thyrotoxicosis. However, onycholysis with a proximal erythematous border is more specific for nail psoriasis.

Other signs of nail psoriasis due to nail bed inflammation include oil drop discolouration, subungual hyperkeratosis and splinter haemorrhage. The oil drop sign or salmon patch appears as a translucent yellow-red discolouration in the nail bed resembling a drop of oil under the nail plate. It is the most specific sign of nail

**Table 1.** Clinical signs of nail psoriasis

<b>Nail matrix psoriasis</b>	<b>Nail bed psoriasis</b>
Pitting	Onycholysis
Lunula erythema	Oil drop discolouration
Leukonychia	Subungual hyperkeratosis
Nail plate crumbling	Splinter haemorrhage

psoriasis. Subungual hyperkeratosis is due to excessive proliferation of keratinocytes in the nail bed that fail to shed off from the stratum corneum. It is also commonly seen in onychomycosis which may co-exist with nail psoriasis. Splinter haemorrhages are longitudinal black lines due to minute foci of capillary haemorrhage between the nail bed and the nail plate. It is analogous to the Auspitz sign of cutaneous psoriasis.

### Assessment of nail psoriasis

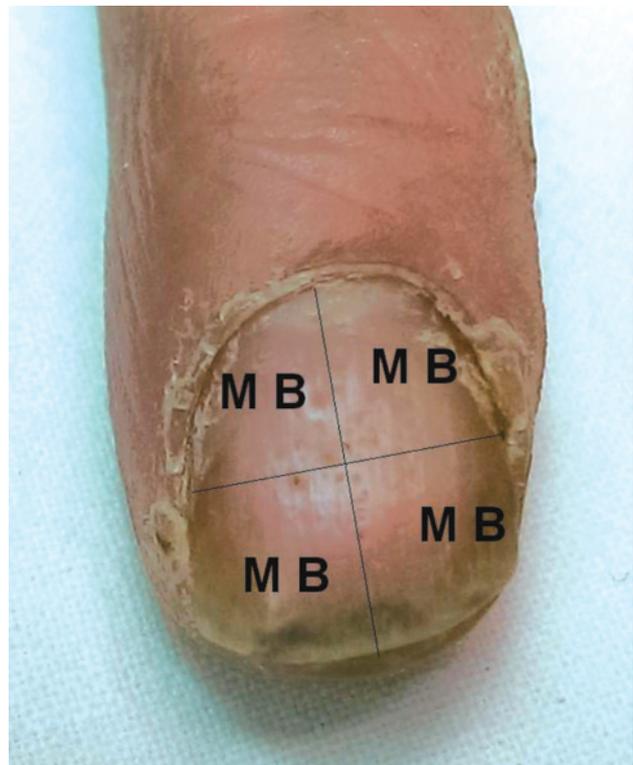
The Psoriasis Area and Severity Index (PASI) score is widely used for the assessment of psoriasis but it does not encompass an assessment of nail psoriasis. To assess the severity of nail lesions, Rich et al introduced the Nail Psoriasis Severity Index (NAPSI) which divides the nail into four imaginary quadrants (Figure 1). Each quadrant is rated with 0 or 1, based on the absence or presence of pathological signs resulting from involvement of the nail matrix and the nail bed. Therefore, NAPSI ranges from 0 to 8 for one nail and 0 to 160 for 20 nails.<sup>12</sup> Although it is time-consuming to use in clinical practice, NAPSI has significantly helped to standardise the outcome assessment of therapeutic studies.

### Management of nail psoriasis

In patients with nail changes affecting individual fingers or toes, onychomycosis should be ruled out with a plain specimen and fungal culture. If the nail changes are of uncertain origin, without accompanying skin changes, a biopsy may be useful in order to confirm the diagnosis. For confirmed cases of nail psoriasis, patients should also be evaluated for the possibility of PsA because of their close association.

The Koebner phenomenon is well-known to occur in psoriasis and it may also affect patients with nail psoriasis. Patients should be informed that meticulous nail care and measures to protect the

nails can be an important part of treatment success. These include protecting the fingernails by wearing gloves when handling chemically or physically aggressive materials at home or at work. Patients should preferably keep their fingernails and toenails short. Injuries to the nails, especially the cuticles, should be avoided. When washing the hands, it is important to dry off the tips of the fingers carefully to absorb any moisture that may get under the fingernails. Patients who have nail psoriasis of the toes should wear non-occlusive footwear that reduce the pressure on the feet. Routine visits to a podiatrist may be indicated in patients with severe disease because this can help avoid mistakes in proper nail and foot care.



**Figure 1.** NAPSI calculation – each nail is divided in four quadrants and the presence of lesion(s) of nail matrix (M) or nail bed (B) is counted as 1 point (max 2 points for each quadrant, 8 points for each nail).

M (nail matrix disorders): pitting, lunula erythema, leukonychia, crumbling.

B (nail bed disorders): onycholysis, oil drop, hyperkeratosis, splinter haemorrhage.

## Specific treatment of nail psoriasis

There is a common perception that nail psoriasis is very difficult to treat, thus only a minority of patients received specific treatments for it. However, various studies in the literature suggest that effective treatments do exist. Treatments include topical agents, intralesional injection, phototherapy and systemic agents (Table 2). The choice of the treatment depends on various factors which may include the patient's factors such as age, co-morbidities, regular medications and treatment preferences. Knowing the pathological origin (i.e. nail matrix or nail bed psoriasis) of specific clinical signs will facilitate the use of appropriate therapy that target that site, hence maximising therapeutic efficacy. Generally speaking, topical agents and intralesional injections are indicated for mild to moderate nail psoriasis and systemic agents are indicated for severe disease, especially if there are concomitant severe psoriatic skin lesions or PsA.

### Topical agents

The problem with topical therapy is that it is difficult to achieve a sufficiently high concentration of anti-psoriatic agent in the nail bed or nail matrix due to their anatomical structure. As a result, nail psoriasis takes at least months to show any improvement. This gives the patients a perception that the topical agent is not effective, thus affecting their treatment compliance. Hence, it is important to inform the patients about this expected slow response and to maintain their motivation and discipline to complete the therapeutic course.

**Corticosteroids** – The most commonly used topical agents in the treatment of nail psoriasis are corticosteroids which may be applied as a cream or solution to the nail fold and periungual regions, if necessary under occlusion. The response rates vary, depending on the strength of the steroid and duration of treatment.<sup>13-18</sup> In a study by Rigopoulos et al, an 82% improvement of NAPS I for oil drop, 66% for pitting and hyperkeratosis and 50% for onycholysis was reported for clobetasol propionate

0.05% cream after 12 weeks.<sup>18</sup> Potential side effects of prolonged use of potent topical corticosteroids include cutaneous atrophy, erythema, telangiectasias, striae, tachyphylaxis and distal phalangeal atrophy.

**Calcipotriol** – A case series of 24 patients with nail psoriasis which investigated the safety and efficacy of topical calcipotriol showed that it reduced onycholysis, hyperkeratosis and nail discoloration.<sup>19</sup> There were also studies supporting the use of combination therapy with calcipotriol and corticosteroid for nail psoriasis.<sup>16,20</sup> The advantage of combination therapy is to reduce the possible side effects of topical corticosteroids. Calcipotriol is relatively safe with possible minor side effects of local irritation, erythema and burning.

**Fluorouracil, Dithranol, Tazarotene** – There are conflicting results in the literature on the treatment of nail psoriasis with these agents. So far, there is still insufficient evidence to recommend their use for nail psoriasis.<sup>21-24</sup>

**Table 2.** Specific treatment of nail psoriasis

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#### Topical treatments:

1. Corticosteroids
2. Calcipotriol
3. Fluorouracil
4. Dithranol
5. Tazarotene

#### Intralesional corticosteroid injection

Phototherapy:

1. Systemic PUVA
2. Topical PUVA

#### Systemic treatments:

1. Ciclosporin
  2. Acitretin
  3. Methotrexate
  4. Biologic agents:
    - i. Infliximab
    - ii. Adalimumab
    - iii. Etanercept
    - iv. Ustekinumab
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### **Intralesional therapy**

Intralesional steroid injection is an effective treatment of nail psoriasis especially if the nail matrix is involved. To target psoriatic lesions originating from the nail matrix such as pitting, it can be accessed from the overlying proximal nail fold. The nail bed can be accessed from the lateral nail folds. The procedure should be preceded by ring block or distal block anaesthesia as it is invariably very painful. Most patients prefer the Dermo-jet syringe over needle injections as it is significantly less painful. Triamcinolone acetonide is the most commonly used corticosteroid, at concentrations ranging from 2.5 to 10 mg/ml. Studies showed that 70-90% of psoriatic patients with both nail matrix and nail bed lesions responded to intralesional steroids. However, onycholysis was more difficult to treat than the other psoriatic lesions, with only 20-55% of patients responding.<sup>25-28</sup> Apart from pain, the possible side effects of intralesional corticosteroid injection include nail atrophy, subungual haemorrhage or even tendon rupture.

### **Phototherapy**

Phototherapy has also effectively been used against nail psoriasis. UVA light is able to penetrate the nail bed and the hyponychium. Published case series have shown that continuous irradiation can achieve moderate improvement in onycholysis as well as nail discolouration and subungual hyperkeratosis. In one study on systemic PUVA therapy, symptoms improved by around 50% in 70% of treated patients.<sup>29</sup> Another study on topical PUVA therapy showed that four out of five treated patients had significant improvement in onycholysis and nail pitting decreased.<sup>30</sup>

### **Systemic therapy**

Systemic therapy represents the next step in the therapeutic ladder in patients with nail psoriasis who have not responded to topical agents, intralesional therapy or phototherapy. Commonly used systemic agents include methotrexate, acitretin and ciclosporin. Biologic agents such as

infliximab, adalimumab, etanercept and ustekinumab have also shown promising results. Some of the studies supporting the use of these systemic agents for nail psoriasis are listed in Table 2.

**Ciclosporin** – In an uncontrolled study by Syuto et al on 16 patients, ciclosporin was given at a dosage of 3 mg/kg of body weight. Fourteen out of 16 patients had marked improvement, 10 out of 16 had significant improvement and two healed completely.<sup>31</sup>

**Methotrexate** – In a randomised study by Gümüşel et al, 34 patients received either methotrexate or ciclosporin for 24 weeks. A significant improvement was observed in the methotrexate group for nail matrix findings and in the ciclosporin group for nail bed findings. In terms of overall NAPS I scores, methotrexate and ciclosporin were comparable in their efficacy in treating nail psoriasis.<sup>32</sup>

**Acitretin** – Tosti et al gave 36 patients with isolated nail psoriasis low dose acitretin 0.2-0.3 mg/kg for six months, achieving an average NAPS I reduction of around 41%. Complete or nearly complete healing was achieved in almost 25% of patients. Acitretin particularly makes the nails thinner and therefore benefits patients with thickened nails and subungual hyperkeratosis.<sup>33</sup>

**Infliximab** – In a phase III, multicentre, double-blind, placebo controlled study for the evaluation of long-term efficacy and safety of infliximab in patients with moderate to severe plaque psoriasis, infliximab led to complete eradication of nail psoriasis in 6.9% of patients within 10 weeks, 26.4% after 24 weeks and 44.7% after 50 weeks. The average reduction in NAPS I was 28.9% after 12 weeks of treatment and 51% after 54 weeks of treatment.<sup>34,35</sup>

**Adalimumab** – Van den Bosch et al reported that treatment led to an average NAPS I reduction of about 45% after 12 weeks of therapy and about

65% after 20 weeks.<sup>36</sup> A study by Thaci et al reported that after 16 weeks there was an average NAPSI reduction of 39.5%.<sup>37</sup>

**Etanercept** – In a post-hoc analysis by Luger et al, the administration of etanercept 25 mg twice weekly led to an average reduction in the NAPSI scores of around 51% after 54 weeks (711 patients with psoriasis, of whom 80% had nail involvement). The average NAPSI reduction after 12 weeks of therapy was 28.9%.<sup>38</sup>

**Ustekinumab** – In a phase III study, using a standard dosage of ustekinumab 45 mg, after 12 weeks of treatment, there was a reduction of the median NAPSI of around 25%; and after 24 weeks of around 50%.<sup>39</sup>

In clinical practice, we may consider systemic agents for patients with nail psoriasis under following conditions:

- 1) Psoriasis limited to the nails but failed topical/intralesional therapy and associated with significant morbidities such as pain and functional impairment. The medical board of the National Psoriasis Foundation recommended the following agents in ranking order from highest enthusiasm to lowest: adalimumab, etanercept, ustekinumab, methotrexate, acitretin.<sup>40</sup>
- 2) Nail psoriasis together with moderate to severe cutaneous psoriasis. The recommendations for treatment were, in ranked order from highest enthusiasm to lowest: adalimumab, etanercept, ustekinumab, methotrexate, acitretin, infliximab.<sup>40</sup>
- 3) Nail psoriasis together with cutaneous psoriasis and psoriatic arthritis. The recommendations for treatment were, in ranked order from the highest to the lowest: adalimumab, etanercept, ustekinumab, infliximab, methotrexate.<sup>40</sup>

## Conclusions

Nail involvement is a predictor for a severe disease course in patients with psoriasis. As nail psoriasis

can adversely affect the patient's quality of life and lead to significant functional impairment, its recognition and treatment should be given a greater emphasis.

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