

# Nail psoriasis: a review of the literature\*

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**Abstract:** Nails are considered epidermal appendages, and as such, are commonly affected in patients with psoriasis, 80% of whom are likely to develop nail psoriasis as a result of their condition. Two patterns of nail disorders have been shown to be caused by psoriasis. Nail matrix involvement can result in features such as leukonychia, pitting (punctures or cupuliform depressions), red spots in the lunula and crumbling. Nail bed involvement, on the other hand, can cause onycholysis, salmon or oil-drop patches, subungual hyperkeratosis and splinter hemorrhages. Nail disease causes aesthetic and functional impairment, and is indicative of more severe forms of psoriasis as well as of joint involvement. The treatment for nail psoriasis involves behavioral interventions, topical medications, or systemic therapy in case of extensive skin or joint involvement. This article presents a review of the main features of nail psoriasis, its clinical presentation, diagnostic and assessment methods, clinical repercussions, and of its available treatment options.

**Keywords:** Arthritis, psoriatic; Nails; Psoriasis

## INTRODUCTION

Psoriasis is a chronic and recurrent inflammatory skin disease, with a worldwide prevalence of approximately 1 to 3%.<sup>1</sup> However, few data are available on the epidemiology of this condition in Brazil. The condition is associated with immune dysfunction, and its multifactorial etiology involves both environmental and genetic factors. Its clinical presentation ranges from mild and localized lesions to severe cases of erythroderma.<sup>2</sup>

As specialized dermal appendages, nails are often affected by psoriasis. It is thought that 80-90% of patients with psoriasis will at some point present with nail involvement. Its clinical signs result from the involvement of the nail matrix and nail bed, each of which can lead to distinct clinical features.<sup>3</sup>

In spite of its aesthetic and functional implications, nail psoriasis has only been briefly discussed in the literature, and few studies have investigated its epidemiology and clinical characteristics.

## THE EPIDEMIOLOGY OF NAIL PSORIASIS

The prevalence of nail involvement in psoriasis patients is of approximately 50%.<sup>4,5</sup> A German study conducted in 2010 on 3531 patients with psoriasis found that nail involvement was more prevalent in male individuals (11.2%).<sup>5</sup> Among patients with psoriatic arthritis, the prevalence of nail involvement may be as high as 80.5%.<sup>6,7</sup> In 1 to 5% of patients, alterations compatible with nail psoriasis may also occur in the absence of cutaneous lesions.<sup>8</sup>

## CLINICAL MANIFESTATIONS

The nail consists of the nail plate, a keratin structure with no living tissue, and four distinct epithelial tissues: the nail matrix, the nail bed, as well as the hyponychium and perionychium.<sup>9</sup> The clinical features of nail psoriasis depend largely on the type of nail tissue affected by the condition.

The effects of psoriasis on the nail matrix involve alterations in the nail plate, such as cupuli-

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form depressions, also known as pittings, leukonychia, red spots in the lunula and crumbling. Effects on the nail bed include onycholysis, oil-drop or salmon patches, dyschromias, splinter hemorrhage and nail bed hyperkeratosis. As nail psoriasis is similar to that observed on the backs of the fingers, the condition is considered to be a cutaneous extension of finger lesions.<sup>10</sup>

Although some authors consider pitting (8) to be the most common sign of nail psoriasis, some studies have suggested that other features may be more strongly associated with this condition. An Italian study published in 2012 found onycholysis to be the most frequent symptom among the 178 patients studied.<sup>11</sup> On the other hand, a study conducted by Salomon and colleagues on a sample of 106 inpatients found nail hyperkeratosis to be the most common manifestation of nail psoriasis.<sup>12</sup>

### NAIL MATRIX PSORIASIS

The nail matrix, which is responsible for producing the nail plate, can also be affected by psoriasis. The effects of this condition on skin keratinization may also affect the proximal portion of the matrix, resulting in the presence of parakeratotic cell aggregates on the nail plate surface. As the nail grows, these features may become increasingly apparent and result in large and deep cupuliform depressions, which are irregularly distributed on the surface of the nail.<sup>13</sup> The pitting observed in nail psoriasis may also be present in other diseases, such as sarcoidosis, pemphigus, alopecia areata, eczema and Reiter's syndrome.<sup>8,14</sup>

The nail whitening observed when nail matrix involvement is present is referred to as true leukonychia, and presents as 1 to 2mm-wide bands which involve more than one nail. The exclusive presence of small white dots is generally a result of trauma to the nail, while longitudinal leukonychia has been reported in patients with Darier's disease.<sup>15</sup>

Nail matrix psoriasis has also been shown to lead to other types of alterations. Beau lines, for instance, which present as transversal stripes on the nail, may occur as a result of acute nail-fold inflammation. Onychorrhexis, or longitudinal nail fissures, may also be observed in patients with chronic psoriasis. Erythematous spots on the lunula may also occur as a result of the involvement of the intermediate and ventral nail matrices.<sup>2</sup>

### NAIL BED PSORIASIS

The nail bed consists of the vascular area underneath the nail, which extends from the lunula to the hyponychium and is permeated by longitudinally arranged blood vessels. Focal bleeding in this tissue may manifest as splinter hemorrhaging.<sup>16</sup> This phe-

nomenon results in brown or red lines on the nail, which are displaced distally as the nail grows. Although such manifestations may also occur as the result of trauma to the nail, their simultaneous presence in more than one nail is indicative of an underlying systemic disease. Conditions such as bacterial endocarditis, rheumatoid arthritis, malignancies, systemic lupus erythematosus and antiphospholipid syndrome are some of the possible systemic causes of nail bed psoriasis.<sup>17</sup> The latter condition may also occur in healthy individuals with increased capillary fragility.<sup>14</sup>

Onycholysis refers to the detachment of the nail plate from the nail bed. In psoriasis, this may occur along the distal margin of the nail, which becomes white in color as it detaches from the nail bed. The affected area is usually encircled by an erythematous border.<sup>8,13</sup> Some other possible causes of onycholysis are anemia, hyperthyroidism and peripheral strokes.<sup>18</sup> It is important to note that onycholysis increases infection risk, as it allows microorganisms to penetrate the nail.<sup>8</sup>

Nail bed involvement in psoriasis is usually signaled by the presence of oil-drop or salmon patches, which consist of translucent and discolored red-yellow patches located on the nail plate. The yellow color is a result of parakeratotic and acanthotic processes which occur underneath the nail, while the reddish tones occur due to the presence of plaque on the nail bed.<sup>8</sup>

Nail bed keratosis is associated with increased nail plate thickness due to nail bed or hyponychium hyperplasia caused by chronic focal inflammation or congenital nail bed hyperplasia.<sup>19</sup> In such conditions, cells accumulate underneath the nail plate, and the thickness of the nail increases proportionately to the degree of psoriatic activity. Patients with psoriasis who develop nail bed hyperkeratosis usually present with yellow and oily nails, although white-to-gray coloring has also been reported.<sup>2</sup> Other possible causes of such manifestation include trauma to the nail, congenital ichthyosis and onychomycosis.<sup>19</sup>

Nail bed psoriasis may also manifest as crumbling. This term refers to the nail plate crumbling observed after a prolonged period of disease activity which leads to total nail matrix destruction.<sup>20</sup>

### PERIUNGUAL TISSUE PSORIASIS

Acropustulosis is characterized by the subungual and periungual pustules, which may be caused by Hallopeau's acrodermatitis (HA) or generalized pustular psoriasis (GPP).<sup>21</sup> There is some controversy as to whether HA is a distinct disease or simply a variant of GPP, as there are several reports of patients who were initially diagnosed with HA but went on to develop GPP. Abbas and colleagues believe these to

consist of the same disease, as both can be caused by mutations in the IL36RN gene.<sup>22</sup>

In HA, pustules first appear on the distal extremities of the phalanges, and are more frequent in the first finger of the hand. Nail bed involvement may follow, and result in nail dystrophy, onychia or osteolysis of the distal phalanx.<sup>22,23</sup> Unlike paronychia, these conditions are usually culture-negative. This should be considered when making differential diagnoses.<sup>23</sup>

## DIAGNOSIS

As the clinical features of nail psoriasis are not exclusive to this disease, the clinical differentiation between this and other conditions especially onychomycosis, can present a significant diagnostic challenge. The identification of additional cutaneous manifestations and of joint involvement may provide some diagnostic help. However, cases in which only nail psoriasis is present may be particularly problematic.

Some diagnostic tools have been found to be especially helpful in such cases. Farias and colleagues suggest the use of dermatoscopy, a non-invasive, low-cost and easy-to-use method, as a complementary diagnostic tool in patients with ambiguous diagnoses. For instance, when onycholysis is present, the use of such a method would allow for the identification of the erythematous border, which is specific to nail psoriasis, and is often undetectable by the naked eye.<sup>24</sup>

Periungual capillaroscopy, a method generally used to study the microcirculation of patients with collagen diseases, has also been used to assess patients with suspected psoriasis. A Brazilian study published in 2012 found that avascular areas were especially common in patients with nail psoriasis, suggesting the presence of alterations in nail trophism in these individuals.<sup>25</sup> Therefore, capillaroscopy may be a useful complementary diagnostic tool for detecting nail psoriasis.

The nail yellowing and whitening, hyperkeratosis, onychorrhexis, nail plate thickening, and total nail dystrophy observed in psoriasis are often similar to the manifestations observed in patients with fungal infections. Furthermore, given the high prevalence of onychomycosis in patients with psoriasis, direct mycological tests, fungal cultures and histopathological tests must often be conducted.<sup>26</sup>

Matrix or nail bed biopsies, which could allow for a better examination of the histological characteristics of the lesion, are not usually performed.<sup>21</sup> Given the adverse effects associated with this method, it should only be used when the diagnosis cannot be made by other means.<sup>27</sup>

Hanno and colleagues have suggested the use of the following diagnostic criteria: presence of neu-

trophils in the nail bed epithelium (major criterion), hyperkeratosis with parakeratosis, presence of exudates on the corneal epithelium, focal hypogranulosis and psoriasiform hyperplasia of the nail bed (minor criteria).<sup>28</sup> In addition to these criteria, Grover and colleagues underscore the importance of negative PAS staining in differentiating between psoriasis and onychomycosis.<sup>27</sup>

Grover and colleagues conducted a study on 42 patients whose only clinical manifestations of psoriasis consisted of nail lesions. Of the 22 patients who underwent biopsies, only 12 (54%) were definitively diagnosed with psoriasis. The most frequent histological finding was hyperkeratosis with parakeratosis in the distal portion of the nail bed and hyponychium (91%). Follow-up assessments indicated that 9% of the biopsied patients developed secondary infections, and 44% presented with scarring or reduced nail width.<sup>27</sup>

## QUANTIFICATION METHODS

The collection of data about nail psoriasis is an important step in improving the clinical assessment of patients with this condition. However, since many of the methods used to diagnose nail psoriasis lack standardization and validation, the impact of this condition in individuals with psoriasis may be inadequately measured or underestimated. Although it is not without its limitation, the NAPS I index (Nail Psoriasis Severity Index) is the only validated method to diagnose nail psoriasis, and is, therefore, the most widely used tool in this regard.<sup>29</sup>

As part of this method, the nail is divided into four imaginary quadrants, and the presence of lesions on the nail matrix (pitting, leukonychia, red spots in the lunula and crumbling) or nail bed is investigated (oil-drop/salmon stains, onycholysis, hyperkeratosis, and splinter hemorrhage). When these features are present in all four quadrants, the patient receives a score of 4, while the complete absence of such symptoms leads to a score of 0. The matrix (0-4) and nail bed scores (0-4) for each nail are added up to provide a total score ranging from 0 to 8. The sum of scores on all nails provides a severity index ranging from 0-80 or 0-160, if the toenails are included.<sup>10</sup>

It is important to note that the NAPS I does not assess the impact of nail psoriasis on quality of life. To address this gap in the literature, the NPQ10 (Nail Psoriasis Quality of Life Scale) was published in 2010. However, the instrument has not yet been adapted to Portuguese-speaking patients. The NPQ10 contains 10 items which assess the location of the nail lesions, the degree of pain, and the frequency with which the condition leads patients to experience irritability, negative moods and difficulty performing daily tasks, such as putting on shoes, getting dressed, driving and conducting domestic activities.<sup>20,30</sup>

## FEATURES ASSOCIATED WITH NAIL PSORIASIS

Nail inflammation in psoriasis may be a predisposing factor for secondary fungal infections. The association between these two conditions is estimated to occur in 4.6-30% of patients with nail psoriasis, and the morphology of the lesions caused by these two diseases can be similar.<sup>31</sup> The presence of onychomycosis in patients with nail psoriasis may lead to more intense clinical manifestations through the Koebner phenomenon, which occurs as a result of continuous fungal infections.<sup>26</sup>

The disease duration may also influence the severity of the nail lesions observed. Patients with nail involvement have usually had cutaneous manifestations of psoriasis for a longer time than those without nail involvement.<sup>3,5,32</sup>

The presence of nail psoriasis is also associated with the severity of the skin condition. Hallaji and colleagues described the relationship between these two variables through the following equation: for each one-point increase in the severity of cutaneous psoriasis, 10 points are added to the severity of the nail condition.<sup>32</sup>

The presence of nail abnormalities may also help to diagnose patients with psoriatic arthritis, especially when cutaneous lesions are absent.<sup>33</sup> The association between nail and joint involvement in patients with psoriasis is well established in the literature.<sup>4,5,34,35</sup> One possible explanation for this phenomenon is the intimate microanatomical relationship between the nails and the musculoskeletal system, through which focal inflammation associated with tendon enthesitis may lead to alterations on the nails.<sup>36</sup> As a result of this process, approximately 80% of patients with psoriatic arthritis present with nail involvement at some point in the course of their lives.<sup>3,6,7,36</sup>

Nail psoriasis may also be responsible for a decrease in patients' quality of life. One study reported that 58.1% of 1728 patients reported to feeling pain in the affected nails and 58.9% experienced impairments in their daily lives.<sup>37</sup> Another study found that 90% of patients with nail psoriasis were uncomfortable with the aesthetic impact of their condition. Some authors have also suggested that impairments in manual function, such as that involved in buttoning up clothes or handling small objects, may also increase depression and anxiety in patients with severe nail diseases.<sup>3</sup>

## TREATMENT

To ensure that patients with nail psoriasis receive adequate treatment, the severity of the nail condition, the extension of the skin condition and/or the presence of joint involvement must all be careful-

ly assessed. Behavioral interventions which minimize the Koebner phenomenon, especially those related to footwear, nail care, and intense manual activities, are also a key part of treatment.<sup>8</sup>

## Topical therapy

The most commonly recommended treatments for nail psoriasis involve the use of topical or intralesional corticoids, as well as the use of topical vitamin D3 analogues.<sup>38</sup> Studies suggest that the use of 0.05% clobetasol propionate in gel or cream form in the perungual region may only cause slight improvement in patient symptoms due to the low absorption rates observed in this region. A pilot study of 15 patients published in 2012 compared the efficacy of clobetasol nail lacquer at concentrations of 0.5%, 1% and 8%. The authors identified significant clinical improvement in patients who used the highest concentration of the product. Although the follow-up period was short, no adverse effects were reported following treatment.<sup>39</sup>

The efficacy of hydroxypropyl-chitosan nail lacquer was also tested in a study of 28 patients who were treated for 24 weeks. The treatment was well received by all patients, and resulted in a 72% reduction in pitting, and a 60% reduction in leuconychia and onycholysis.<sup>40</sup>

Other topical treatments for nail psoriasis which have been shown to be effective include tacrolimus, fluorouracil, topical cyclosporine, tazaroten and anthralin. Radiotherapy may be used in recalcitrant cases. However, the risk of fibrosis and malignancies must always be considered before this treatment is recommended.<sup>8</sup> Although phototherapy is an excellent treatment option for cutaneous psoriasis, it has not proved to be as effective for nail psoriasis.<sup>8,18</sup> However, some evidence of the efficacy of a pulsed dye laser (595 nm) was obtained in a study of 20 patients with psoriasis.<sup>38</sup>

## Systemic therapy

Although systemic therapies are a major modality of treatment for cases of combined skin and nail disease, they are not recommended for patients who only present with nail lesions. According to the European Consensus for the treatment of nail psoriasis, when individuals have moderate to severe forms of the disease, methotrexate is recommended in addition to topical therapy. Tumor necrosis factor alpha inhibitors are recommended as a second line treatment (etanercept, infliximab or adalimumab).<sup>41</sup>

Although the efficacy of methotrexate and cyclosporin in the treatment of cutaneous psoriasis has been described in numerous studies, its applicability to patients with nail psoriasis has been much less extensively studied. A randomized clinical trial

comparing six-month treatments with methotrexate and cyclosporin found that both were moderately effective in treating nail psoriasis, and that their effects did not significantly differ from one another.<sup>42</sup>

The use of acitretin in treating nail psoriasis is controversial. Studies such as that by Tosti and colleagues found this treatment to be effective, as a six-month course of 0.2 to 0.3 mg/kg/d acitretin led to a 50% reduction in NAPSI scores.<sup>43</sup> Conversely, a Brazilian study conducted on 20 patients found no significant improvements after a four-month treatment course.<sup>44</sup> However, it is important to note that acitretin may cause adverse effects such as nail thinning, which may impact areas of the nail plate which have normal thickness.<sup>8</sup>

The recently introduced immunobiological therapy has also led to some interesting results. Infliximab is the most widely studied immunobiological agent, and has proved to be safe and effective in a year-long phase III double-blind study conducted on 378 patients with moderate to severe common psoriasis.<sup>45</sup> The secondary outcome assessed by this study was the improvement of the nail condition. Infliximab was found to be superior to the placebo in this regard as early as 10 weeks into treatment, and led to growing benefits throughout the remainder of the study.<sup>45,46</sup>

Other immunobiological agents have also proved to be effective treatments for nail psoriasis. The first study to assess the use of adalimumab in nail psoriasis found the medication to be effective in treating both the nail condition, as well as the impact of psoriasis on the skin and joints.<sup>47</sup> A study of etanercept

conducted on 771 patients found that the drug led to significant improvements both in the lesions themselves, as well as in quality of life.<sup>48</sup> A phase III study has also found that ustekinumab, a human monoclonal antibody which targets the p40 subunit of interleukins 12 and 23, has been shown to be effective in treating moderate to severe common psoriasis.<sup>49</sup> The drug was also found to be safe and effective in a study of 27 patients, although this particular investigation did not involve a control group.<sup>50</sup>

## CONCLUSION

In spite of its clinical repercussions such as pain, functional impairment and aesthetic consequences, nail psoriasis is still a poorly studied condition. Nail involvement in psoriasis is a marker for more severe cutaneous manifestations and joint involvement. Both dermatologists and rheumatologists should be familiar with the different clinical presentations of nail psoriasis, so as to allow for early diagnosis and a more precise determination of patient prognosis. The quantitative assessment of nail psoriasis also allows for a more objective evaluation of the evolution of the disease. The therapeutic management of nail psoriasis may pose a series of challenges, and must take into account the extent of skin involvement and the presence of joint involvement. Although several topical and systemic treatments have been studied for their effectiveness in treating nail psoriasis, some patients remain refractory to therapy, which underscores the need for further investigations into additional therapeutic methods. □

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