Nail Psoriasis and Psoriatic Arthritis for the Dermatologist

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Abstract

Psoriatic arthritis (PsA) may affect up to a third of patients with psoriasis. It is characterized by diverse clinical phenotypes and as such, is often underdiagnosed, leading to disease progression and poor outcomes. Nail psoriasis (NP) has been identified as a risk factor for PsA, given the anatomical connection between the extensor tendon and nail matrix. Therefore, it is important for dermatologists to screen patients exhibiting symptoms of NP for joint manifestations. On physical exam, physicians should be evaluating for concurrent skin and nail involvement, enthesitis, dactylitis, and spondyloarthropathy. Imaging modalities, including radiographs and ultrasound, may also be helpful in diagnosis of both nail and joint pathology. Physicians should refer to Rheumatology when appropriate. Numerous systemic therapies are effective at addressing both NP and PsA including DMARDs, biologics, and small molecule inhibitors. These treatments ultimately can inhibit the progression of inflammatory disease and control symptoms, thereby improving quality of life for patients.

Introduction

Psoriasis is a chronic inflammatory disease that affects up to 3% of the population¹. Of those patients, 30% may develop psoriatic arthritis (PsA), a complex disease characterized by diverse clinical phenotypes²-⁶. Among psoriasis patients followed by dermatology, about 15% were found to have undiagnosed PsA⁵. One study found that a delay of just 6 months in diagnosis can contribute to peripheral joint erosions and poor functional outcomes⁷.

The pathogenesis of PsA, similar to psoriasis, involves the complex dysregulation of T-cell subtypes (Th1, 2, 17, 19, Treg) and other dendritic cells producing pro-inflammatory cytokines that affect synovial fibroblasts, chondrocytes, and osteoblasts³. PsA is most common in North America, with a peak age of onset at >50 years of age and no differences in gender². It can present peripherally, with variable joint distributions, and/or with axial involvement. Distinguishing features of PsA include enthesitis (inflammation at the site of tendon insertion into bone) and dactylitis (inflammation of two or more consecutive joints in the same finger). Enthesitis is observed in 30-50% of PsA patients, and is most commonly found at the Achilles tendon and plantar fascia. Some theories postulate that biomechanical stress at the entheses may result in the release of cytokines, leading to an articular inflammatory response and contributing to the pathogenesis of PsA⁸. Dactylitis occurs in 40-50% of patients, most commonly in the toes, and is associated with more severe disease⁸.

Risk factors for developing PsA include both genetic and clinical
Diagnosis

With the diagnosis of NP, dermatologists should also examine for additional psoriatic skin involvement as well as concurrent PsA. When examining, assess for dactylitis by comparing the affected versus unaffected hands and feet, which helps distinguish between normal joint size and shape from abnormal joint swelling and sausage digit formation. Enthesitis can be examined by applying pressure to entheseal points (knee, elbow, pelvis, spine, ribcage, shoulder; Achilles tendon, and plantar fascia). Assessment for spinal disease includes testing the patient’s neck for range of motion in all directions. If restriction in movement is suspected, a validated assessment measure such as the modified Schober’s test or lateral lumbar flexion test is warranted.

Several screening questionnaires have also been developed to assist in the early detection of PsA including the Toronto PsA Screen (ToPAS), Psoriasis Arthritis Screening Questionnaire (PASQ) and the Psoriasis Epidemiology Screening Tool (PEST). Formal classification criteria was proposed in 2006 based on the Classification of Psoriatic Arthritis (CASPAR) study which considers the presence of skin or nail involvement, dactylitis, negative rheumatoid factor, and juxtaarticular bone formation.

Imaging modalities may be helpful to improve diagnostic accuracy. Radiographs can show joint erosions, joint space narrowing, bony proliferation, osteolysis (pencil in cup deformity), ankylosis, and spondylitis. Recently, musculoskeletal ultrasound (US) has been studied as a non-invasive and inexpensive modality to assess for joint and tendon inflammation as well as nail disease. Given the distal extensor tendon’s close association with the nail matrix, inflammation of the enthesis in the early phase of disease can affect the nail. This results in clinically significant pathology that can be identified with US. Nail plate alternations can be seen with US in a majority of PsA patients, even in up to 75% of clinically normal appearing nails. PsA patients have significantly increased nail matrix and nail bed thickness when compared to controls. One study even recommended the use of US to examine the DIP joints in patients who had at least 5 dystrophic nails.

Further research is required for guidelines on how to use US in the clinical setting for diagnosis or monitoring of disease progression.

Dermatologists should feel comfortable doing a brief physical exam for patients who complain of joint pain and/or present with NP, obtaining imaging studies, and initiating a timely referral to Rheumatology. Understanding and identifying features of PsA at the time of presentation will help more patients get access to disease modifying treatments and prevent disabling disease progression.

Management

Management may depend on whether patients present with isolated or concomitant nail and joint involvement, as well as the severity of disease. Figure 2 identifies treatments for NP and PsA as well as the overlap of therapies with efficacy for both. This article will focus on exploring treatment options to address concurrent psoriatic nail and joint disease.

When discussing evidence based therapies for both NP and PsA, studies have used indexes such as the Nail Psoriasis Severity Index (NAPSI), and the American College of Rheumatology (ACR) criteria to evaluate response to treatment. For NAPSI, each nail is divided into four quadrants and evaluated for nail bed and nail matrix symptoms.
Figure 2. Treatment options for Nail Psoriasis and Psoriatic Arthritis

One nail can score up to 8 points, for a maximum of 80 among 10 fingernails. ACR assesses for a certain percentage (20%/50%/70%) of improvement in tender and swollen joint counts, patient and physician global assessments, pain, disability, and acute phase reactant measures.

Traditional DMARDs

Methotrexate (MTX) is one of the most common first line disease modifying anti-rheumatic drugs (DMARDs) used to treat PsA that also has efficacy for NP. Cyclosporine, a calcineurin inhibitor, is typically reserved for more refractory PsA and limited to short-term use (up to 12 months), given its association with nephrotoxicity, hypertension, and malignancy.

Biologic Therapies

2018 recommendations from the American College of Rheumatology (ACR) and National Psoriasis Foundation (NPF) suggest utilizing TNF alpha inhibitors (TNFi) even prior to DMARDs for treatment-naïve patients. These TNFi include adalimumab, etanercept, infliximab, golimumab, and certolizumab pegol, all of which have shown great efficacy in treating both NP and PsA, including decreasing radiographic progression. While no studies have compared the efficacy of all 5 TNFi on NP and PsA, there is data demonstrating nonsignificant differences between select TNFi. Notably, combination therapy of biologics (etanercept, infliximab, golimumab) and MTX have shown superior efficacy compared to MTX monotherapy. When selecting a TNFi, physicians should consider the patient’s preference for route of administration, frequency of treatment, and insurance coverage.

IL-17 and IL-23 inhibitors

Psoriasis research has identified the central roles of the IL-17 and IL-23 pathways for both NP and PsA pathogenesis, and thereby developed targeted anti-interleukin therapeutics. IL-17 inhibitors currently available include secukinumab and ixekizumab, both with significant efficacy in addressing NP and peripheral articular symptoms, in addition to inhibiting radiographic progression. When compared to a TNFi (adalimumab), by 24 weeks ixekizumab showed a significantly greater improvement in treating both PsA and NP. Brodalumab is another anti-IL17 drug currently under investigation for PsA. Phase 2 studies found significant superiority over placebo with higher rates of ACR20 and ACR50. It has also been shown to significantly improve NP by week 12. Physicians should note that some patients receiving brodalumab reported suicidal ideation, although no causal relationship has been identified. Therefore, we caution use in those with known psychiatric comorbidities. Ustekinumab is an IL-12 and IL-23 inhibitor that also demonstrated efficacy in treating NP and peripheral PsA with decreased radiographic progression.

Other treatments that selectively target IL-23 have not been FDA approved for use in PsA; these include guselkumab, tildrakizumab, and risankizumab. Guselkumab has demonstrated efficacy for NP. Post hoc data analysis from VOYAGE 1 and VOYAGE 2 studies showed a significant improvement in NAPSI score over adalimumab by week 16. However, by 6 months, the magnitude of improvement did not differ between the two treatments. A placebo-controlled phase 2 study with a primary endpoint of ACR20 for PsA showed significant improvement in symptoms as well. Preliminary data from a phase 2B trial of tildrakizumab has shown significant efficacy in treating joint symptoms as early as 8 weeks, however limited data is available regarding its effect on NP. Risankizumab, in a phase 2 head-to-head comparison with ustekinumab, had superior efficacy in measured secondary outcomes including NP and joint pain for PsA patients. Authors suggested that the blockade of the p19 subunit of IL-23, as opposed to the p40 subunit (blocked by ustekinumab), may have greater inhibited IL-23 activity, and improved efficacy of treatment.

Phosphodiesterase Inhibitor

Apremilast is a phosphodiesterase 4 inhibitor that works intracellularly to downregulate many of the inflammatory mediators involved in psoriasis pathogenesis. NP and PsA trials have shown significant improvement in NAPSI and ACR20 scores by week 16. It is generally well tolerated and does not require laboratory monitoring.

Small Molecule Inhibitors

Tofacitinib is an oral Janus kinase (JAK) inhibitor that can be used to treat both NP and PsA. Its safety profile, however, is concerning for malignancy, risk of serious infection, and herpes zoster reactivation, which often limits its use clinically. Other JAK inhibitors undergoing clinical trials for PsA include filgotinib and upadacitinib. Filgotinib, evaluated in EQUATOR, a multicenter phase 2 randomized trial, demonstrated efficacy in patients
who had previously failed conventional DMARDs with improvements in psoriatic skin disease and enthesitis\textsuperscript{46}. Upadacitinib is currently in phase 3 testing with no published data as of yet.

## Treating Isolated NP

For NP without joint or significant cutaneous involvement, localized therapies may be considered to avoid the associated adverse effects of systemic medications. This includes corticosteroids (betamethasone), calcipotriol, retinoids (tazarotene and acitretin), calcineurin inhibitors (tacrolimus), as well as intralesional injections (triamcinolone acetonide or MTX). Phototherapy options include pulse dye laser (PDL) psoralen-ultraviolet light A (PUVA), and narrowband ultraviolet B (NBUVB)\textsuperscript{15}.

### PsA Only Treatment

Some treatment options for PsA do not provide the additional benefit of addressing psoriatic nail disease. These include conventional DMARDs (leflunomide, sulfasalazine) and the immunomodulator abatacept, which we will not delve into further in this paper\textsuperscript{47}.

## Conclusion

Nail psoriasis should alert the dermatologist to further investigate for PsA. Examination for enthesitis, dactylitis, and spondylarthropathy along with radiographic imaging and prompt referral to Rheumatology can improve the detection of PsA. Multiple new biologic therapies are available to treat both NP and PsA, decreasing the disease burden of afflicted patients.

## Conflicts of Interest

The authors have no conflicts to declare.

## References


