Focussing on the foot in psoriatic arthritis: pathology and management options

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Abstract:

Introduction

Psoriatic arthritis (PsA) is a heterogeneous chronic inflammatory arthritis characterised by a range of musculoskeletal conditions including enthesitis, dactylitis and synovitis as well as skin and nail manifestations. The foot is a complex mixture of tissues all of which can be involved in this disease and is frequently the presenting feature.

Areas covered

In this under researched area articles were taken from the authors publications and known other authors. This review will discuss how PsA affects the foot and ankle with particular focus on synovitis, tenosynovitis, enthesitis, dactylitis, bone erosion and psoriatic skin and nail disease. The use of imaging is discussed. Conventional radiography is consistently used, however magnetic resonance imaging and ultrasound should be used routinely to diagnose, assess and monitor the disease appropriately. The complex nature of PsA in the foot and ankle should be considered when managing the condition and treatment should be individualised to relieve pain, maintain mobility and improve quality of life.

Expert commentary

The foot and ankle remains a neglected area in PsA. Problems with the foot and ankle should be prioritised as they can significantly impact on patients' quality of life. Focussing treatment on the foot and ankle can significantly improve outcome.

1. Introduction

Psoriatic arthritis (PsA) is a heterogeneous chronic inflammatory disease which forms part of the spondyloarthropathy family. In addition to gastrointestinal, ocular and cardiovascular involvement, patients can present with several musculoskeletal manifestations including polyarthritis, oligoarthritis, sacroiliitis, enthesitis, dactylitis, and tenosynovitis [1, 2]. Peripheral joint and soft tissue involvement in the foot can manifest around the forefoot, midfoot and hindfoot right from the onset of disease with forefoot deformity affecting over 90% of patients with established disease [3, 4].

2. Clinical Features

2.1 Skin and Nail Disease

Generally patients present with psoriasis before developing PsA (60-80%) [5] and around 30% of patients with psoriasis will go on to develop PsA [6, 7]. Psoriatic plaques can often be found on the dorsum of the foot (Figure 1) but patients can also present with palmoplantar pustulosis, which is considerably rarer (3-4%) [4, 8] . The main features of palmoplantar pustulosis include intraepidermal pustules, erythema, scaling and fissuring skin on the palms and/or soles of the feet which can greatly impact quality of life. Management usually consists of topical treatment as a first-line approach (corticosteroids, salicylic acid, etc.) but often requires systemic treatment (oral retinoids, methotrexate, etc.)[8].

The incidence of nail disease in PsA is reported to be around 65% [1, 9] yet it is often overlooked despite patients reporting that it can impact activities of daily living and cause pain and discomfort [10]. Researchers propose that nail changes in PsA may arise due to Koebner phenomenon [11, 12] and research by Tan et al, revealed the fascia of the nail root has a tenuous connection to the extensor tendon before insertion into the distal phalanx [13].

Nail disease in PsA (Figure 1) can be divided into changes arising from the nail matrix and changes involving the nail bed. Typical nail matrix disease includes leukonychia (white discoloration), onychorrhexis (nail ridging), nail pitting and blood spots on the lunula whereas nail bed disease can present as onycholysis (separation of the nail from the nail bed) (Figure 2), splinter haemorrhages and subungal hyperkeratosis [9]. There are a number of scoring systems to assess the extent of nail disease including the Nail Psoriasis Severity Index (NAPSI) and the Psoriasis Nail Severity Score (PNSS) [14, 15] but it is often difficult to differentiate from bacterial and fungal infections which can mimic the presentation of psoriatic nail disease.

2.2 Enthesitis

Enthesitis is a prominent feature of PsA presenting as inflammation at the insertion sites of tendons, ligaments, fascia and joint capsules to bone [16], and was initially noted as a possible manifestation of the disease that could distinguish spondyloarthropathies from rheumatoid arthritis (RA) [17]. It is present in 28%-35% [18-20] of patients who have PsA and may be the initial presenting clinical feature of the disease. The presence of enthesitis may be an adverse prognostic factor: one study found an association with elevated disease activity and self-reported pain and fatigue, poorer functional status and greater overall burden of disease [21].

The insertion of the Achilles tendon at the heel is the most prevalent site affected (3, 6) (Figure 3) however enthesitis can also typically be detected in the foot at the insertion of the plantar fascia at the calcaneus, tibialis posterior at the navicular tuberosity and peroneus brevis tendon at the base of the fifth metatarsal. A clinical enthesitis index, specific to PsA, has been developed which examines tenderness at six points of the body: bilateral lateral epicondyle of the humerous, medial condyle of the femur and the Achilles tendons at the posterior prominence of the calcaneus [22] however the

location and presentation of enthesitis in the foot can make it challenging to differentiate clinically from synovitis, bursitis and other inflammatory joint manifestations [23] (Figure 4). Enthesitis was typically under-diagnosed in patients with PsA however the routine use of ultrasound and MRI for assessing and monitoring the disease has increased the detection of enthesitis and enables more detailed investigation. Both modalities provide different, valuable information: MR imaging allows assessment of soft-tissue, entheseal and bone oedema, bone erosion and enthesophyte formation while ultrasound assesses vascularisation (power Doppler ultrasound (PDUS)), echogenicity, fluid, ligament abnormalities and tendon thickening [24]. The severity of enthesitis detected by ultrasound is a potential marker for peripheral and axial radiographic joint damage [25] however a recent study found no correlation at the insertion of the Achilles tendon [26].

The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) recommend the use of NSAIDs as the first-line treatment for targeting enthesitis then TNF inhibitors and/or IL-12/23 inhibitors as there is no empirical evidence to suggest traditional DMARDs have any effect [27]. In addition, the use of IL-17 inhibitors have demonstrated benefits in treating enthesitis as well as better outcomes overall, particularly for skin disease [28]. Due to the high risk of tendon rupture, local corticosteroid injections should be used with extreme caution at load-bearing entheses - particularly at the Achilles tendon insertion - however it is possible to inject into the retrocalcaneal bursae to achieve some therapeutic effect [4, 27]. Podiatry and physiotherapy are often prescribed despite the lack of evidence, but the benefit shown in managing foot disease in RA and clinical experience suggests they may be able to provide relief through the provision of orthoses, stretching and footwear modification and advice.

2.3 Dactylitis

Dactylitis, also known as ‘sausage’ digit, is a hallmark clinical feature of PsA and other spondyloarthropathies presenting as an acutely painful, uniformly swollen digit. Of the 39-48% of patients with PsA who have dactylitis, 75% of these cases occur in the foot [29, 30]. Dactylitis can be an early indicator of PsA and forms part of the classification criteria for diagnosing PsA [31, 32]. Similarly to enthesitis, the presence of dactylitis is a potential adverse prognostic factor and is associated with elevated disease activity, poorer functional status and greater disease burden compared to those without dactylitis [21]. Dactylitis may be a marker for arthritis mutilans in which typical changes such as erosion of the terminal phalangeal tufts, juxta-articular and entheseal new bone formation, periostitis, and severe osteolysis are seen on plain radiography [33]. MRI may show inflammation in several tissues, including tenosynovitis, synovitis, enthesitis and bone oedema. The European League Against Rheumatism (EULAR) and GRAPPA recognise the significance of dactylitis and recommend the use of biologics for patients with active dactylitis (and/or enthesitis) who do not respond to NSAIDs or local corticosteroid injections [27, 34].

Imaging studies have shown dactylitis to be a complex disorder with a wide range of features including synovitis, tenosynovitis, enthesitis, capsulitis, soft tissue thickening, bone oedema, and nail abnormalities (plate and bed) in the acute stage. However when the acute inflammation subsides, MRI scans still show abnormalities in the affected digit [35]. Current evidence suggests active foot disease persists in many patients despite recent treatment advances and the concept of “tight control” of disease [36]. Only a small proportion (20%) of those with moderate to high levels of foot related impairment and disability will receive foot care [3] with no evidence to support the use of interventions such footwear and orthoses in PsA.

Dactylitis most commonly occurs in the fourth toe and index finger and trauma has been hypothesised as a potential trigger for PsA. High levels of stress at entheses are suggested to be a biomechanical trigger to enthesitis and other manifestations of this disease [37, 38]. The load bearing function of toes during activities of daily living supports the mechanical pathogenesis hypothesis of toe dactylitis. A previous study, undertaken by Wilkins et al, found no significant evidence linking plantar forefoot pressures (a measure of vertical stress) and the prevalence of toe dactylitis suggesting that examining plantar pressure alone provides limited understanding of toe dactylitis [39]. Knowledge of plantar shear stress distribution (a measure of stress in anterior/posterior, medial/lateral and vertical directions) could provide a greater insight into pathological foot function which is a potential trigger for toe dactylitis. To our knowledge, the only related study examining shear stress in inflammatory arthritis patients demonstrated increased plantar shear stresses and resulting pain [40].

2.4 Synovitis and Tenosynovitis

Synovitis is commonly found in the distal and proximal interphalangeal joints of the foot and other peripheral joints and is also present in around 14% of patients with PsA at the metatarsophalangeal (MTP) joints [41]. The synovium is a primary site of inflammation in PsA and can be characterised by a thinner synovial lining than patients with RA, increased vascularity in both synovium and psoriatic plaques and an overabundance of proinflammatory cytokines [42]. Due to the complexity and proximity of midfoot and forefoot pathology in PsA, it can be incredibly difficult to diagnose and assess synovitis clinically without the use of imaging.

Unlike RA, patients with PsA can have residual synovial inflammation detectable by ultrasound even when they are in clinical remission [43] and recent research has found PDUS-detected synovitis

during remission is in fact a strong predictor of short-term flare [44]. Interestingly, subclinical synovitis is detected in around 30% of patients using PDUS at the MTP joints [45].

Tenosynovitis, namely exudative and proliferative tenosynovitis, is commonly found in the foot and ankle in patients with PsA. Tenosynovitis also occurs in the dactylitic toe, primarily affecting the flexor tendons, which can be detected using MRI and ultrasound imaging [46]. Common areas for tenosynovitis include the tibialis posterior, common peroneal sheath and the long flexor tendons of flexor digitorum longus (Figure 4) and flexor hallucis longus at the ankle.

Even in tendons which are not encased within a synovial sheath e.g. Achilles tendon, ultrasound can still detect inflammatory changes such as tendon thickening, intratendineous power Doppler signal and hypoechogenicity as a result of tendon oedema [47].

2.5 Onychopachydermoperiostitis

Psoriatic onychopachydermoperiostitis (POPP) syndrome is a clinical variant of psoriatic arthritis originally described by Fournie et al in 1989 [48]. Typically both hallux are involved in the presence of skin psoriasis, however it can occur in other digits, with associated nail changes, painful swelling of the soft tissue close to the distal phalanx as well as specific radiologic changes such as periosteal reaction and bone erosions of the distal phalanges. However, distal interphalangeal joint involvement is characteristically absent.

2.6 Juvenile psoriatic arthritis

The diagnosis of juvenile PsA is defined by having two of the following: dactylitis, nail pitting/onycholysis, and/or psoriasis in a first-degree relative. The ankle and small joints of the

forefoot are often affected, including the painful presentation of dactylitis resulting in reduced physical function [49, 50]. Typical psoriatic skin and nail lesions are more subtle and less common in the juvenile PsA compared with that seen in adults.

3. Imaging

3.1 Conventional Radiography

Conventional radiography (x-rays) is still routinely used to detect and monitor joint erosions, narrowing of the joint space and assess the density of subchondral bone [51]. Research has shown that within two years of developing PsA, around 32% of patients will present with radiographic joint erosions in the hands and feet despite clinical advances [52]. Overall factors predicting progression of radiological damage come from prospective cohort studies. In Toronto, the factors predicting progression were: erosions at presentation, higher baseline inflammation, and number of swollen and damaged joints [53]. However the predictors for radiological damage in the foot and ankle have not been determined.

When imaging the foot and ankle it is often useful to take a weight-bearing x-ray as this is a more accurate representation of the foot structure and may also have greater relevance as the patient may be asymptomatic when non weight-bearing [4]. Conventional radiography does however have limitations: it is ineffective for assessing soft-tissues such as enthesitis, synovitis, tenosynovitis, tendinitis, bursitis and intraarticular effusions, all common features of PsA which must be detected and monitored throughout the disease course [54]. Other imaging modalities including ultrasonography and magnetic resonance imaging (MRI) are able to assess these changes and allow identification of inflammatory lesions soon after symptoms occur and before there is structural damage.

3.2 MRI

MRI is the most sensitive imaging modality for detecting inflammatory changes and is therefore the gold standard for assessing soft tissue and bone pathology in patients with PsA [55]. The structures and inflammatory processes you can visualise using MRI include: synovitis, bone erosions, bone oedema, enthesitis and dactylitis. However the disadvantages of using MRI over ultrasound imaging or conventional radiography include: high cost, limited clinical availability, few clinicians are able to interpret foot images and you may need to use an intravenous contrast agent if you aim to assess the soft tissues and bone simultaneously [4].

3.3 Ultrasound

The complex nature of anatomical structures and proximity of soft tissues, tendons, ligaments and bones in the foot and ankle can make it difficult to obtain information from standard imaging modalities and differentiate clinically relevant pathology. However, ultrasound is a practical imaging tool that allows the clinician to identify and assess a number of PsA pathologies. Ultrasound imaging of PsA patients typically involves grey scale/B mode assessment to assess structural change and PDUS to detect inflammation through measuring vascularity [55]. There are a number of structural changes detectable by grey scale/B mode ultrasound in the foot and ankle including bone erosions, enthesitis, synovitis, tendonitis and bursitis which would be difficult to distinguish clinically. In addition, PDUS is a useful tool for determining whether there is active inflammation or residual degenerative changes [56]. PDUS can detect changes in vascularity in soft tissues such as the synovium but also has the potential to assess changes at a superficial level e.g. the skin and nails [57].

4. Management

When managing the foot in PsA the aim is for a zero-tolerance approach to active disease through pharmacological and non-pharmacological interventions and treatments. The evidence for managing foot and ankle disease in RA has shown there is a lack of basic foot health services for these patients and their foot health needs are not being met [58-61]. Despite the fact there is no evidence on the efficacy of podiatry involvement in the management of patients with PsA, it is well recognised that regular podiatry input is essential for holistic management of these patients.

Only 20% of patients with PsA currently receive foot care despite over 60% self-reporting pain and moderate to severe levels of impairment and disability [3]. Research into RA has shown foot problems have a significant impact on patients' quality of life by restricting mobility and the ability to work and socialise [61]. With similar manifestations, and the addition of enthesitis, dactylitis, psoriatic skin/nail disease and further pathology, it is fair to extend this observation to patients with PsA.

Foot problems can be divided into primary i.e. they arise as a manifestation of PsA (synovitis, tenosynovitis, dactylitis etc.) or secondary i.e. loss of hand dexterity and function and/or axial involvement which can make it impossible for patients to carry out basic foot care, tie laces or fasten appropriate footwear. Redmond et al. advocate five areas of foot health provision for patients with rheumatic conditions including: education and self-management advice, provision of orthoses and footwear, general e.g. nail care, corn enucleation and callus reduction, the management of the high risk foot (ulceration, vascular insufficiencies, neuropathy) and foot and ankle surgery [60].

The feet should be assessed regularly by members of the rheumatology multidisciplinary teams and should be incorporated as part of the overall joint/skin assessment. Helliwell et al. published a 'Look, Feel, Move' model encouraging clinicians to carry out a simple, quick foot and ankle assessment: looking for changes in foot posture, swelling, and skin and nails changes then palpating joint margins and soft tissue structures and finally moving the ankle, subtalar, midfoot, MTP and interphalangeal joints to assess the range of motion and detect structural changes [62].

Forefoot deformity such as hallux abducto valgus, often in conjunction with changes to foot posture, can result in difficulty finding suitable footwear particularly when, as previously mentioned, the patient is unable to manage due to hand and/or axial involvement. Patients should be encouraged to wear a wide-fitting shoe with more depth to accommodate the structural deformity and laces or a fastening to secure the shoe to the foot. Foot and ankle problems often result in a prolonged compensative gait typically leading to weakened muscles e.g. posterior calf muscles, and require muscle strengthening exercises specific to the muscle group affected. Although there is no evidence to support the benefit of using mechanical therapies in PsA, it is reasonable to assume that orthoses designed to attenuate mechanical stresses and used in patients with RA [63] would be beneficial in joints and soft tissues that are acutely inflamed or in those where disease remains locally persistent. The use of corrective functional foot orthoses, particularly in early disease to relieve pain and reduce mechanically driven inflammation by correcting the foot position, providing joint stabilisation, resting key anatomical structures and resisting the deforming forces will likely prevent the development of deformity. Foot orthoses can also be used to redistribute high pressure areas and offload painful tendons and/or soft tissue structures.

The management of PsA nail disease depends on the severity, duration of symptoms and how much it impacts the patients' quality of life. When psoriatic nail disease is present, podiatrists can reduce

the thickness of onychauxic (thickened) nails to prevent onychocryptosis and subsequent infection - a serious consideration for immunosuppressed patients - and advise on safe topical treatments if there is a suspected infection. When nail disease is widespread and significantly impacting the patient's quality of life, or presents along with significant skin and/or joint disease, then systemic therapy is justified with strong evidence supporting the efficacy of TNF and IL-12/23 inhibitors [27].

Despite the lack of research around the peripheral vascular supply of patients with PsA, it is important to assess the vascular supply to the lower limb as we know PsA is actually equivalent to RA and diabetes mellitus in terms of general cardiovascular risk [64]. Clinically this can be assessed by looking for skin colour changes, presence of hair and potential tissue breakdown/ulceration. It is important to check the vascular supply to the foot by palpating the dorsalis pedis pulse as it runs over the dorsal prominence of the navicular bone and the posterior tibial pulse as it runs behind the medial malleolus. If they are not palpable a hand-held vascular Doppler should be used to locate these pulses and assess the strength of the blood flow to the peripheries.

Local corticosteroid injections are advocated for chronic foot disease in PsA patients, despite a lack of evidence, to relieve symptoms and target areas of persistent inflammation. Ultrasound guided injections have been shown to improve the accuracy of intra-articular injections and may be more beneficial for the smaller joints of the feet and when there is significant structural abnormality present [65, 66].

Surgery should be considered if pharmacological and conservative approaches are not effective, although the evidence to support surgical strategies is lacking in this group of patients. Guidelines typically recommend that patients are referred for a surgical opinion at an appropriate time,

although identifying when a patient should be referred for foot surgery is yet to be determined. Surgical synovectomy and radioactive synovectomy are seldom undertaken nowadays, possibly because of more effective systemic therapies for this disease.

5. Conclusion

Management of the foot in PsA should not be over-looked by clinicians as foot and ankle problems can have a significant impact on patients' quality of life and foot focussed interventions can significantly improve this.

6. Expert Commentary

Unfortunately there is no high quality evidence to support the management of foot problems in people with psoriatic arthritis. It has been proposed that the key to effective management of foot problems in people with rheumatoid arthritis is through staged and targeted interventions in early disease with the ultimate aim of zero tolerance of active disease in the foot; we advocate this approach to managing foot disease in people with psoriatic arthritis. Strategies should combine pharmacological anti-inflammatory agents, including intraarticular and soft tissue steroid injections with physical therapies to prevent and reduce mechanical articular and peri-articular stresses. In practice, however, there is evidence to suggest active foot disease persists in many patients despite recent treatment advances and the concept of "tight control" of disease. Our future research needs to be directed at gaining a better understanding of the pathogenesis of foot disease in this group of patients to enable us to identify effective management strategies, aimed at preventing long term damage.

A previous study, undertaken by our team in Leeds, found no significant evidence linking plantar forefoot pressures (a measure of vertical stress) and the prevalence of toe dactylitis, suggesting that examining plantar pressure alone provides limited understanding of toe dactylitis. Exploring other biomechanical reasons will provide a greater insight into pathological foot function which may act as a potential stress trigger for toe dactylitis and help us understand why it most commonly occurs in the fourth toe. We can then direct our further research to identifying appropriate interventions to reduce the impact of dactylitis.

It is widely accepted that high levels of stress at entheses are suggested to be a biomechanical trigger to enthesitis and other manifestations of this disease; pharmacological therapies such as local steroid injections and systemic disease modifying drugs are used to treat the inflammation. However, we must also address the clinical question 'do mechanical therapies work for enthesitis?'

And should they be combined with pharmacological therapies such as local steroid injections to provide the most effective treatment?

Skin and nail disease have both physical and psychosocial impacts on the person involved, which extends to include the foot. Clinically we experience patients finding it difficult to wear a fully enclosed shoe due to pressure/rubbing on the skin and often discomfort from thickened nails. Therefore it is important that we understand what influence skin and nail disease has on the patient's ability to wear orthoses and footwear, required to manage the biomechanical aspects of the disease. This leads to a further question; should we be treating the skin (and nails) aggressively for this reason?

A research strategy aimed at understanding both the biomechanical and inflammatory mechanisms of foot disease in people with psoriatic arthritis provides the opportunity to address foot impairments and resulting disability and develop a personalised targeted approach to treatment.

7. Five-year review

This review has given us the opportunity to highlight the impact of foot disease, the potential mechanisms that cause the resulting impairment and disability and propose targeted treatment strategies. We speculate that in five years our understanding of the manifestations of how the disease process affects the feet will have improved so that we can stratify patients to ensure that we target those who are a risk of developing deformity and disability. This approach will enable us to design studies to determine the clinical and cost effectiveness of treatment strategies aimed at preventing and managing the mechanical and inflammatory outcomes of the disease.

Key issues

- Peripheral joint and soft tissue involvement in the foot can manifest around the forefoot, midfoot and hindfoot right from the onset of disease; forefoot deformity affects over 90% of patients with established disease.
- The Achilles tendon insertion is the most prevalent site affected however enthesitis can also typically be detected in the foot at the insertion of the plantar fascia at the calcaneus, tibialis posterior at the navicular tuberosity and peroneus brevis tendon at the base of the fifth metatarsal.
- Dactylitis can be an early indicator of PsA forming part of the classification criteria; of the 39-48% of patients with PsA who have dactylitis, 75% of these cases occur in the foot and most commonly in the fourth toe.
- The load bearing function of toes supports the mechanical pathogenesis hypothesis of toe dactylitis, however recent evidence suggests that plantar forefoot pressures (a measure of vertical stress) are not linked to the prevalence of toe dactylitis.
- Synovitis is commonly found in the distal and proximal interphalangeal joints of the foot as well at the metatarsophalangeal (MTP) joints. Clinical synovitis is present in 14% of patients with PsA at the MTP joints; interestingly, subclinical synovitis is detected in around 30% of patients using power Doppler ultrasound at the MTP joints.
- Common areas for tenosynovitis include the tibialis posterior, common peroneal sheath and the long flexor tendons of flexor digitorum longus and flexor hallucis longus at the ankle.
- Only 20% of patients with PsA currently receive foot care despite over 60% self-reporting pain and moderate to severe levels of impairment and disability.
- The feet should be assessed regularly by members of the rheumatology multidisciplinary team and should be incorporated as part of the overall joint/skin assessment.

- Due to the high risk of tendon rupture, local corticosteroid injections should be used with extreme caution at load-bearing entheses i.e. the Achilles tendon insertion; injecting into the retrocalcaneal bursae will achieve some therapeutic effect.
- Despite the lack of evidence, clinical experience suggests that foot symptoms are relieved through the provision of orthoses, stretching and footwear modification and advice.
- Functional foot orthoses offer the potential to relieve pain, redistribute high pressure areas and offload painful tendons and/or soft tissue structures.
- Surgery should be considered if pharmacological and conservative approaches are not effective, although the evidence to support surgical strategies is lacking in this group of patients.

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Annotated Bibliography

* of interest

These references highlight the manifestations of psoriatic arthritis including the impact of foot disease and the need for management strategies.

** of considerable interest

These references identify the impact of foot problems in patients with foot disease in people with psoriatic arthritis.

Figure Legends

Figure 1: Plaque psoriasis on the dorsum of the foot and psoriatic nail disease.

Figure 2: Psoriatic nail disease: onycholysis in the finger nails also seen in toe nails.

Figure3: Pronounced enthesitis at the Achilles tendon insertions

Figure 4: Tenosynovitis of the tibialis posterior tendon and a large synovial cyst arising from the flexor digitorum longus tendon sheath of the right foot.