Psoriatic arthritis: a clinical diagnosis

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There have been great advances in the identification and understanding of the pathogenesis of psoriatic arthritis, and new biological therapies have improved the options for patients with this potentially disabling condition.

Psoriasis is a common skin condition afflicting approximately 2 to 3% of the world's population. Between 10 and 30% of patients with psoriasis suffer from the associated inflammatory arthritis.

Typically, five types of arthritis are associated with psoriasis (Table 1). In most patients, rash usually precedes arthritis by 8 to 10 years, but in 15% rash and arthritis start concurrently and in another 10% seronegative arthritis develops first with rash following sometime later, making diagnosis difficult.

The psoriatic rash can be minor and hidden in sites such as the scalp, genitals, external auditory meati, skin folds or nails, and most often its severity does not correlate with that of the inflammatory arthritis. Indeed, in many patients psoriatic arthritis can be a severe and destructive arthritis, with half of all affected patients having a deforming arthritis, and up to 20% being disabled by their arthritis. Males and females are equally affected.

Pathogenesis

Psoriasis together with its arthritis is understood to be an immune-mediated disease characterised by infiltration of activated T-cells predominantly in the dermis. These cells release inflammatory cytokines, such as tumour necrosis factor (TNF) and interferon, as part of a cascade of inflammatory events, culminating in cutaneous inflammation and causing hyperproliferation of epidermal keratinocytes and recruitment of neutrophils into the epidermis.

An inflammatory infiltrate is also the pathological finding in psoriatic arthritis synovium (see the case study on page 71). This infiltrate is characterised by mononuclear cells, neutrophils and excess inflammatory cytokines, including TNF, interleukin (IL)-1, IL-23, and interferon gamma. Effective new therapies target these cytokines.

Table 1. Types of arthritis associated with psoriasis

- Distal interphalangeal predominant (DIP) arthritis affecting a psoriatic nail (onycholysis and especially pitting) – distinguished from primary nodal osteoarthritis in which the nails are normal
- Asymmetric pauciarthritis, which affects a few joints (usually a mixture of small and large joints) in an uneven pattern – e.g. one finger, one ankle and an elbow
- Symmetrical polyarthritis – i.e. the bilateral involvement of small joints (e.g. hands and feet), resembling rheumatoid arthritis but with negative rheumatoid factor and the presence of psoriasis
- Axial involvement – inflammatory back pain (i.e. back pain and stiffness that causes a patient to wake up in the second part of the night, fluctuates from side to side, is felt in the buttocks, is associated with morning pain and stiffness for prolonged periods, improves with exercise and heat, and is present for extended periods rather than occurring in attacks)
- Arthritis mutilans, which is rare and causes complete destruction of fingers or toes with collapse of the digits

Clinical features

Several clinical features are strongly suggestive of psoriatic arthritis, including:

- painful and swollen small and large joints in an asymmetrical pattern

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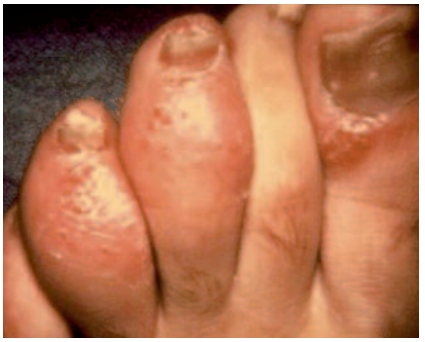

Figure 1. Dactylitis of the third and fourth toes.

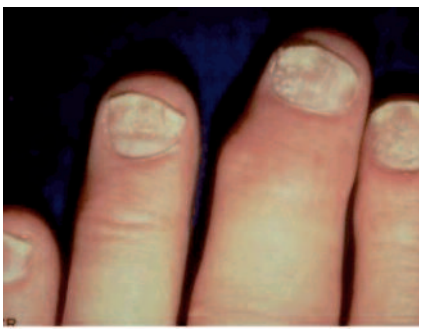

Figure 3. Distal interphalangeal predominant joint inflammation and psoriatic nail disease (onycholysis, ridging and pitting).

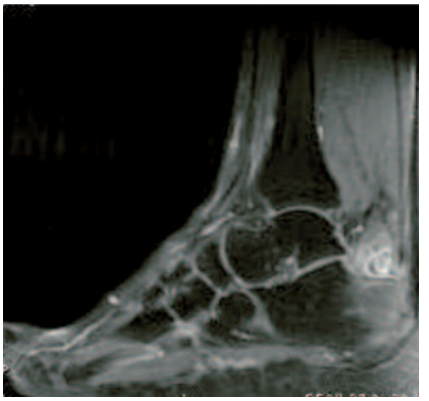

Figure 2. MRI showing Achilles enthesitis. Severe diffuse posterior calcaneal bone oedema extending a long way from the site of attachment of the Achilles tendon is present, as well as retrocalcaneal bursitis and Achilles tendinosis.

- dactylitis – the uniform swelling of a digit, characterised on MRI by the presence of severe tenosynovitis, together with arthritis and digital oedema (Figure 1)
- enthesitis, the inflammatory reaction occurring at the bony attachment of a ligament or tendon, typically found at the Achilles insertion and plantar fascia attachment to the calcaneum (Figure 2).

Psoriatic arthritis may affect the whole spine and frequently manifests with sacroiliitis. Extra-articular features include uveitis. Patients with psoriatic arthritis are more likely to manifest nail disease (pitting and onycholysis) as a feature of the psoriasis (Figure 3).

Conditions such as HIV infection have been shown to flare psoriasis and psoriatic arthritis and can initiate disease de novo, as can interferon therapies. Paradoxically, the anti-TNF therapies, which have proven to be effective for psoriasis and psoriatic arthritis, can rarely be associated with a new pustular psoriasis rash, typically occurring on the palms and soles.

Diagnosis

The diagnosis of psoriatic arthritis is clinical; a list of clues to its diagnosis is given in Table 2. Laboratory tests are often unhelpful as there is no characteristic

Table 2. Clues to diagnosis of psoriatic arthritis

- Assess whether the patient has psoriasis (present, past or family history)
- Look for nail pitting and onycholysis
- Examine hidden anatomical sites for psoriasis (the patient may not be aware the rash he or she has is that of psoriasis)
- Look for the 'sausage' digit (dactylitis) in fingers or toes
- Ask the patient if he or she has a history of inflammatory joint pain (spine or limbs), early morning stiffness lasting more than 30 minutes, or stiffness after periods of rest (gel phenomenon)

Table 3. CASPAR criteria[1]

To meet the CASPAR criteria for psoriatic arthritis a patient must have inflammatory articular disease and score 3 or more points based on the following categories.

Category	Points
1. Evidence of psoriasis	
• Current psoriasis	2
• Personal history of psoriasis	1
• Family history of psoriasis	1
2. Psoriatic nail dystrophy	
• Pitting, onycholysis, hyperkeratosis	1
3. Negative test result for rheumatoid factor	1
4. Dactylitis	
• Current swelling of an entire digit	1
• History of dactylitis	1
5. Radiological evidence of juxta-articular new bone formation	
• Ill-defined ossification near joint margins on plain x-rays of hand/foot	1

Abbreviation: CASPAR = Classification Criteria for Psoriatic Arthritis.

autoantibody production. Rheumatoid factor and anti-cyclic citrullinated peptide (anti-CCP) antibodies are negative, and the inflammatory markers erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are normal in up to half of patients with active disease.

To help diagnosis, the CASPAR criteria (Classification Criteria for Psoriatic Arthritis) have been developed (Table 3). According to these criteria, the presence of an inflammatory arthritis is mandatory and a score of at least three points must be attained from five categories to confirm the diagnosis of psoriatic arthritis.

Genetic studies have served to differentiate this condition from rheumatoid arthritis, as gene associations classify psoriatic arthritis within the spondyloarthropathic group of diseases (ankylosing spondylitis, inflammatory bowel disease-associated arthritis and reactive arthritis). These are distinct

Case study. Reaching a diagnosis of psoriatic arthritis

The case

A 42-year-old storeman, who was a nonsmoker and regular beer drinker, presented complaining of having had a swollen right knee for a few months. He thought it must be injury related. You prescribed him diclofenac 50 mg twice daily and referred him to a surgeon, who requested an MRI and suggested arthroscopy. He has now come back to you wanting to know if arthroscopy is really necessary.

The MRI shows a large effusion with considerable synovial thickening and mild changes of osteoarthritis. The diclofenac you prescribed has led to considerable symptomatic improvement and 'by the way' his hands and feet hurt less.

Further history and examination reveal scaly red plaques on his elbows, which he says 'have always been there' and used to be worse when he was a teenager, occurring also in his scalp and groin. He also reports some hand and foot stiffness in the mornings when he gets out of bed, which improves as the day goes on and worsens again in the evening when resting.

On examination, the knee effusion is large enough to be clearly visible (Figure 4). Many joints, including the wrists, interphalangeal joints, metatarsophalangeal joints and Achilles and plantar fascia insertions, are tender to palpation. You also feel that some of these are swollen.

Discussion

The provisional diagnoses include:

- gout
- psoriatic arthritis
- rheumatoid arthritis
- osteoarthritis
- calcium pyrophosphate deposition disease
- a combination of the above.

Appropriate investigations include: erythrocyte sedimentation rate, C-reactive protein (CRP), rheumatoid factor, anti-cyclic citrullinated peptide (anti-CCP) antibodies and serum uric acid measurements.

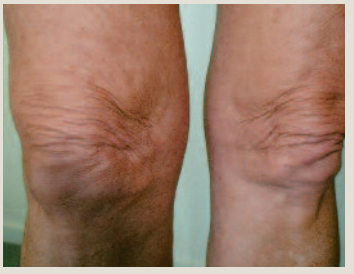

Figure 4. Swollen right knee of the 42-year-old man in this case study.

Case continued

Only the CRP and uric acid levels are mildly elevated (CRP, 15 mg/L [normal range, 0.0 to 10.0 mg/L] uric acid, 0.52 mmol/L [normal range, 0.18 to 0.48 mmol/L]); the other tests results are normal. Fluid is aspirated from the knee and shows an inflammatory cell count with no uric acid or calcium crystals.

Discussion continued

The diagnosis is psoriatic arthritis, given the inflammatory arthritis and long-standing psoriatic rash, in addition to mild knee osteoarthritis. A swollen joint and a raised serum uric acid level do not equate to acute gout. The key intervention is to aspirate the synovial fluid for analysis of the cell count and differential (which is normal in osteoarthritis, elevated in psoriatic arthritis) and a crystal search.

Case continued

The patient's symptoms are stabilised by regular NSAID treatment, and you refer the patient to a rheumatologist for opinion about the use of disease-modifying agents or biological therapies.

Discussion continued

Surgery is not required to make a diagnosis of an inflammatory arthritis and also is not part of the initial treatment algorithm. Very occasionally, however, a surgical synovectomy will be a useful adjunctive therapy for a single joint if systemic treatments and corticosteroid injections have failed to control the synovitis in that joint.

continued

Table 4. Treatment initiation recommendations for psoriatic arthritis*[2]

Peripheral arthritis
- NSAIDs
- Intra-articular corticosteroids
- DMARDs (methotrexate, cyclosporin A, sulfasalazine, leflunomide)
- Biological agent (anti-TNF therapies)

Skin and nail disease
- Topical agents (e.g. corticosteroid and vitamin D analogues)
- PUVA/UVB
- DMARDs (methotrexate, cyclosporin A)
- Biological agents (infliximab, etanercept, adalimumab, golimumab and ustekinumab)†

Axial disease
- NSAIDs
- Physiotherapy
- Biological agents (anti-TNF therapies)

Enthesitis
- NSAIDs
- Corticosteroid injection to the inflamed site
- Biological agents (anti-TNF therapies)

Dactylitis
- NSAIDs
- Corticosteroid injection into the tendon sheath or the joints involved
- Biological agents (anti-TNF therapies)

* Recommendations are based on the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) treatment guidelines.

† Infliximab, etanercept, adalimumab and golimumab are indicated for psoriatic arthritis. Ustekinumab and the anti-TNF therapies infliximab, etanercept, adalimumab and golimumab are indicated for plaque psoriasis.

ABBREVIATIONS: Anti-TNF = anti-tumour necrosis factor inhibitor; DMARD = disease-modifying antirheumatic drugs; NSAID = nonsteroidal anti-inflammatory drugs; PUVA = psoralen plus ultraviolet light A; UVB = ultraviolet light B.

from rheumatoid arthritis-associated gene profiles.

Treatment

Traditional disease modifying agents (DMARDs) – sulfasalazine (to treat arthritis), methotrexate (to treat rash and arthritis) and leflunomide (to treat rash and arthritis) – have been 'borrowed' from the rheumatoid arthritis armamentarium and are widely used for psoriatic arthritis despite few controlled clinical trials demonstrating efficacy for this indication. (Sulfasalazine and methotrexate are used off-label for the treatment of psoriatic arthritis.)

The systemic treatments for cutaneous and joint psoriasis partially overlap. The main nonbiological systemic treatments for cutaneous psoriasis are acitretin, methotrexate and cyclosporin. Cyclosporin is not often used for psoriatic arthritis due to toxicity when used long term. Leflunomide is rarely used to treat cutaneous psoriasis.

Oral prednisolone is used less often for psoriatic arthritis than for rheumatoid arthritis, due to the severe rebound effect of psoriasis associated with corticosteroid withdrawal.

Anti-TNF therapies, as targeted biological agents, have dramatically changed the landscape for both psoriasis and psoriatic arthritis. They have demonstrated significant efficacy for psoriasis, treating both rash and nail disease. For psoriatic arthritis, they have been shown uniquely to retard structural damage and are the first agents shown to be effective for dactylitis, enthesitis and spinal inflammatory disease.

The anti-TNF therapies are protein antibodies that target cytokines to block inflammation and its sequelae. They include etanercept, infliximab, adalimumab and golimumab, all of which are PBS listed for the treatment in adults of severe active psoriatic arthritis failing multiple prior therapy.

The biological agents that have restricted PBS approval for the treatment of severe treatment-resistant cutaneous psoriasis are the anti-TNF therapies etanercept, infliximab and adalimumab and the IL inhibitor ustekinumab. Ustekinumab, which blocks the cytokines IL-12 and IL-23, has shown efficacy for the treatment of psoriasis in randomised controlled trials and is currently under investigation in phase III trials for the treatment of psoriatic arthritis.

Table 4 summarises the treatment guidelines for psoriatic arthritis as recommended by the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA).[2]

Conclusion

There have been great advances in the identification, understanding of pathogenesis and therapeutic options available for patients with psoriatic arthritis. Efforts are under way to develop validated questionnaires to identify patients with inflammatory arthritis in psoriasis populations, develop a disease activity index and pursue further novel therapies for skin and joint disease. MT

References

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COMPETING INTERESTS: Dr Feletar and Associate Professor Nash have received research grants for clinical trials, honoraria for lectures or advice for companies manufacturing targeted biological therapies.