Other seronegative spondyloarthropathies

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Abstract

Seronegative spondyloarthropathies are a group of overlapping forms of inflammatory joint disease, the most common conditions being psoriatic arthritis and ankylosing spondylitis. Other less common conditions include reactive arthritis, enteropathic arthritis and SAPHO (synovitis, acne, pustulosis, hyperostosis, osteitis). Shared features include a propensity to affect the spine, an association with anterior uveitis, involvement of the enthesis, the absence of rheumatoid factor and an increased frequency of HLA-B27. Psoriatic arthritis has several distinctive characteristics that may vary from patient to patient and include frequent involvement of distal interphalangeal joints, dactylitis, new bone formation within the enthesis, osteolysis and ankylosis. Genetic factors are important, with HLA-Cw06-containing haplotypes associated with psoriasis and peripheral joint inflammation, and HLA-B27 variants associated with axial involvement, especially sacroiliitis. Psoriatic arthritis patients are managed with physical and occupational therapy, NSAIDs, non-biological disease-modifying anti-rheumatic drugs and local corticosteroid injections. The advent of tumour necrosis factor-α inhibitors has provided an important new dimension to treatment options for those with severe or persistently active disease, and new therapeutic agents are currently in advanced phases of clinical trials.

Keywords Enteropathic arthritis; enthesopathy; HLA-B27; psoriasis; psoriatic arthritis; spondylitis; tumour necrosis factor-α

The seronegative spondyloarthropathies are a group of overlapping forms of inflammatory joint disease including psoriatic arthritis (PsA), ankylosing spondylitis, reactive arthritis, enteropathic arthritis and SAPHO (synovitis, acne, pustulosis, hyperostosis, osteitis). Ankylosing spondylitis and reactive arthritis are discussed elsewhere. This group of diseases has the following common features:

- a propensity to affect the spine
- an association with anterior uveitis and human leucocyte antigen (HLA)-B27 variants
- usual absence of rheumatoid factor and anti-citrullinated peptide antibodies
- variable penetrance and pattern of presentation within families.

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What's new?

- There is a more established link between psoriatic disease and the metabolic syndrome, prompting a new drive to address modifiable risk factors such as obesity, diabetes, hypertension and smoking in order to improve prognosis
- Agents blocking IL-12/IL-23, IL-17, phosphodiesterase pathways and intracellular signalling (STAT3) have shown much promise as future treatment options for psoriatic disease
- The stratified medicine approach of tailoring therapy to a patient's biomarker (genetic, serum, radiological, and clinical) profile is of growing research interest in the seronegative arthritides, and may alter management practices in the near future

Psoriatic arthritis

Epidemiology

Psoriasis affects 2–3% of the population. About 15–20% of individuals with psoriasis attending hospital develop inflammatory arthritis; the incidence may be lower in the community. There is a slight female predominance. The characteristic clinical and radiological pattern of joint involvement in PsA (Figures 1 and 2) strongly suggests that it is a distinct entity. Most patients have pre-existing skin or nail psoriasis; joint inflammation precedes psoriasis in about 15% of cases. There is a strong association between an increased incidence of PsA and the epidemic of HIV infection in sub-Saharan Africa.[1]

Aetiopathogenesis

An array of environmental triggers in a genetically susceptible host is thought to cause abnormal activation of the innate and adaptive immune systems in PsA.[2] The heterogenous phenotype of PsA suggests that different initiating events can take alternative routes, ending in a common network of interactions between cells and messenger molecules, resulting in the varied phenotype of PsA observed.[2] There are increased concentrations in the synovial fluid and membranes of affected joints of cytokines derived from:

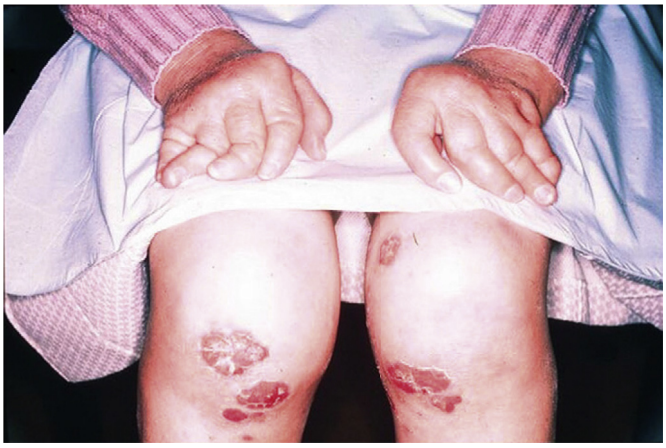
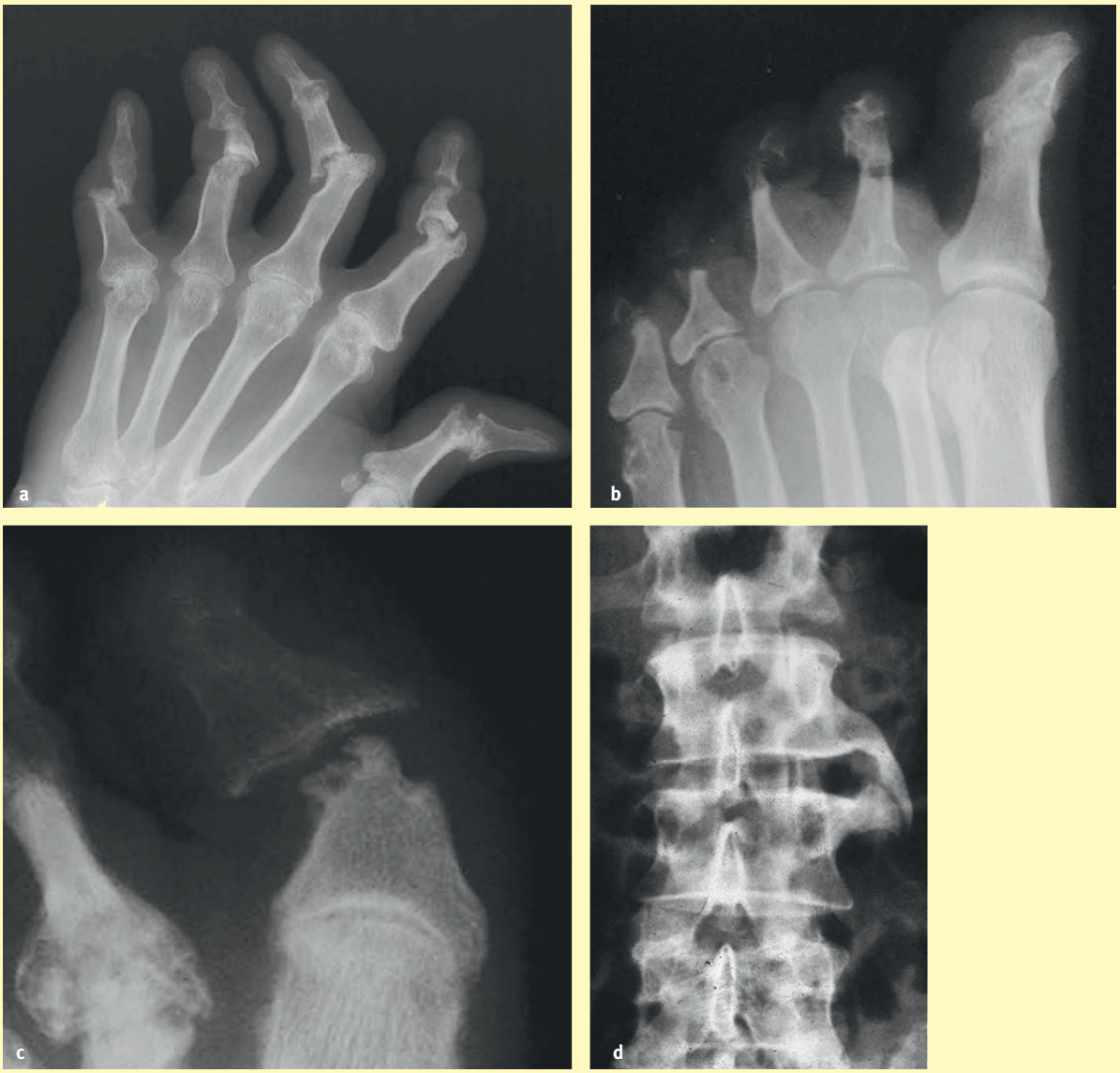


Figure 1 Arthritis mutilans in a patient with psoriatic arthritis.



Characteristic radiological features of psoriatic arthritis including involvement of distal interphalangeal joints of hands (**a**), feet (**b**), lack of periarticular osteoporosis (**a**), osteolysis (**b**), pencil-in-cup deformities (**c**) and paramarginal syndesmophyte formation in axial spine (**d**).

Figure 2

- macrophages, such as tumour necrosis factor-α (TNF-α), interleukin-1, interleukin-6, interleukin-8 and interleukin-18
- Th1 cells such as interleukin-2 and interferon-α
- Th17 cells such as IL-17; the Th17 subset of T cells is likely to be involved in the progression of disease

We know that innate immunity-associated cytokines such as TNF-α are also critically important, given the success of anti-TNF-α therapies in PsA. Defective dendritic cells have recently been implicated in PsA.[3] Increased levels of osteoclast precursors are found in the circulating blood, and increased expression of RANKL (receptor activator of nuclear factor-κ B ligand) in the synovial membrane that may explain heightened erosion and new bone formation.[4] Trauma, stress and infection have been suggested as triggering factors for PsA, though none has been well substantiated. Hormonal factors may have a modifying role — PsA usually improves during pregnancy and may flare post partum, as in rheumatoid arthritis (RA). Development of reactive arthritis to organisms in psoriatic plaques is a reasonable hypothesis but does not account for patients who present before the onset of psoriasis, unless an infective trigger at another site (e.g. the gastrointestinal tract) is responsible.

Genetics: the genetic factors that make individuals susceptible to PsA are likely to be separate from those for psoriasis. There is a high sibling recurrence ratio, with 8% of first-degree relatives of probands with PsA having the condition themselves.[5] Several genes have shown robust association with PsA, including HLA-