Psoriatic arthritis and seronegative spondyloarthropathies

Deepak R Jadon

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, involvement of the enthesis, an association with anterior uveitis and inflammatory bowel disease, the absence of rheumatoid factor, and an increased frequency of *HLA-B27* variants. Psoriatic arthritis has a diverse phenotype with several distinctive characteristics, including frequent involvement of the distal interphalangeal joints, dactylitis, new bone formation within the enthesis, osteolysis and ankylosis. Genetic factors are important, with *HLA-Cw06* haplotypes associated with psoriasis and peripheral joint inflammation, and *HLA-B27* variants associated with sacroiliitis and spondylitis. Psoriatic arthritis patients are managed with physical and occupational therapy, non-steroidal anti-inflammatory drugs, local glucocorticoid injections, conventional synthetic disease-modifying antirheumatic drugs (DMARDs) and biologic DMARDs. The advent of biologic DMARDs, including tumour necrosis factor-α inhibitors, interleukin-17 inhibitors and interleukin-12/23 inhibitors, has revolutionized the management of articular disease, entheseal disease and other extra-articular manifestations in individuals with persistent severe disease. Treatment goals have therefore shifted, with clinicians and patients aiming for disease remission or minimal disease activity.

Keywords Biologics; enteropathic arthritis; *HLA-B27*; MRCP; psoriasis; psoriatic arthritis; sacroiliitis; spondylitis

Key points

- In keeping with other forms of spondyloarthropathy, the enthesis (site of tendon, ligament or joint capsule insertion to bone) is the primary site of involvement in psoriatic arthritis (PsA)
- Different patterns of joint disease occur in PsA, ranging from distal interphalangeal joint disease to spondyloarthritis
- Dactylitis, involvement of the distal interphalangeal joints of the fingers, interphalangeal involvement of the toes and psoriatic nail disease are highly suggestive of PsA
- As psoriatic disease is associated with the metabolic syndrome, it is very important to address modifiable risk factors such as obesity, diabetes mellitus, hypertension and smoking
- Conventional synthetic (methotrexate, leflunomide, sulfasalazine) and biologic (tumour necrosis factor-α inhibitors, interleukin-17 inhibitors) disease-modifying antirheumatic drugs are proving to be very effective treatments for the management of all aspects of psoriatic disease
- The personalised medicine approach of tailoring therapy to a patient's biomarker (genetic, serum, blood, synovial, radiological, clinical) profile is of growing research interest in the seronegative spondyloarthropathies, and will probably alter management practices in the near future

Introduction

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

- a propensity to affect the spine in the form of sacroiliitis and/or spondylitis
- 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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Psoriatic arthritis

Epidemiology

Psoriasis affects approximately 2% of the UK population. About 15–20% of individuals with psoriasis attending hospital develop inflammatory arthritis, although the incidence may be lower in the community. There is a very slight female predominance. The characteristic clinical and radiological pattern of joint involvement in PsA (Figures 1 and 2) strongly suggests that PsA is a distinct entity. Although most patients have pre-existing skin or nail psoriasis, musculoskeletal inflammation precedes psoriasis in about 15% of cases.

Aetiopathogenesis

A variety of environmental triggers in a genetically predisposed host are thought to cause abnormal activation of the innate and adaptive immune systems, leading to the heterogeneous phenotype of PsA. The synovial fluid and tissue of affected joints have increased concentrations of cytokines derived from:

- macrophages, such as tumour necrosis factor (TNF)-α, interleukin (IL)-1, IL-6, IL-8 and IL-18
- T helper type 1 (Th1) cells, such as IL-2 and interferon-α

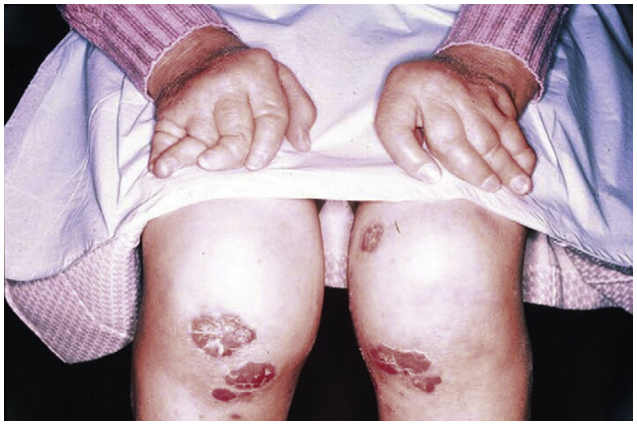

Figure 1 Arthritis mutilans in a patient with PsA.

- Th17 cells, such as IL-17. Additionally, Th17 cells are likely to be involved in disease progression.

We know that innate immunity-associated cytokines such as TNF-α are critically important, given the success of anti-TNF-α therapies in PsA. Defective dendritic cells, increased levels of circulating osteoclast precursors and increased expression of RANKL (receptor activator of nuclear factor-κB ligand) in the synovial membrane are likely to contribute to erosion and new bone formation in PsA. Physical trauma, stress and infection have been implicated in triggering the onset of PsA, but the association remains to be established. Hormonal factors can have a modifying role; PsA usually improves during pregnancy, but can flare in the postpartum period. 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 a microorganism at another site (e.g. gastrointestinal tract) is responsible.

Genetics: the aetiology of PsA has a large genetic component. There is a high sibling recurrence ratio: 8% of first-degree relatives of probands with PsA have the condition themselves. Several genes have shown robust association with PsA: *HLA-B27*, *HLA-Cw06*, *IL12B*, *IL23R*, late cornified envelope *(LCE)* gene cluster and *TRAF3IP2*. Some loci have shown association with PsA independently of skin psoriasis: *HLA-B27*, *IL13*, *IL23R*, *PTPN22* and *5q31*. Conversely, *HLA-Cw06* is more strongly linked to skin psoriasis. PsA and AS share gene associations with

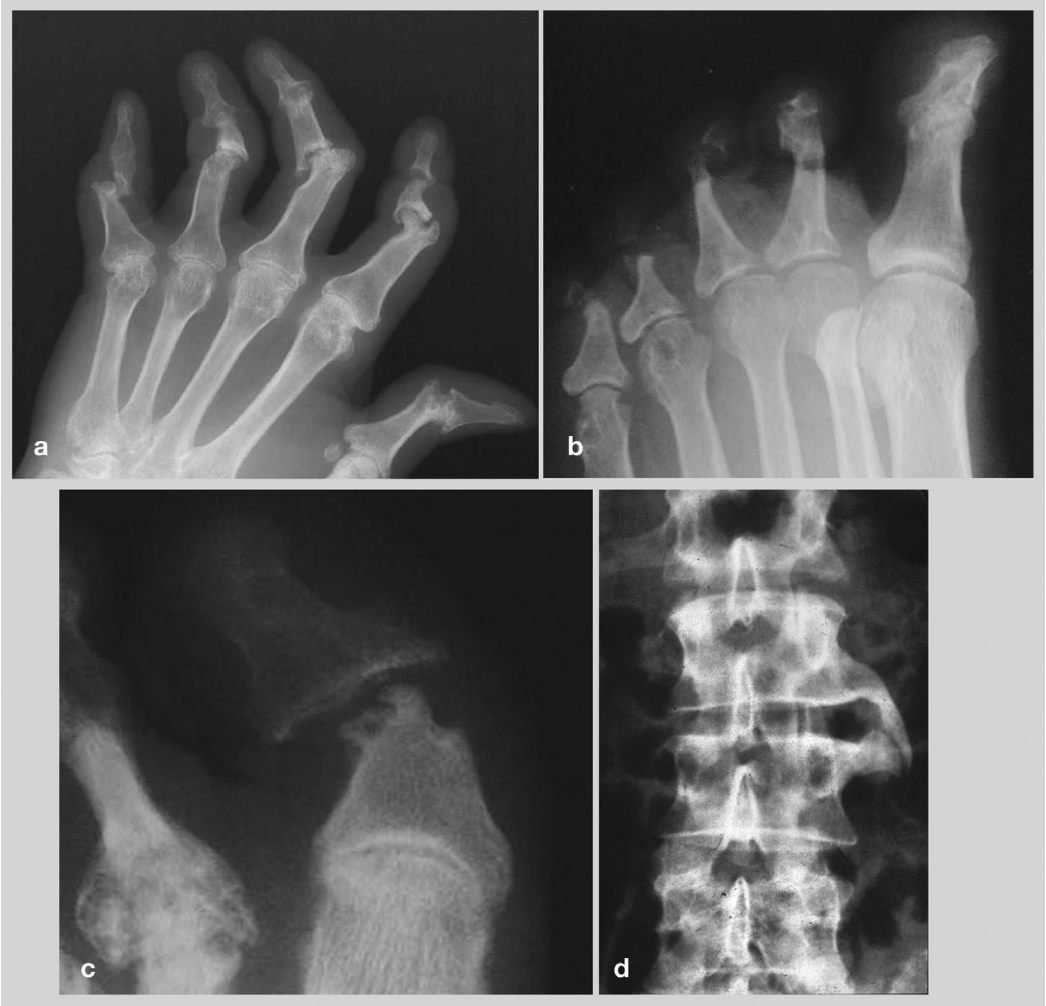

Figure 2 Characteristic radiological features of PsA, including involvement of the distal interphalangeal joints of the hands (**a**) and feet (**b**), lack of periarticular osteoporosis (**a**), osteolysis (**b**), pencil-in-cup deformities (**c**) and paramarginal syndesmophyte formation in the axial spine (**d**).