

## Rheumatology: 5. Diagnosis and management of inflammatory polyarthritis

Alice Klinkhoff

### The case

Three months after an uncomplicated pregnancy and delivery Mrs. D consults her physician about new pain and swelling in her wrists and several proximal interphalangeal joints; 1 wrist is swollen and tender and there is tenderness in the ring metacarpalphalangeal (MCP) and 2 proximal interphalangeal (PIP) joints of each hand. She has morning stiffness which lasts 30 minutes There has been no recent infection or triggering event, and she has no history of a similar problem. Mrs. D has been trying to ignore these symptoms for the last 6 weeks, but she is having difficulty lifting and changing her baby.

It is important to distinguish rheumatoid arthritis from other forms of polyarthritis, including psoriatic arthritis, systemic lupus erythematosus (SLE) and other connective tissue diseases, the relatively benign maturity-onset seronegative synovitis (MOSS) syndrome, crystal-induced synovitis and inflammatory osteoarthritis. The standard of good practice in rheumatoid arthritis includes early and continuous use of disease-modifying antirheumatic drugs (DMARDs), singly or in combination, to prevent damage, deformity and disability. Although treatment may be costly and inconvenient, the costs of medication and monitoring are minor compared with the costs to the patient and society in terms of long-term disability.

### Acute polyarthritis

Patients with inflammatory polyarthritis (i.e., inflammation in more than 4 joints) are a diagnostic and management challenge. When symptoms are of recent onset, the range of possible diagnoses is great. Certain viruses including those that cause rubella, and mumps, human parvovirus B19 and some enteroviruses can cause acute polyarthritis; however, these viral arthritides normally subside within 6 weeks without sequelae. The prodrome of acute hepatitis B infection and infection with the Lyme disease agent, *Borrelia burgdorferi*, may include polyarthritis.<sup>1</sup> The former is recognized by the ensuing hepatitis, while the latter requires a high index of suspicion (i.e., a history of tick bite or a typical rash on a patient from an endemic area) and often involves only 1 or 2 large joints.

### Persistent and chronic polyarthritis

In patients who are under 50 years of age with joint pain and swelling lasting longer than 6 weeks the diagnoses to be considered include rheumatoid arthritis, psoriatic arthritis, other seronegative spondyloarthropathies and SLE. In patients over 50 years of age, MOSS syndrome and crystal-induced synovitis should also be considered. Osteoarthritis may also cause considerable inflammation in the affected joints. For most of these conditions specific therapies aimed at controlling inflammation, preserving range of motion in the joint and preventing joint damage are successful in decreasing morbidity and improving quality of life.

The patient with symptoms in many joints requires a detailed history and physical examination. If there is morning stiffness lasting more than 30 minutes or stiff-

*Review*

*Synthèse*

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ness after sitting, the joint complaints are likely to be caused by inflammation; a convincing history of joint swelling confirms the presence of inflammation (Table 1). The physician should record the onset and progression of symptoms and the distribution of joints affected. A history of psoriasis in the patient or a family member is an important clue to the possibility of psoriatic arthritis. The physician should also inquire about a history of iritis or inflammatory bowel disease, both of which are associated with seronegative spondyloarthropathies. A recent episode of infectious diarrhea or genitourinary infection are clues to possible Reiter's syndrome. Does the patient have symptoms suggestive of SLE (e.g., photosensitive or malar rash, alopecia or pleurisy)? Is there a past history of acute episodes of arthritis or gout? Are the joints tender or swollen? Is movement limited? The choice of laboratory tests that may help depend on the differential diagnosis.<sup>2</sup>

### Rheumatoid arthritis

As in the case of Mrs. D onset of polyarthritis in the early postpartum period is more common with rheumatoid

arthritis than with other forms of inflammatory arthritis. The typical patient with rheumatoid arthritis has inflammation in the wrist and MCP or metatarsophalangeal (MTP) joints, or both, that persists beyond 6 weeks (Table 2).<sup>3</sup> Among patients under 50 years of age more women are affected, but after age 50 incidence is equal for men and women. Morning stiffness and inactivity stiffness are almost always present, and swelling of affected joints is clear with careful examination (Fig. 1). The condition may be episodic at the onset, but within weeks to months the symptoms become persistent and more disabling. A positive rheumatoid factor test supports the diagnosis;<sup>4</sup> however, as many as 30% of those affected have negative test results. Specificity increases with consistent results on more than 1 test and with high titre.<sup>4</sup> The presence of antinuclear antibodies at a low titre may be associated with more severe seropositive rheumatoid arthritis. If the patient has had active polyarthritis for more than 1 year, joint erosion may be seen on radiographs of the hand or foot.

Useful laboratory tests for patients with recent onset inflammatory polyarthritis may include complete blood count, erythrocyte sedimentation rate, rheumatoid factor

**Table 1: Distinguishing clinical and laboratory features of chronic inflammatory polyarthritis**

Diagnosis	Symptoms	Signs	Laboratory tests	Key features
Rheumatoid arthritis	Pain, swelling and stiffness for > 6 weeks	Swelling and tenderness, especially in wrists, MCP and MTP joints	Rheumatoid factor positive in 70% of patients	Symmetry
Psoriatic arthritis and spondyloarthropathies	Pain, tenderness and swelling in joints and tendon and ligament attachment sites	Tenderness at sites of tendon attachments, dactylitis (swelling of entire digit caused by tenosynovitis)	Blood tests are not helpful	May have sacroiliitis, spondylitis, plantar fasciitis, DIP arthritis, nail pitting or onycholysis History of psoriasis in patient or family
Systemic lupus erythematosus	Symptoms of multisystem involvement (e.g., rash, pleurisy) Photosensitivity	Often more joint tenderness than swelling	ANA test always positive Other antibodies, including ENA and DNA antibodies, commonly present Cytopenias may occur	Nonerosive
Maturity-onset seronegative synovitis	Pain swelling and stiffness in joints (often develops suddenly in patients over 60 years of age)	Wrists and shoulders are commonly affected	Rheumatoid factor and ANA tests are negative Marked increase in ESR	Behaves like polymyalgia rheumatica
Polyarticular gout	History of episodic monoarthritis for years before polyarticular disease	Any joint can be affected Tophi are usually present	Marked increase in serum uric acid; urate crystals in joint fluid	Patients are often on diuretics, drink alcohol to excess and have family history of the disease Prevalence higher in men
Osteoarthritis with inflammation	Pain and tenderness in DIP, PIP and CMC, as well as weight-bearing joints	Affected joints may be tender and swollen Heberden and Bouchard's nodes palpable	Laboratory tests not helpful Radiographs show osteoarthritis	Often symmetric Onset common in perimenopausal women

Note: MCP = metacarpophalangeal, MTP = metatarsophalangeal, DIP = distal interphalangeal, ANA = antinuclear antibodies, ENA = extractable nuclear antigens, ESR = erythrocyte sedimentation rate, PIP = proximal interphalangeal, CMC = carpometacarpal.

test, aspartate aminotransferase (AST) test, creatinine level and urinalysis.<sup>5</sup> Erythrocyte sedimentation rate is an inexpensive measure of disease activity in those with rheumatoid arthritis; however, the test is not diagnostic and rates are not elevated in all patients affected. A positive test result for rheumatoid factor is helpful but not essential to confirm the clinical impression of rheumatoid arthritis in the setting of symmetrical inflammatory polyarthritis. If the arthritis has lasted more than a year, the physician should consider taking radiographs of the hands and feet.

The importance of diagnosing rheumatoid arthritis cannot be overemphasized — early intervention with DMARDs has been shown to improve long-term outcomes,<sup>6,7</sup> and once joint damage has occurred erosion and joint instability are irreversible. If rheumatoid arthritis is mild and in its early stages many rheumatologists favour using hydroxychloroquine because it is safe and convenient. If control is suboptimal after 6 months, additional DMARDs are often prescribed.<sup>8</sup> A recent study<sup>9</sup> reported some efficacy with minocycline for patients with early seropositive rheumatoid arthritis. However, long-term efficacy data for patients treated with minocycline are not available, and radiographs show that damage progresses at the same rate as in placebo-treated patients.<sup>9</sup>

If a patient has moderate or severe rheumatoid arthritis, especially if the rheumatoid factor is positive, injectable gold or methotrexate may be the preferred DMARD. Gold treatment has the important advantage of offering the potential for disease remission,<sup>10</sup> but methotrexate is more convenient and better tolerated.<sup>10</sup> Sulfasalazine is safe as a second-line agent and can be used in combination with methotrexate and other DMARDs. Many new DMARDs are becoming available.

There is frequently a delay between the presentation of polyarthritis and the confirmed diagnosis, and there is always a delay before a prescribed DMARD has the expected



**Fig. 1: Hands of a woman with early rheumatoid arthritis. Note the swelling of the metacarpophalangeal joints and wrists.**

benefit. When optimal DMARD therapy or a combination of DMARDs does not control synovitis, low-dose prednisone can provide symptom relief, acceptable low toxicity and joint protection. Bisphosphonate, either cyclical tidronate or daily alendronate, reduces the risk of steroid-induced osteoporosis and should be prescribed prophylactically when the daily dose of prednisone is 7.5 mg or more (see upcoming article in this series on osteoporosis by John P. Wade).

Patients with active rheumatoid arthritis should be assessed by a rheumatologist on a regular basis, and clinical and laboratory evaluations should be repeated to measure the efficacy and toxicity of treatment. The aim of therapy is to minimize pain, stiffness and joint swelling; retard joint damage; and reduce future disability.

### **Psoriatic arthritis and seronegative spondyloarthropathies**

Psoriatic arthritis is almost as common as rheumatoid arthritis. This condition should be suspected when the patient or the patient's family has a history of psoriasis, when distal interphalangeal joints are affected or when there is a history of unexplained chronic or recurring back pain with prolonged inactivity. Another feature of psoriatic arthritis and the spondyloarthropathies is bursitis or enthesitis (i.e., inflammation of the muscular or tendinous attachment to bone). Typical examples of bursitis, tendinitis and enthesitis include trochanteric bursitis, Achilles tendinitis and lateral epicondylitis. Heel pain or plantar fasciitis are commonly associated with psoriatic arthritis, and nails may show pitting and onycholysis (Fig. 2). Careful examination may reveal psoriatic plaques on the scalp or ears that the patient has not noticed. Interestingly, the severity of psoriasis has little correlation with the presence or severity of psoriatic arthritis.

Psoriatic arthritis may be indistinguishable from rheumatoid arthritis in onset and progression,<sup>11</sup> and there

**Table 2: Diagnostic criteria for rheumatoid arthritis\***

Criterion	Definition
Morning stiffness	Stiffness in joints lasting at least 1 hour
Arthritis in 3 or more joints	Pain and swelling in at least 3 joints
Arthritis in hand joints	Swelling in at least 1 of the following areas: wrist, MCP or PIP joint
Symmetric arthritis	Involvement of the same joint area on both sides of the body
Rheumatoid nodules	Subcutaneous nodules over bony prominences or extensor surfaces or around joints
Serum rheumatoid factor	Positive rheumatoid factor
Radiologic changes	Periarticular osteopenia or erosions in joints visible on radiographs of hands or feet

Note: MCP = metacarpophalangeal, PIP = proximal interphalangeal.

\*Criteria 1 through 4 must be present for at least 6 weeks. Confirmation of 4 or more of these 7 criteria by a physician is considered diagnostic of rheumatoid arthritis.

Source: American Rheumatism Association 1997 revised criteria.<sup>3</sup>



**Fig. 2:** Foot of a patient with psoriatic arthritis. Note the interphalangeal joint swelling and onycholysis (i.e., separation of the nail plate from the nail bed).

are no diagnostic laboratory tests for psoriatic arthritis. However, it more typically is asymmetrical oligoarticular or monoarticular. Most cases of psoriatic arthritis are controlled with NSAIDs; for those whose arthritis is not satisfactorily controlled with NSAIDs and for those who are experiencing joint damage the DMARDs used for the treatment of rheumatoid arthritis are effective.

Seronegative spondyloarthropathies such as reactive arthritis and Reiter's syndrome most commonly present as asymmetric oligoarthritis affecting the lower extremity joints. Reactive arthritis is a sterile inflammatory arthritis that occurs as a consequence of infection at a remote site. It should be suspected when there is a recent history of diarrhea, chlamydial infection, unexplained genitourinary symptoms, prostatitis, cystitis or conjunctivitis. Reiter's syndrome is a reactive arthritis that occurs within 3 weeks of a chlamydia infection of the genitourinary tract or after an intestinal infection, typically caused by *Salmonella* spp., *Shigella* spp., *Campylobacter* spp. or *Yersinia* spp. Extra-articular symptoms associated with the full-blown syndrome include conjunctivitis, circinate balanitis and hyperkeratotic skin lesions on the soles called keratoderma blennorrhagica.

The triggering infection should be treated as appropriate; screening of contacts at risk must be included in the management of patients with genitourinary reactive arthritis and selected patients with enteropathic Reiter's syndrome. Management of the arthritis must be individualized and may include NSAIDs, oral or intra-articular steroids and, in resistant cases, DMARDs.

### **Systemic lupus erythematosus**

Patients with SLE (female:male ratio is about 10:1) frequently present with polyarthritis — typically a peripheral polyarthritis with symmetric involvement of both small and large joints. The physician should question the patient in detail about symptoms that reflect multisystem involvement, particularly photosensitivity, unexplained rashes,



**Fig. 3:** Hands of a woman with inflammatory osteoarthritis. Note Heberden's nodes with associated swelling.

malar rash, pleuritic chest pain, history of seizures, oral ulcers, hair loss, Raynaud's phenomenon, fevers and sweats. Deformities including subluxation at the MCP joints, ulnar deviation, "swan neck" and boutonniere deformities (Jaccoud's arthropathy) may develop in about approximately 15% of patients with SLE, but these are not associated with joint erosion.<sup>12</sup>

If, on the basis of the history and the physical examination, SLE is suspected the physician should order an antinuclear antibody test;<sup>5</sup> this is a useful screening test because a negative test result will virtually exclude SLE. If the test is positive and there is clinical suspicion of multisystem disease, the physician should consider further serologic tests and refer the patient to a rheumatologist. For SLE patients without serious internal organ involvement hydroxychloroquine is the drug of choice because it has been shown to improve disease control, prevent flares and improve long-term outcomes.<sup>13</sup> Arthritis and pleurisy respond to NSAIDs. Steroid medications may also be required in low and moderate doses either intermittently or continuously. Immunosuppressant drugs are required for those with serious internal organ involvement (e.g., cerebritis or glomerulonephritis).

### **Other connective tissue diseases**

Diseases such as primary Sjögren's syndrome, polymyositis-dermatomyositis, limited and diffuse scleroderma and mixed connective tissue disease may also manifest as polyarthritis. Primary Sjögren's syndrome may be extremely difficult to differentiate from rheumatoid arthritis when the main feature is polyarthritis. Prominent muscle weakness is a clue to myositis, and patients with scleroderma almost always have sclerodactyly and Raynaud's phenomenon. Mixed connective tissue disease may present with features of rheumatoid arthritis in conjunction with those of other connective tissue diseases.

### **Maturity-onset seronegative synovitis syndrome**

This condition, is distinguished from rheumatoid arthritis on the basis of a negative rheumatoid factor, a markedly elevated erythrocyte sedimentation rate, usual age of onset over 60 years and marked improvement in response to low doses of steroids. Although it is uncommon it is not rare. Onset is often sudden, and there is typically swelling of the wrists and pain, stiffness and restriction of the shoulder joints. The clinical course of MOSS syndrome closely resembles polymyalgia rheumatica in its sudden onset and response to prednisone. Polymyalgia rheumatica typically presents with shoulder and pelvic girdle involvement and an absence of clinically detectable synovitis; MOSS syndrome presents with peripheral synovitis that may be indistinguishable from seronegative rheumatoid arthritis except in its response to prednisone and its course over time. The synovitis disappears with 10–15 mg/day of prednisone, and the condition is nonprogressive and nonerosive. Once the disease is under control the dose of prednisone can be lowered every 1–3 months, aiming for the lowest dose that will control symptoms. Strategies to prevent steroid-induced osteoporosis, specifically bisphosphonates, are required. If the prednisone dose cannot be lowered or if pain and swelling persist in spite of low-dose prednisone, the physician should reassess the patient and consider alternative diagnoses, such as rheumatoid arthritis, psoriatic arthritis, temporal arteritis and other vasculitides. Because this condition is difficult to differentiate from seronegative rheumatoid arthritis and because of the morbidity associated with long-term steroid use in the elderly, it is best to refer these patients to a rheumatologist.

### **Crystal-induced synovitis**

Although uncommon, gout or pseudogout can result in inflammatory polyarthritis. The typical patient with polyarticular gout has had acute attacks of monoarthritis and typical attacks of gout for many years. Any joint may be affected and, in severe cases, the patient may be febrile and have leukocytosis; tophi are commonly found on careful ex-

amination. Patients are usually over 50 years of age or have identifiable risk factors for gout such as diuretic use, renal disease or alcohol abuse. Although serum uric acid level is often high this is not always the case. Synovial fluid aspiration will demonstrate the typical urate crystals.

Calcium pyrophosphate dihydrate deposition disease (i.e., pseudogout) may also cause polyarthritis. Patients are usually over 60 years of age, and this condition commonly coexists with osteoarthritis. The presentation may resemble rheumatoid arthritis — typical distribution of joint inflammation includes the wrists, knees, shoulders, hips and finger joints. Radiographs of affected joints commonly show chondrocalcinosis, but the diagnosis is confirmed when calcium pyrophosphate dihydrate crystals are found in the synovial fluid of inflamed joints.

### **Erosive osteoarthritis and inflammatory osteoarthritis**

Osteoarthritis affecting DIP, PIP and CMC joints may be associated with symptoms and signs of inflammation (Fig. 3). Onset is common in perimenopausal women, and there is often a family history of Heberden's osteoarthritis. Patients complain of joint tenderness and episodes of swelling usually in 1 or several finger joints at a time. Examination discloses Heberden's and Bouchard's nodes in finger and sometimes toe joints; MCP and MTP joints are not affected. Radiographs of affected joints show

narrowing, osteophytes, sclerosis and, in the advanced stages, PIP or DIP joint erosions. Because of the prominent involvement of DIP joints, it may be difficult to distinguish inflammatory osteoarthritis from psoriatic arthritis, which may also develop in older patients. It is important to remember that rheumatoid arthritis can occur in patients who also have osteoarthritis.

### **Treatment for Mrs. D**

Mrs. D's laboratory tests revealed a positive rheumatoid factor in a titre of 1:320 and an erythrocyte sedimentation rate of 40 mm/h (normal range: 0–20 mm/h). Her complete blood count was normal. She experienced slight relief when taking 500 mg of naproxen twice daily. A rheumatol-

#### **Key points**

- Patients with inflammatory polyarthritis are a challenge to diagnose and manage.
- Diagnosis and management are usually based on a detailed history and a focused physical examination of the patient, but it is essential to inquire about family history of diseases (e.g., psoriasis, colitis, arthritis conditions and gout) as well.
- Key symptoms of inflammation are morning stiffness that lasts longer than 30 minutes, worsening of symptoms with rest and improvement with mild exercise.
- In patients with persistent inflammatory polyarthritis, diagnostic considerations include rheumatoid arthritis, psoriatic arthritis and other seronegative spondyloarthropathies, systemic lupus erythematosus, maturity-onset seronegative synovitis, crystal-induced synovitis and osteoarthritis.
- Laboratory tests, such as those for rheumatoid factor and antinuclear antibodies, have value in increasing or decreasing the probability of a specific diagnosis.
- With early diagnosis specific therapies aimed at controlling inflammation, preserving range of motion and preventing joint damage can decrease morbidity and improve a patient's quality of life.

ogist agreed to see Mrs. D two weeks later to confirm the diagnosis of rheumatoid arthritis and recommend specific therapy. Mrs. D was initially reluctant to start DMARD therapy, but after attending rheumatoid arthritis education classes and meeting other young women with rheumatoid arthritis, she agreed to start injectable gold therapy. The rheumatologist explained the expected improvement from gold treatment, the common side effects and the variability in patient responses. Patient and physician agreed that if this treatment did not result in a marked improvement in 6 months, another DMARD or a combination of DMARDs would be selected.

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### Articles to date in the rheumatology series

- Esdaile JM. Rheumatology: introduction to the series. *CMAJ* 2000;162(7):1007.
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