The diagnosis of painful joints

Musculoskeletal disorders are frequently encountered by GPs. They range from simple self-limiting local problems to life-threatening multi-organ diseases. The diagnosis and appropriate treatment of these conditions can be facilitated by adopting a systematic approach.

HAESUNG BAK
MB BS

SIRI KANNANGARA
FRACP, FACSP

Dr Bak is a Rheumatology Registrar, Institute of Rheumatology and Orthopaedics, Royal Prince Alfred Hospital, Camperdown, NSW; Dr Kannangara is a Rheumatologist, Department of Rheumatology, Concord Hospital, Concord, NSW.

Many musculoskeletal conditions are described in syndromic terms because they lack criteria for diagnosis. Formal classifications exist for many arthritic conditions, the most widely adopted being the American College of Rheumatology criteria. While their use in clinical practice is appealing and sometimes useful, it should be borne in mind that these are primarily designed for research and epidemiological purposes (Table 1).[1]

In this article, we describe some of the more common clinical presentations of inflammatory arthropathies and present an approach to joint problems that takes into account key clinical features.

Clinical features and history

It is axiomatic that careful history taking is vital in reaching an accurate diagnosis. Only then can a picture of the disease be established that permits a suitable diagnosis to be recognised. The first step in this process is to confirm that the problem arises from a particular joint or joints. The description given by patients should be analysed carefully. For example, when patients complain of 'hip' pain, it is useful to have them indicate exactly where they mean. They may not point to the groin, the typical site of primary hip pathology, but may experience the pain in the lateral thigh, suggesting the problem is not in the hip joint proper, but in the trochanteric bursa, gluteus medius or lower back.

Pain from periarticular problems, such as bursae, ligament attachments and muscles, or pain referred from distant visceral or musculoskeletal structures needs to be excluded.

Where an articular pathology is suspected, the involved joints need to be examined carefully for evidence of inflammation. If arthritis is present, other joint groups need to be examined carefully as well. Finally, other organ systems are examined to look for systemic involvement.

Important aspects of history taking include: analysis of joint symptoms; enquiry about systemic features such as fever and weight loss, family and ethnic history, travel history, comorbidities, alcohol consumption and drug history including

IN SUMMARY

- **Painful joints are frequently encountered clinical problems that require a careful, systematic approach.**
- **Key features of any joint symptoms are the nature, onset, duration, course and distribution.**
- **It is important to interpret clinical, radiographic and laboratory data together because pathognomonic features leading to a diagnosis seldom exist in these conditions.**
- **Sometimes prompt diagnosis is required, as in cases of septic arthritis, yet at other times careful clinical follow up is more appropriate.**
- **The primary goal in treating patients with painful joint conditions is preservation of joint integrity.**

illicit drug use; and an appropriate system review. Key features of any joint symptoms are:

- the nature (inflammatory or mechanical)
- the onset (acute or subacute)
- the duration and course (transient, chronic or relapsing)
- the distribution (monoarticular, oligoarticular or polyarticular; symmetrical or asymmetrical; predominantly involving small joints or large joints).

Once a particular pattern is established, a list of differential diagnoses consistent with clinical features is checked and a presumptive diagnosis is made. However, it is often impossible to make a definitive or even reasonable provisional diagnosis early in the course of many rheumatic diseases. It may be preferable to leave the 'labelling' open at the initial stage, as a clearer clinical picture often emerges with careful clinical follow up.

Investigations

Investigations need to be targeted. Erroneous conclusions may be reached if test results are not interpreted in the appropriate clinical context. For example, an otherwise well young woman with heel pain and a positive antinuclear antibody at low titre (1:160) is most unlikely to have systemic lupus erythematosus, and should not be labelled as such on the basis of a single laboratory test. Most tests are complementary to good history

Table 1. Criteria for the classification of rheumatoid arthritis1*

Criterion	Definition
1. Morning stiffness	Morning stiffness in and around the joints, lasting at least one hour before maximal improvement
2. Arthritis of three or more joint areas	At least three joint areas simultaneously have had soft tissue swelling or fluid (not bony overgrowth alone) observed by a physician. The 14 possible areas are right or left proximal interphalangeal, metacarpophalangeal, wrist, elbow, knee, ankle and metatarsophalangeal joints
3. Arthritis of hand joints	At least one area swollen (as defined above) in a wrist, metacarpophalangeal or proximal interphalangeal joint
4. Symmetrical arthritis	Simultaneous involvement of the same joint area (as defined in criterion 2) on both sides of the body (bilateral involvement of proximal interphalangeal, metacarpophalangeal or metatarsophalangeal joints is acceptable without absolute symmetry)
5. Rheumatoid nodules	Subcutaneous nodules over bony prominences, extensor surfaces or in juxta-articular regions, observed by a physician
6. Serum rheumatoid factor	Demonstration of abnormal amounts of serum rheumatoid factor by any method for which the result has been positive in <5% of control subjects
7. Radiographic changes	Radiographic changes typical of rheumatoid arthritis on posteroanterior hand and wrist x-rays, which must include erosions or unequivocal bony decalcification localised in or most markedly adjacent to the involved joints (osteoarthritic changes alone do not qualify)

*For classification purposes, a patient shall be said to have rheumatoid arthritis if he or she has satisfied at least four of these seven criteria. Criteria 1 through 4 must have been present for at least six weeks. Patients with two clinical diagnoses are not excluded. Designation as classic, definite or probable rheumatoid arthritis should not be made.

Table 2. Common tests for investigating painful joints

Blood tests

- Full blood count
- Serum biochemistry
- Acute phase reactants (erythrocyte sedimentation rate, C-reactive protein)
- Iron studies
- Liver function tests
- Serum uric acid
- Autoantibodies (rheumatoid factor, antinuclear antibody, extractable nuclear antigens, antineutrophil-cytoplasm antibodies [ANCA] if vasculitis is suspected)
- HLA haplotyping
- Serum viral serology

Joint fluid examination

- Microscopic examination for cells, organisms, crystals
- Culture

Imaging

- Plain x-rays of the painful joints
- Bone scan
- Ultrasound
- Magnetic resonance imaging (rarely)

Figures 1a (left) and b (above). Septic arthritis.

Figure 2. Gonococcal dermatitis.

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taking and physical examination rather than replacing them. Common tests used in investigating painful joints are listed in Table 2, and flowcharts for investigating symptoms are shown on pages 43 and 44.

Acute monoarthritis

Acute pain and swelling of a joint may constitute a medical emergency, and requires prompt and accurate assessment. An infected joint can be irreversibly damaged in a matter of days, with subsequent prolonged morbidity and even mortality if inadequately treated. The conditions to be considered in the differential diagnosis of acute monoarthritis are listed in Table 3.[2] We will now discuss two conditions commonly encountered in clinical practice.

Septic arthritis

Nongonococcal septic arthritides are the most serious conditions to be considered in acute monoarthritis (Figure 1). Approximately 80 to 90% of cases present as monoarthritis. The most common organism responsible for nongonococcal septic arthritis, accounting for 60% of cases, is *Staphylococcus aureus*. Polyarticular cases may occur in patients with predisposing conditions such as rheumatoid arthritis. Systemic features of infections may be masked in elderly patients or patients receiving immunosuppressive therapies. Larger joints such as the knee or hip are the most commonly involved. Intravenous drug use needs to be excluded when atypical joints – for example, the sternoclavicular joint – are involved. Special attention needs to be paid to patients with infection in a prosthetic joint, which can present as an early or late complication of joint replacement. The clinical features can be subtle in those presenting with late infections. Morbidity and mortality rates are high in prosthetic joint infections.

In contrast, gonococcal arthritis caused by disseminated gonococcal infection is associated with the classic triad of dermatitis (Figure 2), tenosynovitis and migratory polyarthritis. Only about 0.5 to 3% of patients with mucosal gonococcal infection develop disseminated infection.

Sometimes septic bursitis, commonly at the olecranon bursa at the elbow and the prepatellar bursa at the knee, can mimic septic arthritis, but can be distinguished by careful clinical examination. Generally, joint function is intact in these patients. With appropriate treatment, the prognosis is excellent.

The single most important test when septic arthritis is suspected is examination of the joint aspirate. Microscopic examination reveals differential cell counts, crystals and sometimes organisms on Gram stain. However, 50% of synovial fluid samples will have a negative Gram stain, and culture is mandatory. Culture allows identification of the organism and determination of antimicrobial sensitivities. The treatment of septic arthritis requires prolonged parenteral antibiotics, often combined with surgical drainage and lavage. Premature antibiotic therapy without obtaining joint aspirate can jeopardise proper care of these patients.

Crystal-induced arthropathies

Crystal-induced arthropathies are important causes of acute monoarthritis.[3,4] They can also present as chronic polyarticular arthropathies mimicking other chronic arthritides such as rheumatoid arthritis. The accurate diagnosis of the different crystal arthritides is vital because their management differs greatly from that of other inflammatory conditions.

Table 3. Conditions to consider in differential diagnosis of acute monoarthritis[2]

Infectious arthritis
Bacteria, mycobacteria, fungi, viruses
Crystal-induced arthritis
Monosodium urate crystals, calcium pyrophosphate dihydrate crystals, apatite crystals, calcium oxalate crystals, liquid lipid microspherules
Trauma
Fracture, internal derangement, haemarthrosis
Osteoarthritis
Foreign body synovitis
Tumour
Metastasis, osteoid osteoma, pigmented villonodular synovitis
Systemic disease presenting with monoarticular involvement

Table 4. Causes of sustained hyperuricaemia

Increased urate production

Genetic causes

- Enzyme mutations (e.g. deficiency of hypoxanthine-guanine phosphoribosyltransferase)

Acquired causes

- Myeloproliferative disorders
- High purine intake
- Obesity and hypertriglyceridaemia
- Alcohol consumption
- Fructose consumption
- Exercise

Reduced urate excretion

Genetic causes

- Reduced clearance or fractional excretion of urate

Acquired causes

- Intrinsic renal disease
- Drugs (e.g. thiazide diuretics and low-dose salicylate)
- Metabolites (lactate, ketones, angiotensin and vasopressin)
- Renal cause (plasma volume contraction, hypertension, reduced urine flow [<1 mL/min] or obesity)

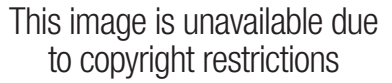


Figure 3 (left). Acute gout.
Figure 4 (above). Chondrocalcinosis.

Monosodium urate, calcium pyrophosphate dihydrate and basic calcium phosphate (hydroxyapatite) are the crystals usually implicated.

Gout has been recognised since antiquity, and typical cases are easy to diagnose on clinical grounds alone (Figure 3). However, both acute and chronic cases of gout can mimic other arthritides and it is important to exclude other diagnostic possibilities. For example, an acute gout attack can easily be mistaken for septic arthritis with a florid presentation of a hot, red and exquisitely painful joint.

On the other hand, monosodium urate crystals may be detected in septic joints, confusing the clinical picture. A high serum urate level is the single most important risk factor. However, people with hyperuricaemia can remain completely asymptomatic, never experiencing a gouty attack. Furthermore, the serum urate level can be in the normal range in a patient during an acute attack. The important secondary causes of gout are listed in Table 4.

Acute gouty attacks tend to occur when there is a change in serum urate levels, either up or down. This often occurs when therapy to manage hyperuricaemia is initiated or discontinued. Urate lowering agents such as allopurinol or probenecid (Pro-cid) are used to prevent frequent gouty attacks in the long term but have no role in acute episodes. Therapy with these agents should be initiated only in the absence of acute inflammation, and then may need to be under anti-inflammatory cover with drugs such as NSAIDs or colchicine (Colgout).

Calcium pyrophosphate dihydrate crystal deposition disease or 'pseudogout' becomes more frequent with increasing age, and affects women more than men. Chondrocalcinosis is the radiographic manifestation of this disease and it can be completely symptom free (Figure 4). Self-limiting acute attacks can involve most large joints, but the knee is by far the most common site. Concurrent attacks affecting more than one joint are unusual.

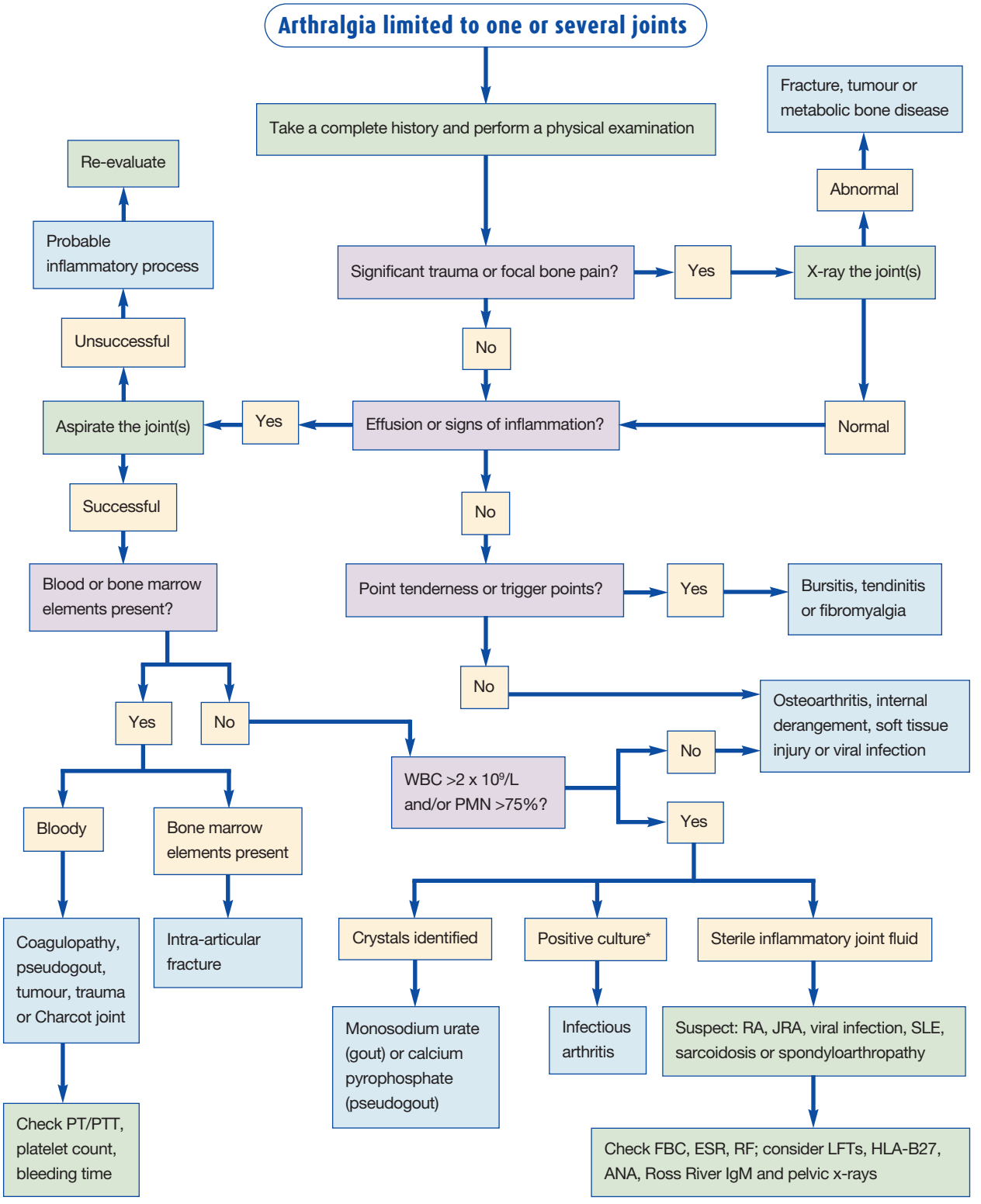
Chronic pseudogout primarily affecting large and medium-sized joints commonly affects elderly patients with osteoarthritis, but may present a picture clinically indistinguishable from rheumatoid arthritis.

Aspirated joint fluid in pseudogout is often turbid and bloodstained. Calcium pyrophosphate dihydrate crystals are less numerous and more difficult to identify than monosodium urate crystals, and negative reporting often indicates failed identification of crystals rather than absent crystals.[5] A high index of clinical suspicion should be maintained when a single aspirate has failed to identify calcium pyrophosphate dihydrate crystals in a suggestive clinical setting. Occasionally, pseudogout may be a manifestation of underlying metabolic disease such as hyperparathyroiditis or haemochromatosis. Simple laboratory investigations such as estimation of serum calcium and ferritin levels allow these conditions to be ruled out.

Polyarthritis

Many rheumatic conditions can cause polyarticular diseases. Some of these cause acute transient episodes, while others run a more chronic course of more than six weeks' duration. Some conditions cause

Investigating monoarticular or oligoarticular symptoms[1]



WBC = white blood cells; PMN = polymorphonuclear neutrophils; PT = prothrombin time; PTT = partial thromboplastin time; RA = rheumatoid arthritis; JRA = juvenile rheumatoid arthritis; SLE = systemic lupus erythematosus; FBC = full blood count; ESR = erythrocyte sedimentation rate; RF = rheumatoid factor; LFTs = liver function tests; ANA = antinuclear antibodies.

*Synovial fluid culture as well as cervical, urethral, pharyngeal and/or rectal evaluations for gonococcus and chlamydia when suspected.

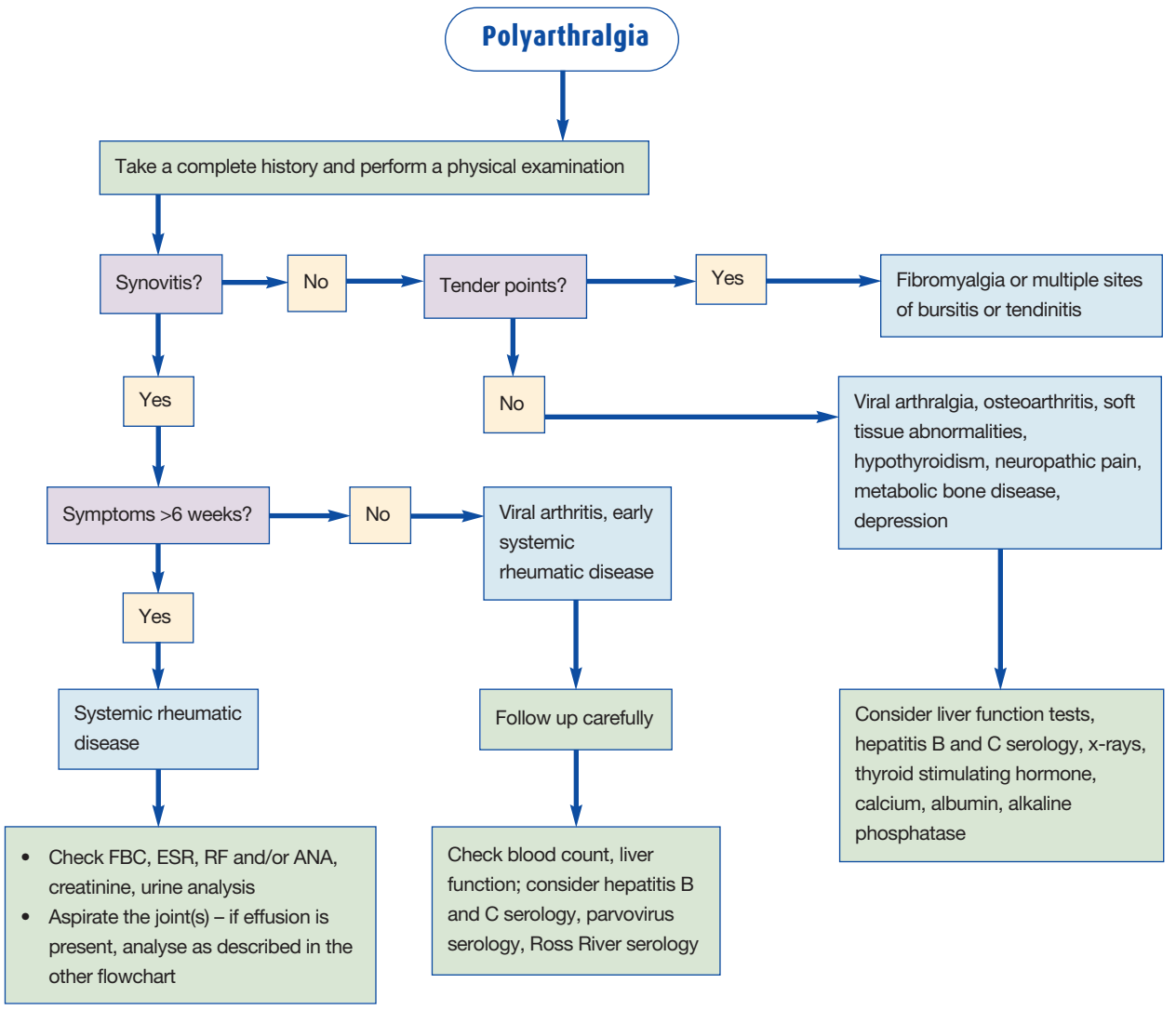
migratory polyarthritis – gonococcal arthritis, viral diseases, acute rheumatic fever, sarcoidosis and the immune complex diseases bacterial endocarditis and systemic lupus erythematosus.

Many patients fear conditions such as rheumatoid arthritis. While it is important to establish a diagnosis early to institute an appropriate management plan, this diagnostic label should be used with care during the acute stage, taking into consideration the psychological impact that will result from the diagnosis. Some of the common causes of polyarthritis are considered here.

Rheumatoid arthritis

Rheumatoid arthritis is a chronic deforming polyarthritis affecting about 1% of the population and thus not infrequently encountered in the primary care setting. The role of primary care doctors in managing patients with rheumatoid arthritis or other chronic inflammatory arthritis is twofold. First, the condition needs to be recognised early. This is especially important because irreversible joint damage tends to occur early and patients may require aggressive treatment, depending on the severity of their

Investigating polyarticular symptoms[1]



FBC = full blood count; ESR = erythrocyte sedimentation rate; RF = rheumatoid factor; ANA = antinuclear antibodies.

disease. Secondly, ongoing monitoring is very important for these patients. Most medications used for rheumatoid arthritis have potentially serious side effects, and regular review of these patients is vital.

There is no simple diagnostic test that can confirm or exclude rheumatoid arthritis. Easily recognisable clinical features, such as various deformities and radiographic evidence of joint erosions, are irreversible late changes. Indeed, the main aim of managing these patients is to prevent these changes from occurring through early diagnosis and intervention.

Rheumatoid factor has prognostic significance, but this may not be helpful in establishing a diagnosis, especially in early rheumatoid arthritis. Many patients (10 to 40%) with rheumatoid arthritis have persistently tested negative for rheumatoid factor and only one-third of patients who become seropositive have detectable rheumatoid factor during the first three months of disease. Moreover, rheumatoid factor is found in 1% of the population without rheumatoid arthritis and is also associated with other diseases such as Sjögren's syndrome, subacute bacterial endocarditis, tuberculosis, pulmonary fibrosis and liver disease. Patients with chronic symmetrical polyarthritis primarily affecting small hand joints and with significant morning stiffness in whom other causes of chronic polyarthritis are reasonably excluded are likely to have rheumatoid arthritis.

Seronegative arthropathies

Seronegative arthropathies are closely related multisystem inflammatory disorders. They include psoriatic arthritis, reactive arthritis or Reiter's syndrome, enteropathic arthropathy, ankylosing spondylitis and juvenile spondyloarthropathy. They share the common features of a close relationship to the HLA-B27 gene, involvement of axial and peripheral joints, involvement of periarticular structures characterised by enthesopathy, and extra-articular involvement.

Peripheral joint involvement in these disorders is usually oligoarthritic, predominantly involving lower limbs. Symmetrical small joint arthritis, resembling rheumatoid arthritis, may occur in psoriatic arthritis. Characteristically, distal interphalangeal joints show inflammatory swelling in psoriatic arthritis. Dactylitis or 'sausage digits' is another characteristic feature when fingers or toes are involved in these conditions (Figure 5). A minority of patients develop rapidly progressing deforming arthritis, as in cases of arthritis mutilans. No treatment has been shown to be effective in retarding progression of axial diseases.

Viral infections

Acute viral illness can often produce prominent arthralgic or arthritic syndromes associated with other systemic features of the infection. The viruses involved include parvovirus B19, arboviruses, rubella, hepatitis B and C, and human immunodeficiency virus (HIV).

Parvovirus B19 infection is common and widespread, and up to 60% of adults have serological evidence of past exposure. Most of those exposed are asymptomatic or experience nonspecific viral illness. In children, parvovirus causes a viral exanthem called fifth disease or erythema infectiosum – with a typical 'slapped cheeks' rash, sore throat, headache, fever, cough, anorexia, vomiting, diarrhoea and arthralgia. In adults, the rash is more subtle, and joint pain and swelling are more prominent, occurring in 75% of patients. The onset is usually acute and the distribution resembles rheumatoid arthritis, affecting smaller joints symmetrically. Henoch–Schoenlein purpura, peripheral neuropathy, aplastic crisis, pancytopenia, hepatitis and miscarriage are more serious but much rarer manifestations. It is usually a self-limiting disease, but some patients experience prolonged symptoms with prominent morning stiffness. Low to moderate titres of rheumatoid factor are present in the early phase of the infection, but rheumatoid nodules and joint erosions are absent.

Figure 5. Dactylitis.

Figure 6. Generalised nodal osteoarthritis.

Ross River virus and Barmah Forest virus are alphaviruses transmitted by mosquitoes that are endemic in many parts of Australia.[6,7] Patients experience severe and incapacitating arthralgia in migratory and asymmetrical patterns. One-third of patients have frank arthritis and some experience chronic joint symptoms for many years. Rash is another prominent symptom. Patients also experience mild flu-like symptoms during the acute phase. Fever is not a prominent feature.

Osteoarthritis

Middle-aged to elderly women can present with generalised osteoarthritis with prominent nodal involvement (Figure 6), and may even present with erosive inflammatory arthropathy. However, the distribution of joints involved and their clinical and radiographic features are quite different from rheumatoid

arthritis. Distal interphalangeal joints and the first carpometacarpal joints are characteristically involved, rather than the involvement of prominent proximal interphalangeal joints and metacarpophalangeal joints seen in rheumatoid arthritis. Superimposed crystal arthropathy in osteoarthritis may further confuse the picture.

Connective tissue diseases

Polyarticular joint disease can be a feature of various systemic inflammatory diseases. Systemic rheumatic diseases causing polyarthritis include systemic lupus erythematosus, systemic vasculitis, systemic sclerosis, polymyositis and dermatomyositis, adult Still's disease, Behçet's syndrome and relapsing polychondritis. Other systemic diseases, such as familial Mediterranean fever, sarcoidosis and malignancy, can also cause polyarticular diseases. Associated clinical and laboratory findings should distinguish these from other polyarticular arthritides.

Conclusion

Painful joints are frequently encountered clinical problems that require a careful, systematic approach to make a correct diagnosis and institute an appropriate management plan. It is important to interpret various clinical, radiographic and laboratory data together because pathognomonic features leading to a diagnosis seldom exist in these conditions. Sometimes prompt diagnosis is required, as in cases of septic arthritis, yet in other settings, careful clinical follow up over time is more appropriate. No matter what the final diagnosis, the primary goal in treating patients with painful joint conditions is preservation of joint integrity by preventing or retarding irreversible joint damage. MT

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