The diagnostic challenge of joint pain—part 2

Polyarthralgia is a common presentation in primary care. Because chronic arthritides may present abruptly, they need to be considered in patients who present with acute polyarticular pain. This pain poses a diagnostic challenge because of extensive differential diagnoses. Many classic rheumatological laboratory tests are non-specific and radiographs can be normal or show only non-specific changes early in the disease process. A thorough history and a complete physical examination are essential for accurate diagnosis.

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Arthritis is joint pain with inflammation, whereas arthralgia is joint pain without inflammation (box 1). Diagnosis and management of arthralgia is a challenge. However, early diagnosis and intervention is important, as seen in patients with inflammatory arthritis, in whom the benefits of early treatment may be significant and long-lasting.[1] Information about disease chronology, patient's demographic, pattern of joint involvement, extra-articular manifestations, and disease course are helpful to elucidate possible causes. Patients with polyarticular pain might need a series of clinic visits to make a specific diagnosis, but a definitive diagnosis may not be possible. Part 2 of this review deals with further investigations into and management of conditions causing joint pain. Part 1, looking at examining the patient and the clinical features of such diseases was published in the June 2009 issue of GM.

Box 1: Definitions

Polyarthralgia: pain in more than four joints

Polyarthritis: joint inflammation affecting five or more joints. A patient with two to four affected joints has oligoarticular disease

Monoarthritis: joint inflammation affecting one joint only. Suspected monoarthritis requires urgent evaluation because of the risk of septic arthritis, gout, or rare bone tumours

Diagnosis

In the absence of definitive rheumatological laboratory tests, the history and physical examination are key to early diagnosis and treatment of conditions causing polyarticular joint pain. Common causes of polyarticular pain should be considered first.

In patients with symptoms in multiple joints, deciding whether the condition is inflammatory or mechanical in nature is important. This is a pragmatic simplification, since mechanical forces, such as weight bearing, may exacerbate most inflammatory arthritides, and osteoarthritis has a variable inflammatory component.[1] Polyarthralgia has a wide range of differential diagnoses (box 2) and diagnosis is often not straightforward. However, history and physical examination should establish a diagnosis in at least 75% of patients (figure).[1]

Laboratory investigations and imaging studies may be indicated to aid diagnosis. However, diagnostic testing to reassure patients is generally unnecessary and test results may be abnormal in the absence of rheumatic disease.[2] Specific testing is guided by the clinical manifestations and should screen organ systems such as the lung, heart, liver, kidney, and bowel, for potential involvement, even without overt signs.[2] Precise diagnosis and effective management require close follow-up as well as consultation with a rheumatologist.

Investigations

Most rheumatological laboratory tests lack the desired specificity and their results should be interpreted with care. Use of tests

with low specificity may increase unnecessary testing and attendant costs, result in inappropriate treatment, and have a negative psychological impact on patients.[3] Antinuclear antibody tests are positive in 5–10% of the general population, a rate that increases with age.[4–6] But, given the high sensitivity of the substrate used for testing, a negative antinuclear antibody test essentially rules out systemic lupus erythematosus.[7] Spondyloarthropathies affect less than 1% of the general population. Indeed, patients who are HLA-B27 positive and do not have a family history of ankylosing spondylitis have only a 2% risk of developing this disorder.[8] Spondyloarthropathies can be overdiagnosed by relying only on a positive HLA-B27 test, because this test is positive in 8% of all white people.[8]

Testing for rheumatoid factor lacks both sensitivity and specificity. The test is positive in 5–10% of the general population and negative in around 20% of patients with rheumatoid arthritis.[9] Therefore, both positive and negative rheumatoid-factor test results must be interpreted cautiously. Rheumatoid factor testing is not useful if a patient lacks other diagnostic criteria for rheumatoid arthritis, especially synovitis.[9] The American Rheumatology Association's revised diagnostic criteria for rheumatoid arthritis uses findings from the history, physical examination, and laboratory tests.[5] These criteria are 91–94% sensitive and 89% specific, and are useful for establishing a diagnosis of rheumatoid arthritis.[5,10,11]

Synovial fluid analysis is done primarily to diagnose infection or a crystal-induced arthritis. A white-blood-cell count of at least 2000 per mm^3 (2×10^9/l) in synovial fluid suggests inflammation, whereas a count higher than 50,000 per mm^3 (50×10^9/l) typically indicates synovial infection[12] (table 1). Fluid with a highly elevated white blood cell count or a predominance of neutrophils should be cultured to exclude infection.

Several radiographic findings are characteristic of specific rheumatic disorders. For instance, sacroiliitis is indicative of ankylosing spondylitis, erosions with periarticular osteopenia are typical of rheumatoid arthritis, and pencil-in-cup deformities are a sign of psoriatic arthritis. However, these radiographic findings take months to develop; early in the disease process, radiographs may be normal or show non-specific changes only. In early rheumatoid arthritis, MRI demonstrates cartilage damage that is not evident on plain-film radiographs.[13] This damage highlights the importance of diagnosing rheumatoid arthritis early on the basis of the history and physical examination so that disease-modifying treatment can be initiated.

Inflammatory arthropathies should be suspected if joint swelling and features of inflammation are present; the most common cause is rheumatoid arthritis. Consider further investigations such as markers of inflammation (erythrocyte sedimentation rate, plasma viscosity, C reactive protein), rheumatoid factor, and radiography of the hands.

Box 3: Differential diagnosis of polyarthralgia

- Osteoarthritis
- Systemic rheumatic disease—polymyalgia rheumatica, rheumatoid arthritis, systemic lupus erythematosus, polymyositis, dermatomyositis
- Spondyloarthropathies—ankylosing spondylitis, psoriatic arthritis, inflammatory bowel disease, reactive arthritis (Reiter's syndrome)
- Endocrine disorders—hyperparathyroidism, hyperthyroidism, hypothyroidism
- Malignancy—metastatic cancer, multiple myeloma
- Systemic vasculitis disease—giant cell arteritis, hypersensitivity vasculitis, polyarteritis nodosa, Wegener's granulomatosis
- Crystal-induced synovitis—gout, pseudogout (calcium pyrophosphate deposition disease)
- Direct bacterial infection—bacterial endocarditis, *N gonorrhoeae*, *Staphylococcus aureus*, Gram-negative bacilli
- Indirect bacterial infection (reactive arthritis)—bacterial endocarditis, *N gonorrhoeae*, *Campylobacter spp*, *Salmonella spp*, group A streptococci (rheumatic fever)
- Viral infection—enterovirus, hepatitis B, varicella-zoster virus (human herpes virus 3)
- Other—fibromyalgia, sarcoidosis, osteomalacia, drug-related arthralgia(proton pump inhibitors, quinolones)

Management

In the absence of active joint inflammation, simple arthralgia should be considered. Patients should be reassured and advised to take simple analgesics or non-steroidal anti-inflammatory drugs (NSAIDs) unless they have a contraindication, such as renal impairment, significant heart failure, active peptic ulceration, or recent gastrointestinal bleeding. Encourage positive lifestyle changes and ask patient to return to the clinic or the practice in 4 weeks.[14] Fibromyalgia should be considered if the patient has generalised pain and signs of depression.[14]

If the clinical features indicate osteoarthritis, reassure the patient and explain the nature of the problem (wear and tear). Advise the patient to take paracetamol or NSAIDs, or both. Taking NSAIDs regularly has lasting analgesic and anti-inflammatory effects, which makes these drugs particularly helpful for treating continuous or regular pain associated with inflammation. Therefore, although paracetamol often gives adequate pain control in osteoarthritis, NSAIDs are more appropriate than paracetamol or the opioid analgesics in the inflammatory arthritides (eg, rheumatoid arthritis) and in some cases of advanced osteoarthritis. Additionally, offer lifestyle education, and encourage exercise and weight loss. Refer patients for physiotherapy if needed.[14]

Corticosteroids are essential for the treatment of polymyalgia rheumatica and temporal arteritis, as they rapidly relieve the incapacitating symptoms and reduce the incidence of blindness.[15] The use of NSAIDs has been advocated in the USA, but most physicians find that steroids are necessary for complete control of symptoms.[15] The response to steroids is dramatic, with relief of symptoms in 48–72 hours and producing very grateful patients. A starting dose of 40 mg prednisolone for giant cell arteritis and 15 mg prednisolone for polymyalgia rheumatica are appropriate initial treatments for most patients. The beneficial effects of treatment must be balanced against the unwanted side-effects.

Consider prescribing a cyclooxygenase-2 selective (COX-2) inhibitor, since the risk of serious upper gastrointestinal events is lower with selective

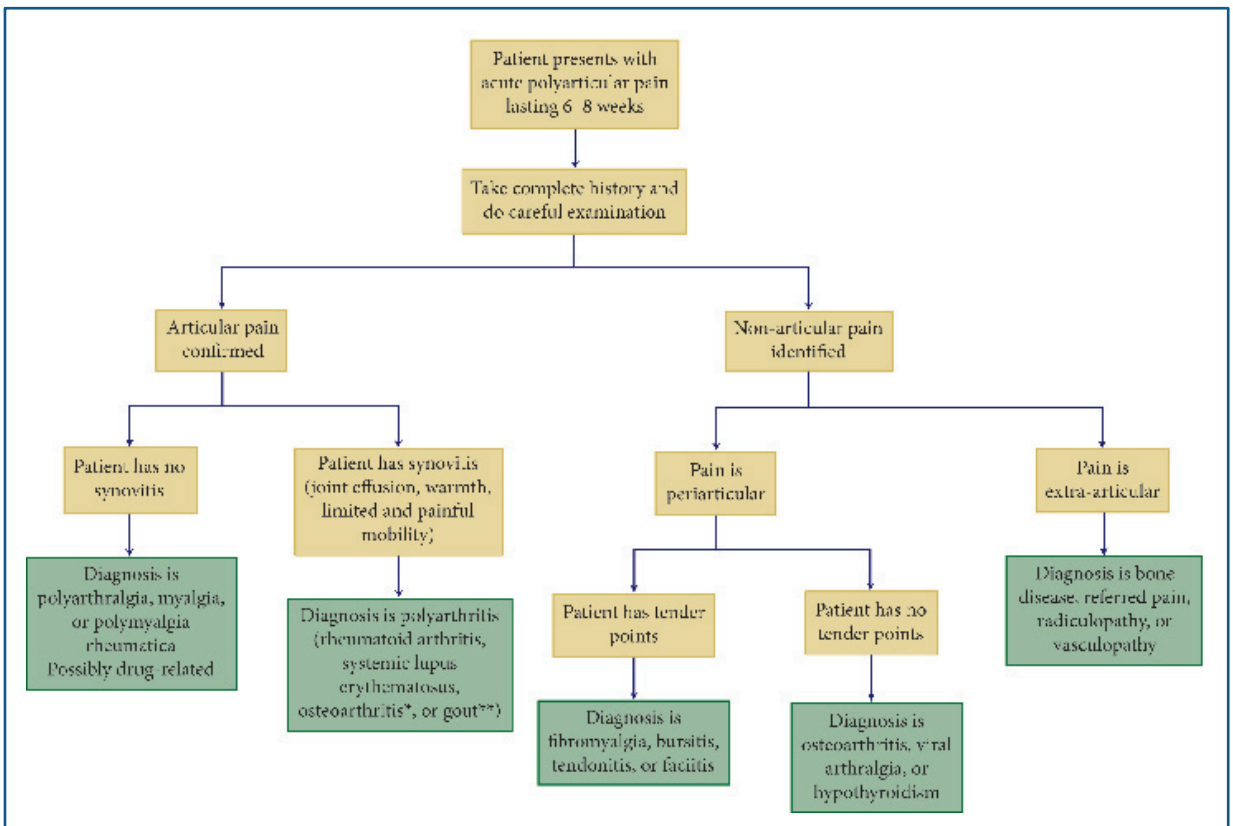

Figure: Diagnosis of polyarticular pain
*Osteoarthritis has a variable inflammatory component. **Acute gout usually affects one joint.

inhibitors compared with non-selective NSAIDs. However, this advantage may be lost in patients who require concomitant low-dose aspirin. Advise patients to rest affected joints when they are inflamed. Consider referring the patient to an occupational therapist for splinting and home aids. If the diagnosis is of rheumatoid arthritis or a seronegative inflammatory arthropathy, explain the nature of the condition and the benefits of referral to hospital for specialist assessment, education, and long-term support.

Give positive messages: several treatment modalities are available that can slow down disease progression; chronic disability and "ending up in a wheelchair" are now the exception rather than the norm.[14] Arrange early referral to a rheumatological service; meanwhile consider starting a disease modifying antirheumatic drug such as sulfasalazine. Initial management of rheumatoid arthritis should be in collaboration with a local rheumatology service, which will provide accurate diagnosis, multidisciplinary assessment, and optimise drug therapy.[16] The disease modifying antirheumatic drugs require regular haematological and biochemical monitoring and are best prescribed under the guidance of a rheumatological specialist. Short-term (6–12 weeks) low-dose oral corticosteroids (eg, up to 7·5 mg prednisolone daily) relieve symptoms and may slow progression.[14] A follow-up clinic appointment after 4–6 weeks should be aranged for clinical assessment, reinforcement of earlier advice, and evaluation of home and social circumstances of the patient.

I have no conflict of interest.

Key points

- Polyarthralgia is pain in multiple joints
- It is more common in women and with increasing age
- It has a wide range of differential diagnoses and diagnosis is often not straightforward
- A systematic approach with a careful history and physical examination commonly lead to the appropriate diagnosis in about 75% of patients
- Clinical parameters, such as distribution pattern of joint involvement and extra-articular manifestations, are helpful in narrowing the possible causes

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	Clarity	White blood cell count per mm³	Polymorphonuclear leukocyte count
Normal	Transparent	less than 200 (<0·2×10⁹/l)	less than 25%
Non-inflammatory	Transparent	less than 2000 (<2×10⁹/l)	less than 25%
Inflammatory	Translucent	less than 75,000 (<75×10⁹/l)	more than 50%
Septic	Opaque	more than 75,000 (>75×10⁹/l)	more than 75%

Table: Analysis of synovial fluid

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