A case of recurrent transient arthritis

Commentary by
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What is causing transient migratory bouts of arthritis in this young man and how should he be managed?

CASE SCENARIO
Anton, aged 38 years, has had an apparent migratory polyarthritis over the past few months. He has had joints affected sequentially with severe pain, heat, swelling and restricted mobility. Symptoms develop in the affected area, last several days to a couple of weeks and then resolve completely, only to be replaced by similar symptoms in a different joint. The sites affected have been his shoulder, wrists, knuckles and interphalangeal joints and, most recently, a knee.

Anton has no systemic symptoms and has been in good general health. He remembers that he had a few months of similar symptoms 10 years previously, but has had no joint problems at all in the interim. He has been happily married for 15 years and has never had a sexually transmitted infection. He has no history of any insect bites or recent travel.

Significant results of initial investigations are:
• elevated inflammatory markers – erythrocyte sedimentation rate (ESR), 40 mm/h (normal range, 1 to 10 mm/h) and C-reactive protein (CRP) level, 75 mg/L (normal range, <5 mg/L)
• mild leucocytosis
• serum uric acid and ferritin levels, low normal
• negative for rheumatoid factor and antinuclear antibodies
• negative by culture and PCR tests for gonorrhoea and chlamydial infection.

What could be causing Anton’s arthritis? How should he be further investigated and treated?

COMMENTARY
This case scenario describes a patient with recurrent transient episodes of arthritis typical of palindromic rheumatism. The latter has been recognised as an entity since 1944 when it was first reported by Hench and Rosenberg. The name derives from Greek palindromos, meaning ‘running back again, recurring’.

Palindromic rheumatism is a descriptive term that refers to recurrent transient (hours to weeks) self-limited episodes of painful arthritis affecting one (monoarthritis) or two to four (oligoarthritis) joints. The mean age of onset is 45 years, with a relatively even balance between the sexes. The most commonly affected joints include the metacarpophalangeal and proximal interphalangeal joints, the wrists, knees, ankles and shoulders. The hips, elbows and feet are less often involved. The spine and jaw are rarely affected. Constitutional symptoms and prolonged morning stiffness are uncommon.

Many forms of arthritis may commence this way. The episodes may subsequently evolve into more clearly defined conditions, such as rheumatoid arthritis or systemic lupus erythematosus. However, in some patients palindromic rheumatism episodes continue without evolving into a systemic disorder. In these patients, the recurrent self-limiting attacks of arthritis are not usually associated with joint damage.
How to evaluate the patient
A thorough history and physical examination are required to exclude infection and evaluate whether there are features of an underlying systemic disease. This includes rashes, fever, weight loss, Raynaud’s phenomenon, mouth ulcers, tophi and nodules. The most common underlying disorder is rheumatoid arthritis (30 to 60% of cases). Other differential diagnoses include crystal arthritis (gout, calcium pyrophosphate deposition disease), reactive arthritis or other seronegative spondyloarthritides, sarcoidosis, familial Mediterranean fever and Behçet’s disease. Migratory arthritis associated with fever and weight loss should prompt investigation to exclude subacute bacterial endocarditis.

Physical examination during an attack may reveal swollen tender joints and surrounding tissue, often in an asymmetric distribution. Between attacks there is usually nothing to find on examination.

Investigations
As a baseline, a full blood count and measurement of ESR and CRP level, a biochemical profile, liver function tests, and serological tests for rheumatoid factor, anticyclic citrullinated peptide antibody (anti-CCP) and antinuclear antibodies are warranted. During attacks there is a mild to moderate elevation of ESR levels. The presence of anti-CCP antibodies is predictive of the subsequent development of rheumatoid arthritis.

Approach to management
Unless there is a contraindication, first-line treatment during attacks involves an oral NSAID. I usually prescribe naproxen sustained release (either 750 or 1000 mg daily) or diclofenac (50 mg twice daily) taken with meals. These are generally well tolerated but may cause dyspepsia. An alternative medication with a lower risk to the upper gastrointestinal tract is celecoxib 200 mg once or twice a day.

If the rheumatism attacks do not settle promptly with an NSAID and the patient has unacceptable symptoms then a short course of a low-dose corticosteroid is warranted, such as prednisone 7.5 to 10 mg daily.

If the attacks become frequent then referral to a rheumatologist for further evaluation and consideration of a disease-modifying antirheumatic drug (DMARD) is warranted. However, there are no prospective randomised controlled trials of drugs in palindromic rheumatism, which makes an evidence-based approach to prescribing difficult. My preferred options include hydroxychloroquine, initially 200 mg twice daily for a month, then reducing to 200 mg daily. Although usually well tolerated, hydroxychloroquine can rarely produce retinal toxicity. A baseline ophthalmological assessment is essential.

An alternative agent is the sulfur-based drug sulfasalazine, which is also used in patients with rheumatoid arthritis and those with inflammatory bowel disease. This is commenced at 500 mg twice daily and, if well tolerated after a week, increased to 1000 mg twice daily. Sulfasalazine can produce skin rashes, nausea, abnormal liver function test results and depression of haemopoietic elements. Monthly blood counts and liver function tests are required to monitor for potential toxicities. Immunosuppressive drugs such as methotrexate are seldom indicated.

Natural history
The natural history of palindromic rheumatism is variable. Approximately 50% of patients with palindromic rheumatism develop rheumatoid arthritis. Less frequently, it evolves into systemic lupus erythematosus or seronegative spondyloarthritis. However, in a substantial number of patients the condition does not evolve and they continue to experience repeated episodes of palindromic rheumatism. It is not easy to predict in individual patients whether palindromic rheumatism symptoms will develop into a more serious condition such as rheumatoid arthritis. The presence of rheumatoid factor, anti-CCP antibodies or high-titre antinuclear antibodies should alert one to the likelihood of subsequent evolution into a systemic disorder.

When to refer to a rheumatologist
If the episodes of rheumatism are frequent and do not settle with NSAID treatment alone then referral of the patient to a rheumatologist is warranted for confirmation of the diagnosis and consideration of DMARDs.

CONCLUSION
Palindromic rheumatism needs to be considered in patients who present with recurrent episodes of transient arthritis. Although palindromic rheumatism does not usually cause joint damage, it may be a source of considerable pain and disability. It may also evolve into a more serious condition, such as rheumatoid arthritis. If attacks are frequent and do not settle rapidly with NSAIDs then referral to a rheumatologist is warranted.

REFERENCES

COMPETING INTERESTS: None.