An approach to reactive arthritis

JANE ZOCHLING MB BS, FRACP

RODGER LAURENT MB ChB, MD, FRACP

Reactive arthritis has a wide spectrum of clinical features but fortunately most cases are relatively mild. Dr Zochling and Dr Laurent present their approach to dealing with this common rheumatological problem.

Reactive arthritis is an inflammatory arthritis that begins 10 to 14 days after an enteric or genital infection. It is different to a septic arthritis in that viable organisms are not present in the joint. Reiter's syndrome, which consists of the triad of arthritis, conjunctivitis and urethritis, is best considered to be a subset of reactive arthritis with more severe disease.

Reactive arthritis has a wide spectrum of clinical features. It can consist of an acute arthritis, inflammatory back pain or an enthesopathy; these features can occur separately or together. The enthesis is the site of insertion of tendons or ligaments into the bone; enthesopathy is the term used to describe abnormalities at the enthesis. Extra-articular features also occur – these most commonly involve the eyes, genitourinary tract and skin.

Reactive arthritis most commonly affects adults aged between 20 and 40 years; equal numbers of men and women are affected. The percentage of people who develop a reactive arthritis following an enteric or genital infection ranges from about 3 to 16%, and the syndrome varies from a mild transient arthralgia to a severe chronic arthritis. Recent studies have shown that reactive arthritis is a mild disease in the majority of cases, with only 20% of patients consulting a doctor and 2% requiring hospital admission.

Aetiology

Reactive arthritis can be triggered by a variety of infective organisms, which are usually Gram negative and intracellularly invasive. The common feature is a cell membrane lipopolysaccharide which is thought to be antigenic and a possible trigger for the arthritis. Organisms known to cause reactive arthritis are:

- *Chlamydia trachomatis*
- *Campylobacter* spp.
- *Salmonella* spp.
- *Shigella* spp.
- *Yersinia enterocolitica.*

Shigella and *Salmonella* infections are more likely to produce a reactive arthritis than other bacteria. The initial infection can be mild, and its severity is not related to the severity of the reactive arthritis. Reactive arthritis may be more likely to develop following an enteric infection if the diarrhoea lasts for more than a week.

Clinical features

Reactive arthritis may produce systemic symptoms of fever, malaise and fatigue, but most patients have arthritis only. There can be other organ involvement in patients who have more severe disease. Reiter's syndrome consists of the triad of arthritis, conjunctivitis and urethritis.

Clinical manifestations of reactive arthritis are listed in the Table.

Musculoskeletal features

The arthritis has an acute onset and is asymmetrical. It usually involves less than four joints. The joints most commonly involved are the knees, ankles, wrists and those of the feet.

Inflammatory back pain occurs in about 20% of cases. This produces pain and stiffness at night and in the morning.

Table. Clinical manifestations

Systemic features
Low grade fever
Malaise
Fatigue

Musculoskeletal
Arthritis
Sacroiliitis
Spondylitis
Enthesopathy
Tendinopathy

Genitourinary
Urethritis
Prostatitis
Cervicitis, salpingitis or vulvovaginitis
Proteinuria
Microscopic haematuria

Ocular
Conjunctivitis
Anterior uveitis

Mucocutaneous
Balanitis circinata
Mouth ulcers
Keratoderma blennorrhagicum
Erythema nodosum

Cardiac
Pericarditis (rare)

Dr Zochling is Research Fellow in Rheumatology and Dr Laurent is Senior Staff Specialist in Rheumatology and Musculoskeletal Medicine, Department of Rheumatology, Royal North Shore Hospital, Sydney, NSW.

continued

Some clinical manifestations of reactive arthritis

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Figure 1. Left Achilles tendon enthesopathy in reactive arthritis.

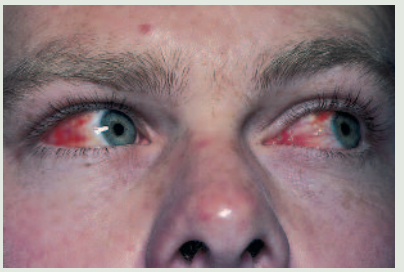

Figure 2. Conjunctivitis in Reiter's syndrome.

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Figure 3. Balanitis circinata in a man with reactive arthritis.

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Figure 4. Superficial ulceration of the tongue in a patient with reactive arthritis.

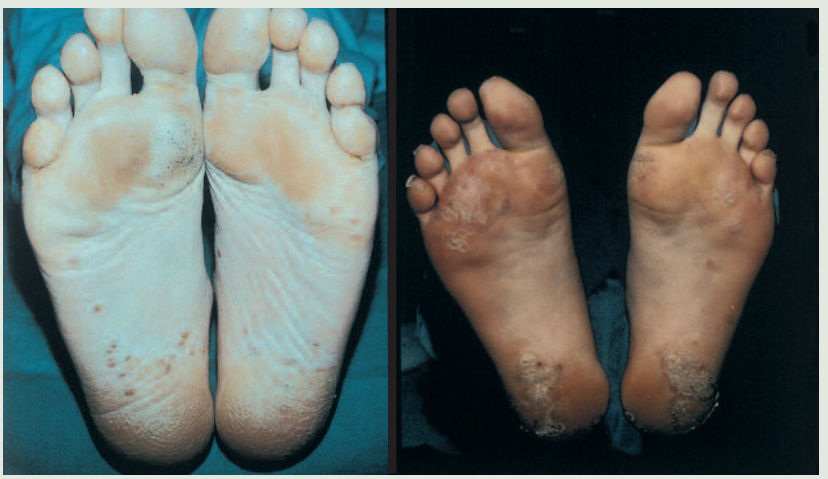

Figure 5. Two examples of keratoderma blennorrhagicum.

FIGURES 1, 3 AND 4 REPRINTED FROM THE CLINICAL TEACHING COLLECTION, 1972. © AMERICAN COLLEGE OF RHEUMATOLOGY.
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It is probably due to inflammation at entheses in the spine and can occasionally progress to sacroiliitis and spondylitis. It is more commonly seen in individuals who are positive for the HLA-B27 surface antigen.

Reactive arthritis includes inflammation at the entheses and in the tendon sheaths. Patients often experience tenderness and pain at the insertion of muscles and along tendons and tendon sheaths. Achilles tendinitis (Figure 1), plantar fasciitis and bursitis are commonly seen.

Genitourinary symptoms

Genitourinary symptoms are common, and it is important to remember that aseptic urethritis occurs even with an enteric infection. Symptoms include urinary frequency, dysuria or discharge. Prostatitis, cervicitis, salpingitis or vulvovaginitis may also occur, and can be asymptomatic.

Urinary sediment is abnormal in up to half of all patients with reactive arthritis, including proteinuria, microscopic haematuria and aseptic pyuria. This rarely progresses to significant renal disease.

Ocular manifestations

Conjunctivitis, which is sterile, is seen in 50% of patients with reactive arthritis who had an initial urogenital infection and in 75% of those with an enteric infection (Figure 2). Anterior uveitis, which manifests as ocular pain, redness and photophobia, is rare, and usually occurs in chronic disease.

Mucocutaneous lesions

Balanitis circinata are small, shallow, painless ulcers on the glans penis that occur in 20 to 40% of men who develop reactive arthritis (Figure 3). Similar painless mucocutaneous lesions can occur in the mouth or on the tongue (Figure 4). Keratoderma blennorrhagicum is a papular rash on the soles of the feet that can often be confused with pustular

psoriasis (Figure 5). Erythema nodosum rarely occurs.

Rare manifestations

Cardiac complications occur rarely in individuals with severe reactive arthritis. These include pericarditis, conduction disturbances and aortic regurgitation.

Investigations

Investigations that may be considered for a patient with suspected reactive arthritis include:

- **Full blood count.** A mild to moderate elevation of neutrophils can occur. Platelets can be elevated mildly as part of the acute phase response.
- **Acute phase response indicators.** These are the erythrocyte sedimentation rate (ESR) and the level of C-reactive protein (CRP). Levels may be normal in very mild disease but are always elevated in patients with severe arthritis or extra-articular involvement.
- **Arthrocentesis.** Joint aspiration is particularly important in a case of monoarthritis to differentiate between infection and a crystal or inflammatory arthritis. The synovial fluid is usually inflammatory (total white cell count >2,000 x 10^9/L, predominantly neutrophils). A sample should always be sent for culture in cases of monoarthritis.
- **Cultures.** Stool and urine cultures and urethral swabs are useful if there are clinical signs of ongoing infection. However, if the infection has resolved clinically then there is little value in cultures.
- **Imaging.** X-rays are not helpful, but a bone scan may be of use to detect early arthritis if there is arthralgia without joint swelling. It may also show areas of enthesopathy or tendinopathy.
- **Bacteriology.** Urine PCR for *Chlamydia* may confirm a presumed genitourinary infection. Serological tests for antibodies to possible infecting organisms are unhelpful.
- **HLA-B27 status.** There is an increased prevalence of HLA-B27 positive status in people who develop reactive arthritis. Recent studies suggest that this increase may be small. This finding is not sufficient to make measurement of HLA-B27 status of any value in the diagnosis of reactive arthritis.

Differential diagnoses

The differential diagnoses for reactive arthritis will depend on the pattern of arthritis.

A monoarthritis can be due to a septic arthritis, gout or pseudogout. The joint must always be aspirated to exclude a septic arthritis. In this age group, gonococcal arthritis always needs to be considered.

When more than one joint is involved, infection is rare unless the patient is severely immunosuppressed. Crystal arthropathies such as gout and calcium pyrophosphate disease generally involve only one joint, are of rapid onset with acutely painful joints, and rarely involve the spine. The other seronegative spondyloarthropathies should be considered, including ankylosing spondylitis, psoriatic arthritis and enteropathic arthritis. The history of infection and the pattern of joint disease are important.

Treatment

Treatment will depend on the severity of the arthritis and CRP level, and may involve analgesics, nonsteroidal anti-inflammatory drugs (NSAIDs), prednisone (Panafcort, Sone) or sulfasalazine (Pyralin EN, Salazopyrin). Consultation with a rheumatologist may be useful if higher dose corticosteroids or sulfasalazine are required.

It is important that all patients with an arthritis receive an appropriate exercise program to restore and maintain normal joint function. Inflammatory back pain and enthesopathies usually respond to NSAIDs and exercises.

Arthralgia or mild arthritis with normal or mildly elevated CRP level

These patients can be controlled with NSAIDs and analgesics.

Arthritis with elevated CRP unresponsive to NSAIDs

Prednisone, 10 to 20 mg a day, is required for this group. The arthritis should improve within two weeks. The pred - nisone is reduced and discontinued, the rate of reduction depending on the clinical features and CRP level.

Arthritis with elevated CRP unresponsive to low dose prednisone

For these patients, the dose of prednisone can be increased to 30 to 40 mg a day. Sulfasalazine should be commenced because patients in this group are generally slow to settle, and it is unusual for them to settle on prednisone alone. Sulfasalazine has a delay of about six weeks before the onset of action, so it should be commenced early.

Once the arthritis is controlled, prednisone is reduced and stopped. The sulfasalazine is continued for six months and then reduced to the lowest maintenance dose or stopped. If there are side effects from the sulfasalazine, methotrexate or azathioprine can be used.

Arthritis, extra-articular features and high CRP

Patients in this group require an NSAID and sulfasalazine early on. Once again, if there is a poor response to NSAIDs commence prednisone.

Using antibiotics in reactive arthritis

There are two aspects to the controversial area of antibiotics and reactive arthritis.

The first is that of antibiotic treatment at the onset of the arthritis. Our view is that if the enteric or genital infection is still present then it should be treated with antibiotics – recent studies have shown that prompt treatment with antibiotics reduces the chances of developing reactive arthritis.

The second aspect concerns treating chronic reactive arthritis with antibiotics. We feel that this is not useful if the cause is an enteric infection. It is still unclear whether a three- to six-month course of tetracycline may help reactive arthritis due to *Chlamydia* infection.

Prognosis

The prognosis is good for most patients who develop reactive arthritis. The majority recover within two to six months, with 85% completely recovered by one year. About 5% will have a chronic arthritis (more common in those with Reiter's syndrome).

Reinfection with the same organism can produce a recurrence of the arthritis. In 15 to 20% of cases, a recurrence in symptoms may occur several years after the initial arthritis has resolved. Back pain, arthritis and enthesopathy are the features that most commonly reappear. These recurrences are usually mild and spontaneous recovery is common.

Conclusion

Reactive arthritis is a common and, in most cases, a mild disease. Involvement of the spine and entheses can occur. As with any arthritis occurring after an infection, it is important to exclude septic arthritis. The long term prognosis is good, with most patients managing on NSAIDs and recovering within about six months. MT

Further reading

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