Sexually acquired reactive arthritis

Authors: Elizabeth Carlin and Sarah Flew

Sexually acquired reactive arthritis (SARA) may present acutely to general physicians. It is important to consider the condition and to identify key features in the history and examination so that appropriate investigations are taken and optimum treatment is given. Involvement of relevant specialists in the management is essential and where sexually transmitted infections are identified, partner notification is required.

Introduction

Sexually acquired reactive arthritis (SARA) is a reactive arthritis (ReA) triggered by a sexually transmitted pathogen in the genital tract. It may also include inflammation of the tendons and fascia and have other systemic manifestations. Reiter's syndrome described the classic triad of urethritis, arthritis and conjunctivitis, with or without other cutaneous or systemic involvement, but is no longer used in current practice.

SARA should be considered with any acute arthritis, especially in a young adult. In such cases it is important to screen for sexually transmitted infections (STIs) and treat appropriately.

Management may require input from several specialities depending on the symptoms and severity.

Aetiology

Establishment of SARA appears to involve an immune response to an infective pathogen and alteration of its usual state to allow it to persist in the synovium in an aberrant form while generating an inflammatory response. It is unclear why some individuals develop STI complications, including SARA, and why not all STIs are associated with the condition.

Lower genital tract infections, either urethritis or cervicitis, are most commonly associated with the condition, with objective features of SARA in 0.8–4% of cases; although this now appears to be much lower in clinical practice.

The most frequently reported infection is *Chlamydia trachomatis* in up to two-thirds of cases and *Neisseria gonorrhoeae* has been reported in up to 16%, independent of its potential to cause septic arthritis.

It has been suggested that ocular strains of *C trachomatis* (trachoma), rather than genital strains, are preferentially associated with SARA but more work is needed to substantiate this and to determine whether ocular serovars are associated with genital tract infection. *Mycoplasma genitalium*, which can cause urethritis, and *Ureaplasma urealyticum* have been reported in a few cases of SARA but a causal role in the development of SARA has not been established.

Risk factors for SARA

There are several predisposing factors for SARA.

- Gender: SARA appears to occur over ten times more frequently in men compared to women but under-recognition or milder disease in women may be a factor.
- HLA-B27: The gene is 10 times more common in those with SARA and is associated with more severe disease.
- HIV infection: A rising incidence of spondyloarthritis, including ReA, has been seen in sub-Saharan Africa in association with HIV. Similar observations have not been seen in Caucasian populations.

Associations with SARA

There is a recognised association with other spondyloarthritides, most commonly with ankylosing spondylitis but also with psoriatic arthritis, inflammatory bowel arthritis and SAPHO (synovitis, acne, pustulosis, hyperostosis, osteitis).

Hence, there may be a personal or family history of spondyloarthritis, iritis, psoriasis, inflammatory bowel disease or SAPHO.

Clinical presentation

There is a history of sexual intercourse, usually with a new partner, within three months of arthritis symptoms.

Most men give a recent history of genital symptoms of urethral discharge, dysuria and/or testicular pain or swelling. The genital symptoms occur on average 14 days before the arthritis develops.

Women are more likely to be asymptomatic but may describe altered vaginal discharge, inter-menstrual or post-coital bleeding, pelvic pain or deep dyspareunia.
Rectal STIs, including gonorrhea and chlamydia, may be asymptomatic but can present with rectal discharge, bleeding, discomfort and tenesmus. Joint pain, with/without swelling and stiffness, especially at the knees, ankles and feet is described. It is typically inflammatory in nature with morning stiffness and nocturnal pain. The distribution is usually asymmetrical and affects less than six joints. Other musculoskeletal symptoms include:

- enthesitis and fasciitis (20–40%), which may cause difficulty in walking,
- tenosynovitis (30%) and dactylitis (16%) 
- low back pain and stiffness is common and sacro-iliitis occurs in approximately 10% of patients.

Extra-articular symptoms include:

- irritable eyes, conjunctivitis (30%) and less commonly uveitis, which is more likely if pain is present (2–11%).
- skin manifestations include psoriasiform rash (12%) with genital lesions, circinate balanitis/vulvitis (14–40%), pustular psoriasis on the soles of the feet (keratoderma blennorrhagica) (5–33%), geographical tongue (16%), oral ulceration (10%) and nail dystrophy (6–12%).

Cardiac:

- left ventricular dilatation, pericarditis, aortic valve disease.

Renal:

- glomerulonephritis, IgA nephropathy.

Neurological:

- meningoencephalitis, nerve palsies.

Other:

- thrombophlebitis, subcutaneous nodules.

Systemic symptoms of malaise, fatigue, weight loss and fever are seen in some patients (10%) and electrocardiographic abnormalities may occur (5–14%).

Renal pathology, such as proteinuria, microscopic haematuria and aseptic pyuria, which may be due to concurrent urethritis, is common (50%) but is usually asymptomatic.

Good clinical examination is essential, specific features to look for are listed in Table 1.

Other clinical features are rare (Box 1).

Management in the acute medical setting

The diagnosis of SARA depends on recognising the typical features of spondyloarthritides and genital infection with a sexually transmitted pathogen.

Close liaison between STI physicians, rheumatologists and the microbiology department is advised to ensure appropriate specimens are obtained (Box 2 and Table 2) and to achieve optimum management. Those with ocular or visual symptoms should be referred to an ophthalmologist for ocular assessment, including slit-lamp assessment.

The condition and prognosis should be fully discussed with the patient.

Treatment

Antimicrobial therapy for genital tract infections should be as in uncomplicated infection. Rapid treatment may reduce the risk of arthritis developing. It is controversial whether treatment alters the natural history of extra-genital aspects of SARA with the most likely position being that it does not once the arthritis is established. Extended antibiotic courses of 3–12 months and combination antibiotic regimens have been trialled but conclusive evidence of benefit with respect to arthritis is lacking.

Comprehensive guidelines on the management of STIs and guidance on ‘look back periods’ have been produced by the British Association for Sexual Health and HIV and should be followed with respect to specific infections.

Partner notification and management will be required for all diagnosed STIs, using standard ‘look-back periods’, to avoid re-infection, and the patient should be advised to avoid all sexual contact until they and their sexual partner(s) have completed treatment.

First-line treatment of arthritis and other musculoskeletal manifestations includes simple measures such as rest, orthotics

KEYWORDS: Sexually acquired, reactive arthritis, Reiter’s syndrome, sexually transmitted infection, urogenital infection
Box 2. Essential investigations

STI tests

- NAAT for Chlamydia trachomatis and Neisseria gonorrhoea (vulvo-vaginal sample in women, urine in men; throat and rectal samples depending on sexual history and symptoms).
- If N gonorrhoeae NAAT is positive further samples for culture confirmation and sensitivity are required.
- NAAT for Mycoplasma genitalium if available, particularly important for men with urethritis (endocervical sample in women, urine in men).
- Urethral (men) or endocervical (women) samples for Gram staining and culture if genital symptoms are present.
- HIV antibody test (fourth generation – antigen/antibody)

Synovial fluid analysis

- Cell count, Gram stain, crystals.
- Culture (where septic arthritis is suspected).

Acute phase response

- Erythrocyte sedimentation rate or C-reactive protein.
- Culture (where septic arthritis is suspected).

Cell count, Gram stain, crystals.

Other

HIV antibody test (fourth generation – antigen/antibody)

STI tests

> NAAT for Chlamydia trachomatis and Neisseria gonorrhoea (vulvo-vaginal sample in women, urine in men; throat and rectal samples depending on sexual history and symptoms).
> If N gonorrhoeae NAAT is positive further samples for culture confirmation and sensitivity are required.
> NAAT for Mycoplasma genitalium if available, particularly important for men with urethritis (endocervical sample in women, urine in men).
> Urethral (men) or endocervical (women) samples for Gram staining and culture if genital symptoms are present.
> HIV antibody test (fourth generation – antigen/antibody)

Synovial fluid analysis

- Cell count, Gram stain, crystals.
- Culture (where septic arthritis is suspected).

Acute phase response

- Erythrocyte sedimentation rate or C-reactive protein.
- Other
- Full blood count.
- Urea

NAAT = nucleic acid amplification test; STI = sexually transmitted infection.

Table 2. Other investigations which may be required

<table>
<thead>
<tr>
<th>Often useful</th>
<th>Sometimes useful</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver and renal function tests</td>
<td>Blood cultures</td>
</tr>
<tr>
<td>HLA-B27</td>
<td>Stool culture (if enteric ReA suspected)</td>
</tr>
<tr>
<td>X-rays of affected joints</td>
<td>MRI of sacro-iliac joints</td>
</tr>
<tr>
<td>Ultrasound of affected joints or entheses</td>
<td>Synovial biopsy</td>
</tr>
<tr>
<td>ECG</td>
<td>Echocardiogram</td>
</tr>
<tr>
<td>Ophthalmic examination with slit lamp assessment</td>
<td>Exclusion tests for other diseases with rheumatological features:</td>
</tr>
<tr>
<td></td>
<td>&gt; rheumatoid factor and anti-cyclic citrullinated peptide antibodies (rheumatoid arthritis)</td>
</tr>
<tr>
<td></td>
<td>&gt; autoantibodies (systemic lupus erythematosus)</td>
</tr>
<tr>
<td></td>
<td>&gt; plasma urate (gout)</td>
</tr>
<tr>
<td></td>
<td>&gt; chest X-ray and serum angiotensin-converting enzyme level (sarcoidosis).</td>
</tr>
</tbody>
</table>

ECG = electrocardiogram; MRI = magnetic resonance imaging; ReA = reactive arthritis.

should be made before prescribing these drugs. Those at risk of GI toxicity may benefit from concurrent gastroprotective agents. All NSAIDs may be associated with increased CV events, with the likely exception of naproxen, which has a more favourable CV safety pattern. NSAIDs should always be used at the lowest effective dose for the shortest time period possible.

Corticosteroid injections may be useful for single troublesome joints, including the sacro-iliac joint, and enthesitis.

Second-line therapies are reserved for those who have moderate/severe arthritis, or where there is erosive joint damage, or who have failed first-line therapy. Individuals falling into this group should be referred for specialist rheumatology assessment.

The most common second line therapies are disease-modifying antirheumatic drugs:

> sulphasalazine
> methotrexate
> azathioprine.

Less common therapies are:

> systemic corticosteroids
> tumour necrosis factor (TNF)-α blockers: experience in SARA is limited although they are well established in treating other spondyloarthritides and they do not appear to reactivate the infective trigger.
> gold salts and D-penicillamine are rarely used.

Surgical interventions are rarely required for musculoskeletal problems but can include synovectomy and arthroplasty.

Mild skin and mucous membrane lesions do not require any specific treatment. Topical keratinolytic agents, corticosteroids, and vitamin D3 analogues are options for mild/moderate cases, while more severe situations may require methotrexate, retinoids or TNF-α blockers.
Eye lesions should be managed with ophthalmological advice and uveitis should be treated promptly with topical or oral corticosteroids and mydriatics to reduce the risk of blindness. In severe cases corticosteroids and mydriatics to reduce the risk of blindness.

**Prognosis**

SARA is a self-limiting condition in the majority of cases with full resolution within 4–6 months on average, although 50% of patients may experience recurrent episodes and up to 17% have chronic symptoms persisting for more than one year. Joint-related complications of SARA relate to aggressive arthritis, and are more common in individuals who are positive for the HLA-B27 gene. Persistent locomotor disability occurs in approximately 15% of cases.

Ankylosing spondylitis has been described in up to 23% of patients, although it is unclear if this is a complication of SARA or a coexisting disease in a genetically predisposed population.

Uveitis that is inadequately treated, or recurrent, may result in cataract formation and irreversible visual loss in some cases.

**Follow-up**

Follow-up should be under the guidance of the relevant specialist and depends on the severity of the symptoms and on the genital infection identified. It is important that patients are actively involved in their care, including self-management, and they should be advised to avoid potentially ‘triggering infections’ in the future. These may be genital or enteric. Therefore, safer sexual practice and good food hygiene should be discussed.

**Summary**

SARA can present with a wide range of manifestations. Although it is self-limiting in most individuals, some will have long-term consequences and disability. It is important to recognise the condition and coordinate treatment with relevant specialists to achieve optimum management.

**References**