Cutaneous and rheumatological manifestations of reactive arthritis: a case report

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Abstract

Reactive arthritis is a rare form of spondyloarthropathies that develops in response to a genital or intestinal infection. We report the case of a reactive arthritis with skin manifestations, occurring after a urethritis. Long term antibiotic treatment associated with sulfasalazine and diclofenac led to the control of disease activity levels.

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Authors’ contributions

- Dr. Maroua SLOUMA: Methodology and Writing - review & editing
- Dr. Siwar BEN DHIA: Roles/Writing - original draft
- Dr. Noureddine LITAIEM and Dr. Rim DHAHRI: data analysis
- Dr. Imen GHARSALLAH: supervision
- Dr. Leila METOUI: conceptualization
- Dr. Bassem LOUZIR: validation

DECLARATION

1
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Abstract:
Reactive arthritis is a rare form of spondyloarthropathies that develops in response to a genital or intestinal infection. We report the case of a reactive arthritis with skin manifestations, occurring after a urethritis. Long term antibiotic treatment associated with sulfasalazine and diclofenac led to the control of disease activity levels.

Structured abstract:
Introduction:
Reactive arthritis is a rare form of spondyloarthropathies occurring after genital or enteric. It is most often self-limited but can progress to chronic spondylarthritis.

Case description:
We report the case of a 30-year-old man who presented with acute arthritis occurring two months after an episode of urethral discharge. Physical examination revealed polyarthritis, dactylitis, sacroiliac joint involvement, and plantar papulosquamous plaques. The human leukocyte antigen B27 was positive. Detection of chlamydia trachomatis and Gonococcus in the first catch urine specimen was negative. Hepatitis B and C, chlamydia trachomatis, Human Immunodeficiency Virus and syphilis serologic test results were negative. Pelvic magnetic resonance imaging revealed left sacroilitis. The patient was treated with antibiotics, diclofenac, and sulfasalazine. After six months of follow-up, a significant clinical improvement was obtained without remission, suggesting an evolution to chronic spondylarthritis.

Conclusion:
Diagnosis of Reactive arthritis is difficult since microbiologic examinations are commonly negative. This disease should be considered in patients with rheumatologic manifestations occurring after a urogenital or enteric infection, mainly when associated with skin manifestations and human leukocyte antigen B27.

Keywords: Reactive arthritis, urethritis, Keratoderma blennorrhagica, HLA-B27 Antigen

Key clinical points
Reactive arthritis should be considered when rheumatologic manifestations follow genital or enteric infection
Negative microbiologic tests should not exclude the diagnosis
Plantar papulosquamous plaques, dactylitis, and HLA-B27 enhance the diagnosis

Introduction:
Reactive arthritis (ReA) is aseptic arthritis occurring 1 to 4 weeks after bacterial infection of the genitourinary and digestive tracts [1,2]. It usually affects a genetically predisposed individual.
Clinical manifestations include mucocutaneous manifestations such as keratoderma blennorrhagicum, circinate balanitis, ulcerative vulvitis, nail changes (dystrophy and thickness), oral lesions, and conjunctivitis [3,4].
The main rheumatological manifestations are asymmetric oligoarticular arthritis of the lower limbs, enthesitis, dactylitis, and inflammatory back pain.
The diagnosis of ReA is challenging since no diagnosis criteria are available.
We report a case of ReA occurring after urethritis. We emphasize clinical signs, radiological features, and management of this disease.

**Case description:**

A 30-year-old man presented to the rheumatology department with a 20-day-history of inflammatory arthralgia. He had no medical history and was a smoker.

The patient claimed to have had a urethral discharge one month before the onset of articular manifestations. He also reported having non-protected sexual intercourse.

Physical examination showed left knee joint effusion, synovitis of metacarpophalangeal joints, and proximal interphalangeal (PIP) joints.

The left sacroiliac joint was tender with positive compression, distraction, and sacral thrust provocation tests. The patient also had right third finger dactylitis (figure 1) and plantar papulosquamous plaques (figure 2). The patient had no fever, urethritis, conjunctivitis, or uveitis.

Laboratory examinations reveal increased C-Reactive protein (CRP) level (97 mg/L, Normal value (N) <8 mg/L), elevated erythrocyte sedimentation rate (ESR) (83 mg/L, N<15 mm). Liver and renal tests were within the normal range.

Anti-nuclear antibodies, rheumatoid factor, and anti-citrullinated protein antibodies were negative.

Polymerase chain reaction (PCR) test for Chlamydia trachomatis (Ct) and Gonococcus in the first catch urine specimen were negative. Detection of Ct by PCR in blood sample was also negative. Hepatitis B and C, Ct, Human Immunodeficiency Virus, and syphilis serologic test results were negative.

The human leukocyte antigen (HLA) B27 was positive. Radiographs of hands and feet did not reveal erosions or joint space narrowing.

The pelvis radiograph did not show sacroiliitis. Pelvic magnetic resonance imaging (MRI) revealed subchondral bone marrow edema of the left sacroiliac joint attesting to an active inflammation of sacroiliac joints.

The diagnosis of ReA was made based on the history of urethral discharge preceding rheumatological manifestations associated with plantar papulosquamous plaques, dactylitis, and the positivity of HLA-B27.

Ceftriaxone (a single dose of 1 g) and doxycycline (200 mg daily for three months) were indicated. Sulfasalazine (2 grams daily) and diclofenac (150 mg daily) were also prescribed, leading to the alleviation of clinical manifestations.

Plantar skin lesions regressed on the third day of antibiotic therapy.

After six months of follow-up, Bath ankylosing spondylarthritis disease activity index (BASDAI) [5] fell from 4.9 to 2.1. Inflammatory biomarkers became within the normal range.

**Discussion:**

We report a case of ReA occurring after urethritis. ReA is a form of peripheral spondyloarthritis occurring after a distant bacterial infection [6].

Causative agents of ReA are most commonly genitourinary (Ct, Neisseria gonorrhoea, Mycoplasma hominis, and Ureaplasma urealyticum) or gastrointestinal (Salmonella, Shigella, Campylobacter, and Yersinia) [7,8]. Bacillus Calmette-Guérin (BCG) therapy [9] or viral triggers can also induce ReA [10].

ReA commonly affects young adults of 20 to 40 years, with a male predominance in the post-venereal form [3,11]. The risk of developing ReA after genitourinary or gastrointestinal infections is about 1 to 4% in the general population. It increases to 25% in patients with positive HLA-B27 [6].
HLA-B27 was found in 30% to 50% of ReA patients [8].

Clinical manifestations appear within one to six weeks after genitourinary or gastrointestinal infection, such as urethritis, cervicitis, or diarrhea [6]. Asymptomatic chlamydia trachomatis infection can also induce ReA [7,12].

Rheumatological manifestations include asymmetric oligoarticular arthritis of the lower limbs [12], dactylitis, enthesitis (42% of patients) [6], and sacroiliitis (30% of cases) [6].

Dermatological manifestations are various. They may include Keratoderma blenorrhagicum, circinate balanitis, ulcerative vulvitis, oral lesions, and nail changes [13,14]. Keratoderma blenorrhagicum typically appears as erythematous macules and papules in the plantar and palmar area, rising into vesicular, often hyperkeratotic plaques and sterile pustules [4].

Only 10% of ReA patients with positive HLA-B27 develop these lesions. [13]

Ocular manifestations include conjunctivitis, anterior uveitis, episcleritis, and keratitis [8]. Cardiac manifestations have also been reported, including conduction abnormalities in the early stages of the disease [15–17] and aortic insufficiency in advanced disease [18,19].

The typical presentation of ReA, known as Reiter’s syndrome, has been rarely reported. This form consists of urethritis, conjunctivitis, and arthritis [20].

Inflammatory markers can be increased in the acute phase of ReA [21].

Microbiologic investigation for C. trachomatis by PCR in urethral swabs, synovial fluid [22], and synovial biopsy [23] are helpful to make the diagnosis of ReA. However, these tests are negative in up to half of the patients [22].

ReA is often misdiagnosed because of the lack of diagnostic criteria.

The diagnosis of ReA can be made if acute oligoarthritis or axial involvement occurs after gastroenteritis or urogenital bacterial infection [23].

In these cases, the diagnosis of ReA can be made based on rheumatological manifestations occurring after genitourinary symptoms, increased CRP, and positive HLA-B27. This association can predict the diagnosis of ReA with a sensitivity of 69% and a specificity of 93.5% [24].

Despite the negativity of microbiologic investigations in our case, the diagnosis of ReA was made based on the history of urethral discharge preceding rheumatological manifestations associated with plantar papulosquamous plaques, dactylitis, and the positivity of HLA-B27.

Nevertheless, if gastrointestinal or urogenital infection cannot be remembered by the patient, the triggering bacteria (Chlamydia, Salmonella, Yersinia, Shigella, Campylobacter) should be identified at the site of primary infection, serologic test, or PCR [23].

Using the Assessment of SpondyloArthritis International Society classification criteria for peripheral spondyloarthritis, the diagnosis of peripheral spondyloarthritis can be established when arthritis, enthesitis, or dactylitis is associated with at least one of these following criteria: psoriasis, inflammatory bowel disease, preceding infection, HLA-B27, uveitis, or sacroiliitis on imaging [25]. These criteria had a sensitivity and specificity of 79.5% and 83.3%.

The management of ReA is not yet codified [26]. Antibiotics can be indicated [3], often for a long time [8]. Although their efficacy is uncertain [26], long-term antibiotic treatment can prevent recurrence and chronic progression of ReA [19,27].

Non-steroidal anti-inflammatory drugs (NSAIDs) are the first-line treatment of articular manifestations. If NSAIDs are contraindicated or have low efficacy, intra-articular glucocorticoids can be indicated. Systemic steroids can be prescribed in patients with many swollen joints [3].
The failure of the first-line treatment or persistent symptoms for more than six months can lead to the prescription of conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) [3]. Sulfasalazine is the main DMARDs used in ReA. Its efficacy has been proved in a placebo-controlled prospective trial [28]. Other csDMARDs (methotrexate, azathioprine, cyclosporin) are supported by less experimental data [29]. Biologic DMARDs can be started if resistance to csDMARDs [3] or severe dermatological lesions [12].

In our case, the prescription of antibiotics aimed to treat urethritis and prevent recurrence and chronic progression of ReA. NSAIDs and sulfasalazine were prescribed to alleviate rheumatological manifestations.

The evolution of ReA depends on the triggering infection (Ct and Ureaplasma Urealyticum), HLA-B27 positivity, gender, and the presence of sacroiliitis [30,31].

ReA is often a self-limited disease [3] with a duration of 3 to 5 months for an acute ReA [32]. Nevertheless, 30% to 50% of patients develop chronic symptoms [7,33]. Chronic gut inflammation and a family history of spondyloarthropathy are risk factors for progression to chronicity [34].

Conclusion:

The diagnosis of ReA is challenging because of the high rate of negative microbiologic examination and the lack of diagnostic criteria. The diagnosis of ReA should be considered in patients with rheumatologic manifestations occurring after a urogenital or enteric infection, mainly when associated with skin manifestations and HLA B27.

The management of ReA is based on the treatment of the triggering infection and the articular manifestations.

References:


Figures legend:

Figure 1: Dactylitis of the right third finger (arrow)

Figure 2: Plantar papulosquamous plaques