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Reactive arthritis: images

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Abstract

Reactive arthritis is an extremely rare spondyloarthritis that affects the peripheral joints and spine, resulting in common symptoms such as arthritis, urethritis, conjunctivitis, and mucocutaneous lesions. On rare occasions, oral lesions such as circinate erosions on the hard and soft palate, gums, tongue, and cheeks may occur. Reactive arthritis may develop during or after genitourinary or gastrointestinal bacterial infections such as *Shigella*, *Salmonella*, *Yersinia*, and *Chlamydia*. A 36-year-old man presented with circinate balanitis, urethral discharge, oligoarthritis, conjunctivitis, lymphadenopathy, pharyngitis, and erythematous lesions on the palate. Culture examination showed presence of *Neisseria gonorrhoeae* and antibiotic treatment resulted in improvement of conjunctivitis and the lesions on the penis. However, severe oligoarthritis, palatal erosions that increased in severity and size, and depilated areas on the tongue were observed. The definitive diagnosis was reactive arthritis. The prevalence of sexually transmitted infections is increasing, highlighting the need to increase awareness of associated risks such as reactive arthritis. Moreover, consideration of non-specific oral manifestations in a systemic context may aid in effective diagnosis and treatment, suggesting the need for multidisciplinary teams.

Keywords: reactive arthritis, reiter syndrome, *Neisseria gonorrhoeae*, *chlamydia* infections, oral ulcers, spondyloarthritis

Introduction

Reactive arthritis previously known as Reiter syndrome, is a type of inflammatory spondyloarthritis that typically affects the axial or peripheral joints and peri-articular tissues of young adults one to four weeks after bacterial infections of the genitourinary and/or gastrointestinal tract. It may be associated with a variety of pathogens and subsequent symptoms affecting several organs. Although usually mild and self-limiting, up to 18% of individuals diagnosed with reactive arthritis may develop chronic arthritis [1,2].

In accordance with the American Rheumatism Association criteria, reactive arthritis may be defined as one month of peripheral arthritis associated with urethritis, cervicitis, or both. Sexually acquired reactive arthritis (SARA; endemic) is more commonly observed than the enteric (epidemic) form. Clinically, reactive arthritis is characterized by the classic triad of symptoms (arthritis, urethritis, conjunctivitis), muco-cutaneous lesions, and oral manifestations such as erosions of the hard and soft palate, gums, tongue, and cheeks in approximately 5%–10% of cases. Balanitis and keratoderma blennorrhagica may be observed very rarely [3-5]. The most common cause of reactive arthritis is *Chlamydia trachomatis* with other sexually transmitted infections such as *Neisseria gonorrhoeae* (distinct from its role in septic gonococcal arthritis) and *Ureaplasma urealyticum* also being implicated [6]. Although synovial fluid cultures of affected joints are often negative for

these bacteria, their nucleic acids and proteins have been observed in the synovium of affected patients [2]. It has been reported that patients with HLA-B27, which plays a role in antigen presentation to lymphocytes, are 50 times more likely to develop reactive arthritis after an infection as it probably shares some molecular characteristics with bacterial epitopes, leading to an autoimmune cross-reaction occurring in the pathogenic process [3]. The global annual incidence of RA ranges between 0.6 and 27 per 100,000 individuals, whereas the prevalence is approximately 30–40 per 100,000 adults, and the incidence of reactive arthritis after genital chlamydia infection has been found to range between 4% and 8% [7,8].

A combination of clinical, laboratory, and radiological imaging data is essential for accurate diagnosis of RA and development of treatment protocols. The current clinical case report focuses on a patient that developed RA subsequent to a sexually transmitted infection.

Case Synopsis

A 36-year-old man presented to the dermatology department of the Therapeutic Diagnostic Center, San Jose Hospital Complex. He reported unprotected, risky sexual behavior (oral and genital), and exhibited skin lesions, circinate balanitis, discrete erythematous areas on the soft palate; conjunctivitis and oral papular and macular lesions.



Figure 1. Lesions exhibited by the patient at the time of first evaluation: circinate balanitis; discrete erythematous areas on the soft palate; conjunctivitis and oral papular and macular lesions.

conjunctivitis (**Figure 1**), lymphadenopathy, right shoulder arthralgia, sacroiliac pain, pharyngitis, urethral discharge, and discrete erythematous areas on the soft palate at the time of initial examination. Empirical treatment included one g of ceftriaxone for 14 days for disseminated gonococcal infection and a single dose of azithromycin one g in case of a possible co-infection with *Chlamydia trachomatis*. The urethral discharge culture was positive for *Neisseria gonorrhoeae*. The patient's conjunctivitis and lesions on the penis were seen to improve with treatment, although severe oligoarthritis (right shoulder, sacroiliac, and metatarsophalangeal joint) and progression of the oral lesions from macules and papules to erosions was observed. He was referred to an oral pathologist at the Odontology Diagnostic Center of the same Hospital Complex.

Intraoral examination showed extensive clearly demarcated circinate erythematous areas on the hard and soft palate (**Figure 2**), angular cheilitis, and depilated areas on the tongue. The treatment protocol included miconazole for angular cheilitis and use of homemade salivary substitutes. Serum analysis revealed elevated acute phase reactants, with high C-reactive protein (107mg/dl; normal range up to 5mg/dl) and high erythrocyte sedimentation rate (ESR: 102 mm/h; normal range up to 13mm/h). The laboratory tests were non-reactive



Figure 2. Appearance of the patient's oral lesions after treatment with ceftriaxone and azithromycin: erythematous well-defined areas located on the hard and soft palates; lesions on the penis and conjunctivitis decreased; depilated area on the tongue; angular cheilitis at the angle of the lip.



Figure 3. Appearance of the patient's oral lesions after one month of treatment: depilated areas on a different sector of the tongue compared to previous; decrease in palatal lesions after 30 days; reduction in fungal lesions on the lip.

for rheumatoid factor, antinuclear antibodies, extractable nuclear antigen antibodies, anti-dsDNA antibodies, human immunodeficiency virus, Venereal Disease Research Laboratory test, and microhemagglutination test for antibodies to *Treponema pallidum* (MHA-TP). The final diagnosis was reactive arthritis.

The patient exhibited obvious improvement of the oral lesions (**Figure 3**) after one month of treatment, as indicated by the dermatologist and oral pathologist. However, oligoarthritis was seen to persist for several months and prednisone therapy (40mg daily with tapered doses) was recommended by the dermatologist. The patient subsequently exhibited substantial improvement in the severity of arthralgia. After three years, the patient returned to the department of oral pathology for examination. He reported that he no longer had joint pain. At the intraoral level, there were no lesions on palate or tongue.

Case Discussion

The current case report focuses on a man diagnosed with RA, a type of oligoarthritis resulting from an existing sexually transmitted infection. The presence of *Neisseria gonorrhoeae* was confirmed in the patient, although detection of *Chlamydia*

trachomatis, the microorganism most associated with this disease, was not possible owing to a lack of necessary implementation. Antibiotic treatment for possible co-infection was carried out nevertheless as previous studies have found that the proportion of co-infection varies considerably, from <4% up to >60% [9]. The inability to demonstrate presence of *Chlamydia trachomatis* in the current case prevented us from ascertaining whether the etiology of reactive arthritis could be attributed to *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, or both. This condition is more frequently observed in males, with the ratio of males to females ranging between 5:1 and 10:1. Although reactive arthritis has been observed in various age groups, it is more likely to occur in adults aged 20 to 40 years owing to the association of the condition with sexually transmitted diseases and at-risk behaviors more commonly observed in this age group [10,11]. The classic triad of symptoms of reactive arthritis include arthritis, urethritis, and conjunctivitis. The current patient profile was typical with regard to gender, age, and manifestation of the classic symptoms [11]. However, what made this case particularly interesting was the presentation of oral lesions. Oral manifestations may occur in the form of shiny and painless ulcers on the palate, tongue, and mucosa of the cheeks and lips; geographic tongue; and gangrenous pyoderma. Our patient exhibited ulcerative lesions on the palate and geographic tongue and these were in accordance with previously reported literature. Mucosal ulcerations and stomatitis of tongue, palate, and buccal mucosa are reported in as many as 17 percent of reactive arthritis cases [12,13].

Accurate diagnosis of reactive arthritis can be challenging, with previous evidence suggesting a strong association with the immunological cross-reaction between certain pathogens and the human leukocyte antigen B27 (HLA-B27). Unfortunately, our patient did not consent to this test on two separate occasions. Therefore, a diagnosis was made based on the presence of clinical characteristics such as severe oligoarthritis with his other clinical findings [5,10]. It is important to note that the oral lesions exhibited by the patient changed from macules and papules to erosions after two weeks of antibiotic treatment, whereas the eye and genital lesions were seen to

decrease. In this case, we must consider the possibility that the patient presented with two types of oral lesions, probably with different diagnoses. During initial *Neisseria gonorrhoeae* infection, the patient developed pharyngitis and macular and papular lesions on the soft palate; these could possibly be attributed to oral sex. However, he then developed demarcated circinate erosions on the soft palate, characteristic of reactive arthritis, and the lesions associated with gonorrhea were seen to disappear.

Recent studies have confirmed no major changes in the microbiological profile and clinical presentation of reactive arthritis in the past 30 years [14]. The pathogens most associated with urethritis include *Chlamydia trachomatis*, *Mycoplasma genitalium*, and *Ureaplasma urealyticum*, although the current case exhibited *Neisseria gonorrhoeae*. Rheumatologic therapy is usually determined based on the presence of underlying infections, articular and extra-articular disease manifestations, as well as the phase of the disease (acute or chronic). Treatment of acute RA includes non-steroidal anti-inflammatory drugs and glucocorticoids, whereas the chronic phase may be treated using disease-modifying anti-rheumatic drugs and biological agents (anti-TNF antibody, interleukin-6 receptor antibody, and interleukin-17a monoclonal antibody), [2].

The diagnosis of syphilis was ruled out by negative VDRL and MHA-TP. When antibody titers are high, as in early syphilis, a false negative may be generated with a nontreponemal test because the overabundance of antibodies interferes with the agglutination of antigen-antibody complexes. In experienced laboratories, the prozone phenomenon can be suspected when an apparently non-reactive

test has a rough or granular appearance. When the specimen is diluted enough the agglutination can be seen and the reactivity becomes apparent.

The correct use of condoms continues to be a fundamental strategy for the prevention of sexually transmitted infections. The Chilean National Health Survey 2016–2017 found that only 12.8% of sexually active men and 7.1% of sexually active women used a condom. Additionally, a greater number of casual partners and high-risk sexual practices are also associated with increased exposure to HIV and other sexually transmitted infections [15]. The World Health Organization reported that approximately one million individuals aged 15 to 49 years were diagnosed with sexually transmitted infections daily. This is equivalent to more than 376 million new cases of chlamydia, gonorrhea, trichomoniasis, and syphilis annually, highlighting the importance of reinforcing prevention measures for sexually transmitted infections which can have serious consequences. Accurate diagnosis and management of these patients requires a multidisciplinary approach and inclusion of an oral pathologist in the diagnostic team is becoming increasingly relevant.

Conclusion

Prevalence of sexually transmitted infections is increasing, highlighting the need to increase awareness of associated risks such as reactive arthritis. Accurate diagnosis and management of these patients requires a multidisciplinary approach.

Potential conflicts of interest

The authors declare no conflicts of interest.

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