Acute onset of rash and oligoarthritis

Angela D. Shedd, medical student, Suraj G. Reddy, MD, Jeffrey J. Meffert, MD, Richard P. Usatine, MD, and Eric W. Kraus, MD
Division of Dermatology and Cutaneous Surgery, University of Texas Health Science Center at San Antonio

EDITOR
Richard P. Usatine, MD
University of Texas Health Science Center at San Antonio

A 29-year-old man sought treatment at our clinic for an extensive rash he'd developed the month before. The rash was on his scalp, umbilicus, glans penis, palms, and soles of his feet. He reported swelling in his left knee and his fourth toes bilaterally that was exacerbated by weight bearing. During the 2 days prior to his visit to the clinic, the patient said he'd had a fever and night sweats; he denied ocular symptoms, GI complaints, dysuria, or penile discharge.

When asked about his sexual history, the patient noted that he'd had unprotected intercourse with a woman a year earlier that resulted in pain on urination and resolved on its own. Other than a resolved case of oral thrush, the patient had a noncontributory past medical history, took no medications, and had no family history of psoriasis.

A physical exam revealed circinate, scaly, and erythematous plaques covering his entire scalp (**FIGURE 1**). The patient's conjunctiva and oropharynx were clear. His fingernails showed hyperkeratosis, subungual debris, and nail fold erythema, without pitting. He also had bilateral swelling of the distal interphalangeal joints of his index fingers.

The patient's umbilicus had a scaly erythematous plaque, while there were confluent erythematous plaques in the groin area, and on the glans penis. There were also similar erythematous plaques in the axilla and inguinal folds; plaques on the lower extremities had a thicker layer of scale. The patient's feet had crusted plaques on the plantar surface, hyperkeratotic nails with thick subungual debris, and swelling and tenderness of the fourth toes bilaterally (**FIGURE 2**).

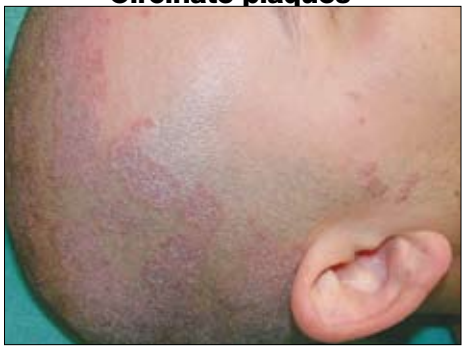
What is your diagnosis

FAST TRACK

During the 2 days prior to his visit, he'd had a fever and night sweats; he denied ocular symptoms or dysuria

FIGURE 1

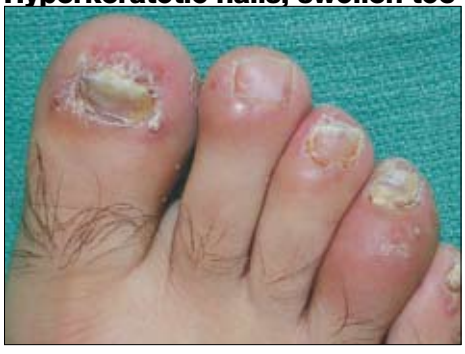
Circinate plaques



A 29-year-old man with circinate plaques on his scalp.

FIGURE 2

Hyperkeratotic nails, swollen toe



The patient had subungual hyperkeratosis, onycholysis, and dactylitis of the fourth toe.

Diagnosis: Reiter's syndrome

This young man had Reiter's syndrome (RS), a form of reactive arthritis that comprises a small subset of cases within the larger family of rheumatoid factor-seronegative spondyloarthritides—conditions noted primarily for inflammation of the axial skeleton.[1]

Of historical interest is the fact that this diagnosis shares its name with the man who first described it, Hans Reiter, a Nazi physician who tested unapproved vaccines and performed experimental procedures on victims in concentration camps. The infamous legacy of Reiter's name has led to the proposal that the syndrome be referred to by another, more descriptive name.[2] For the sake of simplicity, we'll refer to the syndrome by the abbreviation RS.

Look for elements of the classic triad

RS is notoriously inconsistent in its presentation. Only a third of patients will develop the "classic triad"—that is: peripheral arthritis lasting at least 1 month, urethritis (or cervicitis), and conjunctivitis. Nearly half of patients will have only a single element of the triad.[3]

Patients with RS will complain of generalized malaise and fever and will often describe dysuria with concomitant urethral discharge. If conjunctivitis is present, the patient will report reddened, sensitive eyes. Pain will often originate from axial bones, lower extremities (in an oligoarticular asymmetrical pattern), swollen digits, and the heels (from enthesopathy).

Skin manifestations are often very noticeable and include psoriasiform lesions (**FIGURE 3**) on the palms, soles, and glans penis. Specifically, you'll see keratoderma blenorrhagicum (**FIGURE 4**), brown and red macules/papules with pustular or hyperkeratotic features, on the palmar and plantar surfaces. Erythematous and scaly lesions resembling psoriatic plaques often appear elsewhere on the body. On the uncircumcised penis, these shallow ulcerations have a micropustular, serpiginous border and are referred to as balanitis circinata. However, they may also appear psoriasiform in nature on circumcised men, as was the case with our patient.

Coincident findings include onycholysis and subungual hyperkeratosis, lesions mimicking migratory glossitis, and anterior uveitis.

FAST TRACK

Only a third of patients will develop the "classic triad": peripheral arthritis, urethritis (or cervicitis), and conjunctivitis

The typical patient? A young, white man

Patients with RS are almost always Caucasian males in their early twenties and are typically HLA-B27 positive. Seronegativity for this HLA factor may portend a less severe version of the syndrome. Individuals infected with HIV show increased incidence of developing RS.[3]

A microbial antigen is likely responsible for the initial activation of RS. This is followed by an immune reaction involving the joints, skin, and eyes. This theory is supported by the absence of autoantibodies, the frequent association with HLA-B27, and the fact that patients with advanced AIDS experience the same severity of RS symptoms, despite depressed CD4+ T cell function.[1]

Bacteria trigger syndrome via 1 of 2 pathways

The bacteria that trigger RS typically enter the body through one of 2 pathways: the genitourinary tract or the gastrointestinal tract.

- **The sexual transmission pathway** involves infection with *Chlamydia trachomatis* or *Ureaplasma urealyticum* 1 to 4 weeks prior to development of urethritis and possibly conjunctivitis. The arthritic component follows later.

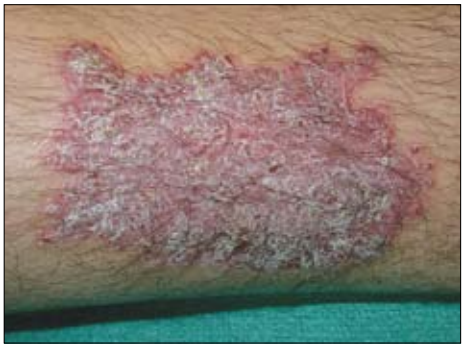
(In our patient's case, his report of a sexually transmitted infection a year earlier did not appear to be the trigger for his RS. We believe that another, subsequent, infection was to blame.)

- **The gastrointestinal pathway** involves an enteric pathogen, such as *Salmonella enteritidis*, *Yersinia enterocolitica*, *Campylobacter fetus*, or *Shigella flexneri* that infects the host and follows the same time frame as noted earlier, though diarrhea rather than urethritis emerges as a chief complaint.[4]

The post-venereal type of RS comprises most cases in adults. Children who develop RS, however, are more likely to present with diarrhea rather than urethritis, leading the clinician to suspect a gastrointestinal infection as the etiology of the condition.[5]

FIGURE 3

Psoriasiform plaque



Skin manifestations of Reiter's syndrome include psoriasiform lesions.

Various forms of arthritis comprise the differential

A number of conditions must be ruled out before the RS diagnosis is considered definitive. The most likely imposters include:

- Gonococcal arthritis
- Rheumatoid arthritis
- Ankylosing spondylitis
- Psoriatic arthritis.

In addition, an attack of gouty arthritis, systemic lupus erythematosus, serum sickness, Behçet's syndrome, rheumatic fever, Still's disease, and HIV could also present in a similar fashion.

The lab work, detailed below, separates RS from the imposters.

Test blood and urine; check the ankles

Although there is no specific test for RS, several laboratory procedures are essential to honing in on the diagnosis. Hematological inquiry will confirm anemia, leukocytosis, thrombocytosis, and an elevated erythrocyte sedimentation rate (ESR). Though the urethral test may not be positive for a suspected organism, this procedure must be done to rule out gonococcal or chlamydial infection. This can now be done on a urine specimen rather than inserting a swab into the urethra. The urine is sent for a polymerase chain reaction (PCR) test rather than a culture. If enteritis was the preceding infection, a stool culture to elucidate potential pathogens is warranted.

You'll also need to order serological tests for antinuclear antibodies (ANAs), rheumatoid factor (RF), and HIV. As you would expect, these tests will be abnormal for systemic lupus erythematosus, rheumatoid arthritis, and HIV respectively. Though these tests are often negative in RS patients, a strong association with HIV infection does exist.

Keep in mind, too, that you can differentiate gonococcal arthritis from RS based on historical features, as well as clinical features, including migratory polyarthritis with necrotic and pustular skin lesions. Patients with gonococcal arthritis will also have a positive gonococcal culture and rapid improvement with antibiotics.

If you order a biopsy, pathology is likely to find a variety of features in an RS patient, such as spongiform pustules, neutrophilic infiltrate in a perivascular pattern, and an epidermal hyperplasia that resembles psoriasis.[3]

Radiographic imaging for a suspected case of RS may reveal a number of signs that resemble psoriatic arthritis (pencil-in-cup deformity, syndesmophytes, sacroiliitis), but enthesitis, particularly in the ankle joint region, should raise your index of suspicion for RS.[6]

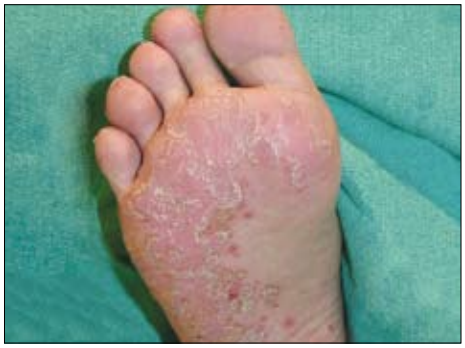
CONTINUED

FAST TRACK

Children who develop Reiter's syndrome are more likely to present with diarrhea rather than urethritis

FIGURE 4

Keratoderma blenorrhagicum



Patients with Reiter's syndrome have brown and red macules/papules with pustular or hyperkeratotic features on the palmar and plantar surfaces.

Tx: Antibiotics, NSAIDs, and steroids

Antibiotic therapy for 3 months is indicated if a patient's case of RS can be traced back to an infection. If a *Chlamydia* species is the offending organism, then doxycycline or tetracycline can be used[7] (strength of recommendation [SOR]: **B**). If the infectious agent is unknown, then ciprofloxacin can offer broad-spectrum coverage[8] (SOR: **B**).

Though few studies have evaluated the long-term effects of NSAID treatment on RS, a regular schedule of high doses for several weeks is appropriate for inflammation and pain management. It's most effective when given early in the disease course[5] (SOR: **B**).

Topical corticosteroids can be used on mucosal and skin lesions. For refractory disease, immunosuppressive agents such as sulfasalazine at 2000 mg/day[9] (SOR: **B**) or a subcutaneous injection of etanercept at 25 mg twice weekly[10] (SOR: **B**) offer relief.

Our patient's treatment included an NSAID and corticosteroids

Because our patient's syndrome involved a variety of systemic manifestations, we used several medications to cover all of his symptoms. We prescribed piroxicam 20 mg daily, clobetasol 0.05% ointment applied daily to legs and feet, triamcinolone 0.1% cream applied to scalp twice daily and genitals and armpits once daily, and acitretin 25 mg daily. We consulted Rheumatology to assess and treat his joint disease. We also consulted Ophthalmology to assess for potential ocular manifestations.

Though the patient did report a history of a sexually transmitted infection, it occurred long before his visit, and we were unable to identify an infectious agent. As a result, we did not start him on any antibiotics.

We instructed the patient to return in 2 weeks. Unfortunately, he was lost to follow-up. Patients with RS, though, typically make a full recovery from their symptoms. Some patients, however—10% to 20%—may go on to have a chronic, deforming arthritis.[3] ■

FAST TRACK

Though most patients make a full recovery, some may go on to have a chronic, deforming arthritis

References

1. Winchester R. Reiter's syndrome. In Freedberg IM, Eisen AZ, Wolf K, Austen KF, Goldsmith LA, Katz SI. *Fitzpatrick's Dermatology in General Medicine.* 6th ed. New York, NY: McGraw-Hill; 2003:1769–1776.
2. James WD, Berger TG, Elston DM. *Andrew's Diseases of the Skin: Clinical Dermatology.* 10th ed. Philadelphia, Pa: Saunders Elsevier; 2006.
3. Wolff K, Johnson RA, Suurmond D. *Fitzpatrick's Color Atlas and Synopsis of Clinical Dermatology.* 5th ed. New York, NY: McGraw-Hill, 2005.
4. Colmegna I, Cuchacovich R, Espinoza LR. HLA-B27-associated reactive arthritis: pathogenetic and clinical considerations. *Clin Microbiol Rev* 2004; 17:348–369.
5. Schachner LA, Hansen RC. *Pediatric Dermatology.* 2nd ed. New York, NY: Churchill Livingstone, Inc; 1995.
6. Gladman DD. Clinical aspects of the spondyloarthropathies. *Am J Med Sci* 1998; 316:234–238.
7. Lauhio A, Leirisalo-Repo M, Lähdevirta J, Saikku P, Repo H. Double-blind, placebo-controlled study of three-month treatment with lymecycline in reactive arthritis, with special reference to Chlamydia arthritis. *Arthritis Rheum* 1991; 34:6–14.
8. Yli-Kerttula T, Luukkainen R, Yli-Kerttula U, et al. Effect of a three month course of ciprofloxacin on the late prognosis of reactive arthritis. *Ann Rheum Dis* 2003; 62:880–884.
9. Clegg DO, Reda DJ, Weisman MH, et al. Comparison of sulfasalazine and placebo in the treatment of reactive arthritis (Reiter's syndrome). A Department of Veterans Affairs Cooperative Study. *Arthritis Rheum* 1996; 39:2021–2027.
10. Flagg SD, Meador R, Hsia E, Kitumnuaypong T, Schumacher HR Jr. Decreased pain and synovial inflammation after etanercept therapy in patients with reactive and undifferentiated arthritis: an open-label trial. *Arthritis Rheum* 2005; 53:613–617.