



Single nontender ulcer on the glans

The patient's history and the clinical appearance of the ulcer led to the diagnosis of this re-emerging condition.

A 42-YEAR-OLD GAY MAN sought care for a nonhealing lesion on his penis that he'd had for 6 weeks. The patient acknowledged having unprotected sex with several partners in the month prior to the onset of the lesion. The lesion was asymptomatic and small, but rapidly developed into a superficial ulcer. The examination revealed a 1-cm ulcerated, erythematous plaque with raised and indurated edges on the glans (FIGURE). There was

minimal drainage in the periurethral area. The patient didn't have any other rashes or lesions on the skin or mucous membranes, or any regional lymphadenopathies.

- WHAT IS YOUR DIAGNOSIS?
- HOW WOULD YOU TREAT THIS PATIENT?

FIGURE

Ulcerated, erythematous plaque on the glans



IMAGE COURTESY OF: HUSEIN HUSEIN-ELAHMED, MD, PhD

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There has been a resurgence of syphilis—not just in men who have sex with men, but in all sexually active populations.

Diagnosis: Primary syphilis

The patient was given a diagnosis of primary syphilis based on his history and the clinical appearance of a syphilitic chancre. While chancres often occur on the shaft of the penis, they can also occur in the periurethral area, as was the case with this patient. The diagnosis of syphilis was confirmed with a positive *Treponema pallidum* particle agglutination assay (TPPA).

Although the primary route of transmission is sexual contact, syphilis may also be transmitted from mother to fetus during pregnancy or birth, resulting in congenital syphilis. In addition, a considerable number of men who are diagnosed with syphilis are positive for human immunodeficiency virus (HIV) antibodies.¹ (Our patient was tested for HIV; the result was negative.)

■ **The resurgence of syphilis.** In 2000 and 2001, rates of syphilis cases reached a historic low (2.1 cases per 100,000).² Since then, however, there has been a resurgence of syphilis—not just in men who have sex with men—but in all sexually active populations. In the United States during 2014 to 2015, the rate of primary and secondary syphilis increased to 7.5 cases per 100,000, which is the highest reported rate since 1994. From 2000 to 2015, this increase was primarily attributable to cases among men and, specifically, among gay, bisexual, and other men who have sex with men. But while the rate increased 18% among men during 2014 to 2015, it also increased by 27% among women.²

Social, epidemiologic, and individual risk factors can lead to higher levels of sexually transmitted diseases (STDs) in gay and bisexual men. In addition, lack of access to quality health care, homophobia, or stigma can all contribute to greater risk for this population.³ For these reasons, it is important for family physicians to immediately recognize this disease. (To learn more about the resurgence of syphilis, listen to the audiocast from Doug Campos-Outcalt, MD, MPA at <http://bit.ly/2mRvYQe>.)

The 4 stages of syphilis

The signs and symptoms of syphilis vary by the stage of disease.

■ **Primary syphilis** is the stage of initial inoculation with *T pallidum*. It is during this

stage that a firm, nonpruritic skin ulceration—a chancre—appears. Although the classic chancre is typically painless, it can be painful.

■ **Secondary syphilis** presents as a diffuse rash that frequently involves the palms and soles.

■ **The third or latent stage of syphilis** may last for 2 years with few, or no, symptoms. However, secondary and latent syphilis may entail a broad range of manifestations, which is why syphilis is known as the “great imitator.”

■ **In the final stage—tertiary syphilis—**gummas and neurologic or cardiac symptoms may be seen.

Differential includes fungal, bacterial infections

The differential diagnosis of syphilis includes other infections such as chancroid, condyloma acuminata, candidiasis, granuloma inguinale, and lymphogranuloma venereum.

■ **Chancroid** presents as multiple painful necrotizing genital ulcers that may be accompanied by inguinal lymphadenopathy. It is caused by the bacterium *Haemophilus ducreyi*.

■ **Condyloma acuminata** is characterized by skin-colored, nontender warts and is caused by the human papillomavirus (HPV).

■ **Candidiasis** is a fungal infection that is characterized by pruritus and whitish-colored patches on the penis.

■ **Granuloma inguinale (Donovanosis)** is a chronic bacterial infection caused by *Klebsiella granulomatis*. It initially appears as nodular lesions that evolve into ulcers, which progressively expand and are locally destructive.

■ **Lymphogranuloma venereum** is an STD that can be caused by 3 different types (serovars) of the bacteria *Chlamydia trachomatis*. It presents with self-limited genital papules and ulcers followed by painful inguinal and/or femoral lymphadenopathy.

Diagnosis can be confirmed with serologic tests

The diagnosis of syphilis can be made by direct identification of the bacterium or serologic tests. Direct tests include dark field microscopy of serous fluid from genital lesions. This provides an immediate diagnosis with a sensi-

tivity rate of up to 97%.⁴ However, hospitals do not always have the equipment or experienced staff to perform this technique, which must be done within 10 minutes of acquiring a sample. A polymerase chain reaction test can also be used to detect *T pallidum* DNA from specimens of any lesion exudate, tissue, or body fluid, but these tests can be costly compared with other tests used to diagnose syphilis.⁵

Serologic tests are divided into 2 groups: treponemal (specific) and nontreponemal (nonspecific) tests. Treponemal tests, which include TPPA, *T pallidum* hemagglutination assays, and enzyme-linked immunosorbent assays, will yield a positive result for current or previously treated syphilis because a positive result remains so for life. Nontreponemal tests, such as the rapid plasma reagin (RPR) test and the venereal disease reference laboratory (VDRL) test, yield a titer that is a measure of disease activity (the titer drops with treatment and rises with reinfection). Because these are nonspecific tests, biological false positives may occur if the patient has other acute or chronic infections or autoimmune diseases.⁵

Treat with penicillin

The first-choice treatment for uncomplicated syphilis is a single dose of intramuscular (IM) penicillin G (2.4 million units). A single dose of oral azithromycin 2 g or doxycycline 100 mg orally twice a day for 14 days can be used for patients who are allergic to penicillin.⁵⁻⁷ Ceftriaxone, either IM or intravenous 1 g/d for 10 to 14 days, is also effective.

■ **Our patient** declined parenteral treatment, so he was treated with oral azithromycin 2 g in a single dose. His RPR titer was taken again one week after completing the azithromycin, at which time there was a 4-fold drop (1:32 to 1:8), indicating a good response to therapy. At a follow-up appointment 6 months later, the infection hadn't recurred. We also educated the patient on the nature of the infection, how he became infected, and safe-sex practices to prevent reinfection. **JFP**

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