



Painless penile ulcer and tender inguinal lymphadenopathy

Our patient had previously been treated for syphilis. But when his symptoms persisted, further testing revealed that he was being treated for the wrong STD.

A 38-YEAR-OLD MAN presented to our emergency department with a 2-day history of fever, general malaise, and a painless genital ulcer. He denied having any abdominal pain, myalgias, arthralgias, or other rashes. He had been treated about a month earlier on an outpatient basis with penicillin for a presumed diagnosis of syphilis, but his symptoms did not resolve. His medical history included well-controlled human immunodeficiency virus (HIV), hepatitis B, hypertension, anxiety, and fibromyalgia for which he took lisinopril, emtricitabine/tenofovir, metoprolol, and darunavir/cobicistat. He smoked a half-pack of cigarettes a day and had unprotected sex with men.

On physical examination, the patient was febrile (103.1° F) with otherwise normal vital

signs. A genital examination revealed a nontender, irregularly shaped 8-mm ulcer at the base of the glans penis (FIGURE). Tender unilateral inguinal lymphadenopathy was noted on the right side.

A chart review showed a normal CD4 count (obtained 2 months earlier). We were unable to access the results of his outpatient rapid plasma reagin test for syphilis. Due to the patient's degree of pain from his lymphadenopathy, fever, and general malaise, he was admitted to the hospital for overnight observation.

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

FIGURE

Penile ulcer



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A nontender, irregularly shaped 8-mm ulcer at the base of the glans penis.

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Lymphogranuloma venereum is more commonly reported in men—primarily men who have sex with men.

Diagnosis: Lymphogranuloma venereum

Based on the patient's history and clinical presentation, we suspected lymphogranuloma venereum (LGV). A positive nucleic acid amplification test (NAAT) for *Chlamydia trachomatis* confirmed the diagnosis.

LGV is an infection caused by *C trachomatis*—specifically serovars L1, L2, and L3—that is transmitted through unprotected sex.¹⁻³ During intercourse, the serovars cross the epithelial cells through breaks in the skin and enter the lymphatic system, often resulting in painful lymphadenopathy. LGV is more commonly reported in men (primarily men who have sex with men [MSM]), but can occur in either gender.⁴ The true incidence and prevalence of LGV are difficult to ascertain as the disease primarily occurs in tropical areas, but outbreaks in the United States occur predominantly in patients infected with HIV.

The 3 stages of infection

Following an incubation period of 3 to 30 days, LGV progresses through 3 stages. The first stage involves a small, painless lesion at the inoculation site—usually the prepuce or glans of the penis or the vulva or vaginal wall. The lesion typically heals in about one week.^{1,2,4}

Two to 6 weeks later, LGV enters the second phase, characterized by painful unilateral inguinal or femoral lymphadenopathy or proctitis. Inguinal and femoral lymphadenopathy is more common in men.^{1,4} The “groove sign”—lymphadenopathy occurring above and below the inguinal ligament—is seen in 10% to 20% of men with LGV.^{1,3} In women, lymphatic drainage occurs in the retroperitoneal or intra-abdominal nodes and may result in abdominal or back pain.^{1,4} Proctitis is reported primarily in women and in MSM.^{1,4}

Tertiary LGV (aka genitoanorectal syndrome) is also more common in women and MSM, due to the location of the involved lymphatics. In this stage, chronic inflammation causes scarring and destruction of tissue.^{1,4} Left untreated, LGV can lead to lymphatic obstruction, deep tissue abscesses, chronic pain, strictures, or fistulas.^{1,3,4}

Other genital ulcers can mimic LGV

LGV can be confused with other causes of gen-

ital ulcers (such as syphilis, chancroid, herpes simplex virus, and Behçet's disease). Identification of the causal bacteria is often needed to make a definitive diagnosis.

■ **Syphilis**, caused by the spirochete *Treponema pallidum*, initially manifests as a chancre (a single, well-demarcated, painless ulcer). It is less commonly associated with inguinal lymphadenopathy and can be diagnosed via serologic testing.^{5,6}

■ **Chancroid** is caused by *Haemophilus ducreyi* and manifests as a painful ulcer with a friable base covered with a necrotic exudate. It can be associated with tender unilateral inguinal lymphadenopathy.⁵ Due to the widespread availability of culture media to test for *H ducreyi*, the diagnosis of chancroid is based on the clinical exam plus a handful of clinical criteria: painful genital ulcers, no evidence of *T pallidum* infection, and negative culture or polymerase chain reaction testing (PCR) for herpes simplex virus (HSV).

■ **HSV**, the most common cause of genital ulcers in the United States,⁵ typically manifests with multiple vesicular painful lesions, with or without lymphadenopathy. Constitutional symptoms, including fever, headache, malaise, and myalgias, occur in 66% of females and 40% of males.^{5,7} Identification of HSV on culture or PCR can confirm the diagnosis.⁵

■ **Behçet's disease** is a noninfectious syndrome associated with intermittent arthritis, recurrent painful oral and genital ulcers, uveitis, and skin lesions. While most symptoms of Behçet's are self-limited, recurrent uveitis can result in blindness. A biopsy may be warranted to diagnose Behçet's disease; the results may show diffuse arteritis with venulitis.^{5,8}

NAAT is recommended to confirm the diagnosis

In the outpatient setting, diagnosis of LGV relies on physical exam, clinical presentation, confirmation of infection, and exclusion of other causes of genital ulcer, lymphadenopathy, and proctitis.³ Diagnostic tests include culture identification of *C trachomatis*, visualization of inclusion bodies on immunofluorescence of bubo aspirate, and positive serology for *C trachomatis*.¹⁻³ (Serology to differentiate LGV from non-LGV *C trachomatis* serovars is difficult and not widely available.)



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Recommendations regarding lab studies have shifted away from serologic testing and toward the use of NAAT. NAAT via PCR has a sensitivity and specificity comparable to invasive testing methods: 83% and 99.5% with urine samples and 86% and 99.6% with cervical samples, respectively.⁹ NAAT has a sensitivity and specificity that is superior to culture for detecting chlamydia in rectal specimens¹⁰ and is preferred by patients because it doesn't require a pelvic exam or a urethral swab.

Treat with antibiotics

Oral antibiotics are the treatment of choice for LGV. Standard treatment includes doxycycline 100 mg bid for 21 days. Women who are pregnant or lactating may alternatively be treated with macrolides (eg, erythromycin).^{1,2,4} Buboec may be aspirated for pain relief and to prevent the development of ulcerations or fistulas.^{3,4}

■ **Our patient** was started on oral doxycycline, which resolved his fever and reduced the size of his ulcer. He was discharged on oral doxycycline and continued on the full 21-day course. Two weeks later, the ulcer and lymphadenopathy had completely resolved. On follow-up in our office, the resident physician who treated the patient in the hospital discussed future use of safe sexual practices. **JFP**

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