Young Man With Painless Penile Ulcer

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For 2 weeks, a 30-year-old homeless man has had an enlarging ulcer on the shaft of his penis.

**History.** The patient had sexual relations with an unknown partner about 3 weeks earlier. The lesion started as a red papule that quickly eroded to form a painless ulcer with serous discharge; it was associated with asymptomatic swelling in the groin.

The patient denies fever or chills, urethral discharge, and urinary symptoms. He has no history of genital or mouth ulceration. There is no rash or joint swelling and no history of chest pain, dyspnea, palpitations, ankle edema, headache, vision problems, cognitive dysfunction, muscle weakness, paresthesia, syncope, seizures, or ataxia.

The patient smokes 1 pack of cigarettes and drinks 6 beers a day; he uses marijuana regularly. He is a sexually active heterosexual with multiple partners. He takes no medication.

**Examination.** This fairly well-built and well-nourished man is unkempt but not in undue stress. The heart rate is 74 beats per minute and regular; respiration rate, 20 breaths per minute; blood pressure, 124/72 mm Hg. Hydration status is good. There is no evidence of anemia, clubbing, or cyanosis. Examination of the head and neck is unremarkable. There is no thyroid enlargement. The patient has a single large, painless, punched-out ulcer on the penile coronal sulcus. The ulcer has wide rolled edges and an indurated base and exudes a clear serous discharge. Mildrubberly, nontender, nonfluctuant inguinal adenopathy is noted on the right side. Other systemic examination results are normal.

**Laboratory studies.** White blood cell (WBC) count, 7200/µL with a normal differential. Hemoglobin level, 12.9 g/dL; platelet count, 180,000/µL; erythrocyte sedimentation rate, 28 mm/h. Urinalysis results are normal. Gram staining of serous discharge from the ulcer reveals a few WBCs but no organisms. No giant cells are seen on Tzanck testing.

The patient is promptly sent to the public health department for dark-field examination of the serous discharge.

Based on the clinical picture and the initial laboratory findings, what is the most likely diagnosis?

A. Primary syphilis
B. Herpetic penile ulcer
C. Chancroid
D. Granuloma inguinale
E. Squamous cell carcinoma of the penis

*(Answer and discussion begin on the next page.)*

**WHAT'S WRONG:**
The dark-field examination shows typical *Treponema palladium* spirochetes. This finding in a patient with a history of multiple sex partners and a single painless, clean-cut ulcer with indurated base and rubbery, nontender inguinal adenopathy on the ipsilateral side points to a diagnosis of primary syphilis.
primary syphilis, A.

Further evaluation revealed positive results on rapid plasma reagin (RPR) and fluorescent treponemal antibody absorption (FTA-ABS) testing. Culture of the discharge was negative for herpesvirus. Results of HIV testing were negative.

Management. The patient was treated with benzathine penicillin G, 2.4 million units IM. When he was examined 10 days later, the chancre had healed completely.

EPIDEMIOLOGY AND CLINICAL MANIFESTATIONS

Since 2000, the incidence of primary and secondary syphilis has increased significantly, from 2 to 6 cases per 100,000 to 4 to 7 cases per 100,000. About 64% of cases are in men, many of whom engage in homosexual activity.

The incubation period of primary syphilis is usually between 3 and 4 weeks. The first clinical manifestation is a chancre at the site of the initial treponemal invasion of the dermis, usually on or near the genitals. Chancres are typically larger than 0.5 cm and solitary, although they can be multiple. Most patients do not have constitutional symptoms. DIFFERENTIAL DIAGNOSIS

Genital ulcers are generally categorized as either painful or painless (Table). A painless, discrete solitary ulcer is a hallmark of syphilis.

Painful ulcers may be associated with the following conditions:

- **Herpes simplex virus** (HSV) infection caused by HSV-2 or HSV-1. Genital herpes ulcers are discrete or confluent. They are small, well-demarcated, and shallow; have a red base; and are associated with painful regional adenopathy.
- **Chancroid**, a contagious infection of genital skin, is caused by *Haemophilus ducreyi*. The multiple ulcers (at times "mirror image" ulcers) may be superficial or deep with an irregular, undermined, erythematous margin and a beefy, granular base. The inguinal lymph nodes become enlarged, painful, and suppurative; a chronic draining fistula may result.
- **Granuloma inguinale**, which is rarely seen in the United States, is caused by *Calymmatobacterium granulomatis*. The initial lesion is a painless nodule that enlarges into a painful hypertrophic, velvety, indurated, beefy red ulcer. Absence of lymphadenopathy is a diagnostic characteristic; however, in patients with complicated granuloma inguinale, secondary infection may produce inguinal adenopathy.
- **Squamous cell carcinoma** of the penis presents with a painful, progressively worsening deep ulcer that has shaggy borders and a necrotic base. It is associated with painful, hard regional adenopathy.
- **Behçet disease** is characterized by recurrent nonspecific, painful ulcers of the oral and genital mucosa.
- **Traumatic ulcer** of the penis is usually painful; it is characterized by sharp, angled borders.

DIAGNOSTIC TESTING

The workup begins with a targeted clinical history and physical examination. Laboratory studies include serologic tests and, if appropriate, dark-field microscopic examination of serous fluid from the primary chancre. The dark-field examination, which is ordered when primary syphilis is strongly suspected and quick confirmation is needed, reveals typical bright, corkscrew-shaped spirochetes with narrow coils, deliberate forward and backward movement, and rotation about the longitudinal axis.

Serologic testing is more widely used in the diagnosis of syphilis. Two classes of test are used:

- Nontreponemal tests, which detect syphilitic reagin, include VDRL and RPR tests. These tests may be either qualitative or quantitative. Qualitative nontreponemal tests are used in screening and must be followed by confirmatory specific treponemal tests. In patients with primary syphilis, reactivity in these tests does not develop until 1 to 4 weeks after the chancre first appears. Thus, if results of the first test are negative, the test should be repeated at 1- and 3-month intervals. False-positive results may occur with disorders such as
systemic lupus erythematosus, malaria, and hepatitis.
- Specific treponemal tests include FTA-ABS, \textit{T palladium} particle agglutination, and microagglutination assay for antibodies to \textit{T palladium}. These confirmatory tests usually become positive with 3 to 6 weeks and remain so for many years, despite effective treatment.

**TREATMENT**

Parenteral penicillin G is the drug of choice to resolve the lesions and prevent sexual transmission and late sequelae. The recommended treatment for adults is a single dose of benzathine penicillin G, 2.4 million units IM. Patient who are allergic to penicillin may be given a 14-day course of oral doxycycline, 100 mg bid, or oral tetracycline, 500 mg qid. Ceftriaxone, 1 g IV or IM per day for 8 to 10 days, is effective for early syphilis. A single 2-g dose of azithromycin has been effective in primary syphilis. However, evidence of widespread resistance to azithromycin in \textit{T palladium} has recently been reported in San Francisco.

### Table — Differential diagnosis of common genital ulcers

- **Painless**
  - Syphilis
  - Uncomplicated granuloma inguinale
  - Staphylococci
  - Neisseria
  - Corynebacterium
  - Anaerobes

- **Painful**
  - Sexually transmitted infection with herpes simplex virus type 2 or type 1
  - Chancroid
  - Complicated granuloma inguinale

- **Nonsexually transmitted**
  - Behçet syndrome
  - Squamous cell carcinoma
  - Traumatic

**References:**

**FOR MORE INFORMATION:**


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