Case Presentation & Question 1

History of Present Illness

A 43-year-old black woman presents with the chief complaint of increasing vulvar swelling and discomfort over the past 6 months, as well as fever and malaise over the past 4 weeks. She states that approximately 1 year ago, she had a tender, swollen right inguinal lymph node, which was surgically drained and then resolved. However, this edematous process began again approximately 6 months ago, which now includes her entire vulva. She also notes passage of stool from the vagina.

Past Medical History

The patient has no significant past medical history and takes no medications. Her past surgical history is significant only for a right breast biopsy for a nontender mass that was found to be benign. She has normal menses at regular monthly intervals and a history of multiple sexual partners, but has not had any sexually transmitted diseases or abnormal Pap smears. Her last Pap smear, taken 18 months ago, was normal. She is married and states that she has been monogamous for 6 years. There is no significant family history. The patient has smoked a pack of cigarettes a day for 25 years and drinks a liter of alcohol a week. She denies the use of illicit drugs. She reports no travel over the past 4 years; however, her husband travels for business.

Physical Examination

The patient appears well but in discomfort. She is afebrile; her weight and other vital signs are normal. General physical examination and mental status examination are unremarkable. No skin abnormalities are noted, with the exception of the findings on pelvic examination, which reveals enlarged, irregular, edematous labia bilaterally, with complete distortion of the right labia majora caused by edema and fecal soiling. Tissue bridges and draining sinuses were visually noted, as well as rectovaginal fistula and several nonconnecting sinus tracts. An internal examination could not be performed because of pain. The patient did not recall receiving any antibiotics.

1. What is the most likely diagnosis?

☐ A) Lymphogranuloma venereum

☐ B) Granuloma inguinale

☐ C) Vulvar carcinoma

☐ D) Hidradenitis suppurativa
E) Primary genital herpes

Discussion 1

Discussion of Answer

Lymphogranuloma venereum (LGV) is correct (Figures 1-4). LGV is rare in North America, with fewer than 350 cases a year occurring in the United States.[1] It is more commonly encountered in Southeast Asia and Africa. The causative organism for LGV is *Chlamydia trachomatis* serotype L1, L2, or L3. The incubation can last from a few days to 21 days. The primary lesion of this disease is a painless ulcer, which often goes unnoticed and resolves spontaneously. In the following weeks, the secondary stage presents as painful lymphadenopathy in the inguinal lymph nodes. In the absence of treatment, the overlying skin becomes brawny and wrinkled, with a characteristic violaceous hue, and the abscesses within the nodes coalesce and drain from one or more sinus tracts. The tertiary stage is manifested as an anogenital syndrome with formation of perirectal abscesses, rectal strictures, and fistulas; this stage is usually seen in women and homosexual men. The patient usually has a mild leukocytosis with elevated monocytes and eosinophils.[2]

![Figure 1. Vulva and perineum. Right labia with distortion from lymphedema. (personal photo)](http://www.medscape.com/viewarticle/407785_print)
**Figure 2.** Vulva and perineum. Right labia with distortion from lymphedema. (personal photo)

**Figure 3.** Vulva and perineum. Right labia with distortion from lymphedema. (personal photo)
LGV is best diagnosed by combining clinical and serologic data. Cell culture is available at most large medical centers but has variable specificity. Furthermore, stringent transport requirements and high cost make this method of detection less appealing. Serologic detection of antibodies to *C. trachomatis* by complement fixation or by enzyme-linked immunosorbent assay (ELISA) in the correct clinical setting suggests the diagnosis. Although highly sensitive, the complement fixation test also cross-reacts with other *Chlamydia* species, especially *C. psittaci*.[3] By contrast, ELISA has greater specificity, especially in high-risk populations. *C. trachomatis* antibodies are common in the general population, but LGV as an invasive disease appears to induce significantly higher antibody titers. Therefore, a high titer is generally required to confirm the diagnosis. However, given the nonspecificity of these tests, these should be used as an adjunct to the clinical diagnosis.

Histopathologically, a typical "stellate" abscess may be seen. This is highly suggestive of the diagnosis. More often, the nonspecific changes of abscess and chronic inflammation are noted and organisms cannot be seen.

The presumed risk factor in this patient was her spouse, who maintained an occupation that required international travel. Although they are not asked about in a typical social history, risk factors of sexual partners must be investigated. This patient probably acquired her disease from her husband.

Granuloma inguinale (b) is incorrect (Figures 5, 6). Granuloma inguinale is an ulcerative bacterial infection of the genitalia that is endemic in New Guinea, Southeast India, southern Africa, the Caribbean, and nearby areas of South America.[4] Cases in the United States are probably imported. The causative agent is *Calymmatobacterium granulomatis*. The infectious process begins as painless, subcutaneous nodules that erode the skin and ulcerate. Secondary infection may occur with necrotic debris on or around the ulcer. The time course for the appearance of such nodules is typically days to weeks, which is inconsistent with the lapse of several months seen in this patient. Fever and other systemic symptoms are also uncommon in granuloma inguinale, as is lymph node involvement, but pseudobuboes in the inguinal area occur. To rule out granuloma inguinale, a smear or biopsy specimen of the ulcer margins should be obtained to identify Donovan bodies, which are the *C. granulomatis* organisms and appear as pleomorphic rods with a characteristic "safety-pin" shape. Giemsa stain, Wright's stain, and various silver stains can be used to identify the organisms, which appear blue or black on staining.
Figure 5. Typical "beefy appearance" of perineum in a woman with granuloma inguinale. Reprinted from Morse SA, Moreland AA, Holmes KK, eds. Atlas of Sexually Transmitted Diseases and AIDS. 2nd ed. St. Louis, Mo: Mosby-Wolfe; 1995:90, Fig. 5.8.

Figure 6. Granuloma inguinale of the vulva with labial edema and perianal extension. Reprinted from Morse SA, Moreland AA, Holmes KK, eds. Atlas of Sexually Transmitted Diseases and AIDS. 2nd ed.
Vulvar carcinoma (c) is incorrect. Vulvar carcinoma is more likely to occur in older populations and may present as epithelial and dermal breakdown that leads to fistula formation. Genital ulceration is a common presentation of this entity. Biopsy is necessary to make a definitive diagnosis of vulvar carcinoma. Given this patient's symptoms, the diagnosis of vulvar carcinoma must be considered in the differential diagnosis. However, given the normal gynecologic examination and Pap smear 18 months before presentation, vulvar carcinoma is much less likely than the other choices.

Hidradenitis suppurativa (d) is incorrect (Figures 7A,B). Hidradenitis suppurativa is a chronic, suppurative inflammatory disease that affects apocrine glands, usually in the axillary and inguinal areas. The exact prevalence of this disorder is unknown, but it is estimated to be 1:300.\(^5\) The cause of hidradenitis suppurativa remains obscure, but hyperkeratosis of the terminal hair follicle is evident with ensuing occlusion and dilatation. Bacterial involvement is not the primary pathogenic event but is secondary to the disease process. Onset is insidious with erythema, itching, and the appearance of firm pea-sized nodules. These nodules may rupture spontaneously and produce a purulent discharge. Lesions fibrose and eventually recur in surrounding areas. With time, the formation of scars, multiple sinus tracts, and subcutaneous abscesses may occur. Lymphadenopathy is rare in advanced disease. Surgical resection of the involved areas may be necessary in severe cases. Antibiotics can be used for acute superinfections but have no role in long-term treatment.

This entity can progress to anal, rectal, or urethral fistulas, as is demonstrated in this patient. However, hidradenitis suppurativa is typically chronic and recurrent, often beginning in adolescence with premenstrual-associated exacerbation. Although hidradenitis suppurativa must be considered in the differential diagnosis, this patient's history is inconsistent with this disease.

Primary genital herpes (e) is incorrect (Figure 8). Primary genital herpes caused by the herpes simplex virus (HSV) occurs in persons who are newly exposed to the virus. The illness usually begins with a flulike syndrome (ie, fatigue, malaise, myalgia, nausea, and fever) 3 to 5 days after sexual activity with the source contact. Lesions begin as vesicles that soon progress to painful ulcerations. The classic description of these ulcers is a cluster of painful white ulcerations of varying size on an erythematous base. Although primary genital herpes can cause extensive ulcerations and tissue destruction, the course of the disease is self-limited and the lesions heal without scarring. Chronic ulceration with sinus tract and fistula formation is not a manifestation of primary genital herpes. The diagnosis is often made on clinical grounds but can be confirmed with a Tzanck smear of vesicular fluid or a viral culture. This patient gave neither a history consistent with this description of vesicles and ulceration nor a time course consistent with genital herpes.
Case Continuation & Question 2

The patient is admitted to the hospital. Biopsies and wound cultures are obtained. Titers for *Chlamydia* and cultures for *Nocardia*, acid-fast bacilli, and HSV are taken. Biopsy shows benign squamous epithelium with submucosal chronic inflammatory changes. Given the clinical findings, *Chlamydia* serology is considered positive with the complement fixation titer greater than 1:32. Stains for *C. granulomatis* and viral cultures are negative. The diagnosis of LGV is confirmed.

2. Which of the following choices represent the most appropriate management of this case?

- A) Surgery with excision of involved tissue
- B) Tetracycline
- C) Erythromycin
- D) Corticosteroids

Discussion 2

Discussion of Answers

Management of LGV varies by stage of disease. The early stages of genital ulcers and lymphadenitis respond to a 3-week course of tetracycline (100 mg twice daily). Erythromycin (500 mg 4 times daily) is considered an alternative treatment but would be the primary treatment if the patient were pregnant. Sulfadiazine also appears to have some activity; it is administered at a loading dose of 2 g, followed by 4 g per day for 10 to 28 days. Once the disease progresses to the tertiary stages, devastating complications can occur; antibiotic therapy alone may not suffice, and surgical intervention may become necessary.

As a result of the extensive destruction, this patient required a prolonged, stepwise approach with surgical and medical therapy. She was given a 6-week course of tetracycline because of the tissue induration and suspected poor perfusion with gross fecal contamination. A temporary diverting colostomy was performed 1 week after pelvic and rectal examination under anesthesia. Examination revealed visible draining sinuses in the perirectal area. Proctoscopic examination revealed involvement of the anal margin with a large LGV lesion. The rest of the anal canal was essentially normal.
After a healing period of 17 weeks, the patient underwent a partial vulvectomy, repair of a rectovaginal fistula, and debridement of the remainder of the affected perineum. A split-thickness skin graft of the debrided area was performed 1 week later.

Three months later, after the skin graft had healed, the patient underwent closure of the colostomy. At that time, there was no evidence of fistula in the rectum or vagina.

**Conclusion**

Although LGV is rare in the United States, Epling and Reich in 1988 reported an outbreak of LGV in central Florida that was linked to prostitution.[8] In fact, 2 months after the presentation of this patient, a second woman came to the same clinic with a case of LGV. The prevalence of LGV is rising as a result of increased global travel, migration, and immigration. Because LGV starts as a painless ulcer and resolves rather quickly, it is often misdiagnosed in the primary stage. Because of the seemingly harmless first stage of this disease, it can be transmitted unknowingly to other people. Although LGV is rare in developed countries, all clinicians should be mindful of this entity to prevent the spread and the destructive tertiary stage of this disease.

**References**