VISUAL DIAGNOSIS

Vulvar Ulcers in a Non–Sexually Active Adolescent

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PRESENTATION

A 16-year-old girl with no significant medical history presents with 5 days of vulvar pain and dysuria. She endorses a constant, sharp, burning labial pain. She has been febrile intermittently, with an initial maximum temperature of 103°F (39.4°C) 2 days earlier. She has been nauseous and experienced 1 episode of nonbloody, nonbilious emesis yesterday. Due to fear of urination, she has stopped eating and drinking the past 2 days. She has been using acetaminophen and ibuprofen every 6 to 8 hours for the past 5 days with no improvement in pain. She denies vaginal discharge, hematuria, urinary urgency or frequency, any sexual activity or trauma, new body products, or douching. She denies a history of arthralgias, rash, fatigue, hematochezia, visual changes, weight loss, recent upper respiratory tract infection symptoms, or recent vaccinations. Her menstrual periods come regularly every 28 days and last approximately 4 days. The first day of her last menstrual period was 2 days ago, and she is actively menstruating. She endorses a history of oral "cold sores" but denies previous genital lesions. Family history is negative, including no family history of autoimmune processes.

She has been seen by her primary care physician twice and in an emergency department once this week, diagnosed each time with a suspected urinary tract infection or yeast infection. Before admission, an initial complete blood cell count and complete metabolic panel in the emergency department were normal, and a urine pregnancy test was negative. A urinalysis in the emergency department was notable for amber color and a specific gravity of 1.028, protein level of 100 mg/dL, greater than 80 mg/dL ketones, positive nitrites, large blood, large leukocyte esterase, white blood cell count greater than 200 WBC/hpf, red blood cell count greater than 200 RBC/hpf, positive bilirubin, and moderate bacteria. However, urine culture data from these visits show no bacterial growth. She has now completed 2 days of cefalexin therapy, 2 days of metronidazole therapy, 1 day of nitrofurantoin therapy, and 1 dose of fluconazole. She was also prescribed trimethoprim/sulfamethoxazole but has not taken it yet. None of these antimicrobial agents, or phenazopyridine, have relieved the pain.

Vital signs on presentation are notable for tachycardia to the low 100s beats/min. She is otherwise afebrile, normotensive, and has a normal respiratory rate and oxygen saturation on room air. She has dry mucous membranes, but no oral lesions are noted. Genital examination is pertinent for bilateral, shallow, tender vaginal ulcerations along the labia minora and vaginal introitus, as well as edema of the labia majora (Fig 1). There is no visible discharge or bleeding or any perianal lesions. A pelvic examination is deferred due to patient discomfort. Examination is not notable for inguinal lymphadenopathy.

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Figure 1. Vulvar ulcerations on arrival.

Due to the need for intravenous pain control and Foley catheter placement for urination (Fig 2), the patient is admitted to the hospital. Gynecology and rheumatology are consulted on arrival at the general pediatrics floor, recommending a full laboratory evaluation for sexually transmitted infections. Testing for chlamydia, gonorrhea, trichomonas, human immunodeficiency virus, syphilis, bacterial vaginosis, and yeast are unrevealing. Polymerase chain reaction (PCR) testing for herpes simplex virus (HSV) types 1 and 2 was negative. There is low concern for a systemic autoimmune process, such as Bechet disease or systemic lupus erythematosus, given the lack of other features on history/clinical examination, including pathergy, oral ulcers, eye or brain involvement, joint involvement, lack of recurrent symptoms, and lack of typical ethnicity. Similar, "knife-life" ulcerations can be seen with cutaneous Crohn disease. However, inflammatory bowel disease is deemed less likely given her lack of gastrointestinal symptoms.

Dermatology is also consulted, recommending antibody titers for Epstein-Barr virus (EBV), cytomegalovirus, and mycoplasma. This infectious evaluation is significant for EBV IgG elevation to 3.2 Ab index, and an EBV nuclear capsid antibody elevation to 63.3 U/mL (positive result >21 U/mL). The patient's history and examination findings confirm the diagnosis.

Figure 2. Vulvar ulcerations on hospital day 2, with Foley placement.

DIAGNOSIS

The patient was diagnosed as having Lipschutz ulcers, also known as non–sexually acquired genital ulceration.

DISCUSSION

Genital ulcers, although less common in pediatrics than in the adult population, have an annual global incidence estimated near 20 million cases. When considering the etiology of genital ulcers, one may first investigate infectious, which are more common, followed by noninfectious causes. (1) The most common infectious causes (in order of frequency) are genital HSV-1/2, syphilis, chancroid (although rates have vastly declined in the United States in the past decade), lymphogranuloma venereum, granuloma inguinale (donovanosis), fungal infection such as candida, or a secondary bacterial infection of preexisting trauma. The most common noninfectious causes include Behcet syndrome, fixed drug eruptions, psoriasis, sexual trauma, and Wegener granulomatosis. (1) Less common causes of noninfectious genital ulcers to consider also include inflammatory bowel disease and other autoimmune processes, such as systemic lupus erythematosus.

Lipschutz ulcers, although often described as an immunologic response to infection or inflammation, are a noninfectious etiology of genital ulcers most commonly found in non–sexually active women younger than 20 years. (2) The exact prevalence is unknown. Symptoms typically begin with prodromal flulike symptoms, followed by the appearance of 1 to 3 large (>10 mm), well-demarcated, painful vulvar ulcerations in a "mirrorlike" distribution. (2)(3) They are often accompanied by labial edema. (4) Dysuria to the point of requiring catheterization is relatively common, affecting nearly 10% of documented Lipschutz cases. (2) Inguinal lymphadenopathy, although not observed in this patient, can also accompany ulcerations in close to 10% of cases. (2)

The most commonly associated infections include (in order of frequency) EBV, mycoplasma, cytomegalovirus, and influenza. (2) Recently, cases of vulvar aphthous ulcers after COVID-19 infection and vaccination have also been reported. (5) This rare diagnosis is one of exclusion, namely, of the aforementioned infectious and rheumatologic causes

of similar presentations. Evaluation should entail skin swabs for PCR testing and culture. PCR remains the most sensitive and specific testing modality for HSV-1/2. Biopsy tends to be traumatic, and findings are nonspecific. (4)

Lipschutz ulcers tend to resolve without recurrence or scarring within 3 weeks, with approximately 10% of cases lasting longer than 1 month. (2) Treatment typically includes reassurance, local hygiene and removal of irritating factors (such as tight clothing or scented soaps or panty liners), wound care, and pain control. (2)(4) Topical corticosteroids are useful for pain control and facilitating healing. A recent systematic review of Lipschutz ulcers did not support the use of systemic corticosteroids in treatment because disease duration was shorter in patients who did not receive systemic corticosteroids. However, this review did not account for clinical severity of disease. (2) Although topical lidocaine 5% ointment was not used in this case, it remains a safe and viable option for local pain control in vulvar ulcerations.

PATIENT COURSE

This patient had a severe course that required a several-day admission for pain control, requiring intravenous morphine. Per dermatology recommendations, she was started on systemic prednisone 0.5 mg/kg once daily and 2.5% topical hydrocortisone ointment twice daily. She required intravenous fluid resuscitation and Foley placement to maintain normal urination while the systemic corticosteroids facilitated healing. She was discharged on hospital day 4 with resolution of her pain using naproxen, prednisone, and topical hydrocortisone. Her lesions were nearly completely resolved by her 1-week follow-up appointment with the pediatrician and have not since recurred.

Summary

- Lipschutz ulcers should be considered when young, non–sexually active females present with painful vaginal ulcerations. They may be associated with labial edema, dysuria, and inguinal lymphadenopathy.
- Lipschutz ulcers are a diagnosis of exclusion and should be considered after more common causes of vaginal ulceration (both infectious and noninfectious) have been ruled out.
- The treatment of Lipschutz ulcers is mainly supportive care and pain control. Topical corticosteroids (and even systemic corticosteroids) may be beneficial in healing; however, further randomized controlled trials are warranted to investigate efficacy.
- Nearly all Lipschutz ulcers resolve within 4 weeks of onset without recurrence or long-term sequelae.