CLINICAL VIGNETTE

"Razorblade" Dysuria: A Case of Primary Genital HSV-1

Heng-Yi Liu, BA and Sarah Goldgar, MD

Introduction

Dysuria is an often-seen symptom in the outpatient primary care clinic and is most commonly due to a urinary tract infection (UTI).[1] But there are other causes of dysuria clinicians should keep in mind. We present a case of a young woman with dysuria that was first treated as pyelonephritis but ultimately found to be primary genital HSV-1. We will review the presentation, testing, and treatment of this disease. We will also discuss changes in HSV-1 infection and HSV seroprevalence that are producing increasing cases of primary genital HSV-1, a trend likely to continue.

Case Presentation

A 27-year-old female presented to an urgent care clinic after two days of "peeing razorblades." She reported dysuria with increased urgency and frequency along with chills, fatigue, nausea without emesis, and a mild headache. She denied hematuria, vaginal discharge, muscle aches, diarrhea, chest pain, dyspnea, cough, or loss of taste and smell. Past medical history included recurrent urinary tract infections and dyspareunia following coitarche that was successfully managed with pelvic floor physical therapy, serial dilation, and topical estrogen. No contributory social or family history was obtained. During initial evaluation, her vitals were significant for a temperature of 100.3 F and pulse of 104. Although physical exam was unremarkable per review of the chart and showed no costovertebral angle tenderness, point-of-care urine testing was positive for nitrites and leukocytes. The suspicion for pyelonephritis was high, with coexisting acute COVID-19 infection also being considered. The patient was given intramuscular ceftriaxone and discharged home on oral cephalexin, with pending urine culture and respiratory infection tests. The urine culture later showed no growth and her COVID-19 testing was negative.

Three days later, she returned for follow-up. Although the fever, headache, and chills had improved, her severe "razorblade" dysuria was persistent. She had taken over-the-counter phenazopyridine for symptom relief. During her visit, she noted vaginal redness and sensitivity to friction from undergarments. She reported having one lifetime sexual partner with a history of cold sores and unspecified negative STI screens. Pelvic inspection revealed mild erythema and three small vesicular lesions on the left labia. Urinalysis and comprehensive STI screening were obtained, and valacyclovir was started for suspected genital herpes simplex virus (HSV) infection. The diagnosis of HSV-1 was confirmed by positive lesion and blood PCR results, and the patient reported complete resolution of symptoms after finishing a ten-day course of valacyclovir.

Discussion

Dysuria is a common complaint in the outpatient setting. Acute dysuria is most often due to an infectious etiology, with acute cystitis the most common cause in women. Although clinicians typically associate dysuria with a UTI, dysuria can have several causes. Along with cystitis, these can include pyelonephritis, vaginitis, pelvic inflammatory disease, cervicitis, balanitis, sexually transmitted infections (STI), local trauma, interstitial cystitis, urethral stricture, noninfectious urethritis (i.e., reactive arthritis), dermatitis, or Bechet syndrome.[1,2] Dysuria associated with vaginal irritation, discharge, or lesions should prompt physical examination, and the presence of genital ulcers should specifically trigger consideration of STIs such as syphilis, genital herpes, chancroid, and donovanosis.[1] We discovered genital HSV-1 as the cause of dysuria and discuss the reasons practicing clinicians may see increasing cases of genital HSV-1.

Genital herpes is a common, sexually transmitted infection in the United States, with around 1 million new cases each year.[3] The responsible infectious agent is the herpes simplex virus (HSV), an enveloped linear double-stranded DNA virus with two main serotypes, HSV-1 and HSV-2. Transmission results from physical contact during periods of viral shedding from skin or secretions. HSV infection classically presents with painful single or clustered vesicles that often ulcerate. Symptoms of active disease can also include prodromal pain, tingling, burning, or itching at the exposure site.[4] Primary infections may cause fever, headache, myalgia, and lymphadenopathy.[3,4] Most cases, though, are asymptomatic or lack recognizable clinical signs or symptoms.[3,5] Symptomatic HSV-1 and HSV-2 genital infections are clinically indistinguishable. After symptom resolution, viral DNA persists in the sensory ganglion. Many patients are unaware of this latent infection, which can cause milder subsequent outbreaks upon reactivation. Recurrence is common in the first year after primary infection, though frequency and severity of episodes typically diminish over time.[3]

HSV infection may be suspected based on history and examination, but the diagnosis is generally confirmed with PCR testing of an active lesion, which has sensitivity and specificity greater

than 95%.[3] Serologic testing is not typically indicated because antibodies are absent at the onset of initial infection or remain positive indefinitely after exposure. Serologic testing can be used if the history is consistent with HSV and no lesions are present, but is not recommended as a screening test without a history of HSV symptoms.[3] If obtained, HSV type-specific serology can guide patient counseling.[3,6] HSV-2 infection is nearly always sexually acquired, so positive serology localizes infection to the anogenital region.[3] Presence of HSV-1 antibodies is less informative because both oropharyngeal and genital infection can have positive serology. HSV-1 is also commonly acquired from salivary exchange in childhood, rather than sexual transmission. Regardless, treatment should not be delayed while awaiting lab results.

The treatment of genital HSV infections relies on antiviral medication and is the same for both serotypes. Acyclovir, famciclovir, and valacyclovir are three equally effective inhibitors of viral DNA polymerase that have been shown to provide clinical benefit in randomized trials for treatment of HSV infection.[3,6] The latter two have high oral bioavailability, although valacyclovir is sometimes preferred due to less frequent dosing. The first episode of genital HSV should always be treated given the risk of severe or prolonged symptoms.[6] Subsequent treatment of HSV can be either episodic or suppressive. Daily suppressive treatment reduces episode severity, duration, and recurrence and also lowers the risk of transmission but does not eliminate latent infection, which is lifelong.[3] Episodic treatment is used as-needed for recurrent symptoms. The choice of episodic versus suppressive therapy depends on the frequency of recurrences, number of sexual partners, and a patient's psychosocial needs. Treatment with topical acyclovir has been shown to be ineffective, and there is currently no vaccine for HSV prevention.[3] Patient counseling on the clinical course of HSV, condom use, and avoidance of sexual activity during recurrences is also important for preventing transmission of the virus.

Although the clinical presentation and treatment of genital HSV-1 and HSV-2 are similar, the prognosis is not. HSV-1 infections produce fewer symptomatic recurrences and have lower viral shedding, making risk of transmission lower and improved the overall prognosis for patients.[7,8] One study noted that the recurrence rate for genital HSV-1 is about 20% of the recurrence rate for genital HSV-2 in the first year of infection, and the recurrence rate for genital HSV-1 declines around 50% between the first and second years.[8] This difference should be considered when counseling patients and may affect whether to use patient-initiated episodic rather than suppressive antiviral therapy.

Traditionally, genital herpes infections have been associated with HSV-2 and orofacial disease with HSV-1. But more recent studies have shown a rise in HSV-1 genital infection compared to HSV-2, an important trend for clinicians to know about. A 1999 study monitoring HSV incidence found equal rates of new HSV-1 genital infections and HSV-1 oropharyngeal infections.[9] A 2003 retrospective review from a university health system showed an increase in the proportion of HSV-1 genital isolates from 31% in 1993 to 78% in 2001.[7] In a 2010 study of college students, HSV-1 accounted for 78% of female and 85% of male genital HSV infections.[10] A 2013 prospective study of U.S. women found that clinically recognized HSV-1 infections presented as genital disease three times more often than oral disease.[5] The same study also found primary genital herpes more likely to be caused by HSV-1 than HSV-2.[5] This increase in genital HSV-1 infections has been attributed to more oral-genital contact during sex, the use of condoms for vaginal intercourse (reducing exposure to genital HSV-2), and changes in viral evolution.[7]

Another reason genital HSV-1 infections are increasing is the declining rates of HSV-1 infection in young people. Studies of the U.S. population from 1999-2016 using NHANES data found declining HSV-1 seropositivity.[11,12] This results in an increased number of people vulnerable to primary HSV-1 infection. Since HSV-1 antibodies can lessen the severity of primary HSV-2 genital infections as well, reduced HSV-1 seroprevalence portends not only increased risk of primary HSV-1 infections in adults but also potentially more severe HSV-2 genital herpes cases.[11] With the declining seropositivity in young people and the rising rates of genital HSV-1, genital herpes should be considered in the differential diagnosis for complaints of dysuria in sexually active patients.

Conclusion

(1) When evaluating dysuria, the sexual history and genitourinary exam are important diagnostic tools. The potentially sensitive nature of questions and maneuvers demands clear, nonjudgmental communication and thorough examination. Poor information-gathering can lead to misdiagnosis and undertreatment.

(2) Considering recent seroprevalence trends and rising rates of HSV-1 genital infection, genital HSV infection should be part of the differential diagnosis for dysuria. Viral etiologies should especially be considered if dysuria persists despite antibiotic therapy. Complications of HSV can be serious and can include acute urinary retention, aseptic meningitis, disseminated infection, increased risk of HIV infection, and vertical transmission to neonates if disease is active in pregnancy.

(3) Understanding the increase in HSV-1 relative to HSV-2 genital infection should also influence patient counseling and management.

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