Follmann Balanitis: An Unusual Case of Syphilis

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ABSTRACT

A 33-year-old man presented with suprapubic abdominal pain and small vesicular lesions on the foreskin of the penis. Based on the presentation, he was empirically treated for genital herpes, although the herpes simplex virus swab was negative. He returned to the emergency department 4 months after his initial presentation with worsening symptoms that were consistent with balanoposthitis and cystitis. He was tachycardic and febrile on presentation. He denied any sexual contact for the last 3 months, with previous negative screening tests for sexually transmitted infections. Syphilis was eventually diagnosed during this admission. The incidence rates of syphilis have increased in recent years, and the infection is often undiagnosed given atypical manifestations. Here we present an atypical manifestation of syphilis that was initially misdiagnosed as herpes simplex virus.

INTRODUCTION

Treponema pallidum is a sexually transmitted infection that has been on the rise in the United States and internationally.[1] In the United States, men who have sex with men have the highest infection rates.[2] Minority women also tend to experience high infection rates, and internationally, there has been a concerted effort to improve testing and screening in low- and middle-income countries.[3] With the increased incidence worldwide, greater vigilance is needed for atypical presentations of syphilis.

CASE PRESENTATION

A 33-year-old heterosexual man with past medical history of gastroesophageal reflux disease and herpes simplex virus (HSV) infection presented to the emergency department (ED) in August 2022 with suprapubic abdominal pain and small painful lesions on his foreskin for the last day. He reported that the pain was worse with movement and palpation but relieved with rest. He stated that he was last tested for a sexually transmitted infection (STI) in August 2018 owing to concerns about penile discharge, but test results were negative at that time. On physical examination, he was found to have small, painful linear lesions on the foreskin of his penis. The lesions were swabbed for HSV, and he was discharged home with prescriptions for lidocaine 2% jelly, meloxicam 7.5 mg, and valacyclovir 1000 mg.

The patient saw his primary care clinician for follow-up 1 month later because the lesions were not improving. He stated that his pain was under control, but he was having persistent erythematous lesions with purulent discharge on his penis that would emerge and then scab over. He denied any hematuria, dysuria, fevers, or scrotal pain. His prescription for valacyclovir was continued at 1 g 3 times daily for 10 days followed by a suppressive course of 500 mg daily.

Three months later, after he was seen by his primary care clinician, the patient presented to the ED with signs of sepsis. He reported worsening abdominal pain, nausea, vomiting, fever, progressive penile lesions, and dysuria. He was febrile and tachycardic on presentation. Initial physical examination revealed edema, erythema, and purulent erosive lesions on the glans penis. Lymph nodes were not palpable, and no other cutaneous lesions were present. He was diagnosed with cystitis and balanoposthitis.

Admission laboratory results revealed mild leukocytosis of 11.3 × 103/μL (reference 3.9-11.2 × 103/μL) with 89% neutrophils (reference 43%-74%) and 6% lymphocytes (reference 17%-46%). His urinalysis showed elevated leukocyte esterase and

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white blood cell count and the presence of bacteria. On computed tomography (CT) of the abdomen and pelvis with contrast, he was found to have prominent bilateral inguinal lymph nodes. While in the ED, he underwent tests for STIs and urinary tract infection. These included urine cultures that were positive for Streptococcus pyogenes and Streptococcus agalactiae, negative urine nucleic acid amplification test for Chlamydia trachomatis/Neisseria gonorrhoeae, and negative serologic tests for HIV-1 and HIV-2 antibodies.

The patient was admitted and empirically treated with fluids, ceftriaxone 2 g in 0.9% NaCl intravenously, and 1 dose of fluconazole 150 mg orally. He was discharged with prescriptions for augmentin 875 mg twice daily for 7 days and topical clotrimazole cream 1% for 10 days and with discharge instructions to refrain from sexual activity and to follow up with his primary care clinician. After discharge, he was found to have a positive rapid plasma reagin titer of 1:256, as well as positive treponemal IgG and IgM. Furthermore, the lesion cultures taken in the ED showed no bacterial or fungal growth, and blood cultures were negative for growth after 5 days. Upon follow up with his primary care clinician, the patient was successfully treated with weekly penicillin G injections (2.4 million units) for 3 weeks.

DISCUSSION

Syphilis is an STI caused by the spirochete *Treponema pallidum* (*T pallicum*). Although syphilis typically is characterized as following a progression through primary, secondary, latent, and tertiary stages, its clinical presentation varies greatly. Primary infection generally presents as a painless genital chancre and inguinal lymphadenopathy that occurs after an incubation period of about 21 days. Secondary syphilis generally presents with a maculopapular rash on the palms and soles of the feet, along with condyloma latta that appear as smooth, flat wart-like papular erosions that are white in color in the anogenital region, intertriginous folds, or oral mucosa. Secondary syphilis also can present with a host of other nonspecific systemic symptoms affecting any organ, such as alopecia, polymorphic rash, lymphadenopathy, and malaise. These secondary symptoms occur weeks to months after infection. Latent syphilis refers to a period in which the infection has no clinical symptoms, although the patient remains seropositive. Tertiary syphilis is the chronic clinical stage in which patients present with systemic complications. Some of these manifestations include gummas, which are chronic granulomatous lesions with necrotic ulcerations in the center; Argyll Robertson pupils, in which the pupils accommodate but do not respond to light; neurocognitive symptoms; and tabes dorsalis, which is the progressive demyelination of the dorsal column, leading to deficits in proprioception, tendon reflexes, touch, vibration, and pain sensation. Though classically described as late-stage manifestations, neurological and ocular symptoms can present at any stage of infection.

Treponema pallidum is also classically associated with vertical transmission resulting in congenital syphilis in the absence of treatment. Congenital syphilis typically manifests as miscarriage, stillbirth, hydrops fetalis, hepatomegaly, rhinorrhea, rash, or skeletal abnormalities. Later in life, children with congenital syphilis may have frontal bossing, saddle noses, peg teeth, and sensorineural losses.[4]

Syphilis incidence was at a historic low in the early 2000s, but in recent years, there has been a resurgence in its prevalence, with almost 6 million new cases and over 300 000 fetal and neonatal deaths annually worldwide. The majority of new cases are in men who have sex with men and often involve HIV coinfection.[3]

Follmann balanitis is an atypical presentation of primary syphilis that was originally reported in 1948 by Eugene Follmann.[5] It is a rare subtype of primary syphilis, accounting for less than 0.5% of cases,[6] and it is defined as erosive balanitis with lymphadenopathy and positive serology for syphilis.[7] Balanitis is the inflammation of the glans penis, whereas balanoposthitis is the inflammation of the glans penis and the foreskin in uncircumcised males. Skin findings of balanitis also have various presentations, such as edematous erosions or smooth white/pink coalescent papules and plaques.[8] Lymphadenopathy may or may not be present based on the phase of the infection.

Current methods for detection include darkfield microscopy, which allows for direct visualization, and venereal disease laboratory testing or rapid plasma reagent testing, which detects anti-cardiolipin antibodies that can result in false positives.[9] Final confirmatory testing includes the fluorescent treponemal antibody absorption assay (FTA-ABS), which detects serum antibodies specific for *T pallidum*. The most prominent histopathologic finding in the presence of syphilis infection is a perivascular infection resulting in ischemic necrosis of tissues. When these effects are close to nerves, they also can result in the loss of sensation--a hallmark of syphilis infection. This damage occurs despite the lack of exotoxin from *T pallidum*, which seems to indicate that the damage is from the host's own immune system.[10] Serum testing is especially important in the treatment of syphilis, because only about 40% of cases present with typical characteristics.[11] While studies from 1948 suggest that the incidence of balanitis as a manifestation of syphilis is around 0.3% to 0.5%, recent studies suggest that this presentation is much higher though specific values are still unknown.[5,7]

Our case had the classic rare presentation as Follmann balanitis, but it was originally likely misdiagnosed as HSV. The classic triad of Follmann's balanitis is lymphadenopathy, balanitis, and positive serum syphilis test. Our case presented with balanitis, and while the patient was not found to have inguinal lymphadenopathy on examination, CT of the abdomen found reactive nodes. Additionally, similar initial presentation has been confused with HSV in previous cases, thus, syphilis should be included in the dif-

ferential diagnosis when HSV is suspected but not confirmed.[7,12] Fungal and other bacterial causes of balanitis also were considered. Given the negative lesion cultures, the patient being nondiabetic, immunocompetent, and the lack of recent broad-spectrum antibiotic use, primary fungal or other bacterial causes were less likely.

Treatment with 2.4 million units of penicillin G benzathine intramuscularly has been the mainstay of therapy, with physical examination findings resolving after 2 to 4 weeks.[6,7] A single dose is typically sufficient, and increasing dosages does not seem to result in faster clearance; penicillin G benzathine maintains adequate serum concentration for about 3 weeks, and there is generally no resistance.[13,14] Additionally, there does not appear to be improvement with multiple doses for individuals with HIV or those who are immunocompromised.[15,16] Doxycycline/tetracycline, ceftriaxone, and azithromycin are all second-line alternatives with good clinical effectiveness in the treatment of syphilis in those who cannot tolerate penicillin or have concomitant STIs.[17]

The diagnosis of Follmann balanitis is often challenging, even for experienced clinicians, given the resemblance to genital herpes or candida infection. Therefore, it is important to rule out other causative organisms such as *Candida*, HSV, streptococci, and anaerobic infections in patients presenting with genital lesions. If untreated, syphilis can progress to the secondary or tertiary stage, resulting in significant morbidity. This case report highlights an atypical manifestation of primary syphilis that was originally misdiagnosed as HSV. We suggest that clinicians keep syphilis in the differential diagnosis when a patient presents with balanitis or balanoposthitis to enable early intervention in the syphilis course to prevent long-term sequalae of secondary, latent, or tertiary infection and possible congenital spread.

CONCLUSIONS

Follmann balanitis can be an atypical presentation of primary syphilis. This abnormal presentation can be confused with HSV infection resulting in delays in appropriate care. With increasing incidence of syphilis infection in recent years, clinicians should suspect *T pallidum* infection in cases presenting with balanoposthitis. Early management of syphilis can prevent subsequent health care utilization and long-term sequalae.

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