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CASE REPORT

# Syphilis: an atypical case of sepsis and multiple anogenital lesions in secondary syphilis

**Nichole Smith, MD[1]*, Sonu Dhillon, MD[2], John G. Cotter, MD[3] and Zohair Ahmed, MD[1]**

[1]Department of Internal Medicine, University of Illinois Peoria Campus, OSF Saint Francis Medical Center, Peoria, IL, USA; [2]Department of Gastroenterology, University of Illinois Peoria Campus, OSF Saint Francis Medical Center, Peoria, IL, USA; [3]Department of Infectious Disease, University of Illinois Peoria Campus, OSF Saint Francis Medical Center, Peoria, IL, USA

The incidence of syphilis has historically been cyclical in nature, often in relation to the rise and fall of public health initiatives directed toward eradication along with social attitudes toward sexual practices. The incidence of syphilis has increased by 15% in the last 6 years in the United States, with similar increases worldwide. Herein, we present an atypical case of syphilis presenting with severe septic shock and multiple anogenital lesions in an immunocompetent host. A 22-year-old male with no significant past medical history presented with fevers, chills, sore throat, diaphoresis, and diarrhea. He was febrile, tachycardic, hypotensive, and unresponsive to fluid resuscitation requiring short-term vasopressor support. Physical exam revealed diffuse lymphadenopathy; lower extremity macular rash involving the soles of the feet; papular non-pustular lesions on the scrotum; and a 0.5 cm non-tender irregular, healing lesion on the shaft of the penis. Laboratory analysis was significant for leukocytosis and elevated creatinine. Serum screening rapid plasma reagin was positive, and further testing revealed a titer of 1:32, with confirmation via fluorescent treponemal antibody absorption test. The patient was diagnosed with secondary syphilis, which was determined to be the underlying etiology of the sepsis as all other serological evaluations were negative. He was treated with penicillin G benzathine 2.4 million units intramuscular and supportive management, with improvement of symptoms. The patient engaged in high-risk sexual behaviors, including prior unprotected sexual contact with males. New research indicates that up to one-third of patients may present with atypical cutaneous manifestations, as demonstrated by this patient. It is important for physicians to familiarize themselves with the varied clinical presentations of syphilis, which include multiple anogenital lesions and tender primary lesions in primary or secondary syphilis.

Keywords: *acquired syphilis*; *treponema*; *sepsis*; *immunocompetent*; *men who have sex with men*; *resurgence*; *sexually transmitted infections*

*Correspondence to: Nichole Smith, Department of Internal Medicine, University of Illinois Peoria Campus, OSF Saint Francis Medical Center, 530 NE Glen Oak Avenue, Peoria, IL 61603, USA, Email: Nichole.a.smith@osfhealthcare.org

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Syphilis is a treponemal infection known for its variable symptomatology; as such, it has long been known as 'the great imitator'. Sir Williams Osler emphasized the broad differential and complexities of syphilis diagnosis stating 'the physician who knows Syphilis knows medicine'. By the 19th century, syphilis became so widespread that a subspecialty of medicine was developed, known as syphilology (1). The relative ease and effectiveness of treatment, along with global initiatives for sexually transmitted infection (STI) prevention had resulted in syphilis becoming a disease primarily of historical relevance by the early 1990s. However, in recent years, the incidence of syphilis has increased exponentially and thus rapid recognition of syphilis is of paramount importance (2). Classically, the presentation of syphilis initially includes a single, painless genital ulcer, and progresses in 3–6 weeks to rash, mucosal ulcers, and vague systemic symptoms (3). However, more recent research indicates up to one-third of patients may have atypical features, including painful, tender, or multiple anogenital primary lesions complicating the diagnosis (4). With the inclusion of sexual orientation by the Center for Disease Control

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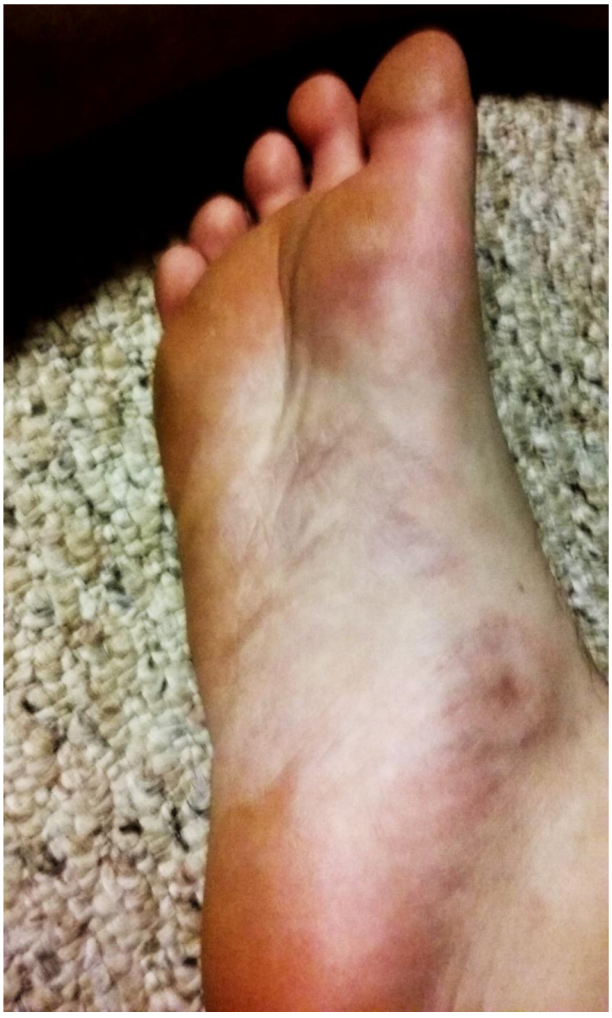

*Fig. 1.* Bull's eye rash of foot.

and Prevention (CDC) in prevalence data beginning in 2005, detailed risk analysis has demonstrated a population subset at higher risk for syphilis infection – men who have sex with men (MSM) (1).

## Case report

A 22-year old male with no significant past medical history presented to the emergency department with complaints of fever, chills, sore throat, diaphoresis, emesis, and diarrhea, which had progressively worsened for 1 week. He ultimately attested to high-risk sexual behavior with men.

Objectively, the patient was hypotensive (BP 75/43), febrile (Tmax of 102.6 F), diaphoretic, and ill-appearing on presentation. The patient remained hypotensive with systolic blood pressure in the 70s despite adequate fluid resuscitation. On physical exam, the patient appeared uncomfortable and profusely diaphoretic. He was noted to have diffuse lymphadenopathy most apparent in cervical and tonsillar regions with mild white exudate and plaque noted of the buccal mucosa. No inguinal lymphadenopathy was noted. There was a blanchable purpuric rash of the bilateral lower extremities involving the soles of the feet, with notable target lesions (Fig. 1). The rash did not involve the upper extremities or hands. The patient initially refused genital exam multiple times, but later remitted. There was a 0.5 cm irregular healing lesion on the shaft of the penis which was non-tender to palpation, as well as multiple scrotal lesions, which were mildly tender. The penile ulcer had been present for weeks, and identification had been complicated by the patient's use of Hydrocortisone cream. Initial laboratory work indicated leukocytosis with white blood cell (count of 30.26 K, with neutrophilic predominance. He was also noted to have an acute kidney injury with creatinine of 1.41 on admission.

After he failed the initial fluid resuscitation, the patient required short-term norepinephrine infusion for blood pressure support. High fevers persisted over the next few days, which required treatment with Tylenol and cooling blankets. After extensive diagnostic workup, serum rapid plasma reagin (RPR) came back positive with a titer of 1:32, and diagnosis was confirmed with fluorescent treponemal antibody absorption test serological testing. Pertinent negative studies include HIV RNA, Herpes simplex virus (HSV) antibody (Ab), Lyme Ab, Q fever Ab, Cytomegalovirus (CMV) serologies, urine gonorrhea & chlamydia (G&C), throat G&C, blood cultures, Ebstein-Bar Virus (EBV) serologies, and Polymerase chain reaction (PCR). He had no recent antibiotic use or prior treatment for STIs to suggest a Jarisch–Herxheimer reaction. Prior STI testing within the last 2 years (including RPR) were negative but suggested a pattern of high-risk sexual behaviors.

## Discussion

The cyclical nature of the incidence of primary and secondary syphilis can be attributed to social health initiatives and changes in culture attitudes toward sexual health. In 2000, the United States had seen the lowest incidence of syphilis since 1941, due to an initiative launched by the CDC which included improved surveillance and health promotion. However, the incidence of syphilis has seen a steady rise since 2000, with a total of 19,999 cases in 2014, compared with 5,979 cases in 2000. This is a 15.1% increase from 2013 and 40% increase from 2010 with a case rate of 6.3 cases per 100,000 population. An increase in prevalence has been noted in other countries as well, including India, Spain, and Canada (5–7).

The majority of these cases ( $>80\%$) are in adult males. In 2005, the CDC began tracking sexual orientation for patients diagnosed with primary or secondary syphilis allowing for more detailed risk factor analysis. MSM accounted for a majority (83.9%) of syphilis cases among men and 61.1% of total cases in 2013–2014. In comparison, men who have sex with women only have a 12.6% incidence. It is important to elicit a detailed sexual history on patients to identify potential high-risk behavior. In


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addition, health initiatives that focus on disease prevention in MSM would help combat the largest at-risk population (1, 2, 5, 8, 13).

Primary syphilis typically presents with a macule at the site of inoculation and transforms into the characteristic single chancre. The chancre is distinguished by a painless, well-circumscribed round/oval ulcer with erythematous base and raised, well-defined margin. Secondary syphilis typically presents with fever, rash, pharyngitis, mucocutaneous lesions, lymphadenopathy, and condyloma lata 2–8 weeks after resolution of initial chancre. The patient may also experience neurological sequelae including cerebrovascular accident, meningitis, uveitis, or focal cranial nerve palsy. The Jarisch–erxheimer reaction, a well-known complication of syphilis, is an acute febrile reaction with associated headache and myalgias that occurs in 10–35% of treated patients. It is theorized to be due to an immunological response to exposed treponemal antigens and typically evolves within the first 24 h after initiating treatment in early stage syphilis (5, 9, 10).

Atypical cutaneous manifestations of syphilis may be more common than previously assumed and can include (but are not limited to) annular, nodular, pustular, nodular-ulcerative (malignant), frambesiform forms; small papular, vesicular, corymbiform, follicular, and psoriasiform rashes; persistent chancre during the secondary stage; tender primary lesion or multiple anogenital lesions. A distinct characteristic of syphilis involves inclusion of the palms of the hands and the soles of the feet for cutaneous manifestations. In a study published by Towns et al., one-third of the patients with syphilis studied were noted to have multiple lesions of the anogenital area, which can often be mistaken for HSV infection (confirmed by negative HSV PCR). This study also demonstrated that painful or tender primary lesions were present in half of the men studied. Other studies indicate that approximately 36% of patients will experience tenderness with chancre, although at times this is due to secondary infection. As demonstrated by our patient, the primary chancre may persist into the secondary stage in up to 30% of patients (11). These presentations contradict the classical scenario of syphilis and 'should highlight the atypical way in which primary syphilis can present'. In addition, atypical cutaneous manifestations are more often associated with HIV superinfection, although it was not the case in our patient as he was HIV negative (4, 10, 12, 14).

Our patient presented with septic shock, and after an extensive workup for potential etiologies, the infectious cause was secondary syphilis. A Jarisch–Herxheimer reaction may present with symptoms concurrent with that of systemic inflammatory response syndrome. However, a high level of suspicion should be maintained for spirochetemia in patients who lack recent precipitant antibiotic use. A literature review fails to demonstrate any other reported cases of septic shock secondary to syphilis infection, although there are case reports of spirochetemia. Dark field microscopy may be performed to confirm the presence of spirochetes in the blood; however, this is limited by local resources and clinical utility. The case presented is an example of the atypical way in which syphilis may present. The systemic symptoms and atypical cutaneous manifestations that syphilis may present with exemplify the need for maintaining a high level of clinical suspicion, especially in a patient with known high-risk behaviors. In addition, treatment should include not only therapy but also risk reduction counseling and education. Our patient was hospitalized for 5 days but made a full recovery with the exception of recurrent perianal abscesses. His repeat RPR remains non-reactive since completing treatment and will continue to have close follow-up with infectious disease.

## Authors' contributions

NS and ZA reviewed the literature, collected the data, and drafted the manuscript. JC and SD reviewed and edited the article to be published, made critical revisions related to the content of the article, and approved the final version of the article to be published.

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This submitted article has not been previously published and is not currently under consideration elsewhere. There are no conflicts of interest to declare.

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