An Atypical Syphilis Presentation

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PRACTICE POINTS

• Syphilis retains its reputation as “the great imitator” due to its wide variability in clinical presentation and propensity for misdiagnosis.
• Lichenoid syphilis is a well-described cutaneous presentation of secondary syphilis, though the characteristics of these lesions remain highly variable and require a high degree of clinical suspicion.
• Treponema pallidum is partially susceptible to most β-lactam antibiotics in primary and early secondary stages of infection; thus, use of these medications can obscure symptoms without adequately treating the infection.

Syphilis is a chronic systemic infection that has been allotted the epithet “the great imitator” for its gross and histologic similarity to numerous other skin pathologies. Well-characterized for centuries, syphilis features diverse clinical manifestations including a number of cutaneous symptoms.1

The primary stage of infection is classically defined by an asymptomatic chancre at the inoculation site. The secondary stage results from the systemic dissemination of the infection and typically is characterized by cutaneous eruptions, regional lymphadenopathy, and flulike symptoms. This stage gained its notoriety as the great imitator owing to its ability to present with a variety of papulosquamous eruptions. The secondary stage is followed by an asymptomatic latent period that may last months to years, followed by the tertiary stage, which is characterized by the neurologic, cardiovascular, and/or gummatous manifestations that represent the major sources of morbidity and mortality associated with syphilis. It is during the primary, secondary, and early latent stages that the infection is communicable.1

Case Report

A 40-year-old man presented with multiple intensely pruritic, scattered, erythematous and slightly violaceous, flat-topped papules on the scrotum (Figure 1A) and penile shaft (Figure 1B) of 1 week’s duration. Some of these lesions were annular in appearance. The patient denied any other dermatologic concerns and showed no other skin lesions. A shave biopsy of the right side of the penile shaft was performed, revealing minimal papillary dermis and superficial perivascular dermatitis with substantial perivascular plasmacytoid infiltration. The epidermal layer was mildly acanthotic with parakeratosis. A tentative diagnosis of secondary syphilis of unknown latency was made and confirmatory laboratory studies were ordered.

Within weeks, the patient developed a painful 7-mm white patch on the right lower mucosal lip followed several days later by the appearance of a painful lesion on the hard palate (Figure 2 [arrow indicates palatal lesion]) and odynophagia. He presented to the emergency department roughly 3 weeks from the time of index presentation and was started empirically on amoxicillin 500 mg 3 times daily for 10 days for suspicion of strep throat. At a scheduled follow-up with his dermatologist 1 week later, physical examination showed complete resolution of the mucosal lip patch and genital lesions. A round erythematous patch on the right hard palate consistent with a resolving mucosal

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patch also was noted. A diagnosis of secondary syphilitic infection was made with a rapid plasma reagin (RPR) titer of 1:32 (reference range, <1:1) and positive Treponema antibodies. The patient was treated with a single dose of intramuscular benzathine penicillin G 2.4 million U to prevent the development of tertiary syphilis.

Comment

Incidence—Syphilis has been well characterized since the early 15th century, though its geographic origin remains a topic of controversy. Although acquired syphilis infections represented a major source of morbidity and mortality in the early 20th century, the prevalence of syphilis in the United States declined substantially thereafter due to improved public health management. Syphilis was relatively rare in the United States by the year 1956, with fewer than 7000 cases of primary and secondary disease reported annually. The incidence of primary and secondary syphilis infections in the United States increased gradually until 1990 before declining precipitously and reaching an unprecedented low of 2.2 cases per 100,000 individuals in 2000. These shifts ultimately have resulted in decreased clinical familiarity with the disease presentation of syphilis among many health care providers. Since 2000, the incidence of syphilis infection has increased in the United States, with the greatest increases seen in men who have sex with men, intravenous drug users, and human immunodeficiency virus–infected individuals.

Pathogenesis and Transmission—The causative agent in syphilis infection is the bacterium Treponema pallidum, a member of the family Spirochaetaceae, which is distinguished by its thin, regularly coiled form and distinctive corkscrew motility. Syphilis is communicated primarily by sexual contact or in utero exposure during the primary and secondary stages of maternal infection. At the time of presentation, our patient denied having any new sexual partners or practices. He reported a monogamous heterosexual relationship within the months preceding presentation, suggesting historical inaccuracy on the part of the patient or probable infidelity in the reported relationship as an alternative means of infection transmission. Untreated individuals may be contagious for longer than 1 year, making transmission patterns difficult to track clinically.

Presentation—The clinical presentation of infection with T pallidum results from dual humoral and cell-mediated inflammatory responses in the host. The primary stage is classically defined by a single chancre, which develops at the inoculation site(s) 9 to 90 days following exposure. The chancre typically begins as a small papule that rapidly develops into a painless ulcer characterized by an indurated border, red base, bordering edema, and a diameter of 2 cm or less. Indolent regional lymphadenopathy often is observed in conjunction with the primary chancre. Our case is notable for the absence of a primary syphilitic lesion and lack of adenopathy. The primary chancre of syphilis typically resolves within 3 to 6 weeks of onset regardless of whether the patient is treated, thus

FIGURE 1. Multiple scattered, erythematous and slightly violaceous, flat-topped papules on the scrotum (A) and penile shaft (B).

FIGURE 2. Pale, macular, right-sided lesion of the hard palate (arrow indicates palatal lesion).
suggested the rare possibility that our patient developed a painless primary chancre without realizing it.

The secondary stage of syphilis infection arises weeks to months after resolution of the primary chancre and is triggered by hematogenous and lymphatic dissemination of the bacteria. The symptoms of secondary syphilis are primarily florid and may include headache, malaise, fatigue, sore throat, arthralgia, and low-grade fever. Non-tender regional lymphadenopathy and splenomegaly also have been reported. Our patient denied any systemic concerns throughout the duration of his illness, with the exception of odynophagia in association with ulceration of the oral mucosa. Abnormal laboratory findings in secondary syphilis are nonspecific and may include an elevated erythrocyte sedimentation rate and/or an increased white blood cell count with absolute lymphocytosis. Laboratory studies drawn at the time of presentation showed no such abnormalities in our patient.

The cutaneous signs of secondary syphilis arise concurrently with systemic manifestations and are a common finding, with lesions of the skin or oral mucosa present in up to 80% of patients, as in our case. Oral lesions classically involve ulcers at the tip and sides of the tongue, which is distinct from our patient who developed oral lesions of the mucosal lip and hard palate.

Secondary syphilis classically features a copper-colored maculopapular rash with sharply delineated margins typically present on the palmar and plantar surfaces. Verrucous lesions appearing as moist exophytic plaques on the genitals, intertriginous areas, and/or perineum also have been described and are referred to as condyloma lata in the setting of secondary syphilis. In contrast to these classic findings, our patient demonstrated lichenoid lesions on the genitalia and white mucosal patches on the oral mucosa. Our case also was highly unusual because of the intense pruritus associated with the genital lesions, which starkly contrasts most secondary-stage cutaneous manifestations and remain permanently detectable even following treatment. Approximately 25% of cases in the United States of primary syphilis are not detected by nontreponemal testing; whereas a nonreactive test nearly always excludes a diagnosis of secondary or latent-stage syphilitic infection. Indeed, nontreponemal studies show the highest antibody titers during the late secondary and early latent stages of infection with declining titers thereafter, even in the absence of antibiotic treatment. In our case, diagnosis was made by biopsy and RPR was used for staging; RPR was reactive at a dilution of 1:32, indicative of secondary or early latent infection.

Treponemal testing, which includes the fluorescent treponemal antibody absorption test, and multiplex flow immunoassay detects antibodies that are specific to syphilis infection. Treponemal antibodies are detectable earlier in the course of infection than nontreponemal antibodies and remain permanently detectable even following treatment. Because of its high specificity, treponemal testing often is used to confirm diagnosis after positive screening with nontreponemal tests. Positive fluorescent treponemal antibody absorption testing and positive multiplex flow immunoassay may be used to confirm the diagnosis of *T. pallidum* infection.
The tertiary stage of syphilis infection can occur years after conclusion of the secondary stage and is comprised of one or more of the following: gummas, aortic dilatation or dissection, and neurosyphilitic manifestations such as tabes dorsalis or general paresis. It is of vital importance to identify syphilis infection prior to the onset of the tertiary stage to prevent substantial morbidity and mortality.

Treatment—Our patient’s symptoms abated after empiric treatment with amoxicillin for presumed streptococcal throat infection after he presented to the emergency department with odynophagia, which is not surprising given the moderate-spectrum coverage of this β-lactam antibiotic as well as the near-complete susceptibility of *Treponema spirochetes* to amoxicillin in primary and secondary syphilis with notably lower efficacy in latent or tertiary disease. It was essential to treat the patient with a single dose of intramuscular benzathine penicillin G 2.4 million U, which has been shown to reliably prevent recurrence of infection or progression to tertiary syphilis.

Conclusion

We present a rare case of lichenoid secondary syphilis in the absence of lesions on the palmar and plantar surfaces. The patient lacked any other cutaneous or systemic manifestations, except for odynophagia in association with oral mucosal lesions. He denied any new sexual partners and did not recall having a primary chancre. Also strikingly unusual in this case was the intense pruritus associated with the genital eruption, which is unlike the classic lack of symptoms experienced in the great majority of eruptions due to secondary syphilis. A clinical appreciation of the many cutaneous manifestations of syphilis infection remains critical to early identification of the disease prior to progression to the tertiary stage and its devastating sequelae.

REFERENCES