Secondary Syphilis: The Great Masquerader: A Case Presentation and Discussion

Gina Caputo, DO,* Roxanne Rajaii, MS, DO,** Gary Gross, MD,*** Daniel S. Hurd, DO****

*Dermatology Resident, 2nd year, LewisGale Hospital Montgomery/Edward Via College of Osteopathic Medicine, Blacksburg, VA
**Osteopathic Intern, Northeast Regional Medical Center, Kirksville, MO
***Clinical Dermatologist, LewisGale Hospital Salem, Salem, VA
****Program Director, Dermatology Residency Program, LewisGale Hospital Montgomery/Edward Via College of Osteopathic Medicine, Blacksburg VA

Abstract
Syphilis has been called “the great imitator” due to its wide range of variable symptoms that often mimic other disease processes. The painless syphilitic chancre can easily go unnoticed, or be mistaken for a folliculitis, abrasion, or benign papule. The non-pruritic, diffuse rash that develops in secondary syphilis, characterized by dissemination and multiplication of the microorganism in different tissues, typically presents anywhere from simultaneously to six months after the healing of the primary chancre.1 We present a challenging case of secondary syphilis that masqueraded as connective-tissue disease, granuloma annulare, and tinea corporis for years despite initial treatment.

Introduction
Syphilis, an entity with origins dating back to the 1530s, was first formally described in 1905. It is a chronic disease with varying presentations and a waxing and waning course. Sexual contact is the main mode of transmission, with the causative organism being Treponema pallidum, a spirochete. The gold standard of diagnosis is serologic testing, and penicillin G remains the treatment of choice. The condition’s varying presentations, along with late manifestations of disease that involve numerous organ systems, explain its distinction as the “great imitator.”1,2 Syphilis is commonly misdiagnosed as connective-tissue disease, granuloma annulare, lupus vulgaris, psoriasis, tinea corporis, and other dermatological diseases. Several case reports in the literature highlight the similarities between these diseases and the importance of accurate diagnosis and early treatment to prevent progression of syphilis to cardiovascular and neurologic sequelae. A high clinical suspicion of disease, coupled with clinical, serologic, and histologic evidence, is optimal for diagnosis and early management of syphilis.

Case Report
A 63-year-old Caucasian male with no documented past medical history presented in April 2015 for evaluation of a pruritic, diffuse rash of seven months’ duration. The patient denied any constitutional symptoms. The patient had diffuse annular, granulomatous, erythematous papules coalescing into plaques with central clearing on the trunk, back, bilateral biceps and forearms (Figures 1-4). The rash was treated with oral terbinafine and steroids and initially improved. Four weeks later, the patient returned without significant improvement, and a punch biopsy was performed with a clinical suspicion of a gyrate erythema or granuloma annulare. Biopsy showed superficial and deep perivascular dermatitis with abundant perivascular lymphocytes and plasma cells. There was focal patchy vacuolar interface change and increased reticular dermal mucin confirmed with Alcian blue/PAS stain (Figures 5, 6).

With further interrogation of the patient and review of the medical record, the patient had been seen in 2010 for a similar rash, also treated with oral terbinafine and biopsied, with results indicating drug eruption versus arthropod-bite reaction. At that time, an ANA, Lyme titer and RPR were performed. The RPR came back positive for syphilis, and the patient was referred to Infectious Disease. He had undergone an extensive workup at that time for Histoplasma, HIV, ANA, Lyme, Blastomyces, and Cryptococcus. The patient was started on cefuroxime 500 mg twice a day for the syphilis.

Upon further questioning in 2015, the patient reported he may have been partially treated by the Centers for Disease Control (CDC) for syphilis.

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The patient denied any extramarital affairs. We performed another RPR, with a result of 1:128. The patient was referred to Infectious Disease for work-up of tertiary syphilis and treatment. Infectious Disease treated the patient with ceftriaxone 2 g IV every 24 hours for two weeks, and he was worked up again for HIV and hepatitis. He also underwent a lumbar puncture to rule out neurosyphilis. Results from the HIV and hepatitis labs and the lumbar puncture were negative. The patient was treated successfully for secondary syphilis.

Discussion

Syphilis is a chronic disease with varying presentations and a waxing and waning course. While sexual contact is the main mode of transmission, with the causative organism being Treponema pallidum, a spirochete, transmission across the placenta is thought to be the second most common mode.2,3 Numerous studies have investigated the transmission probability among partners and have estimated it to be around 60 percent. Three stages of syphilis have been described: The primary stage, presenting with a painless chancre at the site of inoculation; the secondary stage, characterized by a polymorphic rash; and the tertiary stage, characterized by cardiovascular and neurologic sequelae and gumma formation. The tertiary stage is the most destructive.

Syphilis is divided into early (< 1 year) and late (> 1 year) stages, with the early stages (primary, secondary, and early latent) believed to be infectious. Late manifestations of disease involving all organ systems have given syphilis its name as the “great imitator,” with the key to diagnosis remaining a high index of suspicion.2

A single, painless, indurated ulcer with a clean base characterizes primary syphilis. These primary chancre also typically present with a sharply marginated border. Up to 80 percent of patients with primary syphilis have painless regional lymphadenopathy. The incubation period for primary syphilis ranges from three to 90 days. In men, the penis is the most common site affected, while in women, it is the labia majora. Anorectal chancre are common in homosexuals. Extranodal chancre involving the fingers, tongue, anus, and mouth are rare, but when affected, they are typically painful lesions. The most common extranodal chancre location is the mouth, most specifically the lip.3

Secondary syphilis is often subtle and is a cutaneous manifestation of the disease. A primary chancre can be found in up to one-third of patients with secondary syphilis. Skin lesions can often mimic other dermatologic diseases, making syphilis easy to misdiagnose. The rash can have variable morphology, ranging from macular to maculopapular, follicular, and occasionally pustular. Classically, however, lesions are non-pruritic and are universally distributed with a “raw ham” or copper-colored appearance. The palms and soles are typically involved. In up to 7 percent of patients, a patchy, “moth-eaten” pattern of alopecia has been reported. Systemic symptoms of secondary syphilis may include malaise, prostration, cachexia, headache, low-grade fever, asymptomatic meningitis, cranial nerve palsies, gastrointestinal symptoms, painless adenopathy, and vague bone and joint pain, among others.1,2

Tertiary syphilis consists of cardiovascular and neurologic involvement. It is estimated that approximately one-third of patients with untreated primary syphilis develop tertiary syphilis.4,5 Cardiovascular symptoms usually present between 10 years and 30 years after the initial infection. The most common cardiovascular manifestation of disease is syphilitic aortitis, typically involving the ascending aorta.2 Clinical signs and symptoms of neurosyphilis include focal central nervous system ischemia and stroke, tubas dorsalis (progressive ataxia, bladder incontinence), and general paresis (altered mental status, depression, forgetfulness, confusion).4 Cutaneous tertiary syphilis typically presents with nodular lesions that can easily mimic other dermatologic diseases such as granuloma annulare, lupus vulgaris, psoriasis, and sarcoid.2

Diagnosis of syphilis is based on both clinical and laboratory findings. The gold standard for the diagnosis of primary syphilis continues to be visualization of spirochetes under dark-field microscopy. For secondary, latent, and tertiary syphilis, serologic testing is the method of choice for diagnosis. Nontreponemal tests, including VDRL, are often indicated for screening, while treponemal tests, including RPR, FTA-ABS (the serum fluorescent treponemal antibody absorption test), and MHA-TP (microhemagglutination test for T. pallidum), are used to confirm the diagnosis. Nontreponemal tests, however, can lack sensitivity and can give a high rate of false-positive reactions. This is particularly true in patients of increased age, patients who are pregnant or drug-addicted, and those with malignancy, autoimmune diseases (SLE), and viral (EBV and hepatitis), protozoal or mycoplasmal infections. Neurosyphilis is often diagnosed based on a combination of results from serologic testing, abnormalities of CSF cell count and protein levels, or a reactive CSF VDRL.

The first-line therapy for syphilis remains intramuscular benzathine penicillin G.25 Due to the devastating sequelae of syphilis, it is recommended that patients allergic to penicillin be desensitized and subsequently treated with penicillin therapy.5

Despite serologic testing for the diagnosis of syphilis, atypical clinical presentations and false-negative laboratory tests, particularly in HIV-positive individuals, complicate accurate and early diagnosis of disease. This, in turn, has led to an increase in dermatopathological specimens for the diagnosis of syphilis. In addition to the variability in clinical presentation and mimicry of other disease processes, the histopathological features of syphilis also exhibit a wide spectrum, with features ranging from interface dermatitis to granulomatous diseases. However, several well-recognized histologic patterns characteristic of the papulosquamous eruption of secondary syphilis have been described. These include interstitial inflammation, endothelial swelling, irregular acanthosis, and elongated rete ridges. Although not diagnostic, they should raise suspicion for syphilis, particularly in the absence of clinical features.4

Although a variety of diagnostic tools are available for accurate diagnosis, the incidence of false-negative laboratory tests as well as clinical features resembling other etiologies make it one of the most commonly misdiagnosed entities in the field of dermatology. The tragic outcomes that can result from misdiagnosis of syphilis, including but not limited to cardiovascular and neurologic sequelae, demonstrate the importance of early and accurate diagnosis.6

Bittencourt et al. report a different case of secondary syphilis in an HIV patient with palmoplantar lesions masquerading as palmoplantar psoriasis. They present a 32-year-old male with bilateral asymptomatic erythematous-scaly plaques on palms and soles for three months, associated with perungual erythema, subungual hyperkeratosis and onychodystrophy of toenails.7 This case demonstrates the challenge of diagnosing syphilis, in that clinically, it can mimic psoriasis and dermatophytois. However, the unusual alterations typical of syphilis in the case by Bittencourt et al., coupled with a negative result of mycological examination and improvement after treatment, led to the actual diagnosis of syphilis over its mimickers. This validates the importance of clinical suspicion, particularly in the case of atypical manifestations of secondary syphilis.1,4

Conclusion

Syphilis is a disease that skillfully mimics other dermatologic diseases in both clinical and histologic features.6 Furthermore, it is a disease with multisystem effects, one that allows a dermatologist “to highlight the relationship of skin diseases to the rest of the body.”7 The cases by Wu and Bittencourt et al., along with the present case, exemplify this mimicry and the need for a high clinical index of suspicion for syphilis.8 Although a variety of diagnostic tools are available for accurate diagnosis, the incidence of false-negative laboratory tests as well as clinical features resembling other etiologies make it one of the most commonly misdiagnosed entities in the field of dermatology. The tragic outcomes that can result from misdiagnosis of syphilis, including but not limited to cardiovascular and neurologic sequelae, demonstrate the importance of early and accurate diagnosis.6
References


