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Case Report

An Atypical Cutaneous and Histopathological Manifestation of Secondary Syphilis in an HIV-Positive Male: A Case Report

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Abstract

We present an atypical case of secondary syphilis concomitant with condyloma lata in an HIV-positive male. The patient presented with lesions on his lateral neck, soles, and palms. Spirochetes were examined on the biopsy of the palm, consistent with secondary syphilis, but not on the biopsy from the neck. The lesion on the neck was diagnosed as an evolving secondary syphilis lesion due to the extent of the lymphoplasmacytic infiltration, presence of acanthosis and epidermal hyperplasia, the accompanying diagnosis of secondary syphilis on the palm, the patient's history of HIV, and the related diagnosis of condyloma lata on the dorsal shaft of the penis. Following this diagnosis, the patient was referred to an infectious disease specialist who treated him with a single intramuscular injection of 2.4 million units of benzathine penicillin, per CDC guidelines. This case highlights the importance of clinicians taking into consideration a variety of factors when diagnosing and treating cutaneous disorders with a broad-spectrum differential diagnosis, particularly in at-risk individuals.

Introduction

Syphilis is a sexually transmitted disease caused by the bacterial spirochete *Treponema pallidum*. This disease is primarily transmitted through sexual contact, but transmission through the placenta can occur in the case of congenital syphilis [1]. The incidence of primary and secondary syphilis has dramatically increased in the United States on a yearly basis since the 2000s, with the exception of a lull during social-distancing measures at the height of the COVID-19 pandemic. This increase in cases has been particularly prevalent among men who have sex with men, especially those who are African American [2].

As the disease progresses, its signs and symptoms can be categorized into four stages; however, there is no clear-cut delineation between the clinical and histological manifestations of each stage, making the initial diagnosis difficult. The primary stage of syphilis is historically characterized by a chancre, or painless ulcer, at the site where *T. pallidum* entered the body. Secondary syphilis classically involves a maculopapular, copper-colored rash focused on the palms and soles. An asymptomatic latent stage precedes the tertiary stage marked by systemic complications, including but not limited to cardiovascular and neurological involvement [3].

The diagnosis of syphilis according to its stage should be approached with caution because of the diverse range of symptoms that syphilis, also known as the "The Great Imitator," can present with [4]. This is important for all physicians to be aware of, including dermatologists, because syphilis diagnoses are becoming more common in non-STD focused clinical settings [5]. In addition to variable symptoms, syphilis cannot always be diagnosed by biopsy. Spirochetes seen at the histopathological level indicate secondary syphilis; however, silver stains such as the Warthin-Starry stain, are not sensitive enough [6-8]. A secondary syphilis diagnosis is also complicated by the fact that atypical cutaneous and histopathological manifestations of secondary syphilis are especially common in patients concomitantly infected with human immunodeficiency virus (HIV) [9-12]. In the case of an HIV-positive male, we present a unique clinical and histopathological manifestation of secondary syphilis.

Case Report

An HIV-positive 45-year-old man was seen for multiple reddish-brown macules on the palmar and plantar surfaces (Figure 1). The macules were asymptomatic and first appeared two weeks prior to the office visit. A 4-mm superficial shave biopsy was performed on a lesion on the left palm with a differential diagnosis of psoriasis, contact dermatitis, pigmented purpura, and lichen simplex chronicus. The lesion was initially suspected to be lichen simplex chronicus because a biopsy taken on the patient's right anterior shoulder two months prior was read by the pathologist as lichenoid keratosis. The pathology report for the shave biopsy on the left palm, however, revealed lichenoid dermatitis with spirochetes consistent with secondary syphilis (Figure 2).

The patient also presented with a variegated lesion on the left lateral neck, consisting of brown and erythematous macules (Figure 3). A 6-mm superficial shave biopsy of this lesion revealed hyperkeratosis, parakeratosis, acanthosis, mild spongiosis and a dense dermal lymphoplasmacytic infiltrate. The patient was prescribed imiquimod 5% topical cream to treat condyloma lata on the dorsal shaft of the penis.



Figure 1: Reddish-brown macules on the patient's left palm.

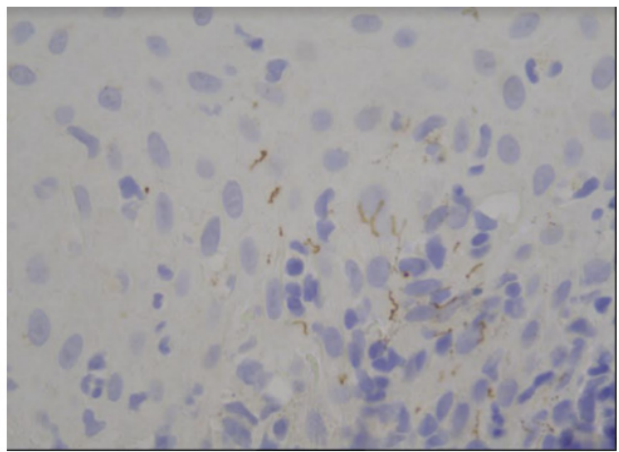


Figure 2: Biopsy from a lesion on left palm. Lichenoid dermatitis with spirochetes consistent with secondary syphilis. (*T. pallidum* immunohistochemical stain, original magnification x630). The slides were read by Dr. Min Zheng and Kathleen Riolo, MHS, PA, consulted by Dr. Zembowicz, and retrieved by Dr. Brian Scott Erler. Jersey Shore University Medical Center Surgical Pathology.



Figure 3: Lesion on patient's left lateral neck presenting with brown and erythematous macules.

The patient was immediately informed on the diagnosis of secondary syphilis and was referred to an infectious disease specialist. He was treated with a single intramuscular injection of 2.4 million units of benzathine penicillin G, as recommended by the Sexually Transmitted Diseases Treatment Guidelines issued by the Centers for Disease Control [13]. The lesions diminished two weeks after treatment. No recurrence was noted, although there are remains of mild residual post-inflammatory hyperpigmentation.

Discussion

The patient presented with a variegated lesion on the left lateral neck which morphologically did not fit the typical profile of a secondary syphilis lesion: the lesion was neither copper-colored nor located on the palms or soles [10]. Despite the unique location of the lesion, there are documented case studies in which individuals have presented with the secondary syphilis rash on body locations other than the palms and soles [14,15]. The histopathological analysis on the lesion performed by the local hospital's pathology department further complicated the diagnosis.

The specimen with Warthin-Starry silver stain, did not reveal spirochetes on histology; however, a growing body of research has shown that the Warthin-Starry silver stain is not sensitive enough for spirochetes (Figure 4), and the presence of a lymphoplasmacytic infiltrate is a more reliable indicator of secondary syphilis [6,7,16,17]. In an analysis of 24 secondary syphilis-positive biopsies, spirochetes were detected in 41% of the specimens when tested with PCR testing and 0% of the specimens tested with silver staining [7]. These results were later confirmed in an analysis of 11 biopsy specimens taken from HIV-positive individuals. Spirochetes were detected in 63.6% of the biopsies when tested with immunohistochemical tests while only 9.09% of the biopsies tested with the traditional silver stain revealed spirochetes [6]. While the absence of spirochetes in the less sensitive test led to false-negative secondary syphilis results, 100% of the biopsies presented with a moderate to excessive lymphoplasmacytic infiltrate [6].

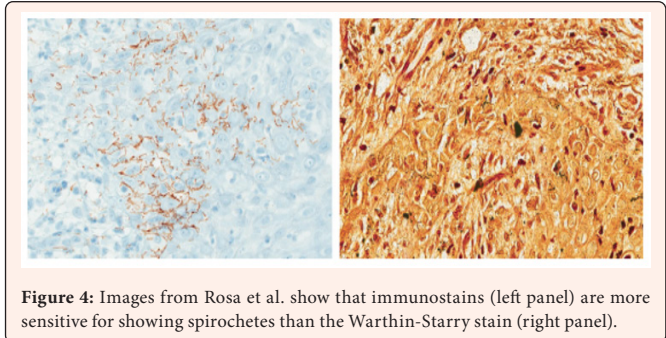


Figure 4: Images from Rosa et al. show that immunostains (left panel) are more sensitive for showing spirochetes than the Warthin-Starry stain (right panel).

The pathology report for the lesion on the neck revealed a dense and extensive lymphoplasmacytic infiltrate without the presence of spirochetes using the Warthin-Starry stain. Despite the lack of spirochetes, the pathology report is diagnostic for secondary syphilis due to the presence of the dense dermal lymphoplasmacytic infiltrate. While the lymphoplasmacytic infiltrate is a key identifying feature of secondary syphilis, there are a plethora of other inflammatory diseases that involve a lymphoplasmacytic infiltrate, and it is the characterization of the infiltrate that helps distinguish between the diseases. These diseases include, but are not limited to, Hashimoto thyroiditis (Figure 5), B-cell lymphoma (Figure 6), and lichen planus [18,19]. (Figure 7) illustrates the difference between the lymphoplasmacytic infiltrate of secondary syphilis versus lichen planus, which was included in our differential diagnosis. (Figure 8) shows a closer comparison of the infiltrate in secondary syphilis lesions mimicking lichen-planus in HIV-positive patients [20]. With respect to syphilis, the immune cells within the lymphoplasmacytic infiltrate are packed much closer together and the overall extent of the infiltrate covers a larger surface area [16]. For a closer comparison, (Figure 8) shows the comparison of the infiltrate in our HIV-positive patient's secondary syphilis lesions to the infiltrate of secondary syphilis previously documented in another HIV-positive patient [20].

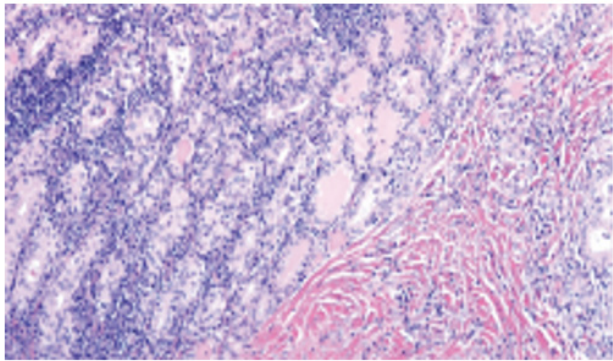


Figure 5: Lymphocytic infiltrate in a case of Hashimoto thyroiditis from Ko et al.

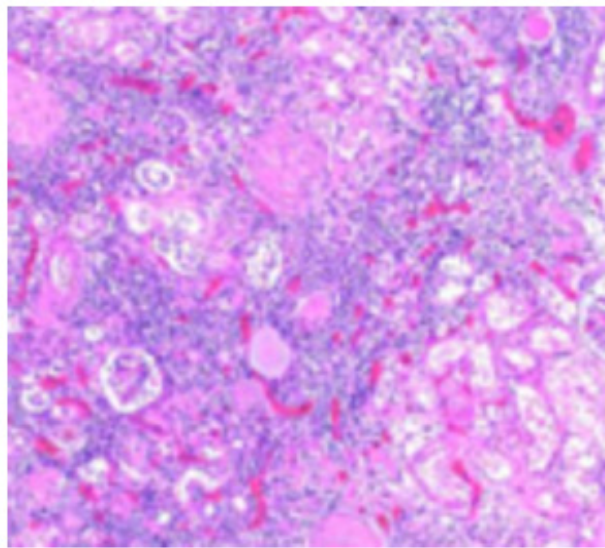


Figure 6: Lymphoplasmacytic infiltration of the kidney in a case of lymphoplasmacytic B-cell lymphoma from Olayinka et al.

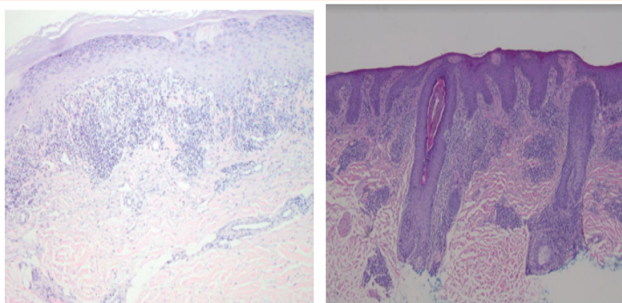


Figure 7: The image on the left from Dinh et al. illustrates the lymphoplasmacytic infiltrate present in a case of lichen planus. The image on the right shows the secondary syphilis lymphoplasmacytic infiltrate from the lesion on our patient's neck (hematoxylin-eosin, original magnification x100). The slides were read by Dr. Min Zheng and Kathleen Riolo, MHS, PA, consulted by Dr. Zembowicz, and retrieved by Dr. Brian Scott Erler. Jersey Shore University Medical Center Surgical Pathology.

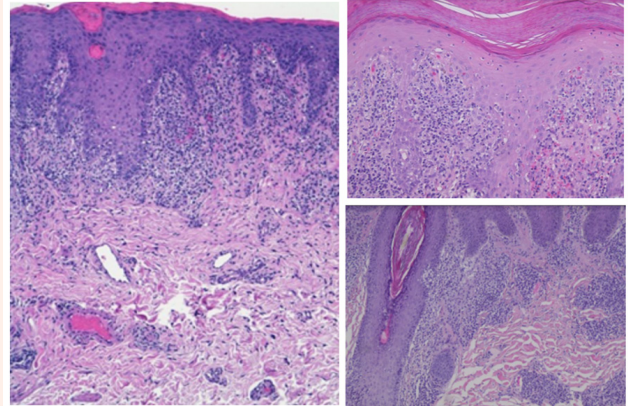


Figure 8: The image on the left from Jiménez-Gómez et al shows a secondary syphilis lesion in a HIV-positive patient that mimicked lichen planus. The top right panel shows the lesion on our patient's palm (hematoxylin-eosin, original magnification x400). The bottom right panel is the lesion on our patient's neck (hematoxylin-eosin, original magnification x400). The density and extent of the lymphoplasmacytic infiltrates are very similar, which supports our diagnosis of secondary syphilis. The slides were read by Dr. Min Zheng and Kathleen Riolo, MHS, PA, consulted by Dr. Zembowicz, and retrieved by Dr. Brian Scott Erler. Jersey Shore University Medical Center Surgical Pathology.

In addition to the presence and extent of the infiltrate, our diagnosis of secondary syphilis for the lesion on the neck is supported by the accompanying diagnosis of secondary syphilis on the palm, which presented with spirochetes, the patient's history of HIV, and the related diagnosis of condyloma lata on the dorsal shaft of the penis, which has been associated with secondary syphilis [14]. This case is an example of an evolving lesion of secondary syphilis, which is supported by research suggesting that syphilis patients co-infected with HIV can present atypical presentations of secondary syphilis [9,10]. The lesion presents with acanthosis, a histological characteristic of primary syphilis, and epidermal hyperplasia, characteristic of secondary syphilis [16]. In addition, the non-uniform healing process of the primary syphilis chancre makes it impossible for there to be a clear histological boundary between primary and secondary syphilis [16].

This case highlights the importance of clinicians taking into consideration a variety of factors when diagnosing and treating cutaneous disorders with a broad-spectrum differential diagnosis, including but not limited to, patient history, histopathological analysis, co-occurring signs and symptoms, and potential atypical presentations of disorders.

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