

Simultaneous Primary and Secondary Syphilis Associated with Syphilitic Alopecia and Folliculitis in an HIV Positive Patient

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Abstract

Syphilis has been classically divided into three clinical stages. The chancre that appears at the site of inoculation is referred to as the primary stage. The secondary stage is characterized by systemic involvement and the appearance of a disseminated maculopapular rash. Cardiovascular, neurologic and gummatous lesions characterize tertiary syphilis. The simultaneous presentation of primary and secondary syphilis has been reported because the chancre can persist into the secondary stage, especially in HIV positive patients. Although syphilitic alopecia is a rare manifestation of secondary syphilis it is an important differential diagnosis in the evaluation of patients with patchy hair loss. This article aims to present the case of a 34-year-old HIV-positive male patient that presented simultaneous primary and secondary syphilis associated with syphilitic alopecia and acute bacterial folliculitis.

Keywords: Syphilis; Primary syphilis; Secondary syphilis; Alopecia syphilitica; Syphilitic alopecia; Patchy alopecia

Introduction

Syphilis is a systemic disease caused by the spirochete *Treponema pallidum*. The disease has been classically divided into a series of stages based on clinical findings [1]. The first stage of syphilis, known as primary syphilis, is marked by the presence of a chancre (a painless indurated ulcer with sharp borders that usually resolves within 3 to 6 weeks) at the site of inoculation (usually the genitals) [1-3]. Secondary syphilis, the stage of spirochaetemia, is characterized by systemic symptoms (fever, headache, myalgias, lymphadenopathy), mucosal lesions, hair loss and the presence of a generalized maculopapular scaly eruption on the torso and extremities [2-5]. The palms and soles are affected in 60% of cases [4]. Tertiary syphilis is characterized by cardiovascular, neurologic and gummatous lesions [1,2]. In HIV positive patients the simultaneous manifestations of primary and secondary syphilis is not uncommon because the chancre is likely to persist into the secondary stage [2,6].

Syphilitic alopecia is a rare manifestation of secondary syphilis affecting approximately 4% of patients [7,8].

Case Report

A 34-year-old HIV-positive Hispanic male patient presented with a 10-week history of a painless, indurated, well-demarcated penile ulcer (Figure 1). His highly active antiretroviral therapy scheme included emtricitabine, lamivudine and atazanavir. On physical examination, the presence of non-pruritic scaly macules and papules on arms, palms and soles were noted (Figure 2). Further examination revealed areas of patchy non-scarring alopecia on the scalp, some of them with normal underlying skin, others with the presence of some crusts and pustules (Figures 3-5). The patient claimed that the scalp lesions had appeared progressively over the past month. The hair pull test was negative. Simultaneous primary and secondary syphilis associated with syphilitic alopecia was immediately suspected. The results of laboratory investigations including complete blood cell counts, blood chemistry and urinalysis were within normal limits. His CD-4 lymphocyte level count was 395 per mm³ and the viral load was undetectable. Darkfield microscopy of the penile ulcer revealed treponema, while the Venereal Disease Research Laboratory (VDRL) was positive at a titer of 1:128. Other confirmatory tests such as EIA, TPPA and IgM-Test, were not performed because the treponema had already been detected by Darkfield Microscopy. Two 4 mm punch biopsies were taken

from scalp, one of them was taken from an area of patchy alopecia without other skin lesions, and the other was taken from a lesion that presented pustules. The first biopsy showed normal epidermis and dermoepidermal junction with decreased number of hair follicles, increased number of catagen and telogen hairs, and a perivascular and perifollicular lymphocytic infiltrate with some scattered plasma cells, compatible with alopecia syphilitica in the presence of a positive VDRL. The second biopsy showed abundant neutrophils near the follicular ostium and a perifollicular and perivascular lymphocytic infiltrate compatible with acute bacterial folliculitis.

Treatment was initiated with one single doses of penicillin G benzathine 2.4 million units administered intramuscularly, as recommended by the Center for Disease Control and Prevention for secondary syphilis in HIV infected patients [1]. The patient was also instructed to clean the pustules and crusts with a povidone iodine solution twice a week. Three months later, the VDRL had dropped to a 1:16 titer, the patient was free of cutaneous lesions and the hair presented partial regrowth, indicating a remarkable response to treatment.

Discussion

Syphilitic alopecia, a non-inflammatory and non-scarring type of alopecia, is a rare clinical finding of secondary syphilis [3,7,9-11]. Hair loss can also occur in primary syphilis but only when associated with a primary chancre of the scalp [7,8]. The frequency of syphilitic alopecia reported in the literature varies significantly, ranging from 2.9% to 48% [7,8,10,12]. Males seem to be more frequently affected than women, and this might be explained by the fact that 60 percent of new cases of syphilis occur in men who have sex with men [13].

The exact pathogenesis of syphilitic alopecia remains unknown

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Figure 1: Painless, indurated and well-demarcated penile ulcer.



Figure 2: Maculopapular scaly eruption affecting the left palm.



Figure 3: Right lateral view of patients scalp and part of the face, showing areas of patchy alopecia and areas of erythema, pustules and crusts.



Figure 4: Close-up of the left parieto-occipital region showing areas of "moth-eaten" alopecia and normal skin, as well as some areas with crusts.

however, recently Nam-Cha et al. were able to detect *T. pallidum* in the peribulbar region and penetrating the follicle matrix using immunohistochemistry avidin-biotin-peroxidase complex technique,

thus supporting the speculation that the alopecia may be caused directly by spirochetes [7,10,12].

Temporary worsening of the alopecia has been reported in association with Jarish-Herxheimer reaction after treatment with penicillin procaine injection [14].

In 1940, McCarthy described two clinical variants of alopecia syphilitica. The first is called the "symptomatic syphilitic alopecia" in which alopecia occurs in conjunction with other cutaneous manifestations of secondary syphilis [3,8,10,11,15]. The second clinical type of syphilitic alopecia is called "essential syphilitic alopecia" and it is characterized by alopecia without other systemic symptoms and signs of secondary syphilis [3,7,8,11,15].

Clinically, syphilitic alopecia can present in a diffuse pattern, a "moth-eaten" pattern or a combination of both [7,9,11,12]. The "moth-eaten" pattern is the most common form of presentation and is considered pathognomonic, as seen in our patient [8,10,12,16,17].

Although the scalp is the most frequently affected area, other hair-bearing sites such as the eyebrows, eyelashes, chest, axillae, pubis and legs can also be affected [11,18-22].

The gold standard for diagnosis of early syphilis is the detection of treponema by dark field microscopy during the chancre phase [1]. Although serologic tests can be helpful, false negatives are common during the primary stage, especially in HIV-positive patients because of a delayed appearance of seroreactivity [1]. For secondary or tertiary syphilis serologic test such as nontreponemal tests (e.g. Venereal Disease Research Laboratory [VDRL] and Rapid Protein Reagin (RPR) and treponemal tests (Fluorescent Treponemal Antibody Absorption [FTA-ABS] tests, *T. pallidum* Particle Agglutination Assay [TP-PA], various Enzyme Immunoassays [EIAs] and chemiluminescence immunoassays) are useful [1]. Because non-treponemal tests antibody titers usually correlate with disease activity, they are especially valuable in monitoring response to treatment [1]. A scalp biopsy can be useful however it is important to note that the histopathological changes are almost identical to those found in alopecia areata.

There are no histopathological distinguishing features of alopecia syphilitica unless the spirochete is found in the hair. The common histopathological findings are a perivascular and perifollicular lymphocytic infiltrate, decreased number of hair follicles, catagenization, telogenization, and follicle-oriented melanin clumping [17]. Plasma cells can be sometimes noted as in our patient [23]. Other than the follicular changes, these findings are similar to those of macular/maculopapular sphilides outside the scalp [23].



Figure 5: Close up of the right parieto-occipital region showing some areas of "moth-eaten" alopecia and normal skin with many pustules and crusts.

The main clinical and histological differential diagnosis is with alopecia areata because both alopecias are inflammatory, non-scarring and present a peribulbar lymphocytic infiltrate [10]. The key distinction between these two entities is the detection of *Treponema pallidum* in syphilis [10]. If no spirochetes are found, a sparse lymphocytic infiltrate and the absence of small or abnormal anagen hair follicles in alopecia syphilitica most reliably distinguish it from alopecia areata [17].

Other differential diagnoses to be considered include other forms of non-scarring patchy alopecia such as trichotillomania, traction alopecia, alopecia neoplastica and tinea capitis, which can all be ruled out by biopsy [7,9,12].

Treatment with penicillin is usually curative [5]. Treatment of primary and secondary syphilis among HIV-infected adults is with penicillin G benzathine, 2.4 million units in a single dose intramuscular injection [1,4]. In case of penicillin allergy, ceftriaxone might be a proper alternative [24]. HIV-infected patients should be evaluated clinically and serologically at 3, 6, 9, 12, and 24 months after therapy [1,2]. Alopecia usually resolves within three months of treatment like in our patient [9,12].

Conclusion

In HIV positive patients, it is important to remember that the described clinical stages of syphilis may overlap, and that simultaneous primary and secondary syphilis is common, even though systemic symptoms of the latter may be absent. Syphilitic alopecia is an uncommon manifestation of secondary syphilis; however it should not be overlooked in patients with localized non-scarring hair loss.

In this case, the diagnosis was immediately suspected because the cutaneous lesions were very characteristic of primary and secondary syphilis. However, the clinical image of the alopecia patches was far from usual. Typically the patches of alopecia in syphilitic alopecia show normal looking skin and this was not the case in our patient [5]. The fact that he presented pustules and crust surrounding some of the alopecia patches made it strictly necessary to take a biopsy and rule out other causes of follicular pustules associated with alopecia. Although acute bacterial folliculitis does not cause alopecia, in our case it explains the presence of the pustules and crusts surrounding some of the patches of syphilitic alopecia.

This patient is presented to highlight the importance of a complete physical examination in hair-loss patients and also to emphasize the need to consider syphilis in our differential diagnosis of patchy alopecia.

Based on a search in PubMed and Google Scholar, using the key words "simultaneous primary and secondary syphilis", "alopecia syphilitica" and "syphilitic alopecia", this appears to be the first case of simultaneous primary and secondary syphilis associated with syphilitic alopecia reported in the English language literature.

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