

Alopecia syphilitica with detection of *Treponema pallidum* in the hair follicle

Alopecia is one of the clinical manifestations of secondary syphilis. It is uncommon for hair loss to be the sole or predominant manifestation, as hair loss is the chief clinical and histologic differential diagnosis of alopecia areata. The main difference between these two entities is the detection of *Treponema pallidum* in syphilis. We present the case of a 24-year-old Hispanic man, human immunodeficiency virus seropositive in treatment, with tiny patches of non-cicatricial alopecia in the parieto-occipital regions of his scalp. The patient denied previous history of genital or other skin lesions. A biopsy from an alopecic patch was performed which showed an inflammatory non-scarring alopecia with a discrete lymphocytic type inflammatory infiltrate localized in the peribulbar region. There was lymphocyte exocytosis into the matrix, associated with vacuolar degeneration, and scattered apoptotic cells were observed. Plasma cells were scattered. Immunohistochemical studies showed the presence of *T. pallidum* limited to the peribulbar region and penetrating into the follicle matrix. To the authors' knowledge, this is the first time that spirochetes have been shown in the hair follicle in alopecia syphilitica, suggesting that the spirochetes may be pathogenetic and responsible for the alopecia.

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Introduction

Alopecia is one of the clinical manifestations of secondary syphilis. In 1940, McCarthy described two types of syphilitic alopecia, 'symptomatic alopecia', associated with other lesions of secondary syphilis, and 'essential syphilitic alopecia', which has no other cutaneous or mucosal manifestations of the disease.¹ The frequency of alopecia syphilitica reported in the literature is variable, ranging from 5% to 48%, but it is uncommon for hair loss to be the sole or predominant manifestation.^{2,3} Clinically, it manifests as diffuse or patchy hair loss. The latter type of 'moth-eaten' loss is the most typical and is considered as a pathognomonic manifestation of secondary syphilis. The diffuse pattern is uncommon and has rarely been mentioned in recent reports. In both cases, the chief clinical and histologic differential diagnosis is with alopecia areata.^{3,4} Both alopecias are inflammatory and non-scarring by

nature and are mediated by a peribulbar lymphocytic infiltrate. We present a case of syphilitic alopecia in which the use of immunohistochemical techniques shows the presence of *Treponema pallidum* in the hair follicles of scalp biopsies.

Material and methods

A 24-year-old Hispanic man reported a 10-month history of increasing hair loss in the occipital regions of the scalp. Three years earlier, serological evidence of human immunodeficiency virus infection had been detected and he was receiving treatment with nevirapine, lamivudine and didanosine. At that time his CD-4 lymphocyte count was 476 per mm³ and the viral load was undetectable. The patient was homosexual and had had several partners in the previous few months. On examination, tiny patches of non-cicatricial alopecia in the parieto-occipital

regions gave his scalp a moth-eaten appearance (Fig. 1). The pull test was negative. He denied any previous genital or other skin lesion. Palpation showed several bilateral lymph nodes in both inguinal regions. Informed consent was obtained and a 4-mm punch was taken from an alopecic patch. The biopsy specimen was fixed in 10% formalin and routinely processed, cut vertically at 4 μ m, and stained with hematoxylin-eosin. An additional paraffin section was obtained for immunohistochemical study by the avidin-biotin-peroxidase complex technique, using the heat-induced epitope retrieval buffer, and a primary antibody against *T. pallidum* (1 : 200; BioCare Medical, Walnut Creek, CA, USA).

Results

Histopathological examination showed an inflammatory, non-scarring alopecia with a reduced number of hair follicles and frequent follicles in catagen. The epidermis was unremarkable and no lichenoid or dense perivascular infiltrate was evident. The only inflammatory infiltrate seen in the biopsy specimen was a discrete lymphocytic type localized in the peribulbar region. There was lymphocyte exocytosis into the matrix, associated with vacuolar degeneration, and scattered apoptotic cells were observed (Fig. 2). Lymphocytes within fibrous streams were also a striking feature. Plasma cells were scattered. Some follicles showed dendritic melanocytes with granular brown intracytoplasmic melanin in the follicle matrix.

Immunohistochemical studies showed the presence of *T. pallidum* limited to the peribulbar region and penetrating into the follicle matrix (Fig. 3). No spirochetes were found in other areas of the cutaneous biopsy and interestingly the follicles in



Fig. 1. Tiny patches of 'moth-eaten' alopecia in the parieto-occipital region.

which *T. pallidum* was present were those exclusively affected by the lymphocytic inflammatory infiltrate.

Serological screening for syphilis showed increased titers for Venereal disease research laboratory test (VDRL), Treponema pallidum hemagglutination assay (TPHA) and Fluorescent treponemal antibody absorption test (FTA-ABS). Lumbar puncture was performed without pathological findings. The patient was treated with three doses of 2.4 million units of benzathine penicillin each at 1-week interval, leading to complete resolution of his alopecia.

Discussion

Histopathologic features of alopecia syphilitica have been described in the literature. The largest series have been reported by Lee and Hsu (nine patients) and Jordaan and Louw (twelve patients).^{3,5} The main histologic findings described by Lee and Hsu were a normal dermal-epidermal junction, frequent telogen and catagen hairs, peribulbar lymphocytes and lymphocytes within fibrous streamers. Two cases showed parabulbar lymphoid aggregates, two cases had a lymphocytic infiltrate in the outer root sheath, and one case each featured a granulomatous infiltrate and an increase in dermal mucin. Plasma cells were evident only in four cases and no eosinophils were found. Lee and Hsu considered eosinophils to be significantly more common in alopecia areata than in syphilitic alopecia. The main histologic findings of Jordaan and Louw were similar to those of Lee and Hsu, differing only in the presence of eosinophils, which were identified in three cases. Melanin clumping was also a notable finding, but it could have been dependent on the skin pigmentation of the patients. Our findings are consistent with the main findings of these authors. The presence of melanocytes in the follicle matrix was also a frequent feature and no eosinophils were seen. There was a scattered plasma cell infiltrate.

The clinical features of secondary syphilis have been reviewed in the literature and an attempt has been made to associate them with the histologic findings.^{4,6,7} Clinically, more evident lesions display a dense, lichenoid, deep perivascular infiltrate with significant numbers of plasma cells. Macular lesions, as in our case, lack epidermal changes, have a sparse inflammatory infiltrate and show scattered plasma cells. The peribulbar lymphocytic infiltrate pattern has already been described as one of the microscopic patterns of secondary syphilis.³ However, scalp biopsies show that peribulbar lymphocytic inflammation is strongly clinically associated with the presence of alopecia areata.⁸ Plasma cells in syphilitic alopecia can be very scattered, as in this

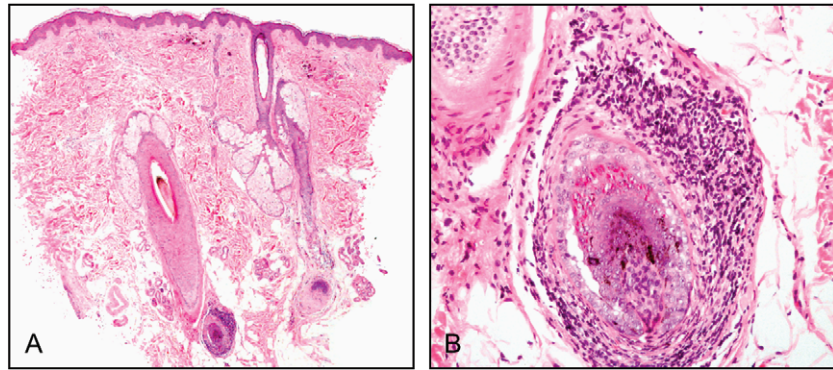


Fig. 2. Dense peribulbar-lymphocytic infiltrate in an anagen hair follicle, with lymphocyte exocytosis into the matrix (hematoxylin and eosin).

case, making the distinction from alopecia areata very difficult. Thus, we have two entities that are clinically and histologically similar, the main difference being the detection of *T. pallidum* in syphilis.

Classically, the detection of spirochetes has been based on silver stains such as the Warthin-Starry or Gomori methods. These types of techniques are prone to significant background artifact, which makes spirochete visualization more difficult and, in many cases, impossible. Attempts have also been made to detect the presence of spirochetes by immunofluorescence methods. Yobs et al. used fresh tissue but their method also yielded many artifacts.⁹ Al-Samarrai and Henderson reported an immunofluorescence technique that was useful in paraffin-embedded tissue sections. However, as described in other tissues, the reactivity diminished after storage.¹⁰ Molecular detection by polymerase chain reaction of *T. pallidum* has also been tried. This technique was the first known method for the direct detection of *T. pallidum* in scalp lesions, but two major risks have been described: the first is the

presence of false-positive cases and the second is the possibility of true-positive results that have no specific pathogenic relevance.² In 1970, Sternberger et al. developed the horseradish peroxidase-anti-horseradish peroxidase (PAP) technique, which allowed the identification of treponemes in tissues.¹¹ Beckett and Bigbee were the first to describe an immunoperoxidase method that was superior to conventional techniques. They compared the results of PAP and indirect immunoperoxidase techniques in syphilitic lesions.¹² Lee et al. compared different *T. pallidum* detection techniques, the immunoperoxidase method being the most sensitive of them.¹³ Recently, Hoang et al. compared the techniques of immunohistochemistry with a monoclonal antibody to *T. pallidum* and silver staining, concluding that the immunohistochemical technique was more sensitive and specific.¹⁴

To the authors' knowledge, this is the first time that spirochetes have been detected in the hair follicle in alopecia syphilitica, suggesting that the spirochetes may be pathogenetic and responsible for the alopecia. This had already been suspected by Lee and Hsu, who stated, 'We suspect that the peribulbar inflammation in alopecia syphilitica might be caused directly by locally present spirochetes'. However, they failed to show the presence of the microorganism in the biopsy specimen.³

In conclusion, we confirm the findings of other authors that alopecia syphilitica should be considered as one of the types of lymphocyte-mediated alopecia that mimics alopecia areata, and that the detection of *T. pallidum* by immunohistochemical techniques may lead to a definitive diagnosis of alopecia syphilitica.

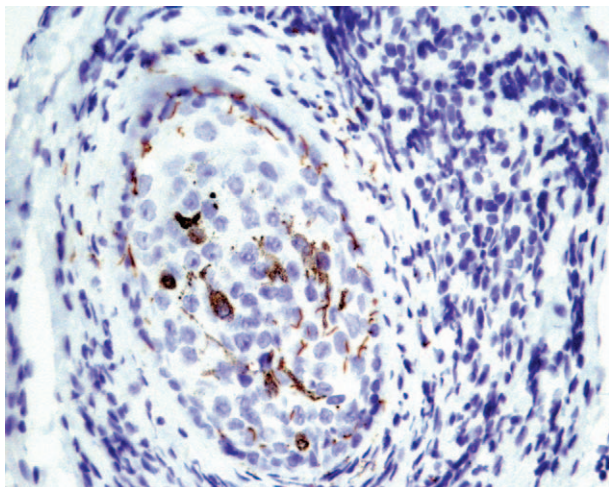


Fig. 3. Immunohistochemistry highlights typical spiral and thread-like organisms in the peribulbar region and penetrating the hair follicle matrix. Dendritic melanocytes inside the matrix are also evident with granular brown intracytoplasmic pigment.

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