JAMA Dermatology Clinicopathological Challenge

Diffuse Alopecia of the Scalp and Eyebrows

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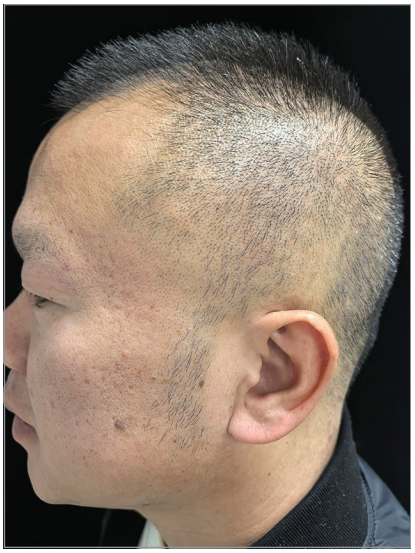
A Clinical image of scalp and eyebrow



B Hematoxylin-eosin staining (original magnification ×200)

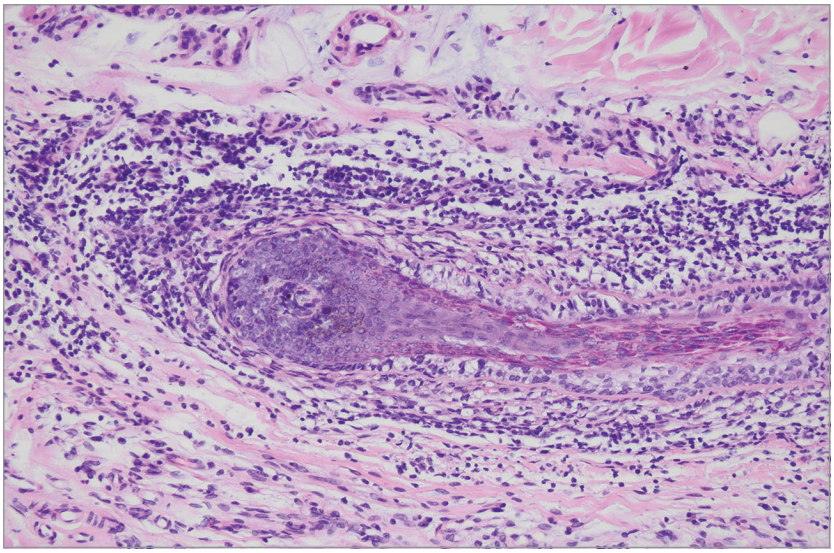


Figure 1. A, Scattered, irregularly shaped areas of hair loss distributed on the scalp and on both sides of the eyebrows. B, Hematoxylin-eosin staining (original magnification ×200) of the biopsy specimen reveals a dense, full-thickness perifollicular inflammatory infiltrate composed of lymphocytes and plasma cells.

A man in hi 30ss presented to our outpatient clinic with a 2-month history of hair loss. He presented with hair loss on the entire scalp and the lateral portions of both eyebrows. Small, diffusely scattered, patchy, irregular foci of alopecia involving the scalp and both eyebrows was observed, and results of the hair-pull test were negative (**Figure 1**A). The alopecic areas were devoid of symptoms, such as pruritus or pain, and there were no secondary changes, such as scaling, scarring, or other cutaneous alterations. The patient denied any history of medication use or previous episodes of alopecia but reported a history of sexual contact. The patient underwent trichoscopy. A biopsy specimen was obtained from the alopecic area and subjected to histopathological staining (Figure 1B).

WHAT IS YOUR DIAGNOSIS?

- **A.** Alopecia areata
- **B.** Tinea capitis
- **C.** Syphilitic alopecia
- **D.** Trichotillomania

CME Quiz at jamacmelookup.com

Diagnosis

C. Syphilitic alopecia

Microscopic Findings and Clinical Course

Laboratory tests revealed a rapid plasma reagin titer of 1:512 and positive findings on *Treponema pallidum* particle agglutination assay. However, findings of the anti-HIV antibody test were negative. Trichoscopy revealed a marked reduction in hair density and increased heterogeneity of hair shaft diameter. Within the alopecic areas, findings included empty follicles, yellow dots, black dots, exclamation mark hairs, and vellus hairs (**Figure 2**). Histopathological examination showed perifollicular lymphocytic infiltration with scattered plasma cells (Figure 1B). Furthermore, direct immunofluorescence staining of scalp biopsy tissue demonstrated the presence of *T pallidum*. Therapy involved the intramuscular injection of 2.4 million units of benzathine penicillin into both buttocks once a week for 3 weeks. After 2 months of follow-up, the patient's hair on the head and eyebrows started to regrow.

Discussion

Syphilitic alopecia (SA) is a relatively rare manifestation of secondary syphilis and can be accompanied by other mucocutaneous lesions. The incidence of this condition has been estimated to range from 2.9% to 11.2%, primarily affecting the temporal and occipital

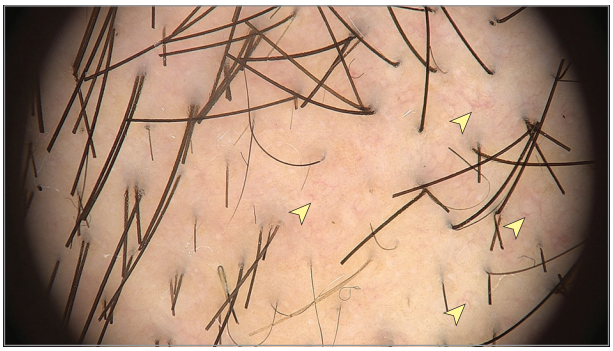


Figure 2. Trichoscopy of the alopecic area shows multiple features: hair shaft abnormalities, including exclamation mark hairs, short brittle hairs, and hair hypopigmentation; and follicular signs, such as empty follicles, yellow dots, and black dots. Additionally, branching and tortuous small blood vessels are visible on the scalp surface (arrowheads).

regions.[1] In some cases, hair loss may be the sole clinical symptom, complicating the diagnosis. Clinically, SA can be categorized into 3 types: moth-eaten, diffuse, and mixed. Of these, the moth-eaten type is regarded as the most common and characteristic form of secondary syphilis.[2] This type manifests as numerous small and scattered patches of hair loss, resembling worm-eaten patterns. In contrast, the diffuse type can cause diffuse hair loss; moreover, eyelashes, the outer one-third of the eyebrows, and body hair can fall out. The immune-mediated small-vessel vasculitis observed in SA can adversely affect the hair growth cycle and trigger reactive phenomena. Consequently, trichoscopic alterations are produced, which are comparable with those seen in telogen effluvium, including reduced hair density per follicular unit, empty follicles, and short regrowing hairs.[3]

When SA appears without other signs of secondary syphilis, trichoscopy can be used as a supplementary tool. The characteristic trichoscopic findings of SA include black dots, patchy alopecia areas, hypopigmented hair shafts, and yellow dots.[4] Nonscarred moth-eaten type hair loss is not limited to SA and can also occur in other conditions, such as alopecia areata, trichotillomania, and tinea capitis.[4] Hence, when encountering a patient whose sole symptom is alopecia, careful differential diagnosis is warranted.

Nonscarring alopecia encompasses a range of conditions, including alopecia areata, trichotillomania, tinea capitis, and SA, each showing distinct clinical presentations. Hair loss in alopecia areata lesions is often localized. The active phase may present with classic exclamation mark hairs, characterized by a fragile, proximally narrowed shaft that appears hypopigmented compared with the intact distal end.[5,6] The crucial histopathological finding is a peribulbar lymphocytic infiltrate, classically described as a swarm of bees. In addition, an increased proportion of catagen/telogen hairs and follicular miniaturization is seen.[7] Tinea capitis is routinely noted in children with inflammatory, scaling, and pustular hair loss. The presence of spores and/or hyphae within the hair shaft is the predominant characteristic manifestation in all endophytic tinea capitis cases.[8] Nonetheless, certain patients may exhibit lymphadenopathy. A superficial or deep perifollicular infiltrate comprising neutrophils, eosinophils, and lymphocytes may be observed.[8] Tinea capitis can be ruled out by the absence of fungal elements on microscopy and the lack of characteristic inflammatory signs. Trichotillomania is caused by repeated hair pulling. Its key features are an irregularly shaped hair loss area, broken hairs of different lengths, and negative findings on the hair-pull test.[9] The prominent morphological alterations include follicular injury, architectural distortion of the follicular anatomy, and perifollicular/intrafollicular hemorrhage, accompanied by a conspicuous absence of significant inflammatory infiltrates.[9] This condition is ruled out in case of complete hair loss without any broken hairs, as the mechanical fracture of the hair shaft is a key feature.

Immunohistochemical staining shows that *T pallidum* was mainly found in the areas surrounding hair follicles and hair roots.[3] These histopathological features are beneficial in differentiating SA from conditions such as alopecia areata, tinea capitis, and trichotillomania.

As an all-purpose imitator, SA can exhibit symptoms indistinguishable from those of other diseases. Hence, dermatologists should suspect SA when evaluating patients presenting with alopecia as the sole symptom, given its tendency to mimic other common hair disorders.

ARTICLE INFORMATION

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