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Mixed-pattern, essential syphilitic alopecia, uveitis, and papillitis in an immunocompetent patient with neurosyphilis

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Abstract

Syphilitic alopecia (SA) and ocular syphilis (OS) are rare manifestations of syphilis, typically reported together in immunocompromised patients. We present a unique case of mixed-pattern, essential, SA of the scalp and OS in the form of anterior uveitis in an otherwise immunocompetent, HIV-negative, 46-year-old female. Briefly, the patient initially presented with sudden-onset scalp hair loss that was initially diagnosed as atypical alopecia areata but failed to respond to typical alopecia areata-directed therapy. Concurrently, the patient developed ocular and neurologic symptoms, and the diagnosis of syphilis was rendered based on the constellation of clinical findings and cerebrospinal fluid/serologic testing. Syphilis-directed therapy resulted in the reversal of ocular and neurologic symptoms, as well as rapid scalp hair regrowth. This case highlights the importance of considering diagnosis of syphilis in the differential diagnosis for atypical alopecia.

Introduction

Syphilis is a sexually transmitted disease caused by the spirochete *Treponema pallidum* (*T. pallidum*). Rates in the United States increased to 40 per 100,000 in 2020, and it is more prevalent among men.[1,2] The natural history of syphilis progresses through several stages – primary, secondary, latent, and tertiary – some of which have a broad constellation of signs that often masquerade as other diseases, earning it the moniker “the great mimicker”. The primary stage is characterized by a painless chancre (an indurated ulcer) typically on the genitals. The secondary stage includes various disseminated mucocutaneous and systemic symptoms (*e.g.*, maculopapular rash, lymphadenopathy, condylomata lata, fever). The latent stage is largely asymptomatic, but serological tests remain positive. This stage is subdivided into early latent (less than one year of disease duration) and late latent (greater than one year of disease duration). Left untreated, approximately one-third of affected patients will progress to the tertiary stage, which can occur years after the primary infection and encompasses neurological, cardiovascular, and cutaneous symptoms (*e.g.*, gummas).[2-4] The term neurosyphilis is applied when the infection involves the central nervous system, and since it can occur at any stage, but is most often associated with tertiary, its clinical manifestations can vary widely from cognitive changes to sensorimotor symptoms, such as hearing loss or vision loss.[5] Syphilis can affect nearly any part of the eyeball, though intraocular inflammation (uveitis) is the most common presentation, particularly in late latent and tertiary stages. Ocular syphilis (OS) is considered a form of neurosyphilis, which can be fatal if untreated, so prompt diagnosis and treatment of these patients is critical.[6] Coinfection with HIV is common, and there is evidence that OS occurs more frequently in individuals with HIV, often presenting with more severe symptoms.[7-9]

Syphilitic alopecia (SA) is a non-scarring alopecia that is a rare presentation of secondary syphilis, with a 3-7% prevalence.[2] There are two classifications of SA: symptomatic SA with hair loss and skin lesions, and essential SA with hair loss alone without visible scalp changes. Essential SA has three presentations: diffuse, moth-eaten, and mixed, with moth-eaten being the most common.[2]

There have been several reports of the co-occurrence of SA and OS, primarily in males and those with HIV.[10-12] Additionally, there is one report of an HIV-negative male with a history of Crohn's disease on immunosuppressive therapy presenting with both SA and syphilitic uveitis.[13] Here, we report a unique case of syphilis presenting with SA and OS in an HIV-negative and immunocompetent female.

Case Report

A 46-year-old female patient presented to the Dermatology clinic for evaluation of diffuse scalp hair loss and mild scalp pruritus of three months' duration with no identifiable triggers and no alleviation from over-the-counter remedies. She was noted to have diffuse, patchy, non-scarring alopecia with bitemporal accentuation and a negative pull test (Figure 1A). She also had madarosis of eyebrows and eyelashes, which had been present and stable for many years. Review of systems and medical history were unremarkable and complete blood counts and thyroid tests were normal. A punch biopsy of the left scalp was obtained (Figure 1A) and showed miniaturization, 40% telogen shift, and robust lymphoplasmacytic inflammatory infiltrate surrounding the bulbs of vellus hairs in the mid dermis. *T. pallidum* staining was negative for spirochetes (Figure 2). A diagnosis of atypical alopecia areata was favored, and the patient was started on oral minoxidil (1.25 mg daily) and intralesional triamcinolone injections. At three months' follow-up, progressive hair loss was noted with minimal regrowth at the injected sites (Figure 1B).

Shortly thereafter, the patient developed acute ocular symptoms, including tearing, photosensitivity, and blurry vision. She was seen by an optometrist, where her visual acuity was noted to be 20/40 in the right eye (OD) and 20/30 in the left eye (OS). She was diagnosed with "acute granulomatous uveitis" in both eyes and treated empirically with topical prednisolone acetate, moxifloxacin, and cyclopentolate. Four days later, she presented to a different optometrist, who noted bilateral optic disc edema and advised her to seek evaluation in the Emergency Department (ED) for neuroimaging and further work-up, which the patient declined. Instead, she was seen by her outpatient neurologist, who obtained magnetic resonance imaging (MRI) with and without contrast, which did not reveal any abnormalities. She was then referred to a retinal specialist (L.Z.). Examination was notable for the absence of anterior chamber cells or keratic precipitates (KPs), the presence of Frisén grade 3 optic disc edema without peripapillary hemorrhages, and the absence of retinal vascular sheathing or retinitis. Macular spectral domain optical coherence

tomography (SD-OCT) was notable for subretinal drusenoid deposits (SDDs) and patchy disruption of the ellipsoid zone (EZ) in both eyes (OU). Green fundus autofluorescence (FAF) revealed peripapillary spotty hyperautofluorescence (hyperAF) OU (Figure 3).

Due to the presence of moderate/severe optic disc edema and macular EZ loss, neurosyphilis was strongly suspected. The patient was sent urgently to the ED for infectious and autoimmune serological tests and a lumbar puncture (LP), which revealed normal opening pressure, pleocytosis, elevated protein, and reduced glucose. Cerebrospinal fluid venereal disease research laboratory was positive. Confirmatory serology for *T. pallidum* antibody was positive, with a rapid plasma reagin (RPR) titer of 1:1,024, confirming the diagnosis of neurosyphilis. The patient was treated with IV penicillin G 24,000,000 units daily for 14 days.

At a follow-up with Ophthalmology the week after her hospitalization, the patient's visual symptoms and optic disc edema had already improved. As for the hair loss, considering the diagnosis of neurosyphilis, the original dermatological diagnosis of alopecia areata was revised to SA, triamcinolone injections were discontinued, and oral minoxidil was continued with close monitoring. At follow-ups approximately four months after treatment with penicillin, her visual acuity improved to 20/20, her optic disc edema and EZ disruption had resolved (Figure 3), and she had complete regrowth of scalp hair (Figure 1C). The timeline summarizes the key events and progression of the case (Figure 1D).

Discussion

We highlight an unusual and previously unreported case of an immunocompetent female patient with mixed-pattern, essential SA and neurosyphilis presenting with OS. Most reported cases have occurred in immunocompromised patients (*e.g.*, HIV) and men. Hair loss as the presenting symptom of syphilis, especially in the absence of coexisting signs of secondary syphilis, is rare.[13] While the patient's history of long-standing madarosis and the biopsy results initially favored a diagnosis of alopecia areata – thereby justifying the original treatment with intralesional steroid and oral minoxidil – the rapid reversal of the scalp alopecia after treatment with IV penicillin G and the complete regrowth of the hair within a few months strongly support a diagnosis of SA. Both SA and alopecia areata can appear similar histologically, with peribulbar lymphoid cell infiltrate, hair follicle miniaturization, and predominant telogen phase shift.[2,3] The presence of peribulbar plasma cells can help distinguish SA from alopecia areata.[3] This is important since staining for spirochetes is challenging and often negative, as in our case.[14] A retrospective review of this patient's scalp biopsy was performed and revealed an increased number of plasma cells among the lymphocytic infiltrate. Though there is no pathognomonic ophthalmic feature

of syphilis, the constellation of findings seen in this case – anterior granulomatous uveitis, patchy EZ disruption and SDDs (*i.e.*, posterior syphilitic uveitis), and papillitis – was sufficient to lead to a diagnosis of syphilis.

Conclusions

This case underscores the importance of considering syphilis in the differential diagnosis of non-scarring alopecia and bilateral uveitis and optic disc edema, especially in the context of an atypical clinical presentation. Prompt recognition and intervention were critical in preventing the progression of symptoms and morbidity associated with syphilis. In this case, treatment not only reversed the vision and hair loss but may have ultimately proved lifesaving.

References

1. Hall CDX, Ryan D, Hayford C, et al. Syphilis Prevalence, Incidence, and Demographic Differences in a Longitudinal Study of Young Sexual and Gender Minority Adults Assigned Male at Birth. J Infect Dis 2023;229:232.
2. Mohammad K Shalabi M, Burgess B, Khan S, et al. Alopecia syphilitica, from diagnosis to treatment. Proc Bayl Univ Med Cent 35:180-3.
3. Stefanato CM. Histopathologic diagnosis of alopecia: clues and pitfalls in the follicular microcosmos. Diagn Histopathol 2020;26:114-27.
4. Henao-Martínez AF, Johnson SC. Diagnostic tests for syphilis: New tests and new algorithms. Neurol Clin Pract 2014;4:114.
5. LaFond RE, Lukehart SA. Biological Basis for Syphilis. Clin Microbiol Rev 2006;19:29-49.
6. Furtado JM, Simões M, Vasconcelos-Santos D, et al. Ocular syphilis. Surv Ophthalmol 2022;67:440-62.
7. Balba GP, Kumar PN, James AN, et al. Ocular syphilis in HIV-positive patients receiving highly active antiretroviral therapy. Am J Med 2006;119:448.e21-25.
8. Becerra LI, Ksiazek SM, Savino PJ, et al. Syphilitic uveitis in human immunodeficiency virus-infected and noninfected patients. Ophthalmology 1989;96:1727-30.
9. Jame R, Al-Saeigh Y, Wang LL, Wang K. Justified Suspicion: Symptomatic Syphilitic Alopecia in a Patient with Well-Controlled HIV. Case Rep Infect Dis 2021;2021:1124033.
10. Chakvetadze C, Monfort JB, Dupin N, et al. A 26-year-old man presenting with loss of vision, skin lesions and wasting. Médecine Mal Infect 2012;42:80-1.
11. Fowler BJ, Winward BK, Scott L. Syphilitic Uveitis and Alopecia. Am J Ophthalmol 2022;242:e3-4.
12. Chang KM, Nadi L, Wallach F. Secondary syphilis with alopecia and ocular manifestation. J Microbiol Immunol Infect 2021;54:758-9.
13. Al-Busani H, Namiki T, Miura K, Yokozeki H. Mixed-pattern syphilitic alopecia of the scalp associated with uveitis and asymptomatic neurosyphilis. J Dermatol 2020;47:e311-3.
14. Lee JY, Hsu M. Alopecia syphilitica, a simulator of alopecia areata: histopathology and differential diagnosis. J Cutan Pathol 1991;18:87-92.

Figure 1. Evolution of Hair Loss and Overall Timeline. (A) Diffuse, patchy, non-scarring, mildly pruritic alopecia with bitemporal accentuation and negative pull test at presentation. A left scalp biopsy was taken (outlined in blue); (B) progressive worsening of alopecia at 3 months; (C) complete resolution of alopecia at 6 months (4 months after treatment with penicillin); (D) timeline summarizing the progression and resolution of SA and OS symptoms.

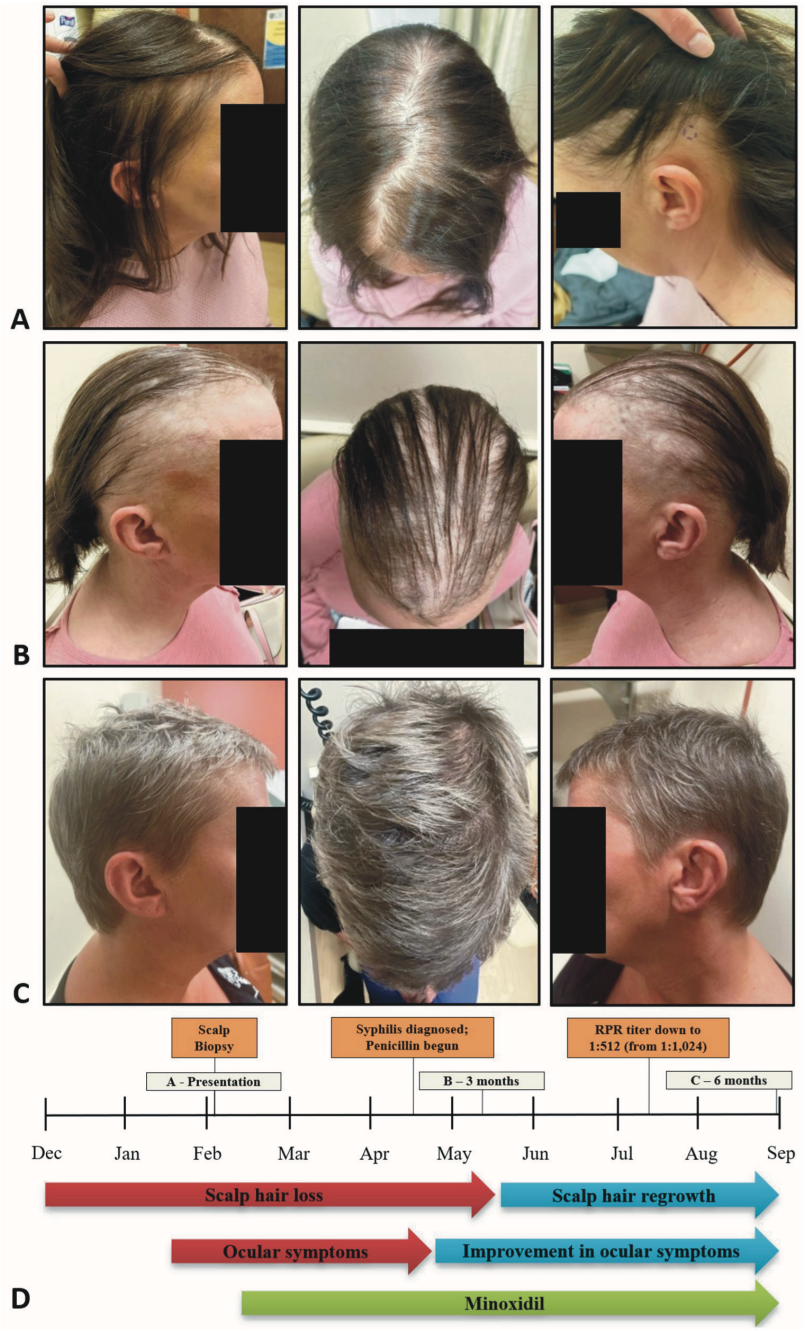

Figure 2. Histopathologic Characteristics of Scalp Biopsy with Hematoxylin and Eosin (H&E) Stain. (A) 40x magnification view of telogen shift; (B) 200x magnification view of plasma cell infiltration.

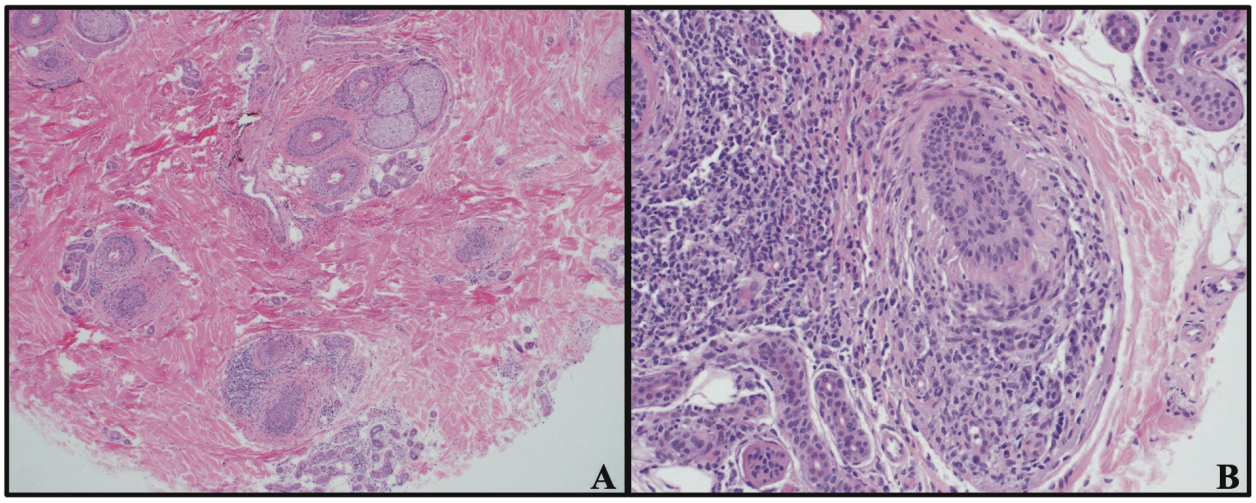

Figure 3. Multimodal imaging of the right eye, obtained with ZEISS Clarus 700 and Cirrus 5000 (Carl Zeiss Meditec, Dublin, CA), from the initial visit (blue rectangle) and follow-up (red rectangle) with the Retinal specialist (L.Z.). The left eye is not shown, but it showed similar findings. (A) Color fundus photograph (CFP) demonstrating Frisén grade 3 optic disc edema; (B) green fundus autofluorescence (FAF) shows spotted hyperautofluorescence (hyperAF) in the nasal macula corresponding to mild irregularities in the photoreceptor ellipsoid zone (EZ) and (C; magnified inset) subretinal drusenoid deposits (SDDs; green triangle) seen with optical coherence tomography (OCT) b-scan; (D; magnified inset) OCT b-scan through the optic disc shows swelling and pre-internal limiting membrane (pre-ILM) epipapillary hyperreflective deposits, which likely represent vitreous cells; (E) CFP shows nearly resolved optic disc edema; (F) green FAF shows resolution of the spotted hyperAF in the nasal macula; (G; magnified inset) OCT b-scan shows resolution of the EZ disruption and SDDs; (H; magnified inset) OCT b-scan through the optic disc shows resolved edema and pre-ILM epipapillary hyperreflective deposits.