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Atrichia with papular lesions: A case report

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Abstract

We present a case of clinically suspected atrichia with papular lesions in an 8-year-old male presenting with alopecia universalis and keratotic papules. We review the literature available on this rare genodermatosis.

Keywords

Alopecia, congenital atrichia, atrichia with papular lesions, pediatric dermatology, genodermatoses

Introduction

Alopecia is a common and distressing clinical complaint in the primary care setting, arising from heterogeneous etiologies. In the pediatric population, hair loss often presents with differing patterns from that of their adult counterparts, and further consideration must be given to rarer congenital and hereditary causes of hair loss, which can occasionally present as part of a multisystem syndrome.[1] Furthermore, psychosocial implications of pediatric alopecia for child and family warrant prompt diagnosis and management.

Alopecia universalis (AU) is a group of disorders with complete or almost complete loss of scalp and body hair, with alopecia areata as the most frequent etiology.[2] Atrichia with papular lesions (APL; OMIM 209500) represents a complex and heterogenous group of genodermatoses characterized clinically by complete and irreversible hair loss shortly after birth and is associated with the development of keratin-filled cysts over the body resulting from mutations in the hairless gene (*HR*).[2]

Case report

An 8-year-old, healthy, Caucasian male was referred to dermatology for evaluation of AU. Upon presentation, our patient demonstrated no hair on the scalp or body, with minimal eyebrows and eyelashes. His mother reported that he was born with hair that fell out within 6 months of birth. There were no known developmental or dental abnormalities (Figure 1). He had no known family history of genetic conditions or consanguinity. On examination, smooth patches of hair loss with no evidence of scarring affected the scalp, body, eyebrows, and eyelashes with few minimal hairs (Figure 2). Pitting was present on nearly every fingernail. Keratotic papules were found on the cheeks and, to a lesser extent, the extremities (Figures 1 and 2). Treatment had been attempted with topical steroids with no improvement. Based on these findings, an ectodermal dysplasia syndrome was suspected. Genetic testing was carried out earlier in life, but his family was unaware of the results and, unfortunately, declined further genetic testing as it would not impact treatment options. The diagnosis of APL was suspected. Vitamin D–dependent rickets was ruled out with normal vitamin D serology.

Discussion

APL is a rare condition that was first observed by Damste and Prakken[3] in three unrelated women with a syndrome of alopecia and numerous follicular cysts tracing back to early childhood.[4] It was first referred to as congenital atrichia by Ahmad et al.[5] APL has been noted for decades among Gypsies known as Irish Travelers, who have existed as a distinct indigenous ethnic minority within Ireland. Published estimates of APL prevalence remain low, despite having the pathogenetic mutations in *HR* identified in distinct populations around the world, often affected by consanguinity.[2–4,6–17] It is suspected to be more common than current estimates, as APL is often mistaken for autoimmune AU,

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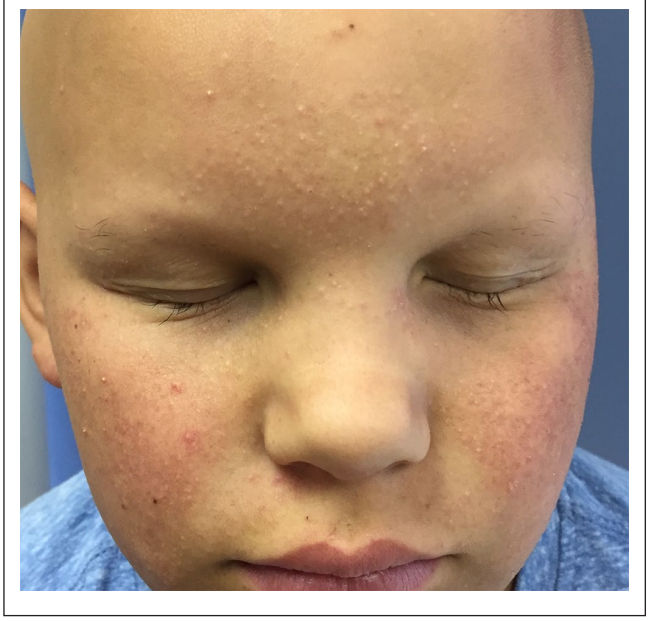

Figure 1. Alopecia universalis, with keratotic facial papules and normal appearing dentition.

achieving the diagnosis after patients fail to respond to standard treatment modalities.[2,18]

In APL, hairs are typically absent from the scalp, axillae, and body, and individuals are almost completely devoid of eyebrows and eyelashes.[11] Lanugo hairs are present at birth, but alopecia is complete within the first year of life as catagen follicles are unable to re-enter the anagen phase. At approximately 2 years of age, progressive keratin retention into follicular structures results in cystic formations clinically evident as papules—a hallmark of the disease.[19] In contrast to ectodermal dysplasia with associated atrichia, patients with APL display no defects in other ectodermal structures (i.e. nails, sweat glands, or teeth) and have normal development and hearing.[10,11,12,16] Heterozygous individuals typically have normal hair and are clinically indistinguishable from genotypically normal persons.[16]

APL is caused by mutations in the *HR* gene, which is situated on chromosome 8p21.2 (short arm) and encodes a single zinc-finger transcription factor that is highly expressed in the brain and skin.[14,16] The *HR* protein functions as a co-repressor of multiple nuclear receptors, including the vitamin D receptor (VDR).[20] It appears to function in the cellular transition to the first adult hair cycle by regulating epithelial stem cell differentiation, lying in a region of the follicle outer root sheath. In its absence, the hair bulb undergoes premature apoptosis during the first catagen stage, resulting in a complete form of inherited alopecia.[6,13,20] The database of allelic series continues to expand as approximately 50 different nonsense, missense, insertion, and deletion mutations have been reported in the *HR* gene.[6] Although the majority of cases of APL involve homozygous mutations, sporadic cases

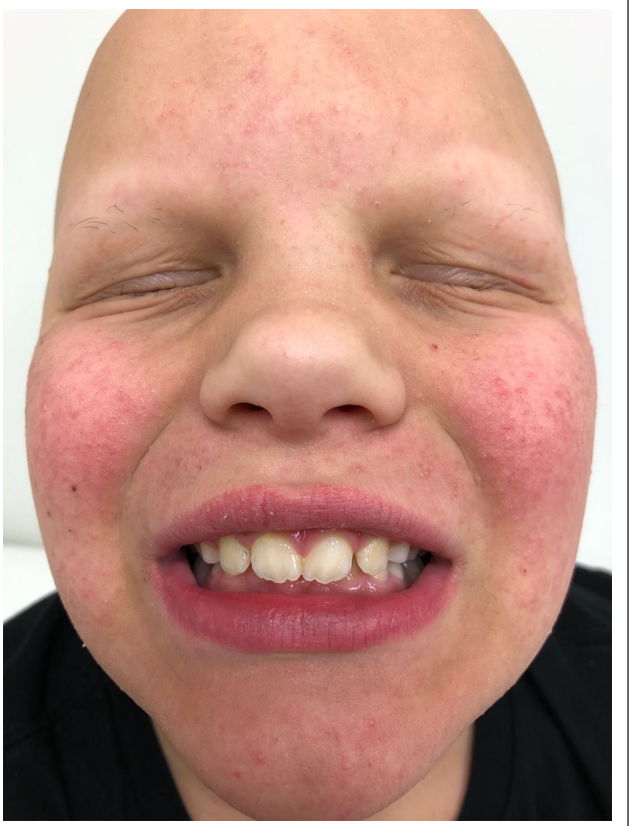

Figure 2. Alopecia universalis and keratotic papules affecting the face.

of compound heterozygous mutations in nonconsanguinous families have been identified over the past decade.[10,17]

The differential diagnosis of APL includes AU, congenital hypotrichosis, vitamin D–dependent rickets type II (same phenotype, mutation in the VDR), and ectodermal dysplasia.[2,16] Consanguinity, the development of AU within the first year of life, disseminated cysts or papules, and nonresponsiveness to therapy strongly suggests the diagnosis of APL.[19] The diagnostic criteria for APL were updated in 2008 by Yip et al.[19] based on review of the literature and personal observations, as shown in Table 1. It is important to note that a scalp biopsy is not required for a diagnosis when clinical and genetic findings support APL.[10] However, scalp biopsy can be safely performed whenever genetic testing is not available.[19] If performed, histopathologic examination in APL reveals empty infundibula with irregular epithelial structures or cysts replacing the lower two-thirds of hair follicles and various sizes of keratinizing epithelial cysts at all levels of the dermis.[21]

In summary, we present a case of suspected APL in an 8-year-old male who presented with AU and keratotic papules. Our patient met three of the five major criteria and three of the minor criteria,[19] requiring definitive genetic testing or affirmative scalp biopsy to confirm the diagnosis of APL; however, the parents were hesitant to pursue either in this case. We are

Table 1. Diagnostic criteria for APL.[19]

Major criteria (four of five required for diagnosis)
1. Permanent and complete absence of scalp hair by the first few months of life
2. Few to widespread smooth, whitish, or milia-like papules on the face, scalp, arms, elbows, thighs, or knees from infancy or childhood
3. Replacement of mature hair follicle structures by follicular cysts filled with cornified material in scalp histology
4. Mutation(s) in the human hairless gene through genetic testing
5. Clinical and/or molecular exclusion of vitamin D–dependent rickets
Minor criteria (supplementary criteria)
1. Family history of consanguinity
2. Absence of secondary axillary, pubic, or body hair growth and/or sparse eyebrows and eyelashes
3. Normal growth and development, including normal bones, teeth, nails, and sweating
4. Whitish hypopigmented streaks on the scalp
5. Lack of response to any treatment modality

APL: atrichia with papular lesions.

reporting this case as it is a rare disorder commonly misdiagnosed as AU resistant to treatment and wrongly treated with steroids with additional adverse effects. When dealing with cases of universal alopecia resistant to therapy and associated with papules, it becomes imperative to consider congenital APL. Vitamin D–dependent rickets should be ruled out as it has similar clinical presentation and is treatable. Unfortunately, there are no treatments currently available for APL.

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Informed consent

Consent to perform and submit this case report for publication was given by the patient's mother.

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