Alopecia areata in a patient with WNT10A heterozygous ectodermal dysplasia

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Abstract

We report a case of a patient with ectodermal dysplasia attributed to a heterozygous 321C>A mutation in *WNT10A* who developed overlying autoimmune mediated hair loss. To the best of our knowledge this is the first reported case of alopecia areata in a patient with *WNT10A* heterozygous ectodermal dysplasia. This case highlights the importance of considering multiple pathways of hair loss in patients with underlying genetic defects and raises the possibility of a shared genetic predisposition.

Keywords: alopecia, ectodermal dysplasia, hair loss, WNT10A

Introduction

Ectodermal dysplasias make up a large group of rare clinically heterogeneous disorders characterized by developmental failure in two or more of the following structures: hair, teeth, nails, sweat glands, and other ectodermally derived structures [1,2]. Since they were described by Freire-Maia in 1971, more than 200 variants have been defined [3]. It is a rare condition estimated to occur in every one in 100,000 live births [4]. *WNT10A* mutations account for approximately 9% of cases of ectodermal dysplasia and cause a broad continuum of phenotypes, ranging from apparently isolated or mild ectodermal dysplasia symptoms to more severe syndromic manifestations [5]. Abnormalities in hair are common, ranging from absent hair growth to sparse or fragile hair in the scalp, eyebrows, and/or eyelashes [6,7].

Alopecia areata is a much more commonly observed form of hair loss in children, in which T-cells infiltrate the hair follicle, leading to patchy, non-scarring hair loss. It affects up to 1.7% of the general US population [8]. Mechanistic studies in mouse models have implicated an IFNγ-driven immune response as the main pathogenic factor [9].

Herein, we describe a patient with *WNT10A* heterozygous ectodermal dysplasia presenting with acute worsening of hair loss, who was found to have alopecia areata in addition to chronic decreased hair density hair related to her genetic disease.

Case Synopsis

The patient is a 9-year-old girl with a complex medical history including autism spectrum disorder and ectodermal dysplasia who presented with new-onset patchy hair loss. Her mother described a life-long history of poor growth of hair and nails, with recent onset of patchy hair loss, most noticeable at the posterior scalp.

The patient was the product of a twin pregnancy, born prematurely at 35 weeks' gestation. She carries a diagnosis of autism spectrum disorder but had been meeting all developmental milestones. Her twin brother has Duchenne muscular dystrophy. The patient had previously undergone genetic testing

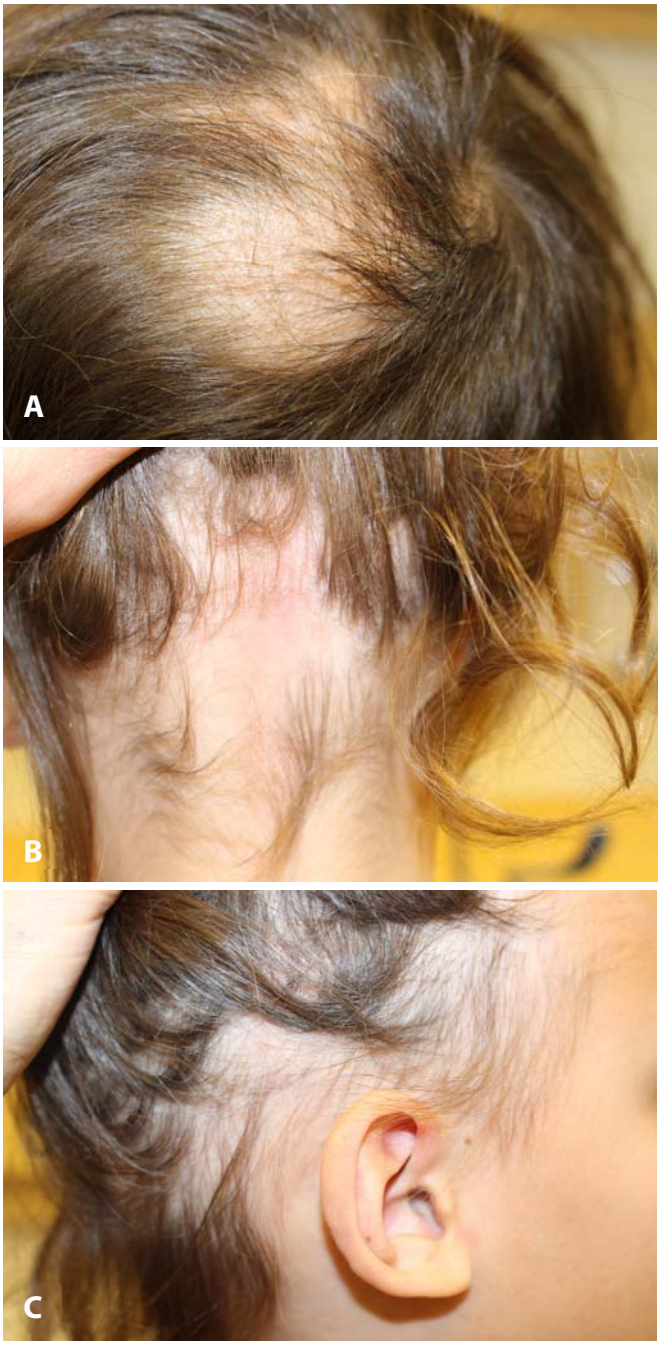

Figure 1. *Discrete patches of non-scarring hair loss on the **A)** vertex of the scalp, **B)** posterior scalp, and **C)** temporal scalp.*

which demonstrated a heterozygous 321C>A mutation in *WNT10A* as well as Duchenne muscular dystrophy carrier status.

On examination, the patient was noted to have cone-shaped teeth and hypoplastic nails. Scalp examination was notable for diffuse thinning and brittle hair with discrete patches of alopecia with exclamation point hairs and no loss of follicular ostia (**Figure 1**).

A biopsy was obtained at another hospital from one of the alopecic patches and revealed peri-bulbar chronic inflammation with lymphocytic infiltrate (**Figure 2**). A diagnosis of new-onset alopecia areata in the setting of ectodermal dysplasia was made.

Treatment was initiated with fluocinonide 0.05% solution and minoxidil 5% foam to affected areas of the scalp. Upon follow-up four months after initiating treatment the patient had experienced near complete regrowth of hair within the affected patches. However, the background diffuse thinning and brittle hair remained.

Case Discussion

WNT10A plays an essential role in the development of skin, hair, nails, and teeth and is required for

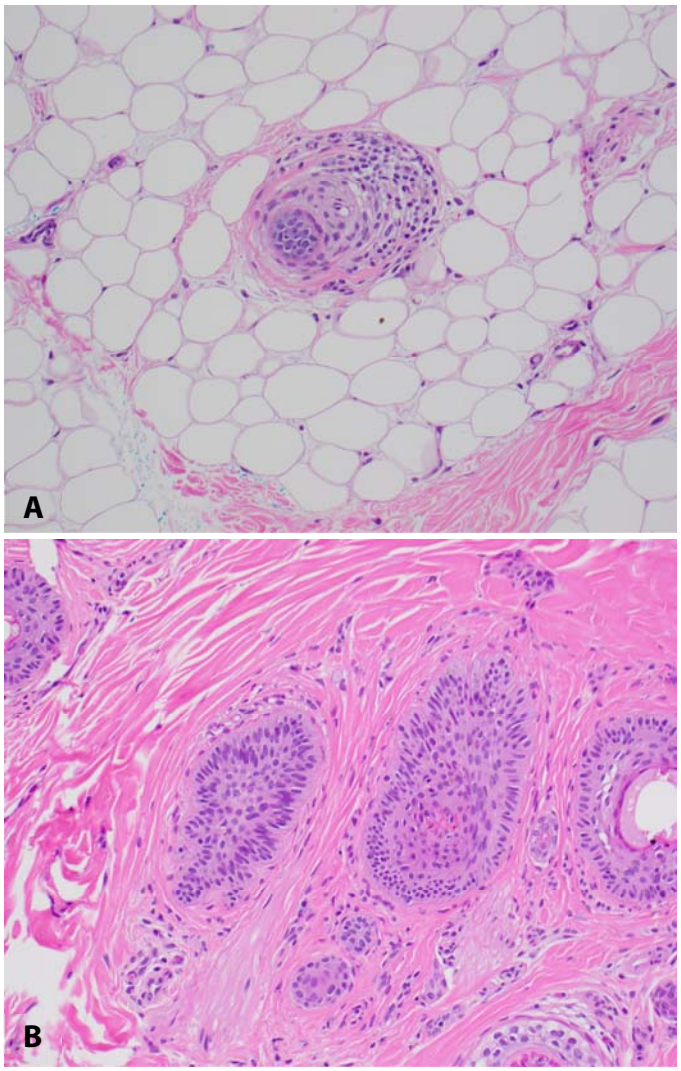

Figure 2. *Histologic features of alopecia areata, including **A)** peri-bulbar inflammation and **B)** several telogen hair follicles.*

proper epithelial progenitor proliferation and subsequent differentiation [5,10]. After embryonic development *WNT10A* plays a role in epithelial renewal via Wnt-activated self-renewing stem cells in adult tissues [10]. Homozygous mutations in *WNT10A* have been implicated in the development of syndromic ectodermal dysplasias including odonto-onycho dysplasia (OOD) and Schöpf–Schulz–Passarge syndrome (SSPS), [5,11,12]. Abnormalities in the hair are also common, ranging from absent hair growth to sparse or fragile hair in the scalp, eyebrows, or eyelashes [6,7]. A 2009 study found approximately 50% of individuals with heterozygous mutations in *WNT10A* showed minor disease-associated symptoms. Heterozygous males predominantly showed dentition defects, whereas heterozygous females showed more nail and hair manifestations [7]. The 321C > A variant noted in this patient has been previously reported in at least 37 patients clinically diagnosed with ectodermal dysplasia and related syndromes [6,7,13-18]. This variant is predicted to cause a premature termination of the gene sequence that may lead to inappropriate decay of mRNA [6].

The importance of *WNT10A* and the Wnt/β-catenin signaling pathway in hair biology is highlighted by the association between polymorphisms and multiple forms of hair loss. In additional to ectodermal dysplasia *WNT10A* polymorphisms are associated with the development of androgenetic alopecia and polymorphisms in other genes involved in the Wnt/β-catenin signaling pathway have been directly linked to alopecia areata [19,20]. Further, differential expression of Wnt/β-catenin associated genes has been observed in alopecia areata patients [21]. Although autoimmune disease, such as alopecia areata, is primarily mediated by autoimmune dysregulation, alterations in the Wnt/β-catenin signaling have been proposed to contribute to alopecia areata by increasing the proportion of quiescent hair follicles and thus decreasing the threshold for clinically apparent hair loss [20].

Conclusion

In the case presented, hair loss appears to have been multi-factorial. The patient's diffuse thinning and brittle hair are likely attributable to her underlying ectodermal dysplasia. However, the acute onset of patchy hair loss with inflammatory infiltrate noted on histopathology points to an autoimmune process, further supported by the rapid improvement with topical corticosteroid therapy. To the best of our knowledge this is the first reported case of alopecia areata in a patient with *WNT10A* heterozygous ectodermal dysplasia. Given the rare occurrence of *WNT10A* heterozygous ectodermal dysplasia and the relatively high prevalence of alopecia areata, further studies are required to determine if there is a true association between the two conditions or if this is an incidental finding. Herein, we describe a commonly encountered diagnosis, alopecia areata, presenting uniquely in a patient with ectodermal dysplasia. This highlights the possibility of multi-factorial hair loss in those affected with *WNT10A* mutations.

Potential conflicts of interest

The authors declare no conflicts of interests.

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