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Case Report

Localized Hypotrichosis Type 1 Due to Intragenic Deletion of Exons 5-8 in Desmoglein Gene in a Neonate from Indian Family

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Abstract

Localized hypotrichosisis a rare genetic disorder characterized by short sparse hairs on the scalp/alopecia with variable involvement of the eyebrows, eyelashes. Pubic and axillary hair is usually spared. Here we report on a neonate who presented with absent scalp hair, body hair and icthyosis of the skin at the time of birth. At the age of 1 year icthyosis subsided with treatment but there was no growth of hair. Whole exome sequencing revealed a likely pathogenic exonic deletion c.(372+1_373-1)_(1005+1_1006-1) encompassing exon 5-8 of DSG4 gene related to autosomal recessive Localized hypotrichosis type 1. The previously reported cases were from Middle Eastern countries and none of them were from Indian descent.

Keywords: Hypotrichosis; Icthyosis; Desmoglein

Introduction

Localized hypotrichosis (OMIM 607903) type 1 is a rare autosomal recessive disorder characterized by fragile sparse scalp hair with or without involvement of eyebrows and eyelashes. It can also affect the hair of trunk and extremities, but sexual hair is largely spared [1]. Hyperkeratotic follicular papules, erythema, and dry ichthyotic skin are associated findings. It is caused by pathogenic variants in *DSG4* gene. This gene encodes a desmosome protein which is expressed in hair follicle and epidermis. It plays an important role in proliferation and differentiation of keratinocytes and adhesion of epidermal cells [2].

Case Report

This is a case of male baby born to healthy third degree consanguineous couple. Antenatal period was uneventful. There were no maternal comorbidities. Nuchal scan was not done. Detailed ultrasound scan was normal. There was history of oligohydramnios from 38 weeks. The male neonate was born at term by caesarian delivery with birth weight of 2.58 kg. After birth he was diagnosed to have absent scalp hair with dry skin. On examination of the child, anthropometry was corresponding to age and sex appropriate values. He had alopecia, absent eyebrows and eyelashes with no hair over the trunk, extremities (Figure 1) and icthyosis of the skin (Figure 2). Teeth and nails were normal. There was no facial dysmorphism except for elevated upper lip and mild retrognathia. Neck, chest, spine and extremities were normal. Systemic examination was normal. Extended newborn screening was normal. Screening for congenital hypothyroidism was also normal. The clinical features were suggestive of non-syndromic congenital alopecia with autosomal recessive icthyosis. The couple was counseled and whole exome sequencing was sent.

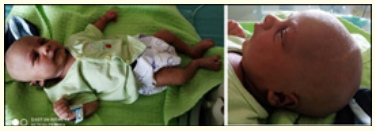

Figure 1: Alopecia, absent eyebrows, eyelashes, and body hair with broad forehead and mild retrognathia in the child at birth.

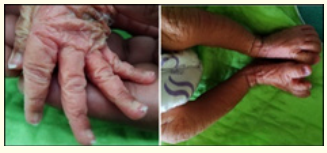

Figure 2: Icthyosis of skin with wrinkling and peeling in upper and lower limbs at birth.

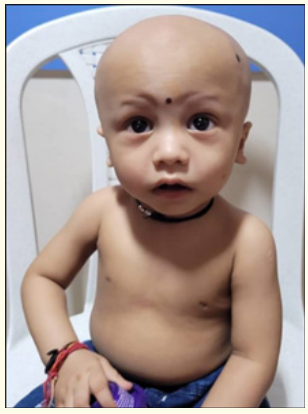

Figure 4: Normal skin with alopecia, absent hair over the face, body and limbs at the age of 1 year.

Results

Whole exome sequencing revealed a homozygoud likely pathogenic exonic deletion c.(372+1_373-1)_(1005+1_1006-1) in exon 5 to 8 of *DSG4* gene related to autosomal recessive localized hypotrichosis type 1. Real time PCR done using primers designed in exon 6 of *DSG4* gene showed that both parents are heterozygous for the variant identified in the child (Figure 3). The child is 1 year at present and has alopecia, absent body hair but icthyosis subsided with treatment (Figure 4). Developmental milestones are normal.

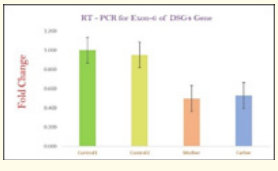

Figure 3: Real time PCR done using primers designed in exon 6 of *DSG4* gene showed that both parents are heterozygous for the variant identified in the child.

Discussion

Hypotrichosis is a complex genetically heterogeneous disorder which can be either syndromic or nonsyndromic and is inherited in an autosomal dominant or autosomal recessive manner [3]. The disease can be diagnosed by excluding other possible causes of hypotrichosis and by genetic evaluation.

There are three types of Localized autosomal recessive hypotrichosis (LAH). Type 1 is caused by mutations in *DSG4* gene which result in the production of abnormal desmoglein proteins and in abnormal proliferation of hair follicles [4]. There is extreme inter and intrafamilial variability and those with severe phenotype have complete absence of hair. Few cases present with keratosis follicularis, scalp erosions and monilethrix-like hairs [1]. These findings suggest that LAH type 1 and recessive monilethrix form a spectrum with variable expressivity [5].Teeth, nails and sweating are normal. Growth and development are normal.

The exact prevalence of autosomal recessive hypotrichosis is not known. Most of the cases of LAH 1 reported till now are from Pakistan, Iraq, Iranian, Moroccan, Japanese descent. The present case is from Indian descent.

DSG4 gene is localized on chromosome 18q21.1. The protein desmoglein is a member of cadherin super-family. A transmembrane domain, an extracellular domain and an N-terminal cytoplasmic domain are three main functional domains in the protein. It is involved in calcium binding, membrane integration, cell-cell interactions, and post-translational modification. Thus this gene plays an important role in morphogenesis of epidermis and of hair follicle [6]. Exon 5 to 8 deletion in *DSG4* gene has been reported in many Pakistani families representing it as their ancestral mutation [7]. Our case is from Indian descent and had deletion of exon 5 to 8. The amino acids deleted are located in extracellular repeat domain of protein.

There is phenotypic variability in cases with LAH type 1, indicating that in addition to mutations in *DSG4* potential modifiers play a role specifically among familial cases [7]. In our case the neonate had severe phenotype with complete absence of hair from head to toe with icthyosis. Later on icthyosis subsided. Exact genotype-phenotype correlations are not established. Differential

diagnosis of LAH are Atrichia congenita and Alopecia universalis congenita. There is no effective treatment of LAH but icthyosis can be managed by using emollients.

Conclusion

Most of the cases of LAH1 reported till now are from Middle Eastern countries, this case report of LAH1 is from Indian descent of Asian origin. Genetic evaluation of such cases helps in exact prognostication of the child.

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Conflict of Interest

The authors declare no conflict of interest.

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