ACTA SCIENTIFIC CLINICAL CASE REPORTS

Volume 4 Issue 11 November 2023

Case Report

Homozygous *WNT10A* Variant in an Indian Boy Manifesting Odonto-Onycho-Dermal Dysplasia

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Received: July 24, 2023

Published: October 06, 2023

Abstract

This is a report of a rare case with biallelic mutation in the *WNT10A* gene with features of hidrotic ectodermal dysplasia. A homozygous pathogenic variant in the *WNT10A* gene, c.1168G>T p.Glu390Ter was identified in the proband by whole exome sequencing. Sanger sequencing of the parents established the carrier status. The mutation was earlier reported in an Asian Indian in UK at the age of 50yr with eyelid cysts as the clinical manifestation.

Keywords: Odonto-onycho-dermal Dysplasia; OODD; Ectodermal Dysplasia; *WNT10A* Gene

Odonto-onycho-dermal dysplasia (OODD; OMIM #257980) [1] is a rare autosomal recessive ectodermal dysplasia caused by mutations in the *WNT10A* [2] gene and account for 9% of all cases of ectodermal dysplasia. Wide range of clinical phenotypes are described with *WNT10A* gene mutation from isolated tooth agenesis, mild form of ectodermal dysplasia to syndromic forms like odonto-onycho-dermal dysplasia (OODD) and Schöpf– Schulz–Passarge Syndrome (SSPS). Schopf–Schulz–Passarge syndrome (SSPS) is a rare type of ectodermal dysplasia that has autosomal recessive inheritance. It is characterized by palmoplantar keratoderma, hypodontia, hypotrichosis, nail dystrophy, and multiple periocular and eyelid apocrine hidrocystomas. In children, SSPS is difficult to differentiate from OODD as eyelid cysts are a late manifestation. *WNT10A* is critical for dentinogenesis and tooth morphogenesis in regulating the odontoblast differentiation [3] and is important for the development of ectodermal appendages, such as hair, teeth, skin, and nails in humans [4]. SSPS and OODD have overlapping phenotypes with hypodontia, nail dystrophy, hypotrichosis and palmoplantar keratoderma but eyelid cysts are reported to be characteristic for SSPS [5]. Around 30 patients with OODD have been reported in the literature [6]. However, the exact incidence of OODD is difficult to estimate due to a lack of a clear phenotypic distinction among the various hereditary ectodermal dysplasias' (HED). A new case of OODD in an Indian patient with features of ectodermal dysplasia is reported in this paper.

Case

A 10-yr-old boy born to non-consanguineous parents presented with failure to thrive and frequent respiratory infections and dental abnormalities. Growth was at 3rd centile with delay in the eruption of teeth. He had two widely spaced hypoplastic upper central incisors (Figure 1). The upper and lower canines were hypoplastic. Scalp hair, eyebrows and eye lashes were scanty and no cystic lesions were seen in the eyes. He had dystrophic finger (Figure 2) and toe nails. Sweating was normal and no other members in the family were affected. He was clinically diagnosed with hidrotic ectodermal dysplasia and genetic testing was performed. Whole exome sequencing identified a homozygous nonsense substitution c.1168G>T (p.Glu390Ter) in exon 4 of the *WNT10A* gene (Figure 1), which is predicted to cause premature termination of the protein. The truncated protein is predicted to have a length of 389 amino acids as opposed to the original length of 417amino acids, which might result in loss-of-function. Both the parents were heterozygous carriers.

Discussion

Odonto onycho dermal dysplasia was first described in 1983 in 2 Lebanese families [7] characterized by a series of core clinical features including tooth agenesis, onycho dysplasia, hyperkeratosis of palms, soles, hyperhidrosis or hypohidrosis of skin, atrophic patches on the face and rarely sparse hair. This is the second case

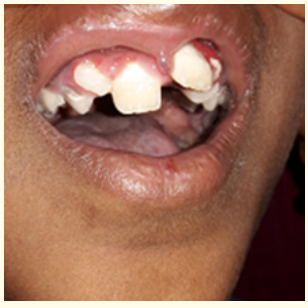

Figure 1: Hypodontia.

Figure 2: Dystrophic nails.

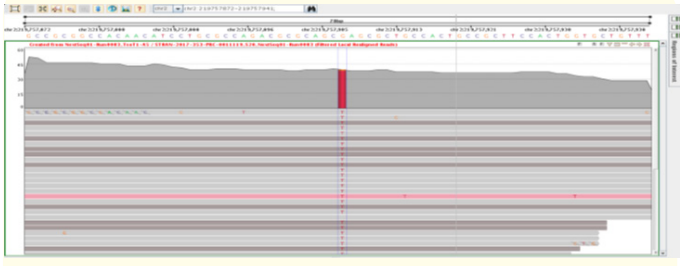

Figure 3: IVG showing homozygous mutation c.1168G>T (p.Glu390Ter) in WNT10A gene.

report of molecularly identified OODD from India. The child did not manifest eyelid cysts and palmoplantar keratoderma. Palmoplantar keratoderma and hyperhidrosis, the presence of eyelid cysts (hidrocystoma) often develop in mid-twenties thus clinical differentiation between OODD and SSPS is difficult in childhood. The identified homozygous nonsense substitution (p.Glu390Ter) in the patient is reported earlier by McGrath (in a study of seven patients) in an Asian Indian patient who manifested eyelid cysts, palmoplantar keratoderma at the age of 50 years [5]. Recently, Biju Vasudevan from Pune reported one case of OODD in a 19 year old boy manifesting thickening of the skin of palms and soles, distortion of toenails, and dry skin [8]. Since there are no reports on Indian specific mutations in the *WNT10A* gene, and finding the same mutation in two Indian patients, it could be possible that this may be the common Indian mutation. The other Indian mutation reported by Biju Vasudevan is the c.433G>A in exon 3. The reported cases are few in number but could be higher due to difficulties in clinical differentiation among the various types of ectodermal dysplasia.

Although there is no effective cure for the disease, dental prostheses should be provided to a patient. Supportive treatment, psychological support, genetic counselling and prenatal diagnosis to the family should be provided.

Conflict of Interest

NIL.

Financial Support

Nil.

Informed consent was obtained from parents for publication.

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