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X-Linked Hypohidrotic Ectodermal Dysplasia: Case Report, Update on Oral Manifestations and Recent Concepts in Treatment

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Abstract: ***X-Linked Hypohydrotic Ectodermal Dysplasia affects 21.9 in 100,000 cases, making it a rare disorder of the ectodermal tissue. XLHED is the most common variant of Ectodermal Dysplasia. This article presents one case report and updates on its oral and craniofacial manifestations along with some of the most recent treatment modalities for the same.***

Keywords: X Linked Hypohidrotic Ectodermal Dysplasia, Oral Manifestations, Treatment

1. Introduction

Ectodermal Dysplasia is a group of syndromes affecting the ectodermal structures. 154 such syndromes have been associated with the group of disorders. [1]Ectodermal Dysplasia primarily affects Hair, Nails, Teeth, Salivary Glands, Cranio-Facial Structure and Sweat glands of the affected individual, although other symptoms may also be seen. Ectodermal Dysplasia is. 77 genes and nine chromosomal regions to 75 are today connected to 75 Ectodermal Dysplasias.[2]Hypohidrotic ectodermal dysplasia is a rare X linked condition. This type of Ectodermal Dysplasia will usually present with features like sparse scalp hair, largely absent body hair, deficiency of major sweat glands, and anodontia or oligodontia with conical teeth. There is also the presence of a distinctive facies, with prominence of the forehead, a depressed nasal bridge, prominent lips, and periorbital wrinkling and pigmentation. Subcutaneous fat is often diminished or absent, as are the mucous glands in the respiratory tree and the gastrointestinal tract.[3]

2. Case Presentation

A 35 year old male reported to the Department of Oral Pathology and Microbiology, School of Dental Sciences, Sharda University. The patient complained of missing teeth and a constant dry feeling in his eyes and mouth that was manifestly connected to halitosis that the patient presented with. Patient's facial profile was symmetric bilaterally, with a marked protuberance on the forehead, a deep nasal bridge was also observed. Also observed was sparse distribution of hair on the patient's eyebrows and scalp along with peri-orbital wrinkling (Image 1). The patient reported of no natural loss of tooth, including loss of primary teeth and gave negative history extraction of his teeth, yet he was observed to be partially edentulous (Image 2).Upon review of the Oral Pantomogram(Image 3)of the patient the patient was found to have had retained 54, 55, 64, 65, 74, 75, 84 and 85. Amongst permanent teeth, 11, 21, 36 and 46 were evident on the OPG. The patient further gave history of constantly feeling warm due to inability to sweat in hot weather. Very few (10-12) hair follicles were found to be present on the entire length of the patient's forehand (Image 4). Patient also gave familial history of the presence of similar symptoms in his maternal uncle.

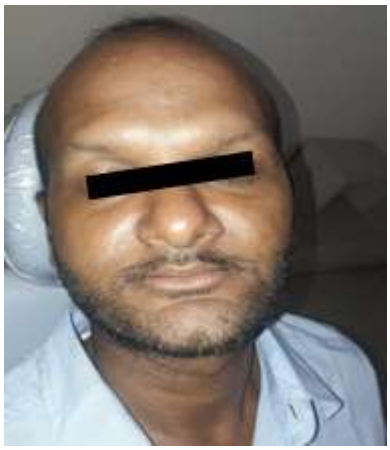

Image 1: Characteristic Forehead Protuberance with Sparse Distribution of Hair on the Patient's Eyebrows and Scalp Along With Peri-Orbital Wrinkling

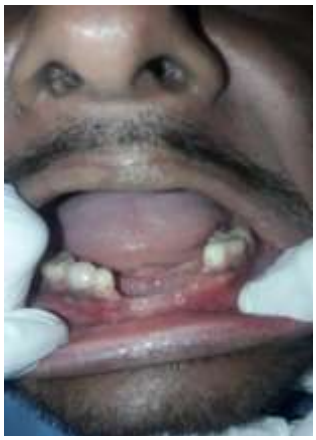

Image 2: Partially Edentulous Mandibular arch

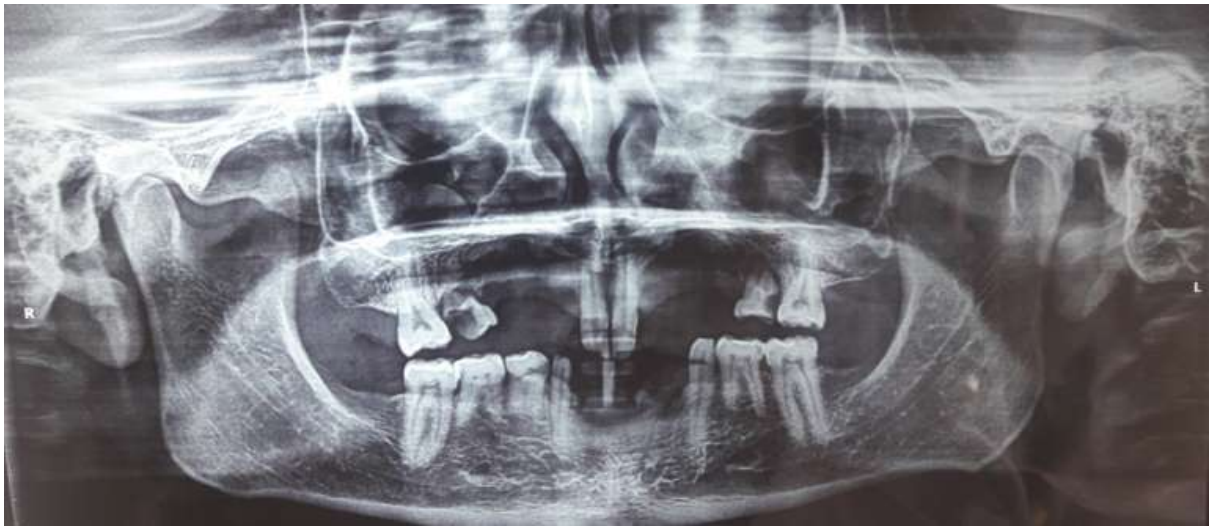

Image 3: Retained deciduous teeth with few Permanent Teeth

Image 4: Only A Few Hair Follicles Seen On the Patients' Forearm

1) Investigations

Oral pantamograph of the patient was done to assess the dental health status of the patient. And on review, it was observed that the patient had retained deciduous teeth and very few permanent teeth in both the dental arches. The numbers of teeth congenitally missing from the patient's oral cavity were indicative of presence of oligodontia, a condition that seldom occurs by itself and is often associated with a syndrome.

2) Treatment/Management

Treatment is focussed on alleviating the symptoms for the patients. Absence of sweat glands will lead to an inability to maintain body temperature in the sun; therefore the patient is advised to avoid prolonged exposure to the sun. Xeropthalmiawas managed with methyle cellulose eye drops and for dry mouth, the patient was advised to have water frequently throughout the day. Partial anodontia or complete anodontia can be managed with removable, fixed or implant based prosthesis used singly or in combination. Although for young patients these prosthesis need to be closely monitored as they need more frequent adjustment. [4]

3) Oral Manifestations of Hypohidrotic Ectodermal Dysplasia

Many people receive their diagnosis of X linked Hypohidrotic Ectodermal Dysplasia (XLHED) after a dental examination when there is no eruption of teeth before 12–18 months of age, or when there is atypia present in either the site or structure of newly erupted tooth. Tooth agenesis is a common feature of XLHED.[5]

The oral manifestation of Hypohidrotic Ectodermal Dysplasia includes, but is not limited to-multiple congenitally missing teeth, crown and rootdysmorphism, presence of conical-shaped crowns, and reduction inflow of saliva. Microdontia is also observed in affected individuals. Moderate to severe taurodontism is known to affect the second primary mandibular molars in few individuals with HED.[6]

Oral manifestations like the presence of dental aberrations, are some othercommon findings in Ectodermal Dysplasias. This is why oral examination, which includes assessment of salivary secretion, should be part of the clinical evaluation in suspected cases. There isalso found to besome co-variation with tooth size and tooth shape in the clinical expression of mutations in genes associated with hypodontia. In more common forms of the condition (like XLHED) the spectrum of oral and dental symptoms varies from very easy to miss to easily recognizable variationsfrom the normal. Female carriers, as well as individuals with IncontinentiaPigmenti, can have no missing teeth.[7]

3. Discussion

(Ectodermal dysplasia protein) EDA, (ectodysplasin 1, anhidrotic receptor) EDAR, and (Ectodysplasia A receptor associated death domain) EDARADD are the three principle genes associated with XLHED.

Mutations inEctodysplasinA(ED1) are responsible for a form of X-linked recessive ED. Allelic mutations in EDAR which encodes a putative ectodysplasin receptor, account for

both autosomal recessive and dominant types of EDA.[9] The exact mechanism of action is unknown.

Features of HED become obvious during early childhood. The scalp hair is thin, lightly pigmented, and rather slow-growing. Perspiration, although not absent entirely, is still deficient, which leads to episodes of hyperthermia until environmental temperature control is achieved by the affected family. Few abnormally developed teeth may erupt, and that too at a later-than-average age. Physical growth and psychomotor development are usually within normal limits.

Diagnosis is usually done by gene sequence analysis of EDA, EDAR, EDARADD and WNT10A genes.[10]There is currently no specified diagnostic criteria for XLHED.

Crawford PJ, Aldred MJ, Clarke A[11] in 1991 suggested that dental radiographs would be useful in diagnosis of XlHED, they also suggested that dental radiographs could also play a role in establishing the carrier status of an individual.

Prenatal Screening is possible with localisation of EDA 1 Gene at Xq12-q13.1.[12]

Nguyen-Nielsen M, Skovbo S, Svaneby D, Pedersen L, Fryzek J in a 2013 study conducted in Denmark found the prevalence of XLHED to be 21.9 per 100,000 overall and 1.6 per 100,000 when they restricted themselves to molecularly-confirmed XLHED cases.

The authors also reported the most frequent age at time of XLHED diagnosis to be between the ages of 11 and 18 years. They further added that they found that teeth abnormalities were present in 79% of all cases.[13]

4. Recent Concepts

Schneider et al in 2015, proposed using EDA agonists, particularly EDI200, which are relevant to optimal therapeutic response windows required for the formation of any EDA-dependent structures like ectodermal appendages. Use of theirdescribed methods allows for the design of targeted therapeutic dosing and administration regimens in order to correct or alter abnormal phenotypes associated with genetic disorders, in particular, XLHED.[14]

Another study that predates this finding was published in 2007, by Casal ML *et al.* conducted a study in canines with X-Linked Hypohidrotic Ectodermal Dysplasia. The authors Fc:EDA1, a kind of recombinant EDA. The authors found the research to show promising results, and suggested that there was significant correction of disease in the canines treated with the new, recombinant EDA.[15]

5. Summary

X-Linked Hypohidrotic Ectodermal Dysplasia follows a very predictable course of inheritance and prenatal diagnosis in utero is possible with current advancements in molecular diagnostic techniques. Recent treatment modalities need further research on a larger sample size to be accepted as effective treatment for the disease.

References

[1] Pinheiro M, Freire-Maia N (November 1994). "Ectodermal dysplasias: a clinical classification and a causal review". Am. J. Med. Genet. **53**(2): 153–62.
[2] Pagnan NA, Visinoni ÁF. Update on ectodermal dysplasias clinical classification. American Journal of Medical Genetics Part A. 2014 Oct 1;164(10):2415-23.
[3] Clarke A. Hypohidrotic ectodermal dysplasia. Journal of medical genetics. 1987 Nov;24(11):659.
[4] Pigno MA, Blackman RB, Cronin RJ, Cavazos E. Prosthodontic management of ectodermal dysplasia: a review of the literature. Journal of Prosthetic Dentistry. 1996 Nov 1;76(5):541-5.
[5] Bondarets N, Jones RM, McDonald F. Analysis of facial growth in subjects with syndromic ectodermal dysplasia: a longitudinal analysis. Orthodontics & craniofacial research. 2002 May 1;5(2):71-84.
[6] de Aquino SN, Paranaíba LM, Swerts MS, Martelli DR, de Barros LM, Júnior HM. Orofacial features of hypohidrotic ectodermal dysplasia. Head and neck pathology. 2012 Dec 1;6(4):460-6.
[7] Bergendal B. Orodental manifestations in ectodermal dysplasia—A review. American journal of medical genetics Part A. 2014 Oct 1;164(10):2465-71.
[8] Kere J, Srivastava AK, Montonen O, Zonana J, Thomas N, Ferguson B, Munoz F, Morgan D, Clarke A, Baybayan P, Chen EY. X–linked anhidrotic (hypohidrotic) ectodermal dysplasia is caused by mutation in a novel transmembrane protein. Nature genetics. 1996 Aug;13(4):409.
[9] Döffinger R, Smahi A, Bessia C, Geissmann F, Feinberg J, Durandy A, Bodemer C, Kenwrick S, Dupuis-Girod S, Blanche S, Wood P. X-linked anhidrotic ectodermal dysplasia with immunodeficiency is caused by impaired NF-κBsignaling. Nature genetics. 2001 Mar;27(3):277.
[10] Wright JT, Grange DK, Fete M. Hypohidrotic ectodermal dysplasia.
[11] Crawford PJ, Aldred MJ, Clarke A. Clinical and radiographic dental findings in X linked hypohidrotic ectodermal dysplasia. Journal of medical genetics. 1991 Mar 1;28(3):181-5.
[12] Mortier K, Wackens G. Ectodermal dysplasia anhidrotic. OrphanetEncyclopedia. 2004 Sep;3:1-6.
[13] Nguyen-Nielsen M, Skovbo S, Svaneby D, Pedersen L, Fryzek J. The prevalence of X-linked hypohidrotic ectodermal dysplasia (XLHED) in Denmark, 1995–2010. European journal of medical genetics. 2013 May 31;56(5):236-42.
[14] Schneider P, Kowalczyk-Quintas C, inventors; Edimer Pharmaceuticals Inc, assignee. Treatment of X-linked hypohidrotic ectodermal dysplasia with a fusion EDA1 protein. United States patent US 9,925,239. 2018 Mar 27.
[15] Casal ML, Lewis JR, Mauldin EA, Tardivel A, Ingold K, Favre M, Paradies F, Demotz S, Gaide O, Schneider P. Significant correction of disease after postnatal administration of recombinant ectodysplasin A in canine X-linked ectodermal dysplasia. The American Journal of Human Genetics. 2007 Nov 1;81(5):1050-6.