CASE REPORT

Hypohidrotic Ectodermal Dysplasia: A Case Report

Aakanksha Suryarao, Chandrashekhar Kadam, Mohammad Nasiruddin and Ashwini Pai

ABSTRACT

Aim: This article reports a classic case of hypohidrotic ectodermal dysplasia and aims at providing a review primarily on aetiology and the factors to be considered while diagnosing this disorder.

Summary: Ectodermal dysplasia (ED) is a rare genetic disorder characteristically affecting the ectodermal derivatives and causing two or more of the following features; Trichodysplasia (hair dysplasia), Dental dysplasia, Onychodysplasia (nail dysplasia) and Dyshidrosis. Hypohidrotic earlier called as anhidrotic (HED) and hidrotic are the two main clinical forms of ED. Here, a case of 21 year old male manifesting as full-blown hypohidrotic ED is presented.

Keywords: Ectodermal dysplasia, hypohidrotic, dental dysplasia.

INTRODUCTION

Ectodermal dysplasia (EDA) may have been recorded as early as 1792 by Danz. In 1838, Wedderburn documented ectodermal dysplasia, describing a case of 10 Hindu male family members in a letter to Charles Darwin.[1]

Dr. Aakanksha Suryarao completed her Graduation (BDS) from Sinhgad Dental College and Hospital, Pune in 2013, and presently pursuing her postgraduation in M A Rangoonwala College of Dental Science and Research Center, Pune, India.

Department of Oral Medicine & Radiology, M.A. Rangoonwala College of Dental Sciences & Research Centre, Pune, Maharashtra, India

Address for Correspondence:
Dr. Chandrashekhar Kadam, Department of Oral Medicine & Radiology, M.A. Rangoonwala College of Dental Sciences & Research Centre, 2390-B, K.B. Hidayatullah Road, Azam Campus, Pune, Maharashtra 411001, India.
Contact: +91 9823053107
E-mail: cmkadam@gmail.com
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Thurman in 1848 described a case of hereditary syndrome presenting as sparse hair, dry skin and missing teethin two male first cousins and their maternal grandmother.[1,2] Similar cases were reported in 1883 and 1886 by Guilford and Hutchinson, respectively. Weech in 1929 introduced the term hereditary ectodermal dysplasia and called those with inability to perspire as 'anhidrotic'. Felsher (1944) studied that anhidrotic forms are not devoid of sweat gland, so he coined the term 'hypohidrotic' instead of anhidrotic'.[1] The prevalence of EDA is estimated to be seven cases/10,000 births, and the incidence of the carriersis higher, probably around 17.3 in 100,000 women.[3] Majority of cases of hypohidrotic ED are transmitted as X-linked recessive trait (XLHED) in which the gene is carried by the female and manifested in the male. However, autosomal dominant and recessive mode of inheritance have also been reported in few families.[4]

The gene responsible for XLHED is EDA (ectodysplasin A) gene located at Xq12q13.1 coding for a transmembrane protein expressed by keratinocytes, hair follicles, teeth, and sweat glands. Epithelial-mesenchymal signaling is affected by this gene which leads to the clinical aspects of the disorder.[4] The first classification system of the EDAs was proposed by Freire Maia and Pinheiro in 1982, with additional inputs in 1994 and 2001.[3]

ED manifests as combination of following defects: ED1: Trichodysplasia (hair dysplasia); ED2: Dental dysplasia; ED3: Onychodysplasia (nail dysplasia); and ED4: Dyshidrosis (sweat gland dysplasia).[1] The classification included the following groups:

Group A: disorders manifested by defects in at least

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two of the four classic ectodermal structures as mentioned above, with or without other defects and

Group B: disorders manifested by a defect in one classic ectodermal structure (1-4 from above) in combination with (5) a defect in one other ectodermal structure (i.e., ears, lips, dermatoglyphics).[3]

Based on the primary ED defects, following constitute the different categories of ectodermal dysplasias- Subgroup 1-2-3-4; Subgroup 1-2-3; Subgroup 1-2-4; Subgroup 1-2; Subgroup 1-3; Subgroup 1-4; Subgroup 2-3-4; Subgroup 2-3; Subgroup 2-4; Subgroup 3; and Subgroup 4. From amongst above, this case belongs to subgroup 1-2-4.

Patho-physiological classification of ED was given by Lamartine in 2003 based on following defects: (1) Cell-to-cell communication and signaling, (2) adhesion, (3) development and (4) other. Functional classification of ED included the following 2 groups: (1) Defects in developmental regulation/epithelial-mesenchymal interaction manifesting as "pure" EDs, with lone involvement of ectodermal derivatives and major skeletal involvement;[5] and (2) defects in ectodermal structural proteins affecting cytoskeleton maintenance and cell stability manifesting as "dermatologic" ectodermal dysplasias with additional involvement of the ectoderm and highly differentiated epithelium.[3,6]

The following are the three most recognized ectodermal dysplasia syndromes, falling into the subgroup 1-2-3-4, as they show features from all four of the primary ectodermal dysplasia defects in association with other anomalies: Ectrodactyly-ectodermal dysplasia-clefting syndrome (EEC); Rapp-Hodgkin HED; and Ankyloblepharon, ectodermal defects, cleft lip/palate (AEC) or Hay-Wells syndrome.[1]

HED is characterized by abnormalities comprising sparse hair (hypotrichosis), abnormal or missing teeth (hypodontia or anodontia), and an inability to sweat (hypohidrosis or anhidrosis).

Oral manifestations of HED are of particular interest to the dentist, because patients with this disorder invariably have missing or malformed teeth, affecting both the primary and permanent dentition, which can pose a significant challenge to the dentist in restoring form and function of the dentition. In addition, there may be involvement of other structures of ectodermal origin, e.g., ears, eyes, lips, mucous membrane of mouth and nose, central nervous system. Defects in tissues derived from other embryonic layers may also be observed.[3] The disorder manifests in its full-blown form in affected males while female carriers may manifest few, none or all of the symptoms in variable distribution.[7]

The diagnosis of ectodermal dysplasia is based principally on: Clinical history as ungula dystrophy, hypotrichosis, anodontia, oligodontia, hypodontia; Histopathology of the skin biopsy showing reduction in pilosebaceou sunits and sweat glands;[7] Examination of hair showing thin, sparse, brittle and fine hair with distorted, bifid, or small hair bulbs and microscopic findings of little pigmentation in the hair shaft and discontinuity of the medulla ora "bar code" appearance when medulla is present;[4] dentaldysmorphia and agenesis seen on panoramicradiography; and molecular genetic analysis.

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A 21 year old male patient reported with a complaint of several missing teeth and severe intolerance to heat since his childhood. There was no history of any systemic disease. None of his family members had similar history. Examination revealed typical features of ectodermal dysplasia, subgroup 1-2-4. Frontal bossing, depressed nasal bridge (Fig. 1 & 2), scarce hair over the scalp (Fig. 3), eyebrows and eyelashes,

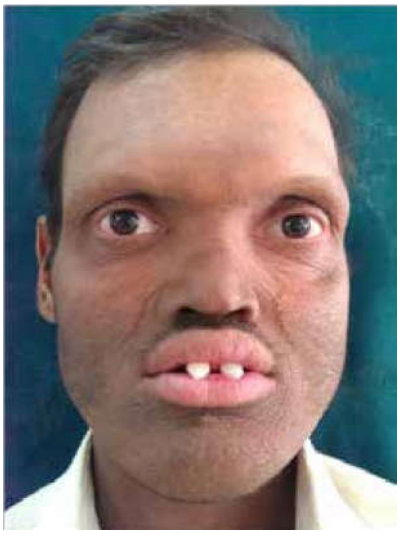

Figure 1: Wrinkled, rough skin around the eyes and mouth

whereas, hair were almost absent over his trunk,

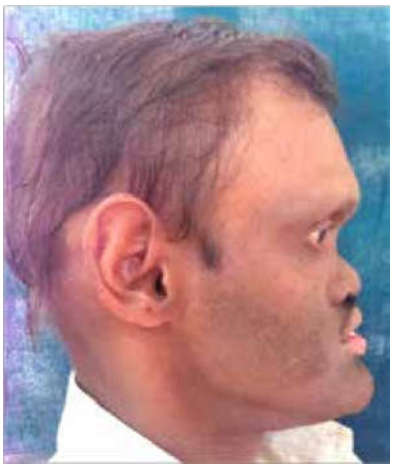

Figure 2:Concave profile with frontal bossing and saddle nose.

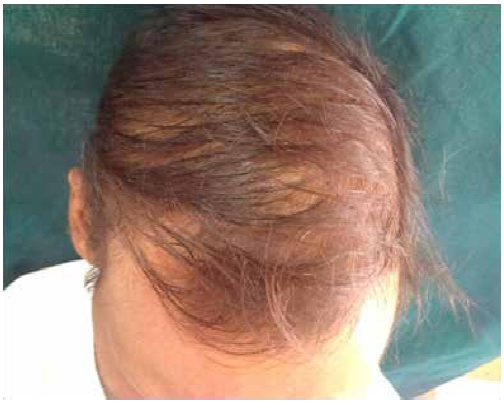

Figure 3: Sparse, fine scalp hair.

hands and leg (Fig. 4 & 5f). Skin showed wrinkling particularly in the perioral and periorbital areas and hyperpigmentation. There was generalized dryness and roughness of the skin. Nails appeared normal.

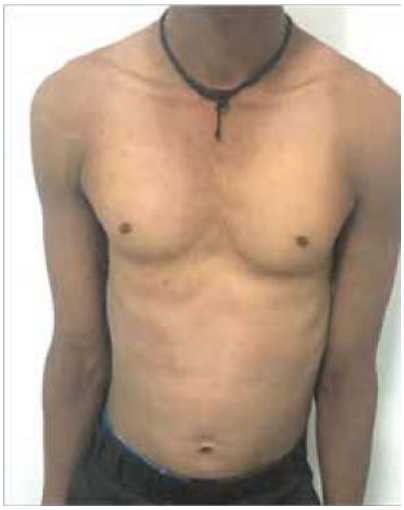

Figure 4: Absence of hair over chest and hands

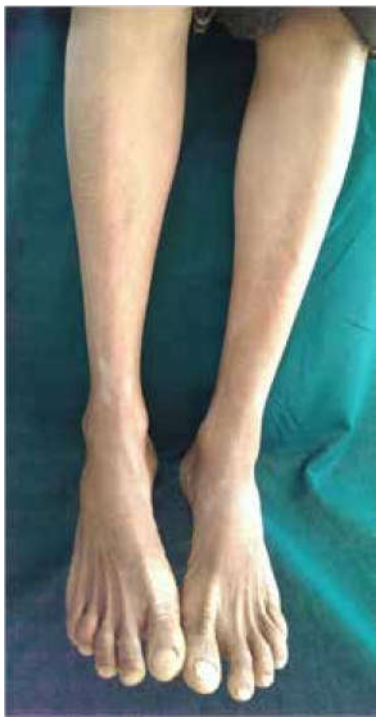

Figure 5: Absence of hair over legs

Intra-oral examination revealed several missing teeth. The teeth present were over-retained deciduous maxillary second molars, permanent maxillary central incisors (Fig. 6), permanent maxillary first molars and permanent mandibular first molars (Fig. 7). Central incisors were conical in shape. The alveolar bone was deficient and the ridges were narrow and thinned (Fig. 8). This might be attributable to the absence of teeth. These clinical features were supportive in diagnosing hypohidrotic ectodermal dysplasia.

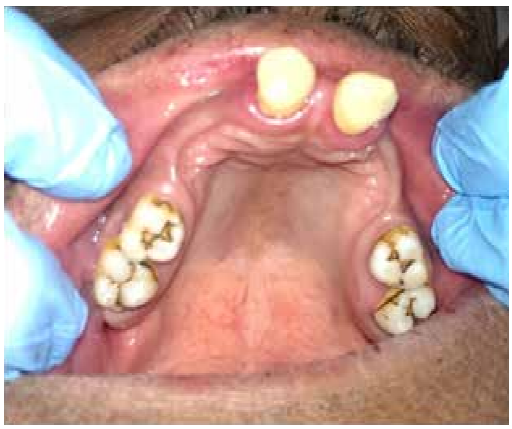

Figure 7: Maxillary oligodontia

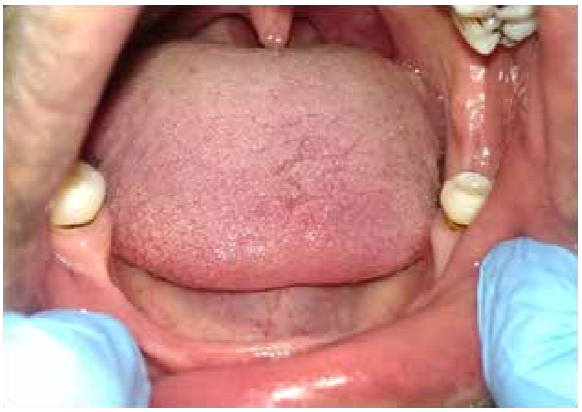

Figure 7: Mandibular oligodontia

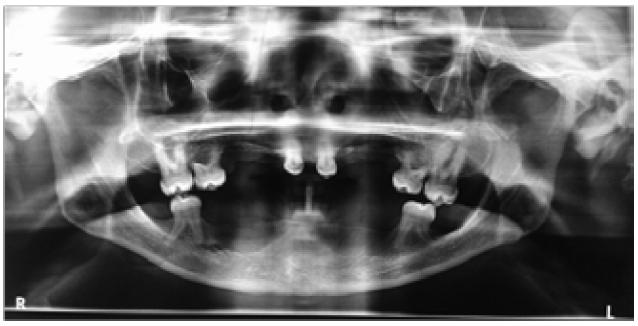

Figure 8: Orthopantomogram showing oligodontia with severe alveolar bone deficiency

DISCUSSION

Ectodermal dysplasias are a group of inherited disorders characterized by dysplasia of ectodermally originated tissues. It has prevalence of approximately 7:1,00,000 live births,[3] caused by genetic defects in ectodysplasin signal transduction pathways located at Xq12q13.1.[8]

To date, more than 192 distinct disorders have been described, most common being X-linke drecessive HED (Christ Siemens Touraine syndrome) and hidrotic EDA (Clouston syndrome).[3] Clouston. in 1929, first described the hidrotic variant with hypotrichosis, ungual dystrophy and hyperkeratosis of the palms and soles.[9] Several genetic mutations can lead to HED: ED1 gene which codes a ligand-ectodysplasinA-A1 (EDA-A1), EDAR gene, coding for ectodysplasinA-A1 receptor, EDARADD gene, concerned with programming the structure of EDAR-associated death domain protein and NEMO gene whose protein product, NFκB essential modulator (NEMO), is necessary for an indirect activation of nuclear factor κB (NFκB). All genes encoding components of the TNFα-related signaling pathway involved in differentiation of skin appendages are localized on the autosomes, while EDA1 and NEMO are localized on the X chromosome.[5] Being a genetic defect, ectodermal dysplasias may be inherited or passed down the family line. In some cases (as in our case), however, they can occur due to a *de novo* mutation in people without a family history of the condition.[1]

HED is the most common phenotype and is inherited in an X-linked recessive, autosomal dominant or autosomal recessive manner. X-linked recessive inheritance is present is about 95% of individuals with HED. The remainder (5%) has either the autosomal recessive or autosomal dominant inheritance.[10] It has full expression only in men. Clinical diagnosis is difficult in female carriers due to insignificant presentation or variable presentation of disorder in most cases.[2,11] Heterozygous females for the XLHED gene may show minor or no clinical evidence of the disorder, due to random inactivation of one of the two X chromosomes during embryogenesis (lionization/ Lyon's phenomenon) leading to two distinct cell lines.[2,4]

HED is characterized by classical triad of hypodontia, hypotrichosis, and hypohidrosis. Patients present with dry scaly skin, unexplained pyrexia and heat intolerance to hypohidrosis due to their diminished ability to sweat, associated with, in certain cases, absence of mucous gland in the esophagus, duodenum, bronchi and the upper respiratory tract. There may be complete absence of hair over the scalp or if present, may be sparse, short, fine and dry. Hair of eyebrows and eyelashes tend to be sparse. Longitudinal grooving, hair-shaft torsion, and cuticle ruffling are the additional structural hair-shaft abnormalities that can be observed. There is high prevalence of atopic eczema in these patients. Individuals with this disorder also commonly present with short stature, eye abnormalities, decreased tearing, and photophobia with normal intelligence. Brittle and thin nails or abnormal ridging of the nails,or grossly deformed nails especially in the hidrotic type are often seen.[12] ED patient presents withtypical facial features like frontal bossing, depressed nasal bridge, sunken cheeks, hyper pigmented skin around the eyes and mouth and large, low set ears.[13]

Intraorally, multiple missing teeth especially permanent teeth root, and crown dysmorphism (such as conical teeth) and reduced salivary flow is seen. The maxillary central incisors, canines, second molar and the mandibular canines are the teeth present in the deciduous dentition in most of the cases.[1] Maxillary central incisors, followed by maxillary first molars and mandibular first molars in the permanent dentition were found to be present in most cases by Guckes et al. Mandibular anterior teeth were least likely to be present.[13] Very rarely; one or both jaws may be edentulous.

The clinical diagnosis of HED is easy, especially after the first year of life when medical history and clinical findings become highly characteristic. However, it is important to determine the pattern of inheritance. After the initial diagnosis, the pattern of inheritance should be determined, since X-linked homozygous males and autosomal recessive forms are indistinguishable phenotypically. Also, examination of the other family members should be done to help define the pattern of inheritance and find if any of the members is a carrier. These above steps would help in early diagnosis and prompt treatment planning of the condition.

HED is managed symptomatically through multidisciplinary approaches such as oral rehabilitation, restorative procedures, and prevention of hyperthermia during any procedure by maintaining cool and ambient temperature.[7] Prosthodontic treatment includes fabrication of complete or partial removable dentures, fixed partial dentures or implants (in cases where sufficient bone is available). The latter treatment is gaining wide acceptance across the world as it has become more predictable, better compliance by the patient and affordable.

CONCLUSION

The diagnosis of ectodermal dysplasia can be easily made based solely upon the clinical examination of the individual. Being a congenital genetic disorder, there is no preventive management for it. It is important to diagnose the condition early in childhood to improve the quality of living of those affected. As dental professionals, early measures to improve affected functions of mastication, speech (due to oligodontia or impaired salivary gland function) and appearance should be implemented, ultimately leading to psychological well-being of the patient.

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