Case Report

Hypohidrotic ectodermal dysplasia: A case report with review and latest updates

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Abstract Ectodermal dysplasia represents a group of inherited conditions in which two or more ectodermally derived anatomical structures fail to develop resulting in most notably anhidrosis/hypohidrosis, hypotrichosis and hypodontia. It is a xlinked recessive disorder with male predominance. We report a classical case in a 17-year-old male with emphasis on review of literature and latest updates.

Keywords: Ectodermal dysplasia, embryonic life, genetic disorder, hypohidrotic

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Submitted: 11-Aug-2021, **Accepted:** 19-Oct-2021, **Published:** 28-Feb-2022

INTRODUCTION

Hypohidrotic ectodermal dysplasia is a rare genetic condition that can result from mutations in one of several genes (these include ectodysplasin A (EDA), EDA receptor (EDAR), EDARADD and WNT IOA). EDA gene mutations are the most common cause of the disorders, accounting for more than half of all cases. It was first described by Thurnam in 1948 and later in the 19th century by Darwin.[1] In 1921, Thadani assigned ED to the X-chromosome.[1] The incidence of ED is relatively rare (1/100,000) births. Classified into hypohidrotic/anhidrotic (Christ–Siemens–Touraine syndrome) or hidrotic (cloustror syndrome) based on the presence or absence of sweat glands.[2,3] ED syndrome affects both males and females of all races and ethnic groups.

The mortality rate is much higher in infancy or early childhood because of intermittent hyperpyrexia.[4-6] Congenital malformation of teeth hair, nails or sweat glands may occur either as single isolated malformations syndrome. Ectodermal dysplasia is considered to be a triad of hypodontia or anodontia, hypotrichosis and hypohidrosis.[7,8] Affected patients usually have prominent supraorbital ridges, frontal bossing, thin eyebrows, fine linear wrinkles, sparse hair, defective nails and saddle nose.[7,9,10]

Characteristic oral findings include complete or partial hypodontia, anadontia, impacted teeth, loss of vertical dimentions of alveolar ridges, protuberant lips, malformed and pegshaped or conical teeth. The palatal arch is frequently high and a cleft palate may be present.

According to Bessermann–Nielsen, the salivary glands including the intraoral accessary glands are sometimes hypoplastic. There may also be hypoplasia of the nasal and pharyngeal mucous glands which leads to chronic rhinitis and or pharyngitis, sometimes associated with dysphagia and hoarseness.[11]

Hidrotic ED (Clouston syndrome) is inherited as an autosomal dominant manner; the homozygous state may be

Access this article online

Quick Response Code:

Website: www.jomfp.in

DOI: 10.4103/jomfp.jomfp_287_21

How to cite this article: Bagdey SP, Moharil RB, Dive A, Bodhade A. Hypohidrotic ectodermal dysplasia: A case report with review and latest updates. J Oral Maxillofac Pathol 2022;26:S12-6.

lethal and clinical features include nail dystrophy associated with hair defects and palmoplantar dyskeratosis. Nails are thickened and discolored; scalp hair is very sparse, fine and brittle. Eyebrows are thinned or absent. Patients have normal facies, normal sweating and no specific dental defect is seen.[11]

Skin histopathology documents show the reduction in the number of sweat glands, hair follicles and sebaceous glands associated with the different syndromes. In hypohidrotic EDS, the epidermis is thin and flattened. Eccrine sweat glands are few or poorly developed or are very Rudimentary. Mucous glands in the upper respiratory tract and bronchi are often reduced in number. Salivary glands may show ectasia of ducts and inflammatory changes. Here, we report a classical case of HED with a review of the literature and latest updates.

CASE REPORT

A 17-year-old male patient reported to the department of prosthodontia of our institute with a chief complaint of poor esthetics due to missing teeth. The patient was a known case of ectodermal dysplasia; he had the complaints of poor esthetics and also of no sweat and increased body temperature. The patient denied a family member with similar features; the patient's vitals and systemic examination were normal. Intraoral examination revealed that the patient had mandibular and maxillary hypodontia with peg-shaped and cone-shaped teeth.

The hairs on the scalp were sparse and hypopigmented and the eyebrows were scanty. Both upper and lower eyelids showed spares eye lashes. The nasal bridge was depressed, appearing like a saddle nose, prominent supraorbital ridges and frontal bossing. His lips more protuberant [Figures 1 and 2].

Intraoral examination revealed midline diastema and Ushaped palatal arch [Figures 3 and 4]. No other significant abnormality was noted.

General examination findings were also normal.

His skin was dry, warm and sensitive. The patient's complete blood count reports were normal. Based on the history and clinical features, the patient was diagnosed as a case of hypohidrotic ED. Apart from medical management, he was referred to prosthodontic department for reconstruction.

DISCUSSION

There are more than 190 subtypes of ED in literature, classified based on the clinical features or the type of genetic

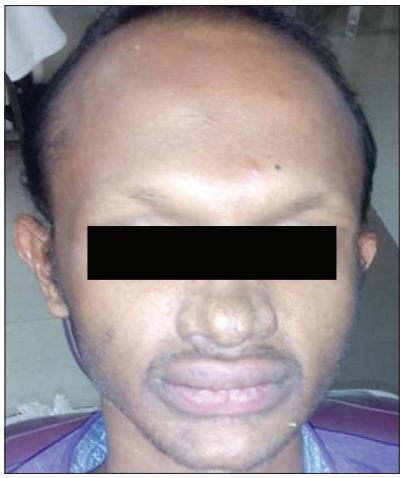

Figure 1: Typical features of ectodermal dysplasia: Frontal bossing, depreeesed nasal bridge and reduced vertical dimension

mutation or the molecular pathway involved. However, the two most common subtypes of ED are hypohidrotic/anhidrotic ED, in which the sweat glands are deficient and hidrotic ED in which the sweat glands are not affected.[12-15]

HED is characterized by partial or complete absence of sweat glands, hypotrichos and hypodontia. The X-linked HED, otherwise called Christ–Siemens–Touraine syndrome, was first described in 1848 by Thurnam.[16,17]

Clinically, HED is characterized by sparse or absent eccrine glands as well as by hypotrichosis and oligodontia with peg-shaped teeth as seen in the present case also.[16,18] The conical and pointed teeth are key features of the syndrome and may be the only obvious abnormality. Usually, incisors and canines are characteristically affected. Because of their severely diminished ability to sweat, patients with HED have a propensity to develop hyperthermia with physical exertion or exposure to a warm environment. The scalp hair, eyebrows and eyelashes are spares, fine and often lightly pigmented. Our patient also had the same features. However, nails were normal compared to several other types of ectodermal dysplasia.

Additional cutaneous features of HED include scaling or pealing of the skin during the neonatal period, periorbital hyperpigmentation and wrinkles, facial, sebaceous hyperplasia and eczematous dermatitis; these features were not present in our case. HED patients have very classic facies with frontal bossing, a saddle nose and full everted lips as seen with the present case also. Abnormal mucous glands result in extremely thick nasal secretions and a propensity to develop respiratory tract infections.[16]

Pathogenesis

Hypohidrotic ED is inherited by X-linked (most common)

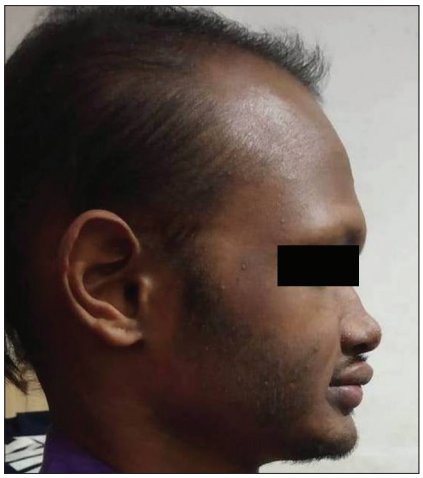

Figure 2: Sparse scalp hairs, thin eyebrows and protuberant lips

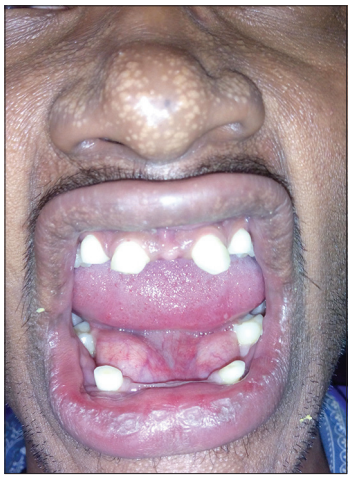

Figure 3: Partial anadontia, truncated or cone shaped teeth

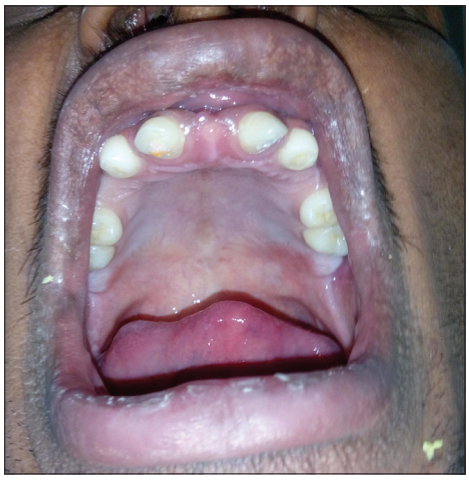

Figure 4: High arched palate and U shaped maxillary arch showing altered morphology of teeth

autosomal dominant and autosomal recessive patterns. The primary gene for the Xlinked inheritance pattern is EDA with locus Xq12q131, encoding a ligand EDA–A1, whereas the pathogenic genes for the autosomal heritance pattern are EDA-EDAR.. On the other hand, hidrotic ED is inherited only by the autosomal dominant pattern by changes in the GJB 6 gene, encoding Connexion-30 and located in chromosome 13 (locus 13q 11– q12).[12] Molecular studies have found that the above mentioned genes are responsible for the formation of several substrates required for the activation of the tumor necrosis factor α (alpha)related signaling pathway, the WNT– signaling pathway and the nuclear factor– KB pathway involved in ectoderm– mesoderm interactions, differentiation of ectodermal appendages and organogenesis during the initiation of embryonic development.[12,19]

In patients with a family history of HED, early prenatal diagnosis can be established by DNA-based linkage analysis and genetic tests for detecting mutations in EDA/EDAR/EDAEADD. In the second trimester of pregnancy, sonography and fetal skin biopsy are suitable diagnostic tests.[12,20,21] Antenatal diagnosis is usually reached before the age of 3 years through the clinical features.

Numerous clinical and psychological aspects need to be addressed in patients with HED; therefore, it requires a multidisciplinary approach.[12] Management of children and adults is a challenge because of their heat intolerance (especially during febrile illness or physical activities and in warm climate) and because of their susceptibility to pulmonary infections. During hot weather, affected individuals must have access to an adequate supply of water and a cool environment, however, external cooling is less effective in these patients because their heat transfer from the core to the skin is also reduced, presumably due to the poor capillary dilatation.[16,22] Affected individuals should learn to control their exposure to heat and to minimize its consequences.[16] Other common manifestations of ED such as atopic dermatitis, xerostomia, dryness of eyes and nose should be treated symptomatically.[12,3,14,21] Patients with xerostomia and reduced lacrimation may benefit from artificial saliva and tears, respectively.[22]

Mortality is as high as 30% in the first 3 years of life in children with hypohidrotic ED, due to numerous complications such as failure to thrive pulmonary infections and hyperthermia. Hence, additional care must be provided to infants and young children by the treating physician. After 3 years of life, life expectancy is normal.[12,23]

Early dental treatment that may range from simple restorations to dentures, dental implants in the anterior portion of the mandibular arch and replacement of dental prostheses as needed should be done to improve esthetics and chewing ability.

In older individuals, dentures, dental implants and orthodontic are usually the preferred treatment options.

Regular visit to an ENT physician may be necessary for the management of the nasal and aural concretions.[16]

Patients with hypohidrotic ED may suffer from low self-esteem, insecurity and depression due to their unusual physical appearances and lack of social acceptance.[12,3,14,21] Hence, psychological counseling should be advised on a regular basis. Advising use of wigs in patients with severe alopecia and early initiation of dental prosthesis may improve their cosmetic appearance. Consultation with a speech therapist and an otolaryngologist is warranted if abnormalities in phonetics and word-articulation are detected.[12]

The management done in our case was full month rehabilitation with implant supported prosthesis in lower anterior region. Toothsupported prosthesis in posterior region and orthodontic drifting of upper anteriors.

The prognosis of the ectodermal dysplasia is very good and the life span of the patients is usually normal except for case of ectodermal dysplasia with immunodeficiency.[22]

Intravenous injections of recombinant EDA-A 1 to newborn dogs with x-linked hypohidrotic ED have found to restore the growth of their teeth, skin structures and mucous glands. Also intraamninotic injections of recombinant EDAA 1 to pregnant mice partially improved the phenotype of the xlinked hypohidrotic ED newborn mice.[12,24] Recombinant EDA–A 1 at present is in phase–II clinical trials and is being administered to newborn males with hypohidrotic ED.

CONCLUSIONS

A multidisciplinary approach comprising restorative, orthodontic, surgical and prosthetic treatment should be done to achieve a satisfactory result.[4] Early prosthetic therapy helps to normalize the functions of masticatary and perioral muscles and consequently the growth pattern of basal bones. Therapy also gives a psychological boost to the selfimage of the child.[1,25]

The pediatrician/treating physician should manage acute complications of ED such as hyperpyrexia and respiratory infections symptomatically. Consultation with a child psychologist, dermatologist, otolaryngologist and speech-therapist should be warranted as and when required.[2]

The ultimate long-term goal is a young adult who is functionally habilitated and psychologically adjusted because the scientific fact that the disease is rare is of no consolation to its victim.[1]

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initial s will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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