Case Report

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STRANDS OF RESILIENCE: TWO SIBLINGS, ONE GENETIC DESTINY IN ECTODERMAL DYSPLASIA

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ABSTRACT:

Ectodermal dysplasia (ED) encompasses a diverse array of syndromes characterized by clinical and genetic variability, marked by anomalies in structures derived from the ectoderm. Hereditary ectodermal dysplasia manifests as a condition linked to ectodermal structure defects, typically inherited as a sex-linked recessive trait, less commonly autosomal dominant and recessive trait, more prominently affecting males than females. The prevalence of various ectodermal dysplasia within a specific population can exhibit significant variability. The aim of this case report is to present two patients, siblings, both exhibiting classic symptoms of hypodontia, hypohidrosis, and hypotrichosis, shedding light on the manifestation of ED in this familial context and a review on ectodermal dysplasia discussing the aetiology, clinical features, diagnosis.

Key words : Ectodermal Dysplasia, Inherited Disorders, Ectodermal Appendages-linked Recessive Trait , Hypohidrotic/Anhidrotic

INTRODUCTION:

Ectodermal dysplasia (ED) is a rare and varied set of inherited conditions characterized by underlying issues in the development of multiple tissues originating from the ectoderm. The main tissues affected include the skin, hair, nails, sweat glands, and teeth. [1]

The epidermis, the central and peripheral nervous systems, neural crest cells, and placodes including (cranial placodes) are all produced by ectoderm. Highly conserved signalling pathways including WNT, BMP (bone morphogenic protein), and FGF (fibroblast growth factor) pathways control cell fate decisions that result in ectodermal lineage specification. Hair, teeth, and nails are examples of ectodermal appendages arise from signaling cross-talk interactions between ectodermal epithelium and mesenchyme. Many hereditary conditions are characterized by abnormal development of ectodermal tissues.[2] One such condition is Ectodermal Dysplasia. The disorders are widespread, nonprogressive, and congenital. [3]

It is usually inherited as an X-linked recessive trait and is more prevalent in men than women. [4] To date, all potential mechanisms of inheritance for over 150 unique syndromes have been

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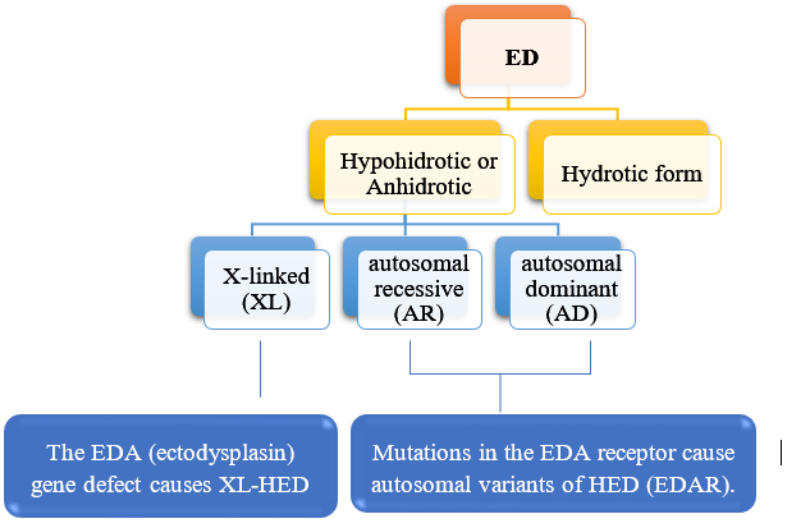
documented. Among the spectrum of ectodermal dysplasia (ED) disorders, two prevalent syndromes emerge: hypohidrotic/anhidrotic ED and hidrotic ED. [5] The term "anhydrotic" was modified to "hypohydrotic" by Felsher in 1944 since people with hypohydrotic forms are not truly devoid of all sweat glands. [4]

In the 20th gestational week, foetal skin biopsy and photoscopy are used to diagnose ectodermal dysplasia in utero. [4]

CASE REPORT:

Two male patients, siblings, aged 20 years and 18 years reported to the department of Oral Medicine and Radiology with a chief complaint of missing teeth since birth. Medical history revealed intolerance to heat, no sweating. There was no family history of a comparable illness or ailment on either side of the parents. The parents had consanguineous marriage. Upon parents' examination, no anomalies were found. Both patients' general examinations revealed palmar plantar keratosis, dry skin, sparse hair on scalp and eyebrows frontal bossing, sunken cheeks, protuberant lips, periorbital hyperpigmentation, depressed nasal bridge in fig.1a, b.

Upon intraoral examination of these patients hypodontia was common in both of them. In the elder sibling a total number of 10 tooth were present those were 11,16,17,18,21,26,27,28,37,47. While in the younger sibling total number of 18 teeth were present those were11,12,13,15,16,17,21,22,23,25,26,27,32,36,37,42,46,47 in fig 2a, b. The mandibular ridge appeared to be atrophic. Salivary flow appears to be normal. To validate the diagnosis, lateral skull views, OPG were taken of both the patients (fig 3a, b). OPG of the younger sibling revealed impacted 33,43. Considering the earlier data, an ED diagnosis was made.



The flow chart showing classification of ED

DISCUSSION:

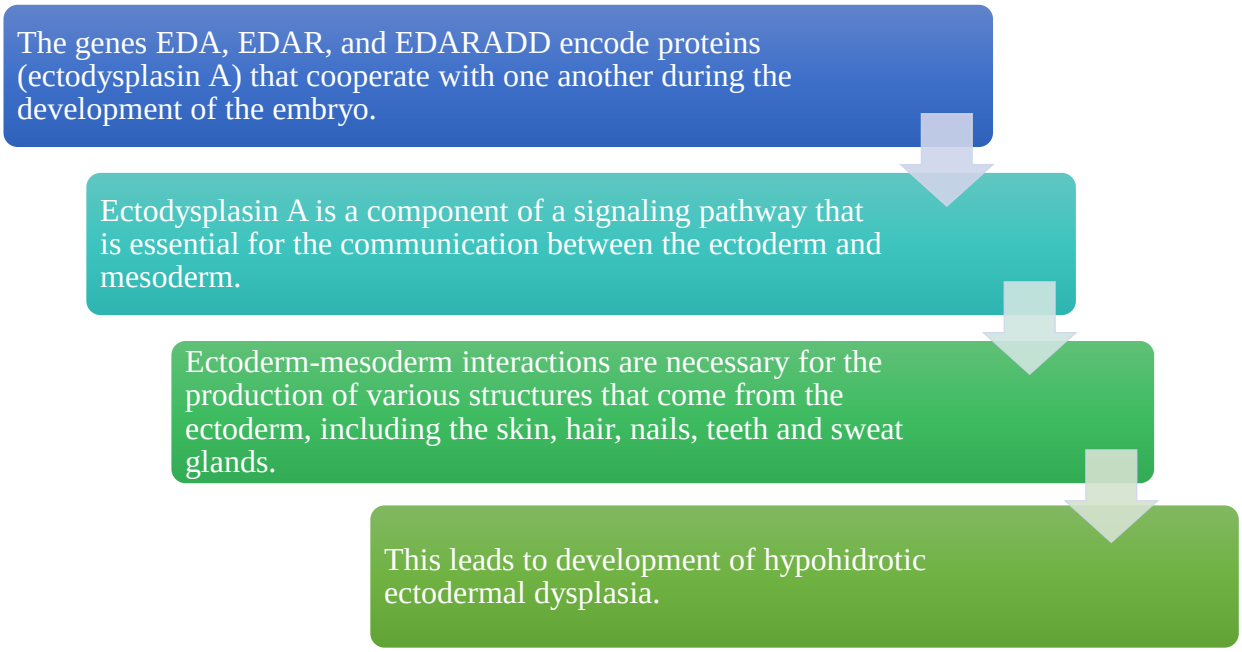
The absence or dysgenesis of at least two ectodermal derivatives, such as hair, nails, teeth, or sweat glands, is indicative of an ED, a hereditary genetic disorder. which occur approximately one in every 100,000 births. [6,7]

ED is basically divided into two broad categories [3]given in the flow chart below. The causing gene has currently been found in roughly 30 distinct cases of ED. The most common type of EDs, known as hypohidrotic or anhidrotic ED [7].

Christ Touraine Syndrome which is X-linked and is characterized by the classical triad of hypodontia, hypotrichosis, and hypohydrosis and the other category, i.e., hydrotic form (Clouston syndrome), which also affects the teeth, hair, and nails sparing the sweat glands. (3)

The EDA-EDAR-EDARADD (EDAR associated death domain) axis is a unique example of naturally occurring mutations in ligand, receptor, and adaptor protein resulting in the development of the defects in epidermal appendages. EDA gene dominates with over 100 mutations in HED cases, while EDAR and EDARADD show limited involvement, with 20 and 2 causal mutations respectively. [7]

The flowchart depicts the genetic mechanisms underlying ectodermal dysplasia (ED). [8]



Approximately 150 ectodermal dysplasia (ED) types exist, categorized based on the presence or absence of the four primary ED defects. [8,9]

1. ED1: Presence or absence of hair anomalies or trichodysplasia
2. ED2: Dental anomalies
3. ED3: Nail abnormalities or onychodysplasia

4. ED4: Eccrine dysfunction or dyshidrosis

ED is further categorized into [9]

Group A disorder which involves defect of at least two ectodermal structures as mentioned above, with or without defects of other structure.

Group B disorder which involves one of the classical ectodermal structures including hair, nail, teeth, or eccrine glands in combination with the defect in any of the ectodermal structure (ear, lip)

Freire Maia and Pinheiro introduced a numerical system for ectodermal dysplasias, assigning numbers (1-4) to affected structures: hair, teeth, nails, and sweat glands. Their review article proposed 10 distinct subgroups, facilitating a systematic understanding of this diverse disorder based on involved ectodermal components. [1]

Table.1 Differences between the hydrotic and hypohydrotic forms of ectodermal dysplasia [5]

Most likely, the illness manifests itself in the first trimester of pregnancy. If it is severe, it emerges before the 6th week of embryonic development, and thus the teeth will be damaged. The other ectodermal structures will be impacted after the eighth week. [8]

Mortality is as high as 30% in the first 3 years of life in children with hypohidrotic ED, due to many comorbidities such as failure to thrive, lung infections, and hyperthermia. As such, newborns and early children require extra attention from the treating physician. Life expectancy is normal after three years of age. [1]

Early prenatal diagnosis can be established using DNA-based linkage analysis and genetic tests in EDAEADD/EDDA/EDAR to detect mutations in participants with a family history of hypohidrotic ED. Diagnostic tests such as sonography and foetal skin biopsy are appropriate during the second trimester of pregnancy. Clinical characteristics are typically used to make an antenatal diagnosis before the child turns three years old. [1]

Recombinant proteins containing the receptor binding domain of EDA fused to the C–terminus of IgG 1 Fc domain have been engineered to cross the placental barrier and administered to pregnant mice. The phenotype of the X-linked hypohidrotic ED neonatal mice was partially alleviated by intra-amniotic injections of recombinant EDA-A1 into pregnant mice. It has been discovered that giving recombinant EDA-A1 intravenously to newborn dogs with X-linked hypohidrotic ED will stimulate the growth of their teeth, skin, and mucous glands. Currently, recombinant EDA-A1 is being given to newborn males with hypohidrotic ED in Phase II clinical trials in the hopes of easing some of their symptoms. [8,1]

Treating hypohidrotic ectodermal dysplasia lacks a specific remedy. A comprehensive approach, encompassing dental treatment for functional and aesthetic restoration, is crucial. Prosthetic interventions and external cooling methods are necessary to prevent multi-organ damage, as

individuals with HED are prone to hyperthermia.[10]

CONCLUSION:

ED underscores the importance of early intervention to address dental challenges and enhance overall well-being. A multidisciplinary approach, of paediatrician, Consultation with a child psychologist, dermatologist, otolaryngologist, and speech-therapist should be warranted, as and when required along with dental and prosthetic treatments, is crucial for functional and aesthetic restoration. Continuous monitoring and adaptive interventions are needed throughout patient's growth phase. This case report emphasizes the significance of personalized care to improve the quality of life for individuals with ectodermal dysplasia

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TABLES:

FEATURES	HYDROTIC	HYPOHYDROTIC
MODE OF INHERITANCE	Autosomal dominant	X linked recessive
SCALP HAIR	Very sparse, fine & brittle	Hypotrichosis
TEETH	No specific dental defects	Conical or pegged teeth, hypodontia or complete anodontia, delayed eruption
LIPS	No abnormality	Thick, everted lips
SWEAT GLANDS	Normal sweating	Hypohidrosis
NASAL BRIDGE	No flattening	Saddle nose
NAILS	Thickened & discoloured	Onychodysplasia
EYEBROWS	Thinned or absent.	Thinned or absent.
EYELASHES/PUBIC/AXILLARY HAIRS	Scanty/Absent	Scanty/Absent
FACIES	Normal facies	Frontal bossing, sunken cheeks, saddle nose, thick, everted lips, wrinkled, hyperpigmented skin around eyes, large low set ears.
EXTENSIVE SCALING & UNEXPLAINED PYREXIA	Absent	Present
INTELLIGENCE	Normal	Normal
PHOTOPHOBIA	Absent	Present

Table.1 Differences between the hydrotic and hypohydrotic forms of ectodermal dysplasia

FIGURES:

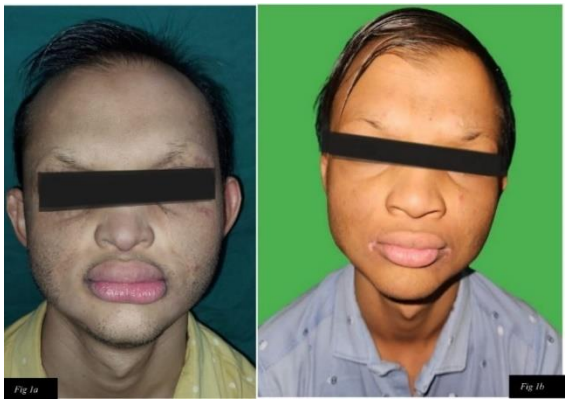

Figure.1a,b : extraoral images of the 2 patients showing sparse hair on scalp and eyebrows frontal bossing, sunken cheeks, protuberant lips, periorbital hyperpigmentation, depressed nasal bridge

Figure.2a,b : Intraoral images of the 2 patients showing hypodontia

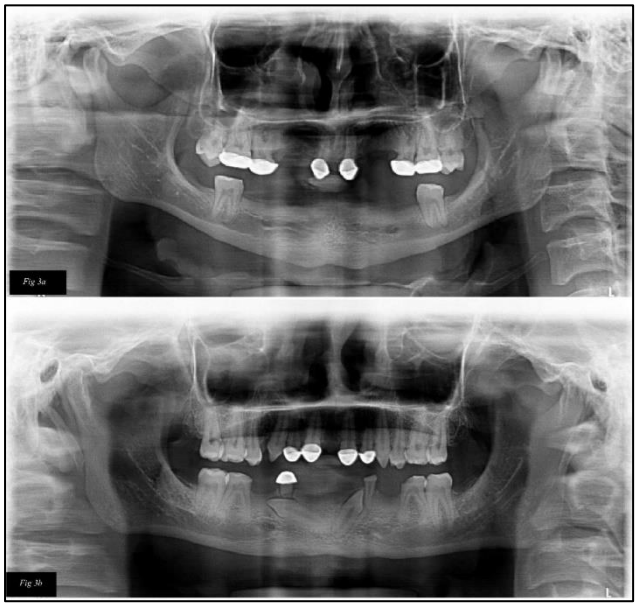

Figure.3a,b : OPG of the 2 patients showing hypodontia in both patients and impacted 33,43 in 2nd patient