Case Report

Hypohidrotic ectodermal dysplasia with autosomal recessive inheritance pattern: Report of a rare and unusual case with a brief review of literature

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Abstract

Ectodermal dysplasia (ED) is a congenital disorder primarily affecting the ectodermal tissue, with infrequent dysfunction of mesodermally derived tissues. Clinically, there are two major forms seen, hypohidrotic/Christ–Siemens–Touraine syndrome and hidrotic/Clouston syndrome, depending on the number and function of sweat glands. A multidisciplinary treatment protocol is usually followed and necessitates collective efforts by medical and dental professionals. Dental intervention should be done as early as possible to ameliorate the patient's esthetics and enhance the emotional and psychological quotient in these patients. This case report aims to highlight a rare and interesting report of hypohidrotic ED in a young female patient with a possible autosomal recessive inheritance pattern.

Keywords: Autosomal recessive, Christ–Siemens–Touraine syndrome, ectodermal dysplasia, hypohidrosis, hypotrichosis, oligodontia

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INTRODUCTION

Ectodermal dysplasia (ED) encompasses an assembly of infrequent genetic disorders characterized primarily by abnormalities of ectodermally derived tissues (hair, teeth, skin and nails), with occasional dysfunction of tissues of mesodermal origin.[1]

Thurman (1848) first documented the condition in two classic patients. Later in the 19th century, ED was also described by Darwin.[2] Weech in 1929 framed the term "ED."[3]

Based on the involvement of eccrine glands, the condition is delineated into two major forms: (a) hypohidrotic or anhidrotic (Christ–Siemens–Touraine syndrome) where eccrine glands are not present or remarkably diminished and (b) hidrotic (Clouston syndrome) with normal eccrine glands. The two types show similarity in teeth and hair involvement although nails and sweat glands show a different pattern.[4]

CASE REPORT

A 19-year-old female patient reported to the outpatient department of oral medicine and radiology with a chief complaint of missing teeth for the past 15 years. The patient also complained of heat intolerance with raised

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body temperature and reduced perspiration. There was a history of delayed eruption of a few permanent teeth, which gradually became carious and got exfoliated on their own. Family history revealed that the parents had a consanguineous marriage (parents were first-degree cousins) although both the parents were asymptomatic. She had three elder sisters, one younger sister and brother. Her elder sister also presented with a similar presentation although the presenting features were milder. Her antenatal and birth history was nonsignificant. Pedigree analysis was done, and it supported a possible autosomal recessive transmission pattern. Physical examination revealed that the patient was calm, cooperative with normal intelligence and was responding to the commands. The patient had a short stature as compared to her siblings. Extraoral examination revealed a concave profile (prognathic mandible), reduced anterior facial height and mild hyperpigmented and wrinkled periorbital skin. Hair examination revealed a receding hairline, thin, lustreless hair with premature graying. There was a scar mark on the right body of the mandible, following the extraction of a retained deciduous molar tooth. Crusted lesion with mild fissuring was also appreciated below the right nostril and lower lip, suggestive of a herpetic lesion [Figure 1a-e]. Hand and feet examination revealed normal-shaped fingers and broad, short and wide-spaced toes. However, nail examination did not reveal any abnormality [Figure 2a-c]. The body temperature of the patient was recorded using a clinical thermometer. The patient had a body temperature of 99°F, thus demonstrating hyperpyrexia. Intraoral examination revealed multiple (16) clinically missing teeth in relation to (irt) 11, 12, 21, 22, 23, 31, 32, 35, 36, 41, 42, 43, 44, 45 and 46, root stumps irt 13, 17, 24 and 26, discolored and restored 33, deeply carious with Grade III mobility irt 37 and 47 and soft-tissue pericoronal flap irt 48. The erupted teeth were small in size, hypoplastic with an altered morphology (generalized microdontia). The maxillary and mandibular arches were underdeveloped with decreased vertical bone height and deficient sulcus depth in the maxillary and mandibular posterior teeth region [Figure 3a-c]. Full-mouth intraoral periapical radiographs (IOPARs) and orthopantomograph (OPG) revealed multiple missing teeth, root stumps irt 13, 17, 24 and 26 and submerged 35, 38, 44, 45 and 48. Periradicular radiolucency with root resorption irt 37 and 47 was also seen. Lateral cephalogram showed maxillary hypoplasia, forward–upward protruded mandible, underdeveloped arches with reduced vertical height and multiple missing teeth [Figures 4a-f and 5a, b].

Based on the presence of multiple missing teeth, a differential diagnosis of nonsyndromic/syndromic oligodontia (ED, Rothmund–Thomson syndrome, Werner syndrome, Van der Woude syndrome and Down syndrome) was taken into consideration. Nonsyndromic oligodontia was ruled out due to the associated hair and sweat gland involvement. Rothmund–Thomson syndrome was ruled out due to the absence of characteristic skin, nail and ocular lesions (juvenile cataracts). Werner syndrome was ruled out due to the absence of premature aging, atrophied skin and ocular lesions (bilateral cataracts). The absence of typical mongoloid facies, mental retardation, high rate of periodontal diseases and protruded and enlarged tongue ruled out the possibility of Down syndrome. The absence of congenital lip pits, clefting (lip/palate) and ankyloglossia ruled out the possibility of Van der Woude syndrome.

Laboratory analysis (complete blood count, liver and kidney function tests, serum calcium and phosphate, Vitamin D3, alkaline phosphatase, parathyroid hormone and serum protein electrophoresis) was performed, and the results were unremarkable. The patient exhibited a positive sweat pore count test (with 2% iodine in alcohol), thus confirming the presence of hypohidrosis [Figure 6a and b]. However, skin biopsy and genetic analysis could not be performed due to financial constraints and nonwillingness of the patient and parents.

Based on the history of consanguineous marriage in the asymptomatic parents, positive family history in another female sibling, presence of pathognomonic clinical and radiographic features and a positive sweat pore count test confirming hypohidrosis, the condition was diagnosed as hypohidrotic ED (HED) with a probable autosomal recessive mode of transmission.

Figure 1: (a-c) Frontal and profile view depicting the dysmorphic features. (d) Family picture showing the short stature of proband. (e) Pedigree analysis showing the autosomal recessive inheritance pattern

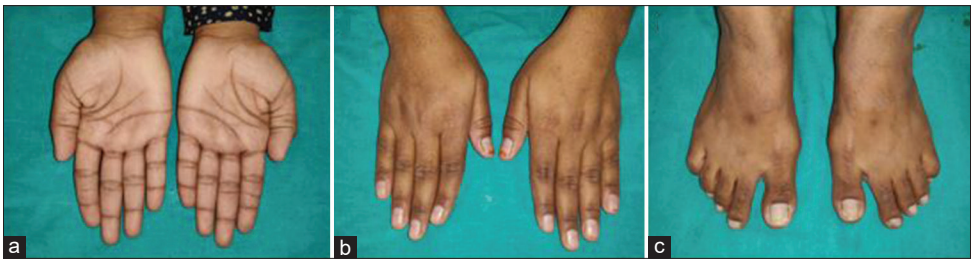

Figure 2: (a-c) Hand, feet and nail examination showing broad, short, widely spaced toes and normal nails

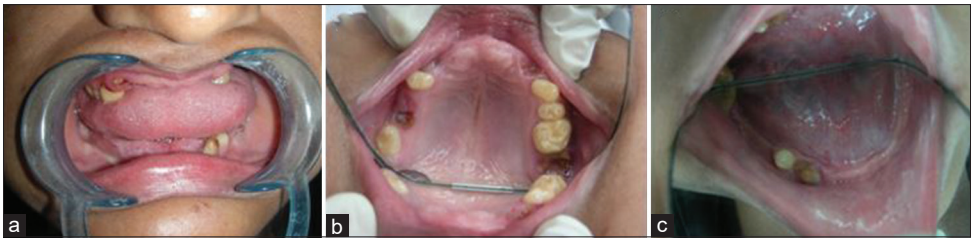

Figure 3: (a-c) Intraoral examination showing multiple missing teeth in the maxillary and mandibular arch. The erupted teeth are small in size and hypoplastic

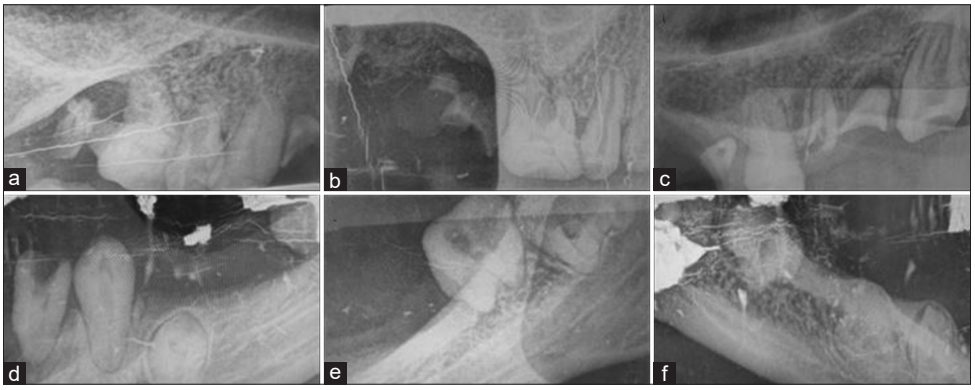

Figure 4: (a-f) Maxillary and mandibular intra oral peri apical radiographs (IOPARs) showing multiple missing teeth, submerged teeth and root stumps. The erupted teeth are small in size and hypoplastic

Extraction of root stumps and Grade III mobile teeth followed by prosthodontic rehabilitation for the missing teeth was considered as the treatment protocol, aiming at improving the esthetics, phonation and mastication. Earlier, it was considered to make interim partial denture for replacement of missing teeth. However, the teeth present in the oral cavity were smaller in size resulting in a decreased vertical dimension, thus imparting a sunken jaw appearance. To overcome this, the option of overdenture was considered. The denture was fabricated using polymethyl methacrylate heat cure resin (Dental Products of India). Furthermore, selective soft relining material (Mollosil long-term relining material) was added around the abutment teeth for comfortable seating and to provide extra retention to the denture. After the final set of soft liner material, occlusal adjustments were done [Figure 7a-f]. The patient was recalled twice for postinsertion checkup after 24 h and after 1 week. The patient was recalled after 2 months for soft liner material resiliency.

DISCUSSION

In 1982, the first classification system of EDs was advocated by Freire-Maia and Pinheiro although additional upgrades were made in 1994 and 2001.[5]

According to this classification, "1" denotes hair abnormality, "2" dental abnormality, "3" nail abnormality and "4" sweat gland abnormality. This classification encompasses more than ten subgroups, depending on the mentioned abnormality.[6]

Since our patient had an abnormality in hair, dentition and sweat glands with no abnormality in nails, she can be categorized in the 1-2-4 subgroup.

Priolo-Lagana and Lamartine, in 2001 and 2003, respectively, proposed the advanced system of classifications employing molecular information. However, this molecular classification is not helpful clinically.[7]

HED is the most frequent type and usually exhibits an X-linked inheritance pattern with the gene mapping to Xq12-q13.1; thus, males are more vulnerable than females. GJB6 is the causal gene for hidrotic ED, which encodes for connexin-30 and has been mapped to the pericentromeric region of chromosome 13q.[8] Most cases of HED exhibit an X-linked inheritance pattern, with females being the carriers and the condition being completely manifested in the males. Occasionally, the disease may have an autosomal dominant or autosomal recessive inheritance pattern.[9]

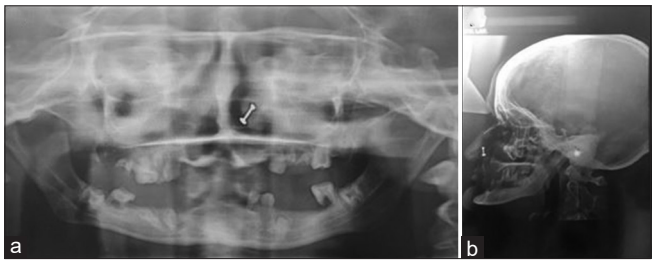

Figure 5: (a and b) Orthopantomogram and lateral cephalogram showing multiple missing teeth, maxillary hypoplasia, prognathic mandible, underdeveloped arches and reduced facial height

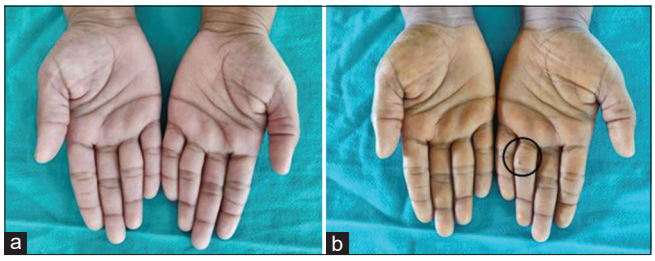

Figure 6: (a and b) Positive sweat pore count test demonstrating hypohidrosis with 2% iodine in alcohol. The encircled part shows the only visible sweat pore

Disease expression in more than one sibling and the presence of consanguinity and asymptomatic parents supports an autosomal recessive inheritance pattern. The autosomal recessive type of inheritance of HED is exceptionally uncommon. Clinically, it is identical to the X-linked type and manifests with a triad of signs encompassing sparse hair (atrichosis or hypotrichosis), anomalous or absent teeth (anodontia or hypodontia) and inability to perspire due to scarcity of sweat glands (anhidrosis or hypohidrosis).[10]

Few published case reports have highlighted the autosomal recessive pattern of inheritance in hidrotic ED.[10-12]

Our case was a rare and interesting presentation as the proband was a female born to asymptomatic parents with consanguineous marriage with disease expression in the elder female sibling, highlighting the possible autosomal recessive inheritance pattern.

Table 1 summarizes the differentiating features of hypohidrotic and hidrotic forms of ED.[13]

HED patients manifest dysmorphic features, oligodontia, friable scaly skin, hypoplastic sebaceous glands (exhibiting diminished sweating), hypoplastic salivary glands (exhibiting oral mucosal dryness) and hypoplastic mucous glands. Skin barrier may be disrupted due to genetic and environmental influences, rendering the patients vulnerable to allergic diseases such as bronchial asthma, atopic eczema, allergic rhinitis, food allergy, pneumonia and otitis media. Oligodontia results in decreased oral intake, poor nutrition and reduced tears leading to corneal erosion.[9]

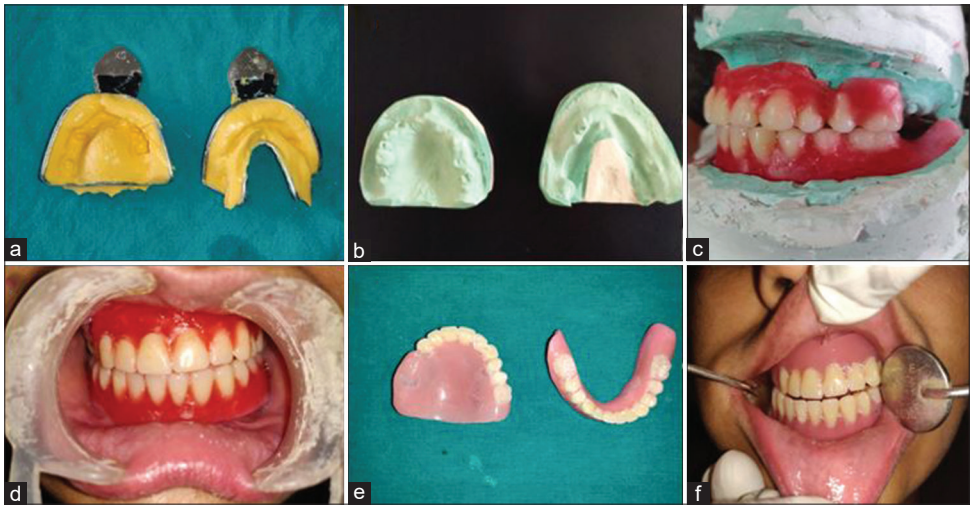

Figure 7: (a-f) Prosthetic rehabilitation of the patient

Table 1: Summarizes the differentiating features of hypohidrotic and hidrotic forms of ED

Features	Hidrotic	Hypohidrotic
Mode of inheritance	Most often autosomal dominant	Most often autosomal recessive
Gene mutation	Mutation in connexin gene	Mutation in ectodysplasin gene
Scalp hair	Soft, downy and dark colored	Fine textured, fair and short
Teeth	Anodontia to hypodontia	Anodontia to hypodontia
Lips	Normal	Protuberant
Sweat glands	Active	Reduced to absent
Nasal bridge	Normal	Flattened
Nails	Dystrophic	Normal
Eyebrows	Frequently absent	Absent
Eyelashes/pubic/axillary hair	Scanty/absent	Variably reduced

Oral manifestations encompass anodontia, complete or partial hypodontia, impacted teeth, loss of vertical dimensions of occlusion, prominent lips, deformed and peg-shaped or conical teeth and deficient alveolar growth. Oral symptoms of ED comprise multiple tooth defects, and an underdeveloped alveolar ridge can complicate the restoration of an ideal occlusion, especially in a growing child.[14]

Children with ED show maxillary retrusion due to sagittally underdeveloped maxilla, forward and upward displacement of the mandible and collapsed anterior facial height. The palatal arch is frequently high, and cleft palate may be present.[15]

Other facial features include reduced facial vertical dimension associated with perioral fissuring (pseudo-rhagades), imparting a senile look at an early age, hypotonicity of the perioral musculature and short stature.

Our patient presented with a concave profile (prognathic mandible) with a reduced anterior facial height, lustreless hair with premature graying, multiple missing teeth, underdeveloped alveolar arches, maxillary hypoplasia and prognathic mandible.

ED is usually diagnosed clinically. Medical history and radiographic evaluation also play an essential role in the diagnosis.[16]

The present case manifested typical radiographic features of multiple missing and submerged teeth, abnormal crown morphology of erupted teeth and deficient alveolar arches.

Sweat pore count is performed employing starch-iodine powder. The powder is applied to dried dorsal/palmar skin surface. In normal individuals, sweat reacts with the powder and produces deep purple color and allows visualization of sweat pores. However, in ED patients, sweat pores are not/poorly seen.[17]

In the present case, sweat pore count test was carried out with 2% iodine in alcohol. The test exhibited hypohidrosis, characteristic for ED.

Histopathology of palmar skin from the hypothenar areas reveals either completely absent or sparse and incompletely developed eccrine glands. Prenatal diagnosis of HED can be done with fetal skin biopsy, obtained by fetoscopy by 20 weeks. However, this practice is intricate and may pose a substantial risk to the pregnancy.[9]

The essential diagnostic aid in ED is genetic testing/genetic mapping. This test reveals the causal gene and the exact site of mutation. The test also forms a basis for genetic counseling, thus ensuring avoidance of consanguineous marriages and provision of essential medical care.[16]

In the present case, skin biopsy and genetic analysis could not be performed due to financial constraints and nonwillingness of the patient and parents.

There is no definitive pharmacological treatment for ED. The patients are managed according to the involved ectodermal structures.[18] The preventive measures for HED patients include wearing light clothes, air conditioning for the environment, a cool water spray bottle, artificial tear use and petroleum jelly application for protection of nasal mucosa.[19]

Our patient was advised to maintain hydration and temperature regulation by frequent intake of water and fluids and wearing light clothing.

Oral rehabilitation should be initiated as early as possible to combat the cosmetic, functional and psychological aspects in these patients. However, prosthetic rehabilitation of these patients may pose therapeutic challenges because of the associated oral deformities and the patient's age.[1]

There exists a range of dental management alternatives for ED. The condition can be managed with removable prosthesis including overdentures, fixed prosthesis, implant-retained prosthesis, implant-supported prosthesis or combination based on the degree of disease.[20]

The standard management protocol for ED emphasizes a series of complete or partial dentures during the dentofacial growth phase and precise prosthodontic rehabilitation following cessation of the jaw growth.[21]

The patient in the present case was treated with a maxillary partial denture and mandibular complete denture. The patient was recalled for postinsertion checkup after 24 h and after 1 week.

CONCLUSION

EDs are rare genetic disorders which manifest with multiple defects in ectodermal derived tissues. The disease usually has an X-linked inheritance pattern primarily affecting males. Our case was exceptionally rare as the proband was a young female born to consanguineous marriage in asymptomatic parents with disease expression in an older female sibling, suggesting a possible autosomal recessive inheritance mode.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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