

HEREDITARY ECTODERMAL DYSPLASIA: diagnostic dilemmas

Displasia ectodérmica hereditária: dilemas diagnósticos

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Abstract

Hereditary ectodermal dysplasia is a condition associated with deformation of one or more ectodermal derivatives which are typically inherited as a cross-linked recessive trait so that the frequency and severity of the condition is more pronounced in males than in females. The objective of this report is to present two female patients with hereditary ectodermal dysplasia, each of hypohydrotic and hydrotic type. These patients showed reduced number of teeth with structural changes which could be explained by X chromosome inactivation i.e., "Lyon" hypothesis, and also the present cases throws light on practical difficulties encountered in clinical diagnosis.

Keywords: Anhydrotic ectodermal dysplasia; Hypohydrotic; Lyon hypothesis; Anodontia.

Resumo

A displasia ectodérmica hereditária é uma condição associada com defeito de um ou mais derivados ectodérmicos que são tipicamente herdadas como traço recessivo por linhagem cruzada, de maneira que a frequência e severidade da condição é mais pronunciada em homens do que em mulheres. O objetivo deste relato é apresentar dois pacientes do sexo feminino com displasia ectodérmica hereditária, tipos hipohidrotico e hidrotico. Essas pacientes apresentaram número de dentes com alterações estruturais que podem ser explicadas pela inativação do cromossoma X, isto é, a hipótese de "Lyon". Igualmente os presentes casos elucidam as dificuldades práticas encontradas no diagnóstico clínico.

Palavras-chave: *Displasia ectodérmica anidrotica; Hipohidrotica; Hipótese de Lyon; Anodontia.*

INTRODUCTION

Hereditary ectodermal dysplasia is characterized by defective formation of one or more structures derived from ectoderm. It was first described by Thurnam in 1848 and was coined by Weech (1) in 1929. In 1875, Charles Darwin documented it amongst a Hindu family of *Scinde* where ten men in the course of four generations were affected, which was communicated to him by Mr. W. Weddenburn. It is remarkable that no instance has occurred of a **daughter** being affected (2).

It is typically inherited as a cross-linked recessive trait so that the frequency and severity of the condition is more pronounced in males than in females (3). Furthermore, it was redefined by Freire-Maia (4) as a developmental defect which at embryonic level affects the ectoderm and therefore the tissues and structures derived from it. Thus it affects the development of keratinocytes and cause aberrations in the hair, sebaceous glands, eccrine and apocrine glands, nails, teeth, lenses and conjunctiva of the eyes, anterior pituitary gland, nipples and the ears.

The disorder might occur during the first trimester of pregnancy. If it is severe, it appears before the sixth week of embryonic life and consequently the dentition will be affected. After eighth week other ectodermal structure may be affected (5). The disease appears in two forms hydrotic and hypohydrotic or anhydrotic (6, 7) whose clinical features are presented in Table 1.

TABLE 1 - Differences between the hydrotic and hypohydrotic forms of ectodermal dysplasia

	Hydrotic	Hypohydrotic
Mode of Inheritance	Most often autosomal dominant	Most often autosomal recessive
Scalp Hair	Soft, dawny, color is darker	Fine in texture, fair and short
Teeth	Anodontia to hypodontia	Anodontia to hypodontia
Lips	No abnormality	Protruding
Sweat glands	Active	Reduced to absent
Nasal bridge	No flattening	Underdeveloped
Nails	Dystrophic nails	No abnormality
Eyebrows/	Frequently absent	Absent
Eyelashes Pubic/Axillary hairs	Scanty/absent	Variably affected

Felsher in 1944 (5) changed the adjective anhydrotic to hypohydrotic because the persons with hypohydrotic form are not truly devoid of all sweat glands. A definitive classification of ectodermal dysplasia (ED) is difficult to formulate since many of the syndrome that involve ED have overlapping features. A simple attempt made by Nelson included five categories, namely *Hypohydrotic (anhydrotic)*, *Hydrotic (Clouston's syndrome)*, *EEC (Ectodactyly ectodermal dysplasia) syndrome*, *Rapp - Hodgkin syndrome* and *Robinson's disease* (8).

While Lamartine (9) has classified the ED genes into four major functional subgroups: cell communication and signaling, cell adhesion, transcription regulation, and development.

One of the most common variant of hereditary ectodermal dysplasia constitutes Ellis-Van Creveld syndrome (10), characterized by ectodermal dysplasia resembling hydrotic form, chondrodystrophy, polydactyly and congenital heart disease probably due to a single autosomal recessive gene with the locus on 4p16.

Furthermore, the characteristic oral features include neonatal teeth, partial anodontia, early involvement with caries, peg-shaped and delayed eruption of teeth (11). The presence of short upper lip, which is bound by frenula to alveolar ridge (lip tie) as well as other defects in mandibular alveolar ridge are also very common.

CASE REPORT 1 (HYPOHYDROTIC)

A female patient of age 24 years attended out patient department of Darshan Dental College and hospital, Udaipur, India, who complained of missing teeth in lower front region since childhood. Dental history revealed the presence of natal teeth in lower front region which were extracted. Patient presented dryness of eyes, lips, thin eyebrows, sparse hairs in hand, fusion of lingual frenum. Patient also presented dry skin and repeated episodes of hyperthermia. The form of finger and toe nails did not reveal any abnormality. Intra oral observations included partial anodontia (missing **15,17,18,22,25,27,28,31,32,33,35,38,41,42,43,45,48**) (Figure 1) and xerostomia following which a provisional diagnosis of hereditary ectodermal dysplasia was made.



FIGURE 1 - Intra oral photograph depicting missing teeth

Presence of natal teeth in mandibular anterior segment, fusion of lingual frenum and short stature are pointing towards Ellis-Van Creveld syndrome. A complete radiographic examination was performed. Skin biopsy was undertaken to diagnose the case which revealed (Figure 2) absence of sebaceous as well as sweat glands thus confirming the diagnosis of hypohidrotic ectodermal dysplasia.

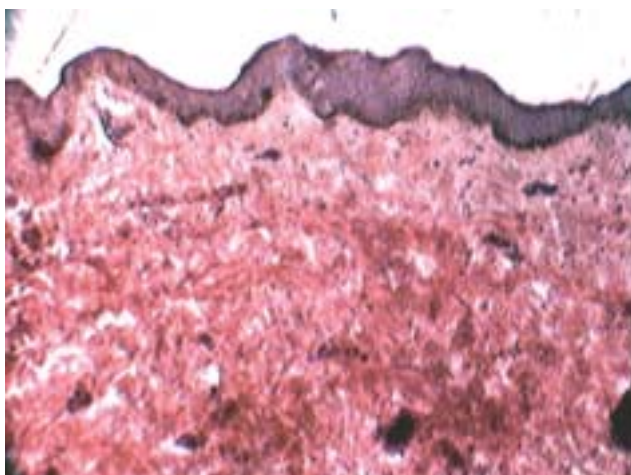


FIGURE 2 - Stratified squamous keratinized epithelium showing absence of sebaceous and sweat glands

CASE REPORT 2 (HYDROTIC)

The second case is a female patient aged 25 years, with a complaint of missing teeth in upper front region since childhood. On extra oral examination, prominent forehead, prominent supra orbital ridges, thin eyebrows, dryness of

lips and mouth were noticed. She had sparse hairs in the hand but did not have dryness of skin or absence of sweating. Partial anodontia (missing **12, 14, 17, 18, 22, 28, 31, 32, 38, 41, 42 and 48**) (Figure 3) comprised the only intra oral finding. Family history disclosed absence of lower teeth in her mother.



FIGURE 3 - Congenital absence of teeth

Furthermore, both her sons of ages 5 and 7 years presented sparse hairs in scalp and prominent forehead with partial anodontia. Her younger son had **55, 61, 62, 65, 75, 83 and 85**, whereas the remaining teeth were congenitally absent (Figures 4 and 5).



FIGURE 4 - Congenital absence of teeth



FIGURE 5 - Patient (second case) with her younger child

The oral and dermal findings were consistent with hydrotic ectodermal dysplasia. The case report of the subject's elder son could not be documented as he didn't report to the department. Pedigree pattern of the case is presented in Figure 6. It is evident from the figure that the three generations are affected with no sex preference.

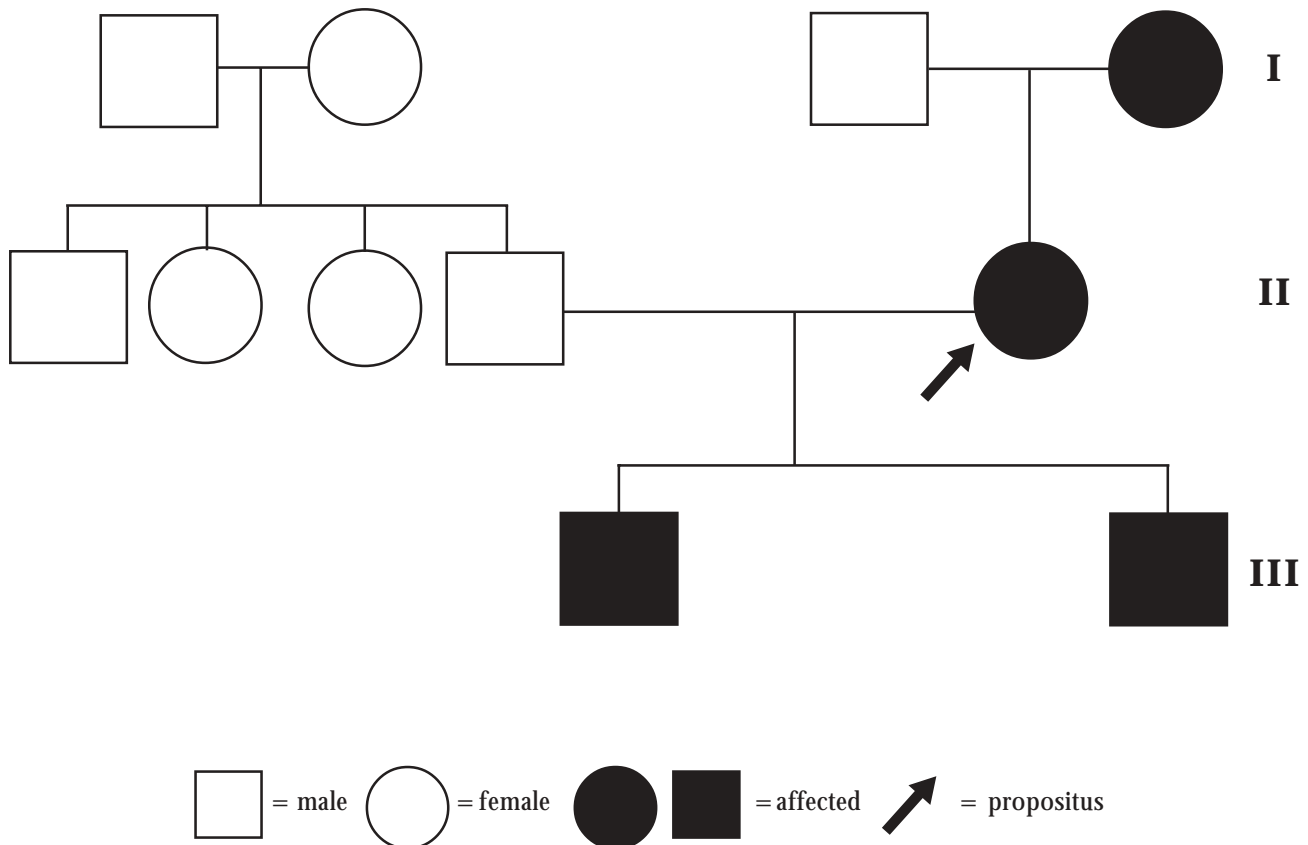


FIGURE 5 - Pedigree pattern.
Note three generations are affected with no sex preference

DISCUSSION

Genetic studies of more than 300 cases have revealed X linked mode of inheritance with its gene locus being Xq11-21.1, the gene is carried by the female but manifested in the male. However there are reports of multiple siblings being affected and of females suffering with this condition (4).

The presentation of thin eyebrows and partial anodontia observed in our cases is in agreement with existing literature (3). Whereas, the observation of normal form and shape of finger and toenails in the present cases is in accordance with previous observation of Shaw (12).

In the first case, the proband was the only child of her parents. No similar case of ectodermal dysplasia has been identified among the relatives, which suggests that the propositus was probably a fresh mutation or due to translocation of genes while in the second case it was inherited from her mother. Female patients may show partial expression of abnormal gene, that is, their teeth may be reduced in number or may have mild structural changes as seen in our cases. This incomplete presentation can be explained by the Lyon hypothesis (X-inactivation), with half of the female patient's X chromosomes expressing the normal gene and the other half expressing the defective gene (6, 13).

Both our cases exhibited xerostomia which could be attributed to rudimentary development of accessory salivary glands in agreement with previous reports (12, 14). The former case had repeated episodes of hyperthermia along with dryness of eyes, hyperthermia can be explained by defective development of skin appendages namely, hair follicles along with sebaceous and sweat glands in accord with existing literature (12, 15) whereas dryness of the eyes may be due to partial absence of lacrimal glands or deformities in gland ducts as suggested by Beckerman (16).

In the former case presence of natal teeth and fusion of lingual frenum, short stature were the features of Ellis - Van Creveld syndrome and - moreover - the presence of abundant hair in the scalp and with no familial history made our diagnosis little complicated, so skin biopsy was carried out to confirm our diagnosis of ED whereas in the latter case the disease was seen in three consecutive generations but the propositus exhibited partial expression of the disease characteristics.

In developed countries diagnosis pertains to laboratory identification of genes (17) and mode of inheritance of mutant genes associated with recessively X chromosome or autosomal dominant or recessive. This may be difficult in developing countries like India where such facilities are insufficient and it requires further probing through genetic analysis. Hence, identification of borderline cases as that of the present instances turns to be difficult and challenging for the physician that demands thorough clinical examination and sound knowledge.

CONCLUSIONS

As quoted by William Goody (1961) syndromes are the signpost, compass and map which direct us through the crowded twisting streets, the oceans and the jungles of medical experience. A full understanding of the logical system implied by the syndromes should enable us to guide our patient with confidence and wisdom; should suggest and direct our researches; and should refresh our sense of gratitude to our medical forefather.

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Received: 08/09/2007

Recebido: 09/08/2007

Accepted: 09/15/2007

Aceito: 15/09/2007