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Anhidrotic Ectodermal Dysplasia: A Rare Entity

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ABSTRACT

Background: Ectodermal dysplasia (ED) is a rare hereditary disorder characterized by congenital defect involving two or more of the ectodermal structures, which include the skin, hair, nails, teeth, and sweat glands. The two most common forms of the disease are hypohidrotic/anhidrotic ED and hidrotic ED. They are caused by the mutations of several genes. Even though usually transmitted as x-linked recessive trait, in about 70 percent of cases, carrier females of hypohidrotic ectodermal dysplasia experience some features of the condition whose presentation varies from very mild to very severe.

Report: A 3years old female child was brought to OPD with complaints of non eruption of teeth and dry skin with repeated history of episodes of high grade fever with no sweating. On examination child revealed peculiar facial features in the form of broad forehead, Flat nasal bridge, dry wrinkled facial skin, low set ears, absent eyebrows and eyelashes , sparse hairs on scalp, Malar hypoplasia and Scaling of skin all over the body. After thorough evaluation and investigations, by ruling out different endocrine, metabolic and infectious causes, the diagnosis of Anhidrotic ectodermal dysplasia was made and multidisciplinary help was sought with dermatologist and dentist to provide a comprehensive medical care to the child.

Conclusion: We report a rare case of anhidrotic ectodermal dysplasia in a 3-year-old female, thus emphasizing the need for considering ED as a differential diagnosis for children with history of repeated episodes of fever of unknown etiology specially when associated with dental, hair and skin issues . An early diagnosis would help in early intervention and improve the future quality of life in child.

Case Report

A 3years old female child was brought to OPD with complaints of non eruption of teeth and dry skin noticed since infancy period. On further eliciting, parents gave history of repeated episodes of high grade fever with absence of sweating. Accordingly many such episodes have been seen till date, more so during hot climatic conditions for which she was consulted regularly with no definitive cause being explained to them.

She is 3rd born child to a 3rd degree consanginously married couple, with previous two child being normal and healthy. They also gave history of NICU admission soon after birth in view of respiratory issues and was on oxygen support for initial 7days ,direct feeding was started from 8th day and was discharged after 2weeks. Parents denied of any similar abnormalities in any of the family members.

On examination, child was febrile with body temperature of around 101*F with other vitals being within normal range for age. Her general physical examination revealed peculiar facial features

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like Broad forehead, Flat nasal bridge consistent with saddle nose, dry wrinkled facial skin, low set ears, absent eyebrows and eyelashes , sparse hairs on scalp which are hypopigmented , Malar hypoplasia and Scaling of skin all over the body.

Her physical and mental development were age appropriate and Systemic examination were within normal limits.

With such a history and examination findings, endocrine dysfunction, metabolic diseases, genetic disease and bone diseases were kept in mind and investigated accordingly in addition to routine Complete blood count and sepsis screening to rule out causes for present febrile episode.

Her CBC with inflammatory markers, thyroid function test, Calcium, phosphorus, ALP levels were within normal range. Xray Orthopantomogram was done to rule out local obstruction to teeth eruption but instead it revealed absent tooth bud. After ruling out all the causes, based on history of episodes of hyperpyrexia, lack of the hair, absence of teeth and tooth buds, peculiar examination findings, diagnosis of Ectodermal Dysplasia was made.

Anticipatory guidance were given to parents about the disease, and symptomatic, supportive treatment were given. Parents were advised for skin biopsy examination but they denied of any further evaluation. They were encouraged to use special cooling vests, caps and consume adequate fluids to tackle heat and to maintain hydration. For skin scaling and dryness topical emollients were advised. They were then referred to pediatric orthodontics and prosthodontics for dental implants in order to improve her appearance and mastication. Genetic counselling regarding mode of inheritance and nature of syndrome was offered to the parents.

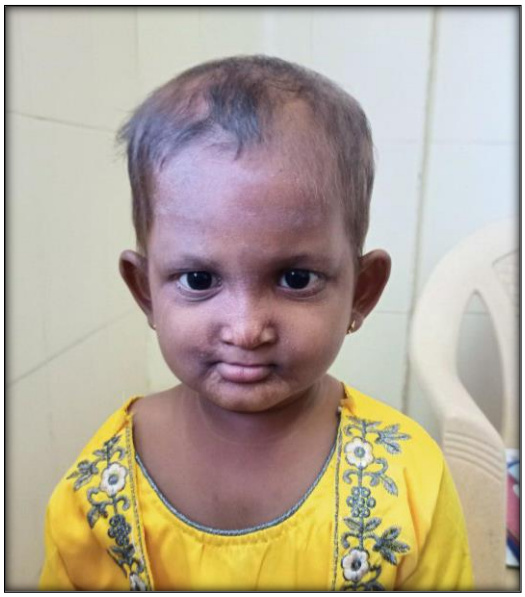

Figure 1: Peculiar facial features (Broad forehead, Flat nasal bridge, dry wrinkled facial skin, low set ears, absent eyebrows and eyelashes , sparse hairs on scalp)

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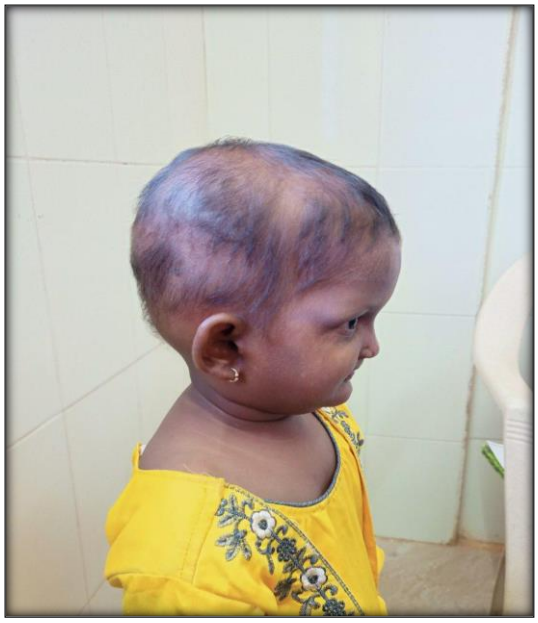

Figure 2: Hypotrichosis: Sparse thin hair , Malar hypoplasia

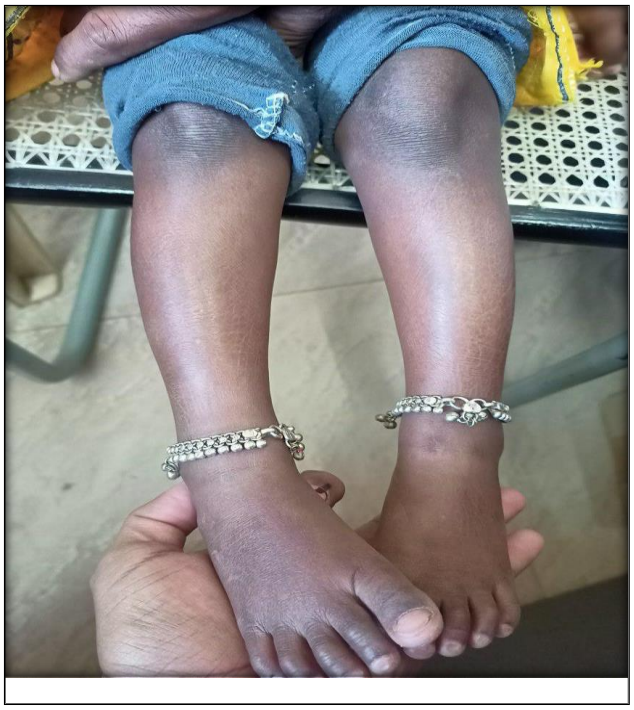

Figure 3: Dry and scaly skin

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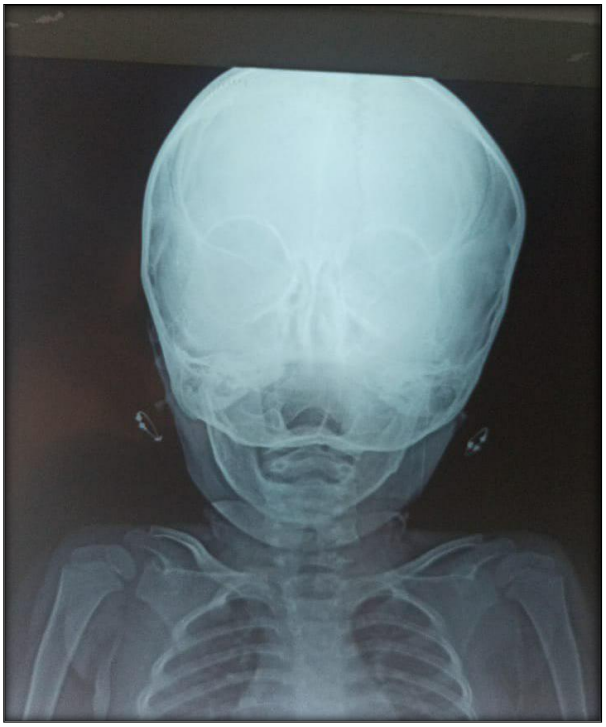

Figure 4: Absence of tooth bud in Orthopantomogram

INTRODUCTION

The skin with its appendages is an important organ in all higher organisms. It forms the primary barrier delineating self from external environment. The development of such a complicated and important structure requires a highly coordinated interaction of several genetic signaling pathways within and between the ectodermal and underlying mesenchymal layers of embryonic tissue. Malfunction in any part of this system or at any point during development of ectodermal structures can lead to a variety of phenotypically distinctive entities which are classified as the ectodermal dysplasia syndromes.[(1)]

It is characterized by a constellation of findings involving a primary defect of the skin; its appendageal structures including hair, nail, exocrine, sebaceous glands and teeth.[(2)]
In addition there might be defect in central nervous system (CNS), the adrenal medulla, the oral, nasal and rectal mucosa and their associated glands. The pharyngeal and laryngeal mucosa may also be sometimes get atrophied resulting in dysphonia and hoarseness of voice.[(3)]

DISCUSSION

Ectodermal dysplasia is a rare, non-progressive, heterogenous group of genetic disorder resulting from abnormal development of two or more tissues/structures which are derived from the embryonic ectoderm typically involving teeth, skin and its appendageal structures including hair, nails, eccrine and sebaceous glands. Estimated international prevalence of 7 in 10,000 individuals has been noted[(4)(13)] and more than 170 different syndromes have been identified.

These different types are caused by the mutation or deletion of certain genes located on different chromosomes. Most commonly mutations in the genes of EDA, EDAR and EDARADD are noted.

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Normally, these genes provide instructions for making proteins (ectodysplasin A) that work together during embryonic development. Ectodysplasin A forms a part of a signaling pathway that is critical for the interaction between two cell layers that is the ectoderm and the mesoderm. Ectoderm-mesoderm interactions are essential for the formation of several structures that arise from the ectoderm, including the skin, hair, nails, teeth and sweat glands. Hence mutations in these gene results in defective Ectodysplasin A formation thereby preventing normal interactions between the ectoderm and the mesoderm and hence impairing the normal development of hair, sweat glands and teeth. The improper formation of these ectodermal structures leads to the characteristic features of ectodermal dysplasia.(5)

The most common ectodermal dysplasia are hypohidrotic (anhidrotic) ectodermal dysplasia which have hair, nail, sweat glands and tooth defects and anhidrotic ectodermal dysplasia which has hair, nail and tooth defects.
The other most recognized ectodermal dysplasia having all four defectsare:
• Ectrodactyly-ectodermal dysplasia-clefting syndrome (EEC)
• Rapp-Hodgkin HED
• Ankyloblepharon, ectodermal defects, cleft lip/palate (AEC) or Hay-Wells syndrome.(5)
Anhidrotic ED usually has XLR inheritance and some may show AD inheritance while other recognised types usually have AD inheritance. Even though XLR and affecting mostly males with females being the carriers , In about 70 percent of cases, carriers of hypohidrotic ectodermal dysplasia experience some features of the condition. These signs and symptoms are usually mild and include a few missing or abnormal teeth, sparse hair, and some problems with sweat gland function. Some carriers, however, have more severe features of this disorder.(6)(7)
Diagnosis is based on the episodes of hyperpyrexia, lack of hairs or abnormal type of the hair, absence of teeth and tooth buds and tooth morphology. Peeling of the skin at birth, eczema, asthma, and frequent respiratory infections may be additional clues. However, during early infancy diagnosis is difficult because manifestations involving teeth, hair and inability to sweat are hard to detect.(8)

Although primarily diagnosed clinically, further diagnosis of specific syndrome/subtype requires a series of investigations such as, a) trichogram(barcode hair in patient of Hypohidrotic ED); b)skin biopsy (absence of eccrine structures in cases of hypohidrotic ED); c) pilocarpine iontophoresis and skin biopsy (documents hypohidrosis and a reduction in the number of eccrine glands.); d) Sweat pore counts using yellow starch—iodine powder; e) Molecular Genetic testing through GeneDx.(9)
Prenatal diagnosis using genetic mutation analysis may be performed. It is done by linkage analysis applied to chorionic villus samples at the 10th week of gestation for some ectodermal dysplasia.(10)

The management of ectodermal dysplasia (EDs) needs a multifaceted approach requiring physical cooling measures such as frequent drinking of cold liquids, wearing special cooling vests and caps for temperature maintainance; Bone grafting or sinus lift procedures, dental implants, and dental prostheses;3% minoxidil to encourage hair growth; Emollients for xerosis and collodion like presentation; aggressive topical and systemic antibiotics administration for chronic erosive scalp dermatitis; interventions from orthopedician and ophthalmologists for limb and occular abnormalities(11) Speech and occupational therapy; Genetic counselling to parents.

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Complications such as asthma, recurrent URTI, atopic dermatitis, dental caries , difficulty in feeding, growth retardation, disability due to skeletal deformities, ankyloblepharon, recurrent inflammation of the lacrimal apparatus, Genitourinary anomalies have been observed in many unidentified cases.[12][13]

But they usually have a good prognosis with a normal life span if detected early. And timely management of associated dental and skeletal problems with regulation of body temperature in the case of hypohidrotic variants considerably improves these patient's quality of life.

CONCLUSION

We report a rare case of ectodermal dysplasia probably anhidrotic type in a three year old female with delayed eruption of tooth, recurrent episodes of hyperthermia, absence of hair and sweating since infancy, thus emphasizing the need for thorough evaluation of delayed eruption of tooth and even fever of unknown origin in the children and considering ED's as a differential diagnosis especially in children presenting with defects in ectodermal structures.

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