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Original Research Article

Anhydrotic ectodermal dysplasia at tertiary care centre in western region of India

Monica Rime[1]*, **Jay Dhirajlal Modha**[1], **Neela V Bhuptani**[1], **Bharti K Patel**[1]

[1]*Dept. of Dermatology Venereology and Leprosy, Pandit Dindayal Upadhyay Government Medical College, Rajkot, Gujarat, India*

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ABSTRACT

Background: Anhydrotic Ectodermal Dysplasia, a rare genodermatosis, results in developmental anomalies affecting structures derived from the ectoderm. This condition is characterized by a clinical triad encompassing hypodontia, hypotrichosis, and anhidrosis, alongside additional symptoms Anhydrotic.
Materials and Methods: We conducted a retrospective review of the medical records of patients diagnosed with Anhydrotic Ectodermal Dysplasia at the Department of Dermatology, PDU Govt Medical College and Hospital Rajkot over the duration of 14 years from june 2008 to june 2022 Clinical presentations, family history details, and the initial symptoms prompting medical attention were carefully documented.
Results: In this case series, total 6 patients 5 males and 1 female of Anhydrotic Ectodermal dysplasia were identified. Clinical triad was present in all the patients. Family history was positive in 5 patient where 2 males were from the same family. Three patients were born out of consanguineous marriage.Initial presentations most commonly noted were intolerance to heat, recurrent fever, dry skin and abnormal dentition.
Conclusion: Anhydrotic Ectodermal dysplasia is a rare genodermatoses which is invariably characterized by its clinical triad. Early diagnosis is important in order to improve the quality of life.

1. Introduction

Ectodermal dysplasia (ED) represents a rare hereditary disorder characterized by primary developmental anomalies affecting two or more ectoderm-derived tissues, including the skin, hair, nails, eccrine glands, and teeth.[1] The condition is broadly categorized into two main types: the hypohidrotic or anhydrotic form (EDA), also known as Christ-Siemens-Touraine Syndrome, which is X-linked and features the classical triad of hypodontia, hypotrichosis, and hypohydrosis. The second category is the hydrotic form (Clouston syndrome), which similarly affects the teeth, hair, and nails but spares the sweat glands. EDA, initially described by Thurnam, exhibits a prevalence of approximately 1 in 100,000 individuals.[2]

2. Materials and Methods

We conducted a retrospective review of the medical records of patients diagnosed with Anhydrotic Ectodermal Dysplasia at the Department of Dermatology, PDU Govt Medical College and Hospital Rajkot over the duration of 14 years from June 2008 to June 2022. Clinical presentations, family history details, and the initial symptoms prompting medical attention were carefully documented

Clinical diagnosis of Anhidrotic Ectodermal Dysplasia (EDA) was made on the basis of presence of at least two of the following seven features:[3]

1. Reduced skin pigmentation.
2. Wrinkling and increased pigmentation around eyes.

* *Corresponding author*.
E-mail address: rimem2003@gamil.com (M. Rime).

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3. Sparse or absent hair.
4. Hypoplastic or absent sweat glands
5. Hypodontia or anodontia, tendency to delayed eruption, deficient alveolar ridge, or conical anterior teeth.
6. Depressed nasal bridge, small nose with hypoplastic alae nasi.
7. Full forehead with prominent supra orbital Ridges.

3. Results

Total 6 patients 5 males and 1 female diagnosed with anhydrotic ectodermal dysplasia were identified with age ranging from 2 to 17 years. Case 6 is the only female patient. The clinical features and family history are summarized in Tables 1 and 2 respectively. In addition, the initial conditions that made each patient seek medical help and be examined for a diagnosis of EDA are described in Table 2.[4]

Clinical triad of Anhydrotic Ectodermal dysplasia was present in all the patients with additional feature of dry skin, sparse hair, intolerance to heat.

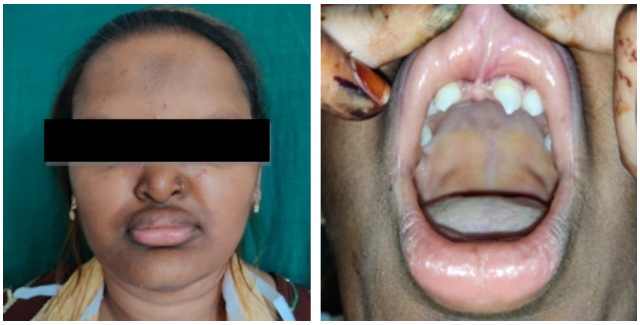

Figure 1: Case no 6, 14 years old girl child with sparse hair, eyebrows, depressed nasal bridge, periorbital wrinkling, fuller lips and conical teeth

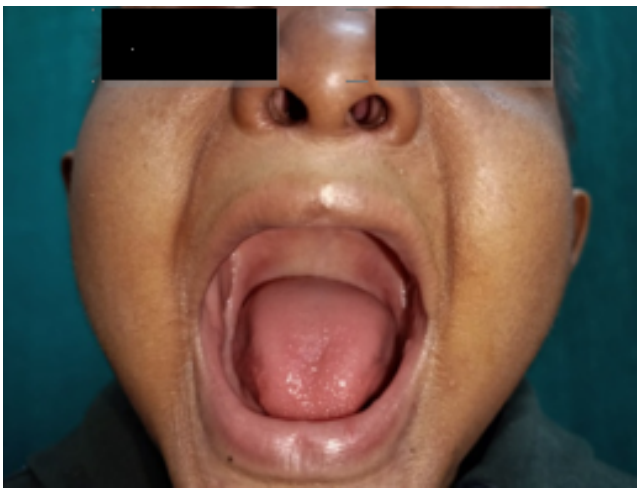

Figure 2: Case no 3 showing complete absence of teeth

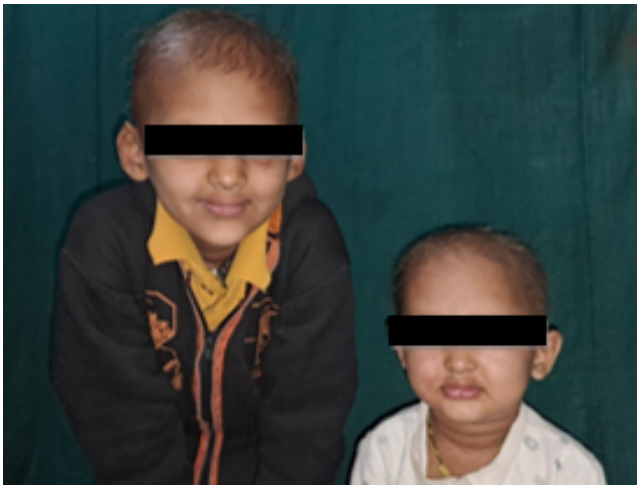

Figure 3: Case 1 and 2 two siblings with anhydrotic ectodermal dysplasia

3.1. Clinical features

Four patients (case 1,2,3 and 6) had periorbital wrinkling, hyperpigmentation and conical teeth. One patient (case 3) had complete absence of teeth. Four patients (case 1,2,5 and 6) had fuller lips. Female patient (case 6) had history of recurrent respiratory tract infections.

3.2. Family history

Family history was positive 5 patients where 2 male children (case 1 and 2) were from the same family, case 3 had similar complaint in mother, case 4 had similar complaint in grandfather, case 5 had similar complaint in younger brother. History of consanguineous marriage was present in three patients (case 1, 2 and 6).

4. Discussion

There exist three primary modes of inheritance in Ectodermal Dysplasia (EDA): X-linked recessive, autosomal dominant, and autosomal recessive patterns. X-linked recessive inheritance constitutes the most prevalent pattern, encompassing about 95% of HED cases.[5] Typically, it manifests in males and is transmitted through female carriers. The remaining 5% may manifest as autosomal dominant or recessive forms, exhibiting similar phenotypic characteristics that pose challenges in clinical differentiation. X-linked recessive EDA results from mutations in the gene responsible for encoding ligand ectodysplasin A (EDA). Conversely, mutations in genes encoding the EDA receptor lead to autosomal dominant forms, while mutations in adaptor proteins less frequently result in autosomal recessive forms of EDA.[6] It's noteworthy that the complete syndrome seldom manifests in females, although affected females may display dental

Table 1: linical manifestations

Case No.	gender	Clinical manifestations						
		H/A T[1]	H/A O[2]	H/A A[3]	H/A H[4]	POW[5]	FL[6]	DS[7]
1	M	Yes	Yes	No	Yes	Yes	Yes	Yes
2	M	Yes	Yes	No	Yes	Yes	Yes	Yes
3	M	Yes	Yes	Yes	Yes	Yes	No	Yes
4	M	Yes	Yes	No	Yes	No	No	Yes
5	M	Yes	Yes	No	Yes	No	Yes	Yes
6	F	Yes	Yes	No	Yes	Yes	Yes	Yes

H/A-T: Hypo- or atrichosis, including scalp hair, eyebrow, eyelash, axillary hair, and pubic hair
H/A-O: Hypodontia including peg-shaped teeth
H/A-A: Anodontia
H/A H: Hypo- or anhidrosis with recurrent hyperthermic episodes and heat intolerance
W: Periorbital wrinkling and hyperpigmentation
L: Fuller lips
S: Dry skin

Table 2: Family history and consangenious marriage

Case No	Family history	Consangenious marriage
1	Yes	Yes
2	Yes	Yes
3	Yes	No
4	Yes	No
5	Yes	No
6	No	Yes

Table 3: Initial conditions leading to seek medical service

Case No.	Gender	Age at time of diagnosis	Initial symptoms leading to medical help
1	M	5 months	Dryness of skin, recurrent fever and family history of EDA
2	M	2 years	Intolerance to heat, abnormal dentition
3	M	2 years	No teeth, dry skin
4	M	10 months	Recurrent fever, family history and clinical features of EDA
5	M	1 year	Abnormal dentition, intolerance to heat, dryness of skin
6	F	2 years	Recurrent fever, abnormal dentition

anomalies, sparse hair, and diminished sweating.[7]

Molecular genetic testing offers a means to pinpoint mutations in the EDA, EDAR, EDARADD, or WNT10A genes associated with EDA. Beyond confirming diagnoses, molecular genetic testing aids in identifying carriers within families and plays a pivotal role in genetic counseling.[5] Through molecular studies, researchers have elucidated that the aforementioned genes participate in the formation of various substrates crucial for activating signaling pathways such as tumor necrosis factor α related signaling, the WNT signaling pathway, and the nuclear factor κB pathway. These pathways are instrumental in ectoderm-mesoderm interactions, ectodermal appendage differentiation, and organogenesis during embryonic development initiation.[8]

Hereditary ectodermal dysplasia (EDA) presents a clinical profile marked by the absence or scarcity of eccrine glands, hypotrichosis, and hypodontia, notably featuring conical or peg-shaped teeth affecting both primary and permanent dentition, particularly the incisors and canines. Affected individuals, unable to perspire, are prone to hyperthermia during physical activity or exposure to warm environments.[9] All 6 patients had history of heat intolerance a consistent with findings from studies by Kuei-L et al.,[4] and Sushita V et al.,[10] where heat intolerance was prevalent among subjects.

Sparse, slow-growing scalp hair, eyebrows, and eyelashes, often with light pigmentation, contribute to the clinical presentation.[11] The hallmark of hereditary ectodermal dysplasia remains hypohidrosis, which may not be immediately evident within the first year of life therefore recurrent unexplained fever often helps in diagnosis this disease.[12]

Additional clinical manifestations consist of frontal bossing, sunken cheeks, a depressed nasal bridge, thick everted lips, and wrinkled hyperpigmented periorbital skin, accompanied by large, low-set ears. The absence or reduced presence of sweat and sebaceous glands results in smooth, dry, thin skin, frequently displaying fine linear wrinkles and increase pigmentation around the eyes and mouth.[13]

Among the notable complaints prompting medical attention are tooth anomalies, often the absence or abnormal shape of teeth, with conical morphology being a characteristic finding. 5 of our patients had conical teeth, while one had complete dental absence, consistent with the observations of Kuei-Chung Liu et al.,[14] and Sushita V et al.[10]

Extremely thick nasal secretions due to abnormal mucous glands makes patient prone to recurrent respiratory tract infections.[14] 1 patient (case 6) had history of recurrent respiratory tract infections which is similar to case series by Keui L et al.,[4] where 1 patient had history of recurrent respiratory tract infection.

X‑linked EDA presents usually in males, with full involvement in females seen only in autosomally transmitted disease.[15] Case 6, the only female patient in our case series had all the clinical features along with history of consangenious marriage in the parents suggestive of autosomal recessive mode of inheritance which is similar to case series by Sushita V et al[10] andcase report by Tashlim A et al[16] and sangita G et al.[17]

Treatment of Ectodermal Dysplasia (EDA) primarily focuses on managing symptoms and alleviating associated challenges. Heat mitigation strategies play a crucial role, involving the use of cooling devices, avoiding excessive heat exposure, staying hydrated, and opting for lightweight, breathable clothing. Creating a cool environment is imperative to mitigate the risk of overheating, necessitating parental guidance to restrict intense physical activities and exposure to high temperatures.[18,19]

Addressing dry skin and potential atopic dermatitis entails the use of moisturizers, emollients, and topical therapies to alleviate discomfort and maintain skin health. Regular skincare routines, including gentle cleansing, are advocated to manage dry skin-related issues effectively.[5]

Dental care is integral and encompasses various interventions such as bonding for conical teeth, dental prosthetics like dentures or bridges for missing teeth, orthodontic treatments, and periodic dental check-ups every six to twelve months to monitor dental development and prevent dental caries.[5] While there's no fixed timeline for initiating dental treatment, it's advisable to provide initial prosthetics before a child enters school.[20,21]

5. Conclusion

Ectodermal dysplasia is a rare genetic disorder affecting hair, nails, and teeth, necessitating a comprehensive clinical approach for effective management. A multidisciplinary team comprising dermatologists, pediatricians, and dentists is crucial in providing holistic care to patients with this condition.

In our endeavor to understand this rare disease, we conducted a retrospective review of medical records of patients diagnosed with Ectodermal Dysplasia at the Department of Dermatology. Through this review, we aimed to highlight significant clinical features and gain insights into the management of this complex condition.

However, our study has certain limitations. Firstly, genetic studies were not conducted, which could have provided valuable insights into the underlying genetic mechanisms of Ectodermal Dysplasia. Additionally, being a retrospective review, we relied on existing medical records and clinical photos, which might have lacked certain crucial information not documented during initial examinations.

6. Source of Funding

None.

7. Conflict of Interest

None.

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Author biography

Monica Rime, 2nd Year Resident https://orcid.org/0009-0006-0929-0683

Jay Dhirajlal Modha, Assistant Professor

Neela V Bhuptani, Professor and Head

Bharti K Patel, Professor

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