

A rare case of anhidrotic ectodermal dysplasia in a six-year-old boy

Bismah Gul, U. Narayan Reddy, Swathi Chacham, S. Ali khurram, Naila Mazher, Taha Mustafa, E. Apoorva

ABSTRACT

Introduction: Ectodermal dysplasia is a rare, non-progressive, genetic disorder resulting from abnormal development of two or more tissues at a time which are derived from the embryonic ectoderm. It classically manifests with skin, eccrine gland, nail and hair changes, with an incidence of 1 in 1, 00,000 births. More than 170 different syndromes have been identified. X-linked recessive anhidrotic dysplasia (XLHED)

being the most common type, which is expressed in males. **Case Report:** A six-year-old boy, was brought to the pediatric outpatient department with the complaints of fever on and off since month months. The parents gave history of recurrent episode of hyperpyrexia, with heat intolerance, absent sweating and delayed dentition in the past. On examination the child had peculiar facies, characterized by malar hypoplasia, flattening of nasal bridge, everted lips, wrinkled periorbital skin, pegged shaped tooth, low set ears, scanty, hypopigmented hair on the head; with absent eyebrows and eye lashes. Even after thorough evaluation and investigation, no focus of infection was found, ectodermal dysplasia was then considered and a skin biopsy done, which showed absence of skin appendageal structures. **Conclusion:** We report a rare case of anhidrotic ectodermal dysplasia in a 6-year-old boy, thus emphasizing the need for considering EDA as a differential diagnosis for neonates and infants with history of fever of unknown origin specially when associated with delayed dentition and hypotrichosis. An early diagnosis would have prevented unnecessary antibiotic misuse.

Keywords: Children, Guillain-Barré syndrome, Herpes zoster, Immunocompetent

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INTRODUCTION

Anhidrotic ectodermal dysplasia is a heterogeneous group of disorders characterized by constellation of findings involving defects of skin, hair, appendageal structures, eccrine and sebaceous glands. There are two major types of this condition depending on the number and functionality of the sweat glands: (1) X-linked recessive anhidrotic or hypohidrotic, (Christ-Siemens Touraine syndrome) in which sweat glands are either absent or reduced in number, and (2) hidrotic (HED), where sweat glands are normal and the condition is inherited as autosomal dominant (Clouston syndrome) [3, 4]. Genetic studies regarding the etiology of EDA revealed that mutations in the ectodysplasin-A and ectodysplasin-A receptor genes are responsible for X-linked and autosomal hypohidrotic ectodermal dysplasia [5]. Various classifications have been proposed based on clinical features, mode of inheritance, gene mutations and pathophysiology, but pure EDA manifests with defects in ectodermal structures alone.

CASE REPORT

A six-year-old boy (Indian), was brought to the pediatric outpatient department during summer season with complaints of fever on and off since three months, his birth history did not reveal any significant events, he was born of a third degree consanguineous marriage, the child had history of recurrent episode of hyperpyrexia, with heat intolerance, absent sweating and delayed dentition in the past, there was no history of similar complaints among the family members. On clinical examination, the child was febrile, temperature 101°F, other vital parameters were normal, but the child had peculiar facies, characterized by recessed Columella, thick everted lips, with absent eye lashes and eyebrows, dry, wrinkled periorbital skin, (Figure 1) with dry scaly skin all over the body. There were scanty, hypo pigmented hair on the head, malar hypoplasia, flattening of nasal bridge, and low set ears (Figure 2). Oral examination of the child revealed hypodontia with presence of only one pegged shaped tooth in the upper jaw (Figure 3). Systemic examination was normal. His physical, mental and sexual developments were as per his age. Otorhinolaryngological and ophthalmological examination were also normal.

Routine investigations for sepsis screen were sent which did not reveal any positive findings. After thorough evaluation and investigation for a focus of infection, EDA was considered and a skin biopsy was done for histopathological examination which showed absence of skin appendageal structures like hair follicles, eccrine glands, and sebaceous glands (Figure 4). The child was given supportive and symptomatic treatment, and was encouraged to consume adequate liquids to maintain hydration. He was advised to wear cool clothing for thermoregulation along with topical emollients.

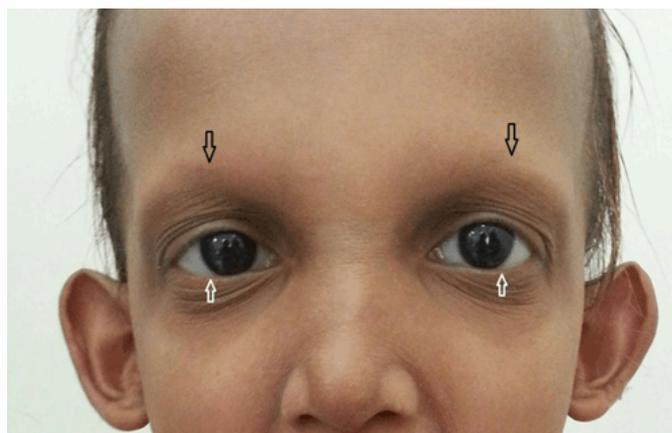


Figure 1: Characteristic facies (malar hypoplasia, flattening of nasal bridge, dry, wrinkled periorbital skin, and prominent low set ears, with absent eyebrows (black arrow) and eyelashes (white arrow)).



Figure 2: Hypotrichosis-sparse, thin, hypopigmented hair (black arrow) with malar hypoplasia (red arrow) and low set ears (white arrow)

The child was referred to a pediatric orthodontist and prosthodontics for dental implants to improve his speech, appearance and mastication. Genetic counseling regarding the mode of inheritance and nature of this syndrome was offered to his parents.

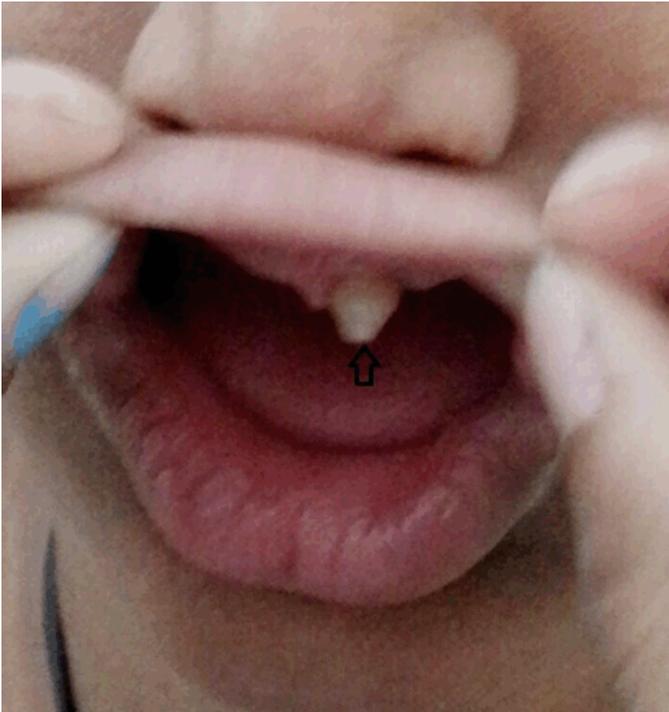


Figure 3: Hypodontia with single, pegged shaped tooth in the upper jaw (black arrow).

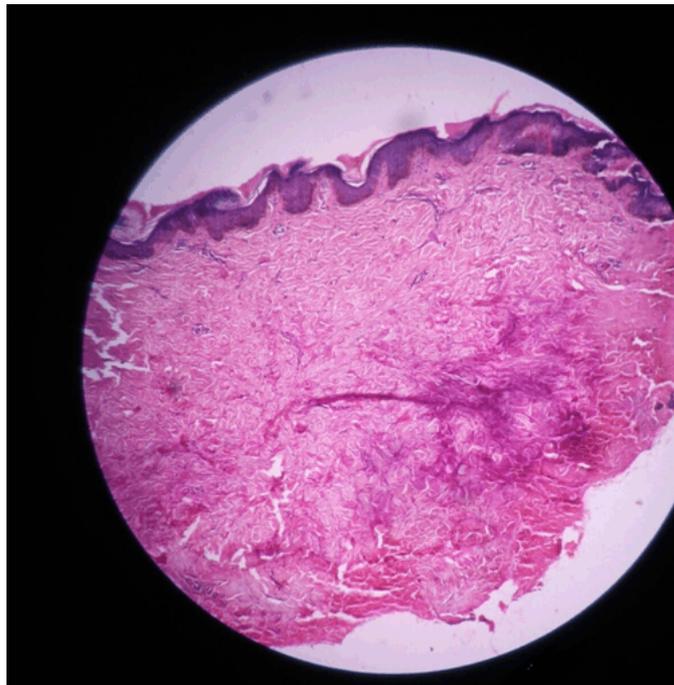


Figure 4: Skin histopathology showing hyperkeratosis of the epidermis with loss of rete ridges, adnexal structures in the dermis.

DISCUSSION

Ectodermal dysplasia is a rare, non-progressive, genetic disorder resulting from abnormal morphogenesis

of two or more tissues at a time which are derived from the embryonic ectoderm. This disorder is characterized by constellation of findings involving defects of skin, hair, appendageal structures, eccrine and sebaceous glands. It has an incidence of 1 in 1,00,000 births [1]. More than 170 different syndromes have been identified [2], of which X linked recessive anhidrotic dysplasia is the most common type with gene mapping to Xq12-q13 mutation, is expressed in males. The number of female carrier, with no or little signs of the disease exceed more than the affected males. It is mostly reported in whites, with rare incidences in people of other races. Hidrotic ectodermal dysplasia has a predilection for people of French-Canadian origin. Genetic studies regarding the etiology of EDA reveals that the mutations in the ectodysplasin-A and ectodysplasin-A receptor genes are responsible for X-linked and autosomal hypohidrotic ectodermal dysplasia [5]. The key transcription factors and intracellular signaling pathways that have been implicated in the etiology of EDA, include the tumor necrosis factor (TNF)-like/TNV receptor signaling pathway, which involves ectodysplasin (EDA); the EDR receptor (EDAR), the EDAR-associated death domain (EDARADD); the WNT signaling pathway; the NF- κ B signally pathway, which involves the NF- κ B essential modulator (NEMO); and the transcription factor p63 [6]. In 2009, 64 genes and 3 chromosomal loci were associated with 62 ectodermal dysplasia [7].

Thurman first reported a patient with ectodermal dysplasia in 1848 [8]. The term ectodermal dysplasia was coined by Weech in 1929 [9]. The first classification system of the ectodermal dysplasia was given by Freire-Maia and Pinheiro in 1982 [10], with additional updates in 1994 and 2001.

Ectodermal dysplasia was later reclassified into the following four functional groups based on the underlying pathophysiologic defect: (1) cell-to-cell communication and signaling, (2) adhesion, (3) development, and (4) other [11]. Similarly, in 2001, Priolo and Laganà reclassified the ectodermal dysplasias into 2 main functional groups: (1) defects in developmental regulation/epithelial-mesenchymal interaction and (2) defects in cytoskeleton maintenance and cell stability [6]. Several ectodermal dysplasia syndromes may manifest in association with mid-facial defects, mainly cleft lip, cleft palate, or both. The three most commonly recognized forms include (1) ectodermal dysplasia, ectrodactyly, and clefting (EEC) syndrome [12]; (2) Hay-Wells syndrome or ankyloblepharon, ectodermal dysplasia, and cleft lip/palate (AEC) syndrome; and (3) Rapp-Hodgkin syndrome, all of which are caused by mutations in the TP63 gene.

Clinical diagnosis is usually made in infancy or childhood when they present with skin, dental, hair, and nail changes, if undiagnosed early, the child may present with complications like seizures (due to hyperthermia), xerophthalmia, conjunctivitis or Xerostomia (due to decreased tear and salivary gland secretions) and dental

caries. Frequent pharyngitis, otitis, and rhinitis; nasal obstruction; hearing loss; and hoarseness has also been reported. On examination, facial dysmorphism (sunken cheeks; saddle nose; thick, everted lips; wrinkled, hyperpigmented periorbital skin; and large, low-set ears) may be seen. Skin is dry and hypopigmented with eczematous dermatitis. Sweating may be absent or reduced. Hair is sparse, hypopigmented and brittle. On microscopic observation hair shaft shows medullation with a “bar code” appearance. Nails may be dystrophic. Dental features may include absent, reduced, rudimentary, or pegged teeth; accompanied by enamel defects and frequent dental caries. Hypogammaglobulinemia with impaired lymphocyte proliferation and cell-mediated immunity have also been associated.

Diagnosis is based on demonstration of absent sweat pore by yellow starch–iodine powder, when applied on the skin of normal individuals will change to a deep purple color on sweating making the sweat pores visible. But there is no color change in people with EDA. Definitive diagnosis is made by skin biopsy done on the hypothenar eminence, which shows reduced or absent appendageal structures with thin and flattened epidermis. Prenatal diagnosis of hypohidrotic ectodermal dysplasia can be made with fetal skin biopsy or by chorionic villus samples at the 10th week of gestation. Genetic testing can determine several forms of ectodermal dysplasia.

Treatment consists of encouraging frequent consumption of cool liquids to maintain adequate hydration and thermoregulation. Patients are advised to wear cool clothing. Topical emollients can be prescribed for xerosis or eczematous dermatitis. Artificial tears to prevent damage to the cornea may benefit patients with reduced lacrimation along with saline sprays to protect nasal mucosa. For patients with dental defects, advise early dental evaluation and intervention and encourage routine dental hygiene. Certain recommendations for the diagnosis, evaluation, and treatment of patients with ectodermal dysplasia, were proposed by an international consensus meeting of experts [13, 14]. Patients with ectodermal dysplasia with immunodeficiency are prone for frequent infections requiring treatment with therapeutic and/or prophylactic antibiotics. Speech and occupational therapy may benefit patients with cleft lip and/or palate. Genetic counseling should be provided to the parents.

CONCLUSION

We report a rare case of anhidrotic ectodermal dysplasia in a six-year-old boy with recurrent episodes of hyperthermia since birth, thus emphasizing the need for thorough evaluation of fever of unknown origin in the new born period and considering ectodysplasin (EDA) as a differential diagnosis especially in children presenting with defects in ectodermal structures.

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Author Contributions

Bismah Gul – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

U. Narayan Reddy – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Swathi Chacham – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

S. Ali khurram – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Naila Mazher – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

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E. Apoorva – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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