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Case Report

Hypohidrotic Ectodermal Dysplasia/ Christ-Siemens-Touraine Syndrome: A case report

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Abstract Hypohidrotic ectodermal dysplasia (HED) is a rare heterogeneous inherited disorder resulting from faulty development of ectodermal structures. It is clinically characterized by the classical triad of hypohidrosis, hypodontia and hypotrichosis. We report a case of 13 years old boy who presented with chief complaints of hypohidrosis and heat intolerance that were particularly troublesome in summer months. Detailed evaluations revealed numerous cutaneous and extracutaneous manifestations of the syndrome. After a clinical diagnosis, patient was managed with a multidisciplinary approach which resulted in remarkable improvement in his quality of life.

Key words
Hypohidrosis; Hypodontia; Hypotrichosis; Multidisciplinary approach.

Introduction

Ectodermal dysplasias (ED) are a highly diverse group of disorders resulting from defect of ectodermal structures that include skin, nails, hair, teeth and sweat glands in different combinations.[1] There are over 200 types of ectodermal dysplasias, and out of them X-linked hypohidrotic form also called Ectodermal dysplasia 1 or Christ-Siemens-Tourane syndrome is the commonest. Its incidence in general population has been reported to be 1 in 17,000 live births.[2]

Genetically, HED is caused by mutations of the genes encoding proteins of the tumor necrosis factor α (TNFα)-related signalling pathway. These proteins are involved in signal transduction from ectoderm to mesenchyme during development of the fetus and are indispensable for the differentiation of ectoderm-derived structures. As a result of mutations in the genes encoding for these proteins, the process of initiation and differentiation of skin appendages is disturbed.[3]

There are no diagnostic criteria defined for HED. Diagnosis is made clinically by findings of hypotrichosis, dry atrophic skin with absent sweating, teeth anomalies and characteristic facial physiognomy. The patients show generalised or patchy hypotrichosis. Hair on torso and extremities is usually absent, scalp involvement is variable. Eyebrows and eyelashes are also usually scanty. The skin is thin, dry and scaly like ichthyosis with hyper or/and hypopigmentation. The teeth are usually small, malformed, taurodontic and widely spaced. The enamel is prone to caries and mechanical damage. Both deciduous and permanent sets of teeth are affected. Besides, many patients exhibit dysmorphic features like prominent forehead, hyperpigmented wrinkled skin around eyes, hypertelorism, depressed nasal bridge, everted nose, prominent lips and deformed ears. The skin on palms and soles is dry, rough, and shows characteristic dermatoglyphic patterns. Some patients show plantar fissured hyperkeratosis.[2] Reduced or

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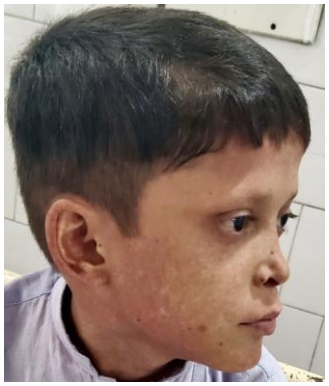

Figure 1

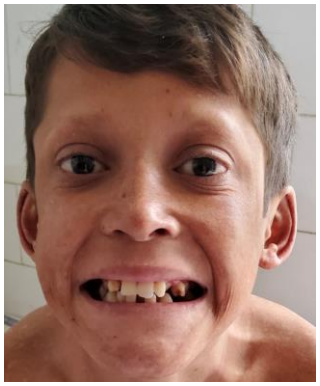

Figure 2

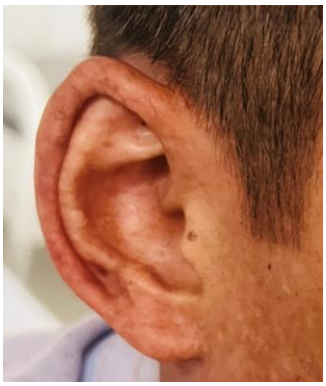

Figure 3
'Spock ears'.

Figure 1&2 Characteristic facial features including sparse eyebrows with absent lateral one third, periorbital and perioral wrinkling, depressed nasal bridge, hypopigmented and hyperpigmented spots, protuberant lips, malaligned teeth and multiple missing teeth.

absent sweating causes problems in thermoregulation resulting in increased core body temperature which is especially dangerous in early childhood. Due to faulty development of other exocrine glands, patients may have dryness of eyes, upper and lower respiratory tract and other mucosal surfaces. Other manifestations include atopic disorders, recurrent infections and restricted physical growth.[2,4]

Case Report

A 13 years old boy was brought to outpatient Dermatology Department of Mayo Hospital Lahore with complaints of inability to produce sweat, and heat intolerance since early childhood causing discomfort and erythema over skin that was particularly troublesome during summer season and after physical activity. Patient was born as the first child to consanguineously married parents, after an uneventful pregnancy with vaginal delivery. During first two years of life, patient had multiple bouts of unexplained fever accompanied with febrile seizures. The parents revealed that patient had extremely dry skin since birth and had recurrent episodes of generalised itchy and scaly skin rashes in early childhood. He had complete absence of hair on whole body since birth. After infancy he gradually grew hair over scalp but hair on torso and limbs never appeared.

Primary dentition was delayed with multiple missing teeth. Teeth which erupted were small, malformed and malaligned. Later on, only some of the deciduous were shed, rest were retained. Among permanent teeth only a few erupted. The malformation and malalignment of teeth resulted in difficulty in mastication and unaesthetic appearance to the face.

Parents also reported history of frequent sinusitis, allergic asthma, recurrent chest infections and frequent bone pains in legs since early childhood. Patient has two brothers and neither of them has any similar features. Parents denied having any other affected family member or any history of early death in family.

On examination, patient's height was 122cm and weight was 18kg. Both these parameters are below 3rd percentile for his age. Patient's mental capabilities and social behaviour was normal. Cutaneous examination revealed pervasive dryness of skin, with numerous post-inflammatory hyper and hypopigmented marks alongwith few excoriations over trunk and limbs. There was complete absence of hair on torso and limbs but hair on scalp seemed normal. Facial features included depressed nasal bridge

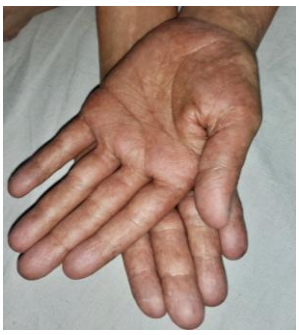

Figure 4

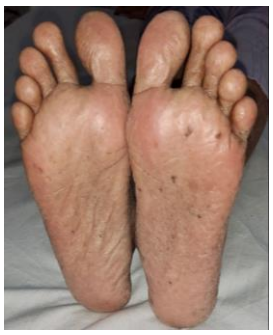

Figure 5

Figure 4 & 5 Thin, wrinkled and dry palmoplantar skin with absent dermatoglyphics.

(saddle nose), peri orbital wrinkling and pigmentation, sparse eyebrows, protuberant lips and characteristic Spock ears **(Figures 1-3)**. Skin over the palms was dry and thin with absent dermatoglyphics and plantar skin was hyperkeratotic and fissured **(Figures 4 and 5)**. Nails were thin, dry and lustreless.

Intraoral examination revealed widely spaced and malformed teeth with most of them having caries **(Figure 2)**. His orthopantomogram confirmed hypodontia, over retained deciduous teeth and absent permanent teeth buds.

Upon investigations, patient was found to have anaemia, neutropenia and had low serum calcium and vitamin D levels. His immunoglobulin levels (IgG, IgA, IgM) were checked to rule out the rare variant associated with immunodeficiency but these levels were found to be normal.

Patient was started on palliative treatment after multidisciplinary consultations involving dermatologist, physicians, dentist, pulmonologist and child psychiatrist. Patient was advised to avoid hot climates, prolonged sun exposure and strenuous physical activity. Episodes of hyperthermia should be dealt with drinking cold liquids, cold showers, cooling the body with vests or clothes soaked in chilled water, avoiding hot beverages and foods, staying in air-conditioned environment if possible. Extreme dryness of skin was treated with moisturisers alongwith topical corticosteroids to for eczematous areas. Monitoring of Vitamin D levels was advised because of sun avoidance and supplements were prescribed. For his over-retained, malformed and carious teeth dental extraction was advised by dentists with subsequent planning of prosthetic implants to improve masticatory function and facial appearance.

Discussion

Hypohidrotic ectodermal dysplasia is a rare developmental disorder involving mainly skin, hair, teeth and eccrine glands inherited mostly in X-linked recessive mode. The main clinical symptoms include hypotrichosis on scalp, body, eyebrows and eyelashes, dyshidrosis, hypodontia affecting both primary and secondary sets of teeth and facial dysmorphism. Because of severely compromised sweating, the newborns experience increases in central body temperature that leads them to develop febrile seizures. The failed thermoregulation is particularly problematic in summer season and/or warmer climates causing about 30% mortality rate in first 3 years of life.[1]

HED is caused by mutations of several genes: EDA1 (encodes for a protein ectodysplasin-A), EDAR (encodes for ectodysplasin A receptor), EDARADD and NEMO (encoding for the protein product NFκB).[2,3] Confirmation of clinical diagnosis can be done by finding the relevant mutations by molecular genetic testing. It could not be done in this patient due to non-availability of genetic studies.

Children with ectodermal dysplasias have been shown to have significantly higher prevalence of atopic eczema, asthma, allergic rhinitis and food

allergies than general paediatric population. Plausible explanation for this predisposition is that a combination of genetic and environmental factors in ED syndromes breach the skin and mucosal barriers, resulting in enhanced transmission and sensitization to irritants, allergens, and pathogens.[4]

Most of the studies have confirmed restricted physical growth in terms of body length and weight since infancy through adolescence in patients of Hypohidrotic ectodermal dysplasia, like found in this patient. It is conceivable that children growing under conditions of poor nutrition because of dental anomalies causing feeding problem, faulty functions of mucosae and recurrent infections are at higher risk of developmental retardation.[5]

A much rare variant of HED is hypohidrotic ectodermal dysplasia with immunodeficiency (HED-ID) which has similar phenotypic picture alongwith a severe immunodeficiency. This immunodeficiency shows high variability among individuals but is characterized by recurrent life-threatening infections (bacterial, mycobacterial, viral) and low level of circulating IgG.[6] Apart from sinusitis and recurrent chest infections since childhood, this patient did not have history of any serious infections and his immunoglobulin levels were normal.

Appearance of clinical features since infancy or early childhood differentiates HED from acquired diseases with similar symptoms like alopecia areata and Sjögren's syndrome. Differentiation from other ectodermal dysplasias (ED) is done by the classical triad of hypohidrosis, hypotrichosis and hypodontia. The second commonest ectodermal dysplasia after HED is Clouston syndrome/ Hidrotic ectodermal dysplasia. Nail dystrophy, alopecia and palmoplantar keratoderma are the 3 major characteristic features of the hidrotic ED. Teeth and sweat gland function are unaffected in hidrotic EDs unlike in HED.[7]

Another differential for hypohidrosis is dermatopathia pigmentosa reticularis which is an autosomal dominant disorder characterized by a triad of widespread reticular pigmentation, non-scarring alopecia and onychodysplasia. Other manifestations include adermatoglyphia, hypohidrosis, palmoplantar keratoderma and acral non-scarring blisters.[8]

As there is no curative treatment for HED, patients need a multi- disciplinary team effort to plan appropriate supportive management. It includes external cooling and regulation of ambient temperature, removal of malformed and damaged teeth, early denture fittings, skin, treatment of associated eczematous dermatitis, asthma, respiratory infections and nutritional deficiencies.[9] Better control of infections and skin issues resulting in reduced absenteeism from school, and improved aesthetic appearance of face after necessary dental care helps in boosting child's self-esteem. All these measures improve patient's overall quality of life.

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