IJMAHS

CASE REPORT

HYPOHIDROTIC ECTODERMAL DYSPLASIA WITH X-LINKED HYPER IgM

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INTRODUCTION:

Ectodermal dysplasia (ED) is a large, heterogeneous group of inherited disorders characterized by a constellation of findings involving defects of 2 or more of the tissues derived from embryonic ectoderm : teeth, skin, and appendageal structures including hair, nails, and eccrine and sebaceous glands.(1) Although 192 distinct disorders having been described till date the majority are rare and most have not been genetically defined.(2)

Thurman published the first report of Ectodermal dysplasia in 1848 and coined by Weech in 1929.

Other names of hypohidrotic Ectodermal dysplasia (ED): anhydrotic Ectodermal dysplasia, Christ Siemens Touraine syndrome.

Anhidrotic ectodermal dysplasia manifests as a triad of defects: partial absence (hypohidrosis) or complete absence of sweat glands, anomalous dentition, and hypotrichosis.(3,4)

CASE REPORT:

A two months old male baby born to a nonconsanguineous marriage presented with complaints of fever since birth and cough and cold with increased work of breathing since 2 days. The family gave a history of near complete absence of sweating since birth, dry skin and repeated episodes of fever since birth.

Birth history was antenatally normal, was full term normal vaginal delivery and cried immediately after birth. On second day of life child was admitted in NICU for high grade fever with respiratory distress for 15 days.

Past history revealed 2 episodes of fever with cough and cold requiring admission was diagnosed to have pneumonia and bronchiolitis. In between these episodes child use to get intermittent fever.

This is sixth child of parents with four elder sons and one elder daughter. No other siblings had similar complains and clinical features.

On general examination of the patient showed very fine hair scarcely present on the scalp with scaly skin, almost complete absence of eyebrows and eyelashes (fig.1&3) and complete absence of hair in the body trunk and extremities. The wrinkled, hyperpigmented periorbital skin and hypopigmented patches over head and face, eversion of the protuberant thick lips, frontal bossing, saddled nose and small jaw were the other notable features of our case. The skin was dry and scaly while mouth cavity was also dry i.e. xerostomia. There was extra nipple on left side. (fig.1) The nails and the digits of the extremities were apparently normal.

On systemic examination respiration was rapid with significant retractions and bilateral wheeze on auscultation and rest was normal.

On investigation chest roentengogram showed hyperinflation with increased vascular markings suggestive of bronchiolitis. The hematological picture was normal. However from the clinical features

anhydrotic ectodermal dysplasis was suspected. Radiographically the jaw showed mild hypoplastic alveolar ridges and teeth were suspected to erupt late. The Starch Iodine test on the forearm was positive. The diagnosis of hypohydrotic ectodermal dysplasia was confirmed in our case after skin biopsy of the scalp (fig. 4).

For classifying the type of ectodermal dysplasia, immunoglobins (IgG, IgM, IgA) were sent to see for immunodeficiency. IgM was increased while IgG and IgA were normal suggestive of associated hyper IgM syndrome(X-Linked Hyper IgM-ED)

Table1: Four recognized types of anhidrotic ectodermal dysplasia [8, 9]

Type	Inheritance	Gene defect
ED-1	X-linked recessive	Ectodysplasin A (EDA)
ED-anhidrotic	Autosomal recessive	Ectodysplasin A anhidrotic receptor(EDAR) EDAR associated death gene(EDARADD)
ED-3	Autosomal dominant	EDAR
ED-anhidrotic with immune-deficiency	X-linked recessive Autosomal dominant	IkKgamma (NEMO) NFkB-IA

DISCUSSION:

Ectodermal dysplasia is a group of conditions in which there is abnormal development of the skin, hair, nails, teeth or sweat glands.

It is a rare genetic condition characterized by a reduced ability to sweat, missing teeth and fine sparse hair. Individuals affected by HED share a similar facial appearance with, dark skin beneath the eye with extra folds or wrinkles, a depressed saddle nose, small narrow jaw and small pointed teeth.

Eruption of the teeth may be delayed or only a few teeth may erupt.

Physical growth and psychomotor development are usually normal.[5,6]

There are 4 recognized types of anhidrotic ectodermal dysplasia. The X-linked form is most common.

ETIOLOGY

Mutations in EDA, EDAR and EDARADD genes are now identified to cause HED by preventing the normal interaction between ectoderm and mesoderm. Ectoderm-mesoderm interaction is essential for the formation of several structures of ectodermal origin, failure of which leads to the characteristic features of HED. [9, 10]

INHERITANCE

Most of the cases of ectodermal dysplasia have X-linked recessive inheritance with the gene responsible being mapped to Xq12-q13 so that males are affected while the females are the carriers only. In autosomal recessive anhidrotic ectodermal dysplasia are identical to those of the X-linked recessive disorder, except that females are affected to the same degree as males. The clinical findings in the autosomal dominant form are also seen in both sexes and are similar to the X-linked recessive form but much milder. Hypohidrotic ED with immune deficiencies causes similar findings in sweating and hair and nail development, in association with a dysgammaglobulinemia. Significant mortality is seen from recurrent infections. [8, 9]

SYMPTOMS

- Unable to sweat and may experience episodes of high fever in warm environments, which may be mistakenly considered to be fevers of unknown origin. This error is particularly common in infancy. This is because the skin cannot sweat and control temperature properly.[13]
- They are unable to tolerate a warm environment and need special measures to keep a normal body temperature
- Typical facies is characterized by frontal bossing and large forehead; malar hypoplasia; a flattened nasal bridge; recessed columella; thick, everted lips; wrinkled, hyperpigmented periorbital skin; and prominent, low-set ears.

- The skin over the entire body is dry, finely wrinkled, and hypopigmented, often with a prominent venous pattern. Extensive peeling of the skin is a clinical clue to diagnosis in the newborn period (fig.2). The paucity of sebaceous glands may account for the dry skin. The scalp hair is sparse, fine, and lightly pigmented, and eyebrows and lashes are sparse or absent. Other body hair is also sparse or absent.
- Anodontia or hypodontia with widely spaced, conical teeth is a consistent feature. Xerostomia may be present.[7]
- Otolaryngeal and ophthalmologic abnormalities secondary to decreased saliva and tear production are seen. Repeated infections of respiratory tract and eyes are tend to occur.
- It may be associated with poor hearing and poor vision.
- The incidence of atopic diseases in children with ED-1 is high.

X-Linked Hyper-IgM Caused by Mutations in the Gene Encoding Nuclear Factor κB (NF-κB) Essential Modulator (NEMO, OR IKKγ); XHM-ED [12, 14]

- This syndrome in males is characterized most often clinically as anhydrotic ectodermal dysplasia with associated immunodeficiency (EDA-ID).
- The condition results from missense mutations in the IKBKG gene at position 28q on the X chromosome that encodes nuclear factor κB (NF-κB) essential modulator (NEMO), a regulatory protein required for the activation of the transcription factor NF-κB. Mutations in the coding region of IKBKG are associated with EDA-ID.
- The immunodeficiency is variable, with most patients showing impaired antibody responses to polysaccharide antigens. Some patients with EDA-ID have hyper-IgM.
- Pharmacologic inhibitors of NF-κB activation have been shown to downregulate CD154 mRNA and protein levels, suggesting the mechanism of hyper-IgM in this condition.
- The hyper-IgM patients with this defect should be easily recognizable because of the presence of ectodermal dysplasia.

DIAGNOSIS

- Starch iodine test will show partial or complete absence of sweat[9,10].
- Palmar or scalp biopsy. Scalp biopsy is the most sensitive and is 100% specific. Biopsy of the skin or of the mucous membrane

TREATMENT

- Live in a cooler environment and take cool water baths or use water sprays to keep a normal body temperature.
- Use of artificial tears to replace normal tearing and prevent drying of the eyes.
- Spray the nostrils with saline nose spray often to remove debris and prevent infections.
- Wear wig and dentures to improve the appearance.
- Efficacy of topical minoxidil and tretinoin in inducing hair growth in the scalp of a patient of the hidrotic type has been reported.[11]
- Administration of recombinant ectodysplasin postnatally can correct the disease in X-linked ectodermal dysplasia.[15]
- Administration of intravenous or subcutaneous immunoglobins regularly will help child from recurrent infections.

COMPLICATIONS

- Brain damage caused by increased body temperature
- Febrile convulsions

PREVENTION

Prenatal genetic diagnosis in family with history of ectodermal dysplasia can be done.

- Histologic analysis of fetal skin obtained by 2nd trimester fetoscopy guided skin biopsy.
- DNA based linkage analysis by gene mapping of the locus to the region of Xq11-21.1 using chorionic villous sample in first trimester.
- Identification of facial features at 30 weeks gestation on 3D ultrasonography.

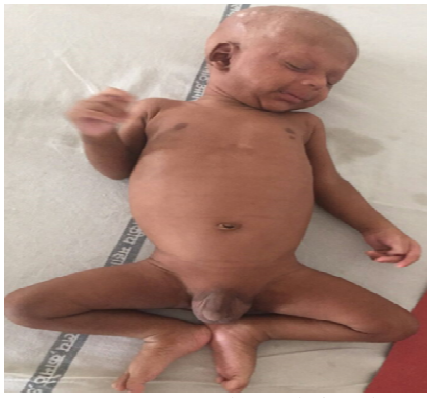

Fig.1. Extra nipple on left side

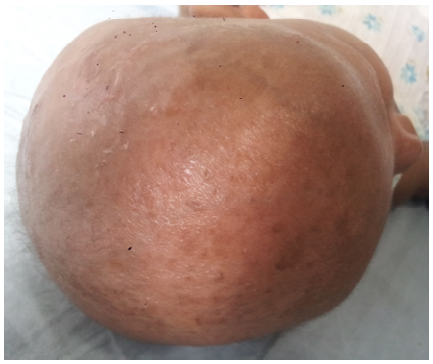

Fig.2. Dry and scaly scalp

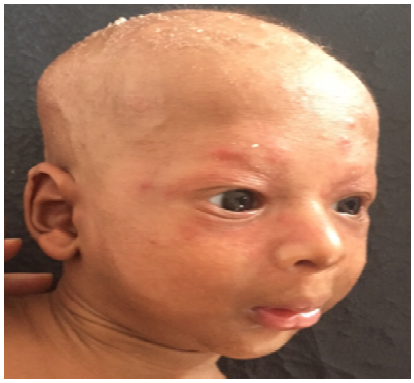

Fig.3. No eyebrows and eye lashes with everted thick lips, periorbital wrinkle.

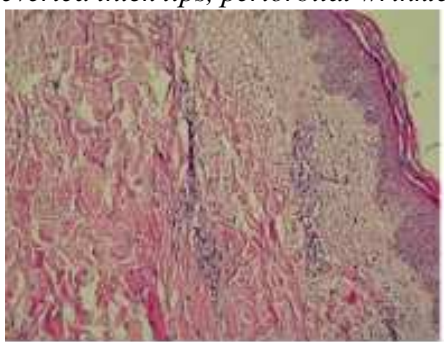

Fig.4. Skin biopsy of scalp showing absence of hair follicle and sweat glands

REFERENCES:

1. Weech AA. Hereditary ectodermal dysplasia. Amer J Dis Child. 1929; 37(6):766.
2. Pinheiro M, Freire-Maia N. Christ-Siemens-Touraine syndrome: a clinical and genetic study of large Brazilian kindred. Am J Med Genet 1979; 4: 113- 122.
3. Hall K.R. Pediatric orofacial medicine and pathology; 4th ed; London; Chapman and Hall; 1994:163.
4. Lowry R.B., Robinson G.C., Miller J.R. Hereditary ectodermal dysplasia: symptoms, inheritance patterns, differential diagnosis, management. Clin. Pediatr 1966; 5:395-402.
5. Crawford PJ, Alred MJ, Clarke A: Clinical and radiographiC findings in X- linked hypohidrotic ectodermal dysplasia. Journal of Medical Genetics, 1991; 28:181-185.
6. Rouse C, Siegfried E, Breer W, Nahass G. Hair and sweat glands in families with hypohidrotic ectodermal dysplasia: further characterization. Arch Dermatol. 2004; 140:850–5.
7. Besserman-Nielsen M. Hypohidrotisk ectodermal dysplasia. Oral manifestations

and genetic aspects. Tandlaegebladet. 1971 Nov; 75(11):1057-76.
8. Itthagarun A, King NM. Ectodermal Dysplasia: a review and case report. Quintessence Int. 1997 Sep; 28(9):595-602.
9. Chassaing N, Bourthoumieu S, Cossee M, Calvas P, Vincent MC. Mutations in EDAR account for one-quarter of non-ED1-related hypohidrotic ectodermal dysplasia. Hum Mutat. 2006; 27:255–9.
10. Gaide O. New development in the history of Hypohidrotic ectodermal dysplasia. Dermatology 2003, 207(2):123-4.
11. Melkote S, Dhurat RS, Palav A, Jerajani HR. Alopecia in congenital hidrotic ectodermal dysplasia responding to treatment with a combination of topical minoxidil and tretinoin. International Journal of Dermatology. 2009; 48:184-185
12. Rebecca H. Buckley. Nelson textbook of Paediatrics, 19th edition, part 14, section 2, chapter 118: 722-727
13. S.N.Ramraje, M. Wasnik and Y.A.Momin, "Anhidrotic ectodermal dysplasia- a report of two cases", Bombay Hospital Journal. Vol. 5, article 12, 2009.
14. A. Kumar, M.T.Eby, S.Sinha, A.Jasmin, and P.M.Chaudhary, "The ectodermal dysplasia receptor activates the nuclear factor –kB, JNK, and cell death pathways and binds to ectodysplasin A", Journal of Biological Chemistry, vol. 276, no. 4:2668-2677, 2001
15. Casal ML, Lewis JR, Mauldin EA, Tardivel A, Ingold K, Favre M, Paradies F, Demotz S, Gaide O, Schneider P. Significant correction of disease after postnatal administration of recombinant ectodysplasin A in canine X-linked ectodermal dysplasia. Amer J Hum Gen. 2007; 81: 1050-1056

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