CONGENITAL ECTODERMAL DEFECT

Two case reports of Hereditary Anhidrotic Ectodermal Dysplasia

By

N. SREEDEVI * L. MARQUIS ** T. K. MEHTA *** S. M. MATHUR ****

The syndrome of hereditary anhidrotic ectodermal dysplasia is characterised by absence or greatly decreased number of sweat, sebaceous and mucous glands, by hypotrichosis, and hypodontia or anodontia. It is usually sex-linked recessive though later reports have established that this abnormality may also be transmitted as an autosomal dominant or recessive manifestation. The preponderance of males over females is in the ratio of about five to one. The striking generalised anhidrosis produces a marked heat intolerance which is generally the predominant complaint of the patient, but other defects of the brain, nails, hair, teeth, mucous glands of nose and throat, adrenal medulla, and thyroid may each show developmental defects of varying severity.

Although there are numerous anomalies of the epidermis and appendages due to faulty evolution of the epiblastic layer of the blastoderm, the term congenital ectodermal defect has been limited to those conditions arising from incomplete development of the epidermis or its appendages or its absence in circumscribed areas thus excluding the keratodermas and the nevi. It is rare to encounter cases of extensive deformation or complete absence of all or nearly all of the cutaneous structures originating from the epidermis. To this group, the term "congenital ectodermal defect" is given.

According to Darwin[1], a description of this syndrome was given by Wedderburn[2] in 1838 in a Hindu family from Sindh. In 1848 John Thurnam[3] of York described this syndrome. The term congenital ectodermal defect was not used until a case was reported by Christ[4] in 1913. Later observers also used this term, until Weech[5] in 1929 designated the group as the anhidrotic type of ectodermal dysplasia. Thadani[6] (1921) also reported a Hindu family from Sindh with this syndrome. Reviews on the subject in world literature have been contributed by Mackie and Andrews (1924)[7], DeSilva (1939)[8], Kaaland-Jrgensen and Christensen[9], Helweg-Larsen and Ludwigsen[10] (1941) and Upshaw and Montgomery (1949)[11]. Kerman (1955)[12] described a case of this defect associated with idiocy. In 1962 Amarject Singh et all[13] reported a case in a female in a Sikh family. Aproximately 125 cases have been reported in world literature. The disease is of world wide distribution.

The facies of patients with anhidrotic ectodermal dysplasia is distinctive and closely resemble that of congenital syphilis. The forehead is large and square with prominent frontal bosses and supraorbital ridges. The nasal bridge is sunken producing saddle-shaped nose. There are high, wide check bones, sunken cheeks and thick lips, the chin may be pointed, eyes slant upward as in mongolism. Radiating

* Skin & V. D. Registrar. ** Clinical Asst. Dermatologist & Venereologist. *** Prof. & Chief Dermatologist & Venereologist. **** Registrar Dep.t of Dermatology and Venereology, T. N. Medical College & Nair Hospital, Bombay 8.

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furrows, pseudorhagades, are found about the mouth. The skin is soft, smooth, shiny and feminine with absence of hair all over the body. The skin temperature is raised especially during the hot weather. The hair on the scalp is scanty and fine, the eyebrows are absent, and the eyelashes may or may not be present. Curiously enough, the moustache and beard are well developed. Axillary and pubic hair are absent, nails are usually normal but may be hard, brittle and deformed.

Dentition is delayed. Both temporary and permanent teeth may be entirely absent, or there may be a few teeth of either or both sets, usually three to ten in number. The incisors, canines and bicuspids bear a striking resemblance to each other, conical in the first dentition; conical and curved with the convexity on the anterior aspect, and very pointed in the second dentition. The molars have long sharped hooked cusps. The teeth are widely spaced, abnormally occluded and the normal anatomic markings are frequently absent. Complete anodontia has been reported by Guilford (1883)[14] and Thomas and Allen[15] (1940) but not proved radiologically.

The chief complaint, as mentioned before is heat intolerance, they do not perspire at all or perspire to an extremely slight degree. Hence in hot weather, they suffer severely with fever and breathlessness and many infants die due to hyperthermia and convulsions. Intelligence is usually normal. The mucous glands may be hypoplastic and may cause chronic atrophic rhinitis associated with foul smelling discharge. Dysphagia, hoarseness and intermittent aphonia may also result. Other anomalies which may be associated are absence of lacrimal, apocrine and mammary glands. Skeletal changes like cleft palate and polydactyly, ocular defects involving the pupil and lens, deformities of the auricles, genital abnormalities like hypospadias, epispadias or undescended testis may be seen.

Histopathology: The epidermis and cutis are thinner than normal, but the collagen and elastic and blood vessels are normal. Most workers have reported a total absence of sweat glands or presence of rudimentary fragments of non-functioning glands and ducts. Except on the face, there is usually a similar marked deficiency of the pilosebaceous structures. Sundermann[16] has reported normal apocrine glands but absent sebaceous glands in the biopsy from the axillae of two patients. However, Upshaw and Montgomery[11], in one case noted an associated absence of apocrine glands in their study.

Biopsies of the mucous membranes of the nose, throat and upper respiratory passages revealed hypoplastic changes in the epithelium as well as in the underlying glands corresponding with the clinical appearances of these structures.

Physiologic characteristics: The evidence of complete anhidrosis based on single or multiple biopsies is incomplete though the sites may not show any sweat glands. At ordinary environmental temperature, the sweat glands are not needed to dissipate heat as the insensible perspiration by cutaneous transudation is enough for maintaining the temperature in a normal person. But at high temperatures, the temperature of an anhidrotic patient rises with a proportionate rise in pulse and respiratory rate. Fleisher[17] has observed that some few sweat glands may be present and functioning in

these patients. By applying starch Iodine mixture he saw a few small areas where sweat was being produced when the skin is exposed to heat. He therefore suggests the term hypohidrosis than anhidrosis to these patients.

Etiology: In the past, congenital syphilis was attributed to be the cause on account of similar facies, others attributed it, to endocrine dysfunction. The only known factor was the hereditary factor. Most observers agree that the pathologic process is probably aplasia and not atrophy because degenerative structures rarely have been seen in tissue sections. Instead, the structures appear not to have begun to differentiate or just barely to do so.

The mode of transmission is a subject of controversy. It is said to be sexlinked, as the disorder is much more common in males and only very rarely females are affected. Goeckermann[4] in a report on a female patient is of the opinion that the condition is not always recessive in females. Such an opinion has also been mentioned by Amarjeet Singh et al. Levit (1936)[18] thought that the condition is always determined by a sex-linked gene which was not always completely recessive and gives the term "conditionally dominant" to indicate that the pathogenic gene might show different degrees of penetration or do not penetrate at all.

Pathogenesis: It is probable that the defective gene or genes in anhidrotic patients begin to affect the development of epidermal structures during the second foetal month The pathogenic process being an aplasia rather than an atrophy.

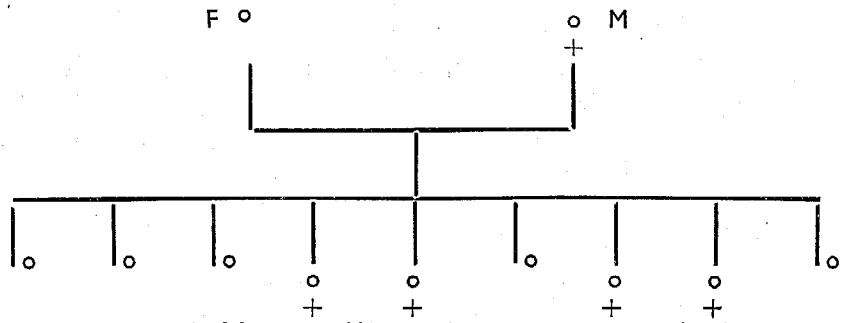
CASE REPORT

Case I. Patient. D. D. Aged 16 years. Hindu. attended the medical out-patient department of the hospital for fever and was referred to skin department on account of peculiar facies and dryness of the skin.

Inquiry revealed that the patient never sweated and was uncomfortable in the warm weather, for which he used to have cold water soaks. He was born at full term with no obstretric complications. His subsequent development was normal.

FIGURE I

CHART SHOWS THE FAMILY OF THE PATIENT WITH THE NO. OF CHILDREN WHO HAD SUFFERED FROM THE DISEASE



Two other brothers were normal and six other siblings, four of which were girls and two boys had similar facial appearance at birth and died due to convulsions about 5-6 months after birth. The maternal brother and sister were normal and healthy with no skin manifestations. No history of consanguinity was present.

Examination: The facies of the patient was typical of congenital ectodermal defect (photograph). No. 1 There was partial alopecia of the hair of the scalp with frontal bossing. Eyebrows were absent. Eyelashes scanty, nose saddle shaped and chin pointed. The upper teeth were deciduous and eight in number. The lower teeth four in number, the two centrals being permanent and the other two deciduous. The individual tooth appeared conical, pointed with notching resembling Hutchinson's teeth. (Photograph No. 2). The skin of the patient was fine, soft and feminine and devoid of hair. Axillary and pubic hair were absent. (Photograph No. 3). Nails normal, no hyperkeratosis of palms and soles. Abnormality of genitalia hypospadias Nasal examination showed chronic atrophic rhinitis. No. endocrine dysfunction was detected. Intelligence of patient within normal limits.

Investigation: Hb. 9.5 G. T. 10,000/cm m. D.C. P 54 L 45 E 1.

Urine-NAD; Stool-NAD; V. D. R. L of patient and mother-negative.

X-ray-Skull-Normal except for absence of teeth.

B. M. R.-within normal limits; Serum cholestrol normal.

Skin Biopsy- (i) showed atrophy of epidermis with absence of sweat and sebaceous glands and hair follicles. (Photograph No. 4).

(ii) Biopsy from axillary region showed absence of apocrine glands. (Photograph No. 5).

Sweat function test: [9] 0.1 cc of 1 in 1000 acetyl choline was injected intradermally on the forearm of the patient as well as on the forearm of a normal control person. After two minutes, a dry bromophenol blue paper (which is yellow when dry and turns blue when moist) was applied over the injected site. There was no change of colour of the paper that was placed on the forearm of the patient, whereas that of the control showed change of colour to blue (photograph). No. 6.

CASE 2

Patient-N. G., Male aged 12 years, Hindu, was referred by the Paediatric out patient department of the hospital to skin deparment for his peculiar syphilitic facies. On enquiry, mother of the patient gave history that the boy felt most uncomfortable during the summer season and preferred to lie down on the wet cool floor. She never noticed any sweating on his body nor any hair except a few, which grew later on the scalp. He was born at full term without any obstetric complications. He had no eruption of the milk-teeth. At the age of 10 years, one upper molar tooth had erupted but it fell out after 2 years. So an artificial denture was fitted. For the last three months, he was suffering from foul smelling discharge from the nose. No history of convulsions.

Family history : Parents–healthy. Mother denies history of any abortion. Father addicted to alcohol. One elder sister only–healthy.

On Examination : The facies of the patient was typical of congenital ectodemal defect, quite identical to case No I. There were sparse hair on the scalp, on eyebrows absent and eyelashes scanty. Nose saddle-shaped chin pointed and frontal bossing. Teeth were absent and artificial denture was fitted Photo No. 7. The skin of the patient was smooth, soft, feminine and devoid of hair. Axillary and pubic hair were absent. Circumoral pigmentation was present. Nails normal, no hyperkeratosis of palms, and soles. Nasal examination showed chronic atroplic rhinitis with foul nasal discharge. No endocrine dysfunction was detected. Development of the genitalia was normal. Intelligence of the patient was within normal limits.

Investigations : Hb–13.5 G; TC–10,850, Dc–P 48 L 44 E 6 M 2.

Urine and stool N. A. D. VDRL of the patient, mother–Negative.

Serum cholesterol–138 mg per cent, Screening of chest: N. A. D.

Sweat function test : Negative while that of the mother (control) positive. (Photo No. 8).

Biopsy : (i) from left forearm: Epidermis–atroplic with absence of sweat, and Sabaceous glands and hair follicles.

(ii) Axilla : Epidemies atroplic. Dermis showed no evidence of skin appendages–sweat, sebaceous or apocrine glands nor any hair follices.

Case II

Discussion : The diverse clinical facets of congenital ectodermal defect, make it an entity of importance, not only to the dermatologist, but also to the internists, dentists, ophthalmologist, otolaryngologist, endocrinologist, plastic surgeon and psychiatrist. Most observers agree that the pathologic processes affect the development of the epidermal structures during the second foetal month, producing an aplasia rather than an atrophy, as degenerative structures rarely have been seen in tissue sections. Instead, the structures appear not to have begun to differentiate or just barely to do so.

Though this entity is usually sex-linked, it may also be transmitted as an autosomal dominant or recessive manifestation. In case I, from the relevant family history available i. e. 2 other brothers were normal and 6 siblings. four of which were girls, and two boys had similar facial appearance at birth and died due to convulsions after 5 to 6 months after birth, it is apparent that the case in point was transmitted as a recessive trait, not sex-linked. In case II, no relevant history is available.

The typical facies of thir syndrome associated with absence of epidermal glandular appendages and dental anomalies, along with symptoms of hyperthermia, make this entity easily recognisable. In our cases, the classical triad of manifestions facial, skin, hair and dental anomalies were evident, besides absence of sweat and apocrine glands, there was associated atrophic rhinitis. Axillary and pubic hair were absent

and examination of genitalia showed hypospadias in case I Intelligence was within normal limits.

SUMMARY

1. Two cases of congenital ectodermal defect are presented showing the typical facies, soft skin and feminine hair distribution.

2. Skin biopsy from the forearm and axillae showed absence of sweat, sebaceous and apocrine structures. Sweat function test with bromo-phenol were negative as compared with a control patient.

3. Clinically patients were uncomfortable in the warm weather for which they used to control their body temperature with frequent cold water soaks.

4. Nasal examination showed associated chronic atrophic rhinitis. Axillary and pubic hair were absent and examination of genitalia showed hypospadias, in case 1.

5. Dental abnormalities seen in case 1. In the upper teeth, 8 deciduous teeth were present and the lower teeth four in number, the two central being permanent and the other two deciduous, in case 2, all teeth were absent, and patient had an artificial denture.

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