Hypohidrotic ectodermal dysplasia, central nervous system malformation, and distinct facial features: confirmation of a distinct entity?

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Abstract

Internal hydrocephalus with partial hypoplasia of the cerebellum was observed in a severely mentally retarded boy who showed signs of ectodermal dysplasia. Diagnostic considerations are discussed. Reports of the triad mental retardation-CNS malformation-ectodermal dysplasia are rare. In 1989 we reported a case with these signs that shows a striking facial similarity to the case presented here.

(J Med Genet 1993;30:245-7)

The diagnosis of ectodermal dysplasia syndrome requires involvement from birth of hair, skin, teeth, or nails without progression of the condition. Diagnosis is often difficult since any ectodermal derivative may be involved in varying degrees. To circumvent this problem, Freire-Maia and Pinheiro designed a classification system which contains over 100 different, clinically distinct conditions. However, assignment of any particular case to a specific subtype in this classification system may still be difficult. We present a case of a severely mentally retarded boy with a medical history and abnormalities of ectodermal derivatives suggesting the diagnosis 'subtype of ectodermal dysplasia'.

Case report

The patient was the first born son of young, non-consanguineous parents. A brother of the mother has Down's syndrome (probably age related) and her nephew has spina bifida. The remaining family history is negative for other congenital malformations or hereditary conditions. The mother of the patient has fine, sparse, fair hair but has an otherwise normal phenotype.

The pregnancy was complicated by premature contractions and hydramnios. A dysmature boy was born after 37 weeks of gestation. Measurements at birth were weight 2530 g, length 46 cm, and head circumference 33 cm. Feeding was difficult, requiring administration by a nasogastric tube, and parameters for weight and length persisted on the 3rd centile while the head circumference stayed on the 10th centile. Clinical examination at 7 months showed a large, open anterior fontanelle, micrognathia, and a cleft palate. He suffered from dacryocystitis of his right eye owing to an imperforate lacrimal duct. He had no hair until 8 months. Neurological examination showed axial hypotonia combined with hypertonic lower extremities. His second toes overlapped the first.

A CT scan showed dilatation of the third, fourth, and lateral ventricles which remained stationary in time without signs of hypertension. Also partial hypoplasia of the cerebellum was observed.

At 13 months of age developmental retardation was obvious. Parameters for weight and length were still below the 3rd centile (6.56 kg and 66.5 cm respectively) while head circumference was on the 10th centile. Admission to hospital was necessary as his condition worsened because of feeding problems, an upper respiratory tract infection, and recurrence of dacryocystitis of his right eye. At 16 months his cleft palate was surgically corrected. However, no remarkable change in the feeding problems (especially for solid food) occurred.

At 3½ years old, he was admitted to hospital for a respiratory infection with febrile convulsions and head banging. His cleft palate was surgically corrected. Since febrile convulsions occurred for the second time that year, anti-epileptic drugs were given. Weight was 10.4 kg (less than the 3rd centile), length was 95 cm (less than the 25th centile), and head circumference was 50 cm (25th to 50th centile). This ratio persisted during the following years.

Clinical observations at that time (figs 1 and 2) were similar to the present. He is now 8 years old and an anxious, pale, and thin child. He is severely mentally retarded. Since the birth of a healthy sister when he was 5 years old he developed serious behavioural problems with anxiety and aggression. The scalp veins are visible and dilated. His hair is fair, curly, and fine. Microscopic examination shows irregular and missing cuticles. Serum copper and caeruloplasmin levels are normal. He shows frontal bossing, hypoplasia of the maxilla, hypertelorism, and ectropion of the right lower eyelid. He has a protruding tongue. Both ears are low set, but hearing is adequate. He has diastema between his upper incisors, and one conical and one peg shaped incisor in the
lower jaw (figs 1 and 3). The lateral incisors in both upper and lower jaws are missing. His skin is thin with little subcutaneous fat, but a biopsy showed normal skin structures. He has small nipples. Sweating seems minimal. A sweat test was performed at the age of 2 years: 139-76 mg sweat was produced with a chloride content of 4.12 mEq/l (normal range). His nails are short and broad. His penis is small and a partially undescended testis can be felt on the right. There is a broad gap between his first and second toes and the third toes are hammer toes. He walks on tiptoe with a broad based gait. Bilateral calcaneovalgus was seen on radiological examination. The karyotypes of both parents and child are normal.

Discussion

In summary, the child was born with a Pierre-Robin sequence and feeding problems were present from birth onwards. He suffered from recurring respiratory tract and eye infections. He combines a specific facies with severe mental retardation and a CNS malformation.

This case presents with many signs pointing to the diagnosis of a subtype of ectodermal dysplasia, maybe 'X linked hypohidrotic ectodermal dysplasia'. In favour of this diagnosis are: (1) the subtle signs in the mother (fair, fine, sparse hair), (2) a history of feeding problems, failure to thrive with parameters for weight and length persisting below the population mean, recurrent infections, and febrile convulsions, and (3) the condition of the hair, skin, and teeth. The variant of hypohidrotic ectodermal dysplasia which is inherited in an autosomal recessive mode is clinically indistinguishable and might be another option since signs in the mother are minimal. Some authors even question whether these two types of hypohidrotic ectodermal dysplasia really exist and imply that in fact only one such condition exists, inherited in an X linked mode. An important diagnostic sign in hypohidrotic ectodermal dysplasia is impaired sweating. Clinical examination of our patient repeatedly showed a dry skin with minimal sweating. However, sweat production was present as shown by a sweat test in which 139-76 mg sweat was collected. Berg et al. reviewed all cases of ectodermal dysplasia reported so far for methods used to estimate objectively sweat production. They concluded that no standardised sweat test had been used in these cases and advocated an accurate evaluation of sweating in ectodermal dysplasia syndromes. However, the methods they recommend for objective testing of sweat production (such as visualisation by dyes or counting of sweat
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Hypohidrotic ectodermal dysplasia (EED), central hypodactyly, and without a sister with AECT hypoplastic phenotype as an example, reports sia are system chosis, hypodontia, are in this be might to its plasia, dysplasia, short stature, we findings to mental retardation, and other conditions which combine syndrome, retardation, and decreased fertility: an autosomal recessive condition in an Amish kindred. Pediatrics 1974;34:201-7.


Halter 35:243-51.


