Hypohidrotic ectodermal dysplasia, primary hypothyroidism, and agenesis of the corpus callosum

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SUMMARY In this report we present the unique combination of hypohidrotic ectodermal dysplasia, primary hypothyroidism, and agenesis of the corpus callosum in a two year old, severely mentally retarded boy.

Hypohidrotic ectodermal dysplasia is a rare and heterogeneous condition. In most patients inheritance is X linked recessive (McKusick *30510), but in a few instances a clinically indistinguishable autosomal recessive variant has been established. The association of hypohidrotic ectodermal dysplasia with primary hypothyroidism was reported by Pabst et al in two brothers.

Case report

The proband was the third son of 31 year old, non-consanguineous, healthy parents. There was no family history of miscarriages, mental handicap, or congenital malformations. The two older sons were also healthy.

The boy was born at term after an uncomplicated pregnancy. Birth weight was 3340 g (50th to 75th centile), length 49 cm (50th centile), and head circumference 36.4 cm (95th centile). Craniofacial dysmorphism was noted from the beginning, including relative macrocephaly with a large anterior fontanelle (7×6 cm), hypertelorism, short and downward slanting eyelids, small nose and mouth, small, dysplastic, and low set ears, and retrognathia.

The neonatal period was complicated by sepsis, transient hypocalcaemia, and swallowing difficulties. Reduced sweating was also noticed in that period and this persisted later in life. Episodes of hyperthermia were not noted. Sweat pores were virtually absent. The clinical suspicion of hypothyroidism was confirmed by measurements of T3, T4, and TSH. A thyroid scintigram with technetium 99 showed absence of normal thyroid gland tissue and the presence of an ectopic goitre at the base of the tongue. Further biochemical investigations including serum immunoglobulin levels, peripheral blood lymphocyte counts, and lymphocyte response to PHA stimulation were normal.

An x ray of the chest showed cardiomegaly. Echographic cardiological examination indicated biventricular trabecular hypertrophy.

FIGURE Craniofacial appearance of the proband at the age of two years.
Case reports

CT scan showed agenesis of the corpus callosum and enlargement of the lateral ventricles. Bilateral vesicoureteral reflex was noticed on intravenous pyelography and cystography. Chromosomal analysis of a peripheral lymphocyte culture showed a normal 46,XY male karyotype after G banding. Psychomotor development has been severely retarded. At the age of two years he was not able to sit without support and social contact was poor without speech development. At that age weight was 10.5 kg (10th to 25th centile), length 83.2 cm (10th to 25th centile), and head circumference 51 cm (90th centile).

In addition to the relative macrocephaly, his face was distinctive with frontal bossing, low nasal bridge, mild malar hypoplasia, hypertelorism, and downward slanting palpebral fissures with epicanthic folds (figure). There was periorbital pigmentation. The scalp hair was sparse, the eyebrows were nearly absent, and the eyelashes were very delicate and thin. The subcutaneous vessels could easily be seen. Dentition was delayed with small teeth and defective enamel. The nails were absent, and coarse enamel. The nails were absent, and coarse enamel. The voice was coarse and high pitched. He has suffered from frequent respiratory and urinary tract infections as well as nearly permanent purulent conjunctivitis. His skin was dry and he had difficulty in heat regulation.

Clinical examination of the mother was completely normal with normal dentition and no other signs of ectodermal dysplasia.

Discussion

The index patient of this report, a two year old severely mentally retarded boy, presents a unique combination of hypohidrotic ectodermal dysplasia, primary hypothyroidism, and agenesis of the corpus callosum. Reviewing other published reports we noticed the similar clinical findings in the present patient and the male sibs reported by Pabst et al.5 They described two brothers with hypohidrotic ectodermal dysplasia and gradual onset of primary hypothyroidism. In addition, these males developed urticaria pigmentosa-like skin pigmentation and structural abnormalities of the ciliary border of the respiratory tract were found. Mental development was normal in both boys, as is seen in the majority of patients with hypohidrotic ectodermal dysplasia.6 7 A CT scan was not performed in these sibs. The mental retardation noted in some patients was attributed to the repeated periods of hyperthermia.8 It is probable that the severe psychomotor retardation in the present patient is related to the agenesis of the corpus callosum.

Familial occurrence of agenesis of the corpus callosum has been reported (for review see Young et al9), but in none of them was athyroidism or hypohidrotic ectodermal dysplasia noted.

In the present patient biventricular trabecular hypertrophy was noted. Reed et al6 reported the necropsy findings in a three year old boy with hypohidrotic ectodermal dysplasia and documented generalised cardiomegaly with left ventricular hypertrophy.

As reviewed by Clarke,1 hypohidrotic ectodermal dysplasia is a heterogeneous condition which includes different, clinically indistinguishable genetic entities. X linked recessive inheritance is most frequently observed, but autosomal recessive inheritance was noted in several studies.3 4 In their report, Pabst et al2 suggested autosomal recessive inheritance of the concurrence of hypohidrotic ectodermal dysplasia and primary hypothyroidism in the two brothers, but, as in our isolated male patient, X linked recessive inheritance cannot be firmly excluded.

Further reports are needed to determine the mode of inheritance and to establish whether agenesis of the corpus callosum is another feature of this entity.

References


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*J Med Genet* 1989 26: 520-521
doi: 10.1136/jmg.26.8.520

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