

trace of the disease in both sets of parents and in the previous generation, the consanguinity of both sets of parents, and the close relation between them.

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Recessive form of Freeman-Sheldon's syndrome or 'whistling face'¹

SUMMARY Freeman-Sheldon's syndrome is a rare genetic disease inherited as an autosomal dominant trait in some families but showing sporadic appearance in the majority of the reported cases. In the present paper we report a family having two affected children born from normal consanguineous parents suggesting that Freeman-Sheldon's syndrome may be heterogeneous from the genetic point of view.

Freeman-Sheldon's syndrome is a rare condition first described in 1938, and mainly characterized by the features of whistling face. Up to 1970 there were 9 cases reported in the world literature, in which familial occurrence of the syndrome was observed in 3 instances, all these families being in concord-

ance for an autosomal dominant type of inheritance (Fraser *et al.*, 1970). In the present paper we report 2 affected sibs born from consanguineous normal parents.

Case reports

Case 1 IV. 1, an 11-year-old boy, the first child of a young mother was born at term by normal delivery after an uneventful pregnancy. Bilateral clubfoot was noticed at birth which required orthopaedic care from the age of 15 days. A few months after birth abnormalities in the mouth and chin were noticed. The boy had normal growth and normal mental development.

Clinical examination showed a bright white boy, weight 30.4 kg, height 132 cm, and an US/LS index of 0.80. The face was round, and masklike, with full cheeks. There was flattening of the supra orbital ridges, moderate blepharophimosis, bilateral ptosis of eyelids, and antimongoloid palpebral fissures (Fig. 1). The nose was 'parrotlike': it was heavily curved, with the nostrils elongated upwards suggesting colobomata. The philtrum was increased in length. The mouth opening was small, and the lips were constantly contracted as if the patient were whistling. The palate was high. The skin over the chin was normal in aspect but it was covering an irregular surface resembling dimples. The hands were normal. The feet had talipes valgus. The genitalia were normal except for a first degree hypospadias.

Laboratory examination showed normal electrocardiogram, electroencephalogram, and audiometry. Electromyography showed paroxysmal spasms of the buccinators muscles. The x-ray films showed a small frontal bone compared with the skull size, hypoplasia of vertebral bodies C-3, C-4, and C-5, spina bifida occulta in C-6, and scoliosis of the lumbar spine. Fingerprint analyses were normal.

Case 2. (IV. 2) a 7-year-old girl, sister of Case 1, was also born at term by normal delivery after an uneventful pregnancy. The mouth anomalies were noticed at birth. Talipes valgus was noticed at the age of 2 years. There was normal physical and mental development after birth.

Clinical examination showed an intelligent white girl, weight 23.0 kg, height 120 cm, span 117 cm, and an US/LS index of 0.93. The face was round, moderately masklike, with full cheeks. The supraorbital ridges were flat and the palpebral fissures were antimongoloid. The nose was curved (Fig. 1). The philtrum was long and the mouth-opening was small. The upper lip was protruding, the lower lip contracted in the whistling manner. The palate was

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Fig. 1 Case 1 (above) and Case 2 (below).

high. There were cutaneous dimples on the chin; bilateral low set ears; normal hands; and talipes valgus. The clitoris was slightly enlarged.

Laboratory examination showed an abnormal electromyography characterized by paroxysmal spasms of the buccinators muscles and levatores labii. The electrocardiogram and electroencephalogram were normal, as was audiometry. X-ray studies showed a small frontal bone in relation to the skull size, and mandibular hypoplasia. The vertebral bodies C-3, C-4, C-5, and C-6 were flattened, with hypoplasia of its apophysis. Bone age was normal. Fingerprint analyses were normal.

The family history showed that the mother of the

propositi had consanguineous parents herself and had married a first cousin. Thus, the total inbreeding coefficient of the affected children was $F = 0.0781$ (Fig. 2).

Clinical examination of the parents of the propositi did not disclose any abnormality which could be interpreted as low expressivity of an autosomal dominant gene.

Discussion

Heterogeneity in genetic disease is not a rare finding. In certain syndromes the clinical manifestations are so similar that the mechanisms of inheritance become a powerful tool in separating the entities. The affected children reported in the present paper have so many findings of Freeman-Sheldon syndrome (Freeman and Sheldon, 1938; Burian, 1963; Rintala, 1968; Weinstein and Gorlin, 1969; Sharma and Tandon, 1970; Fraser *et al.*, 1970) that no one would hesitate in making the diagnosis. However, the pattern of inheritance shown by the present family strongly suggests an autosomal recessive form of the syndrome. On the other hand, those families mentioned by Fraser *et al.* (1970) as having an autosomal dominant type of inheritance, together with the family reported in this paper, show that the Freeman-Sheldon syndrome may represent more than one genetical entity. Finally, if one considers that the majority of Freeman-Sheldon patients reported are

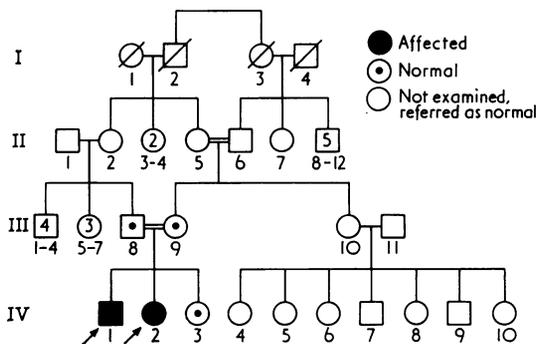


Fig. 2 Family pedigree.

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isolated cases it is possible that some autosomal recessive ones have been misinterpreted as sporadic.

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Fig. 1 The patient at 2 years, showing prominent epicanthal folds.

assessment of delayed speech and motor development. He is the only child of nonconsanguineous parents, born at term to a 21-year-old woman after an uncomplicated pregnancy and delivery. Birth-weight was 3500 g; the head circumference was not recorded. The mother took no medication during pregnancy and had only one x-ray, a diagnostic abdominal film, during the sixth month. There was no other known exposure to potential mutagens or teratogens during gestation, nor during the life of either parent. The family history is non-contributory except for a paternal aunt with epilepsy and delayed speech development. The patient had no feeding problems, and height and weight growth were normal. He sat alone at 12 months and crawled at 15 months. At 2 years he walked poorly with assistance and had no consistently recognizable speech. He had had no seizures.

When admitted to hospital at age 2 years his weight was 14.6 kg (90th centile for age), his height was 98 cm (above the 97th centile), and his head circumference was 47 cm (below the 3rd centile). He had a diffuse angiomatous lesion on the right temporal scalp and prominent epicanthal folds (Fig. 1). General physical examination was otherwise normal. Cranial nerves, reflexes, strength, and tone were normal. Behaviour was conspicuously hyperactive.

Denver Developmental Screening Test confirmed performance at the 10- to 15-month level in all measurements. Complete blood count, urine analysis, bone age, serum thyroxine, and urine metabolic screen (amino acids, FeCl₃, DNPH) were all normal. Skull x-ray films showed only the clinically apparent microcephaly. Electroencephalogram showed a right occipital spike focus and asymmetric spindling.

CYTOGENETIC STUDIES

Karyotype analysis using Giemsa banding and quinacrine fluorescence showed 46 chromosomes in all of

Two reciprocal translocations associated with microcephaly and retardation

SUMMARY The first case is reported of a karyotype containing two apparently unrelated reciprocal translocations, involving chromosomes 1, 2, 5, and 7. It is suggested that the patient's psychomotor retardation and microcephaly may be the result of the loss of a small amount of chromosomal material accompanying these translocations.

This report describes a 2-year-old white boy with psychomotor retardation, microcephaly, and two apparently balanced reciprocal translocations, one between chromosomes 1 and 2, the other between 5 and 7.

Case report

The patient was admitted to Babies Hospital for