

Case reports

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Congenital horizontal gaze palsy and kyphoscoliosis in two brothers¹

SUMMARY In a sibship of 11, two brothers with a congenital complete horizontal gaze palsy developed severe kyphoscoliosis. No-one else in the family has a gaze palsy or comparable skeletal abnormalities. Since the parents are first cousins, an autosomal recessive mode of inheritance seems likely.

Congenital gaze palsy is rare. A vertical, but not horizontal, gaze palsy is seen in neurovisceral storage disease, a progressive neurological autosomal recessive condition in which sea-blue histiocytes are found in the marrow (Neville *et al.*, 1973). Cogan (1953) described autosomal recessive congenital ocular motor apraxia in which there is a defect in horizontal voluntary gaze, but with retention of vertical eye movements (Zee *et al.*, 1977). Crisfield (1974) described a Chinese family in which four sibs had scoliosis and a progressive ophthalmoplegia. Familial congenital horizontal gaze palsy in association with scoliosis has not been described previously.

Case reports

CASE 1 (IV.8)

The younger of the two affected brothers was born in 1941. He, like his affected brother, was the product of a normal pregnancy and delivery. Difficulty with eye movements was noted soon after birth. He did not walk until the age of 20 months. Kyphoscoliosis was first diagnosed at the age of 5 years. He was never thought to have a learning disability and had functioned adequately as a garage mechanic until failing health prevented his working.

He was a 157 cm tall white male with an unremarkable facies. There was marked trunk shortening, secondary to severe kyphoscoliosis. The scoliosis was mainly thoracic and to the right. There was no limb shortening. Neck movements were limited laterally and the neck was short.

Voluntary eye movements in a horizontal plane were impossible. The eyes were fixed centrally and

no random eye movements were noted. Doll's-head eye movements in a horizontal plane were also absent. However, there were full vertical movements in both eyes. Vertical nystagmus was present bilaterally. Visual acuity and fundoscopic examination were normal and the remaining cranial nerves were intact. No muscle wasting was present, power was good, reflexes were preserved and symmetrical, and the plantar responses were flexor. There was no sensory deficit, he was not ataxic, and rapid alternating movements were normal.

At the time of the examination he had cor pulmonale secondary to the kyphoscoliosis.

CASE 2 (IV.6)

The older brother was born in 1936. Abnormalities of ocular movement were noted soon after birth, but the kyphoscoliosis was not noted until the age of 4 years. His motor and intellectual development was, however, slower than his other sibs. He never learned to read or write and had difficulty holding down a job. At the age of 3 he had several major seizures associated with whooping cough. He had seizures intermittently until the age of 8 years.

He was 160 cm tall and, like his brother, his short stature was accounted for by severe kyphoscoliosis. His thoracic scoliosis deviated to the left. He was able to perform moderate exercise without dyspnoea.

The eye findings were identical to those of his brother.

He had complete neural deafness on the left side. The only other positive neurological finding was a brisk jaw jerk.

X-RAYS

X-rays of the long bones and the skulls of both affected patients were normal. The x-rays of the spine showed severe dorsal scoliosis with wedging of the vertebrae and rotation in both patients. The scoliosis was to the right in case 1 (Fig. 1a) and to the left in case 2 (Fig. 1b). In neither patient were hemivertebrae seen. The x-rays of the cervical spine were normal.

FAMILY HISTORY

The patients (IV.6 and IV.8) are the fourth and sixth offspring of a first cousin marriage (Fig. 2). It is possible that the parents are more closely related because the surnames of I.2, I.3, and I.6 are the same. The family has lived in the mountains of North

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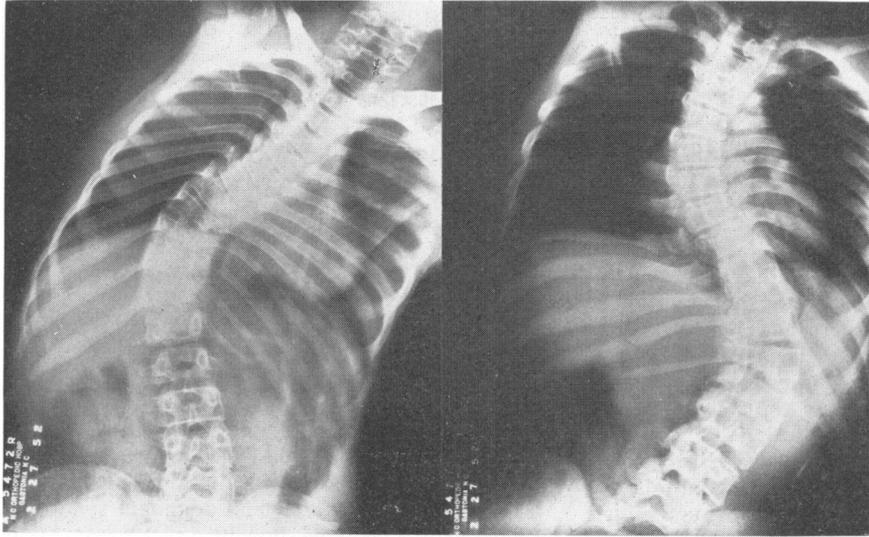


Fig. 1(a) Case 1. X-ray of spine at 11 years showing a right dorsal curve. (b) Case 2. X-ray of spine at 16 years showing right dorsal and left dorsolumbar curve.

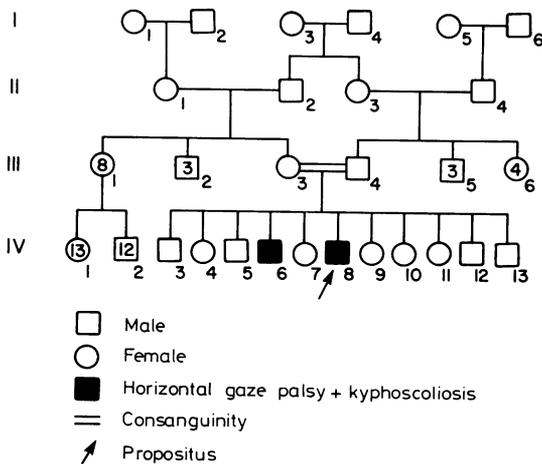


Fig. 2 Pedigree.

Carolina for as long as anyone can remember. There was no history of eye movement disorder or kyphoscoliosis in the remaining sibs, parents, aunts, uncles, cousins, or grandparents.

The mother (III.3) of the propiti was 24 and 29 years of age, respectively, at the birth of her two affected sons. II.3 and IV.3 were examined and neither was found to have kyphoscoliosis or gaze palsy.

Discussion

The central position of the eyes, the lack of lateral movement, but full vertical movement, cannot be explained by an absence or malfunction of any of the external ocular muscles or of their cranial nerves. In the congenital ocular motor apraxia described by Cogan (1953), there is also a deficiency of voluntary lateral gaze and absence of following eye movements in two-thirds of cases (Vassela *et al.*, 1972). However, in ocular motor apraxia, random eye movements are retained and there is contraversion of the eyes on head rotation in a vertical axis (Colenbrander, 1970). The two brothers described in this report did not exhibit the characteristic head jerks or random horizontal eye movements seen in ocular apraxia. The lack of doll's-head eye movements suggests that the lesion in these brothers lies in the paramedian pontine reticular formation adjacent to, or including, the sixth nerve nuclei, bilaterally.

Idiopathic scoliosis occurs eight times more commonly in females than in males and usually presents in adolescence (DeGeorge and Fisher, 1967). Idiopathic scoliosis occurring in infancy has a male predominance over females of 3 to 2 (Wynne-Davies, 1975).

Scoliosis may be seen in connective tissue disorders, such as the Marfan, Ehler-Danlos, and Morquio syndromes, as well as in neuromuscular disorders such as Friedreich's ataxia, the muscular dystrophies,

and Charcot-Marie-Tooth disease. Scoliosis may also be seen secondary to neurofibromatosis. Neurofibromatosis is a tempting explanation for the scoliosis and eye findings in these two brothers, especially in the light of the mental retardation, nerve deafness, and seizure disorder in the older of the two brothers. There were no skin manifestations in the propositi and no family history to support this diagnosis.

X-linked recessive inheritance is a possible, but unlikely, explanation of the findings in these two brothers, in view of the absence of the condition in their mother's three brothers and her sisters' 12 sons.

The close parental consanguinity and the strikingly similar clinical presentation in these two brothers suggest that this is an autosomal recessive condition. The absence of scoliosis or gaze palsy in any of the remaining nine sibs suggests that the scoliosis and gaze palsy are expressions of the same single autosomal recessive gene.

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Re-evaluation of CHANDS

SUMMARY A rare ectodermal dysplasia with the acronym CHANDS (Curly Hair, Ankyloblepharon, Nail Dysplasia Syndrome) was described by Baughman (1971) as being a new autosomal dominant condition. Additional pedigree data obtained after the original report indicate that the mode of inheritance is more likely to be autosomal recessive, with an instance of quasi-dominant transmission as a result of multiple consanguineous matings in the family. These data are provided in this report.

In 1971, Baughman reported a 'new' autosomal dominant trait characterised by curly hair, ankyloblepharon, and nail dysplasia, which was given the acronym CHANDS. The assumption that this trait was inherited as an autosomal dominant syndrome was based on a pedigree showing direct transmission from the mother to 3 of her 9 offspring. Both male and female children were affected, thus ruling out sex linkage of a recessive trait. In addition, ataxia was reported in 3 of the 9 sibs, including 2 of the CHANDS-affected children. The aetiology of the ataxia was not known at the time of the original report, but it was postulated that it could be part of the syndrome.

A more extensive pedigree has subsequently been obtained from this family, and it is the purpose of this report to present evidence that CHANDS is inherited as a recessive, and not as a dominant, trait.

Discussion

The original pedigree showed that V.1 and V.2 are first cousins and have 9 children. V.2 has 7 sibs and is herself the product of a consanguineous mating of second cousins. The family members exhibiting the CHANDS trait are V.3, 4, and 7 of her sibs, and 3 of her children (Fig.). However, when this family was re-evaluated in 1976, it was discovered that V.3 and V.4 have a total of 11 normal children, but none with the CHANDS trait. This was verified by examining recent photographs of all 11 children and noting that all have long, straight hair and normal nails. There is no historical evidence of any of the children having had ankyloblepharon at birth. The CHANDS trait is manifested by curly hair that apparently does not grow past shoulder length, dysplastic nails, and ankyloblepharon at birth. In addition, the ataxia has been shown to be ataxia-telangiectasia based on clinical, phenotypic, and immunological features present in the affected children. Therefore, the CHANDS trait can reasonably be assumed to be a separate entity from the ataxia.