Familial infantile scoliosis associated with bilateral paralysis of conjugate gaze

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SUMMARY A family with two sibs suffering from idiopathic infantile scoliosis associated with bilateral paralysis of conjugate gaze is reported. Although the parental consanguinity and the involvement of patients of both sexes in this family are suggestive of an autosomal recessive mode of inheritance, a dominant or multifactorial pattern remains a possibility.

The familial association of idiopathic scoliosis and conjugate gaze paralysis has been reported in three families (Dretakis and Kondoyannis, 1974; Sharpe *et al.*, 1975). Autosomal recessive inheritance has been suggested. We report two affected sibs in a consanguineous family where the skeletal and ocular manifestations appeared relatively early.

Case reports

A couple was referred for genetic counselling because their two children were affected with the same combination of skeletal and ocular abnormalities. The couple were double first cousins (Fig. 1).

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The mother had given birth to another child who died 40 hours after birth and was reported to have had 'spina bifida', but no further details were available. A fourth gestation ended in a late spontaneous abortion.

The family history disclosed two maternal cousins, an 8-year-old girl (AS) and a 5½-year-old boy (AA), suffering from moderate structural scoliosis of the thoracic spine, first noticed at ages of 6½ and 4 years, respectively (Fig. 1).

CASE 1 (FL)

A 4½-year-old girl presented with obvious deformity of the thoracolumbar spine and some impairment of her eye movements. She was born after an uncomplicated term pregnancy, weighing 3500 g at birth. A suspicion of 'strabismus' was initially noted by the parents at the age of 2 weeks. The skeletal defect was noticed at about 6 months of age when the child

Fig. 1 Pedigree of family.

attempted to sit. Physical findings were consistent with infantile scoliosis of the thoracolumbar spine with no underlying abnormalities of the vertebrae, associated with bilateral paralysis of conjugate gaze. Her head was markedly tilted to the left. X-ray of the cervical spine was normal (Fig. 2). There was no

Fig. 2 X-ray of cervical spine showing tilt to the left with no structural abnormalities (case 1).

shortening of the neck muscles. A detailed re-examination at the age of $4\frac{1}{2}$ years disclosed severe progressive kyphoscoliosis (convex to left, angle 43°) in spite of the continuous use of a Milwaukee brace (Fig. 3). The head tilt seemed to improve spontaneously.

The eye examination showed visual acuity of 3/7 in each eye. The anterior segments and ocular fundi were normal. Refraction under cycloplegia showed emmetropia. There was paralysis of horizontal movements, both saccadic and slow pursuit, to both sides. Optokinetic nystagmus could not be elicited. Vestibular nystagmus, both rotational and that induced by the caloric test using ice cold water, was absent on both sides.

There was slight convergence on attempted dextroversion and levoversion. Convergence, as well as upward and downward conjugate movements, were all normal. The pupils were equal and reacted to light and to near stimuli. Intermittent unilateral blinking movements could be seen from time to time. No abnormal synkinesis could be detected.

Mental development was normal for age. Dermatoglyphic analysis did not disclose unusual findings. Neurological examination did not reveal any additional abnormalities.

CASE 2 (FS)

A $2\frac{1}{2}$ -year-old brother of case 1 was referred to the eye clinic with the suspicion of a similar impairment

Fig. 3 X-ray of thoracolumbar spine showing severe kyphoscoliosis (case 1).

Fig. 4 X-ray of thoracolumbar spine showing severe kyphoscoliosis (case 2).

Fig. 5 Ophthalmological findings showing horizontal conjugate gaze paralysis (case 2). (a) upward gaze; (b) attempted gaze to right; (c) convergence; (d) attempted gaze to left; (e) downward gaze.

of ocular movements. He was born after an uncomplicated term pregnancy, weighing 3750 g. The parents suspected impaired ocular movements and a skeletal deformity at the age of one year.

The scoliosis of the thoracolumbar spine (Fig. 4) was less marked than that of his sister (convex to left, angle 13°), but severe enough to necessitate the use of a Milwaukee brace. There was also tilting of the head to the left.

The eye examination showed a visual acuity of 4/7 in each eye. The anterior segments and ocular fundi were normal in both eyes. Refraction under cycloplegia showed emmetropia.

Again, there was paralysis of horizontal saccadic and slow pursuit movements to both sides. Optokinetic nystagmus and vestibular nystagmus, both rotational and that induced by the caloric test using ice cold water, were absent on both sides. There was slight convergence on attempted dextroversion and levoversion. Convergence, as well as upward and downward conjugate movements, were all normal. The pupils were equal and reacted to light and to near stimuli. Intermittent unilateral blink could occasionally be seen. No abnormal synkinesis could be

detected. The ophthalmological findings are illustrated in Fig. 5. Neurological examination was otherwise normal.

Mental development appeared average. Dermatoglyphic analysis did not show unusual findings.

Physical and x-ray examination of the mother showed a mild non-functional thoracic scoliosis which had not been noted previously.

Discussion

Descending pathways for horizontal saccadic and smooth pursuit movements originate in the frontal and the occipital cortex, respectively, aggregate in the midbrain reticular formation, decussate in the lower midbrain and upper pons, and descend to the pontine paramedian reticular formation (PPRF) near the nucleus of the abducens nerve (Gay *et al.* 1974; Duane, 1976).

Bilateral paralysis of conjugate gaze involving both the frontomesencephalic saccadic and the occipitomesencephalic smooth pursuit systems may be caused by lesions extending between the upper brain stem region, where these two systems converge anatomically, and the PPRF.

Since in both cases described in this report there was bilateral paralysis of both saccadic and slow pursuit horizontal movements and absence of both the vestibulo-ocular nystagmus and the oculocephalic response (doll's eye movement), it is clear that the lesion in these cases was localised in the pons at the level of the PPRF. This is supported by the fact that the vertical conjugate movements and the convergence, the pathways of which descend and synapse with the oculomotor nuclei, were all intact.

Lesions at upper areas spare the vestibulo-ocular nystagmus and the oculocephalic reflexes, whereas conjugate vertical movements and convergence may be affected.

Congenital bilateral paralysis of conjugate gaze may be sporadic (Zweifach *et al.*, 1969) or familial (Dretakis and Kondoyannis, 1974; Sharpe *et al.*, 1975). It may be isolated (Zweifach *et al.*, 1969) or associated with facial palsy and other anomalies, such as are found in Möbius's syndrome.

Only three families have been previously reported where the association of bilateral conjugate gaze paralysis and idiopathic scoliosis was encountered (Dretakis and Kondoyannis, 1974; Sharpe *et al.*, 1975). The Table summarises the clinical features found in our cases as well as in each affected sib in

the families reported before (Dretakis and Kondoyannis, 1974; Sharpe *et al.*, 1975). In the family reported here, the ocular motor manifestations were virtually identical with those described in these reports, apart from the absence of nystagmus. This may denote a similar supranuclear involvement in the pons. Our family is unique in the very early onset of scoliosis, which was therefore of the infantile type. The skeletal deformity in our cases also seems to be more severe.

Dretakis and Kondoyannis (1974) suggested that absence of postural reflexes because of neurological damage could cause the scoliosis associated with the brain stem lesions.

Sharpe *et al.* (1975) reported a family in which four sibs had bilateral paralysis of lateral gaze, pendular nystagmus, and progressive scoliosis. In all sibs, lateral gaze paralysis was not present at birth, but appeared during childhood or early adolescence. The electromyogram suggested a supranuclear lesion. Recessive autosomal inheritance was suggested by the authors, as indicated by absence of these abnormalities in three antecedent generations and involvement of patients of both sexes.

The close parental consanguinity in the family reported here seems to substantiate an autosomal

Table Clinical data on 4 families affected by conjugate gaze paralysis and idiopathic scoliosis

	Family 1 (Dretakis and Kondoyannis, 1974)			Family 2 (Dretakis and Kondoyannis, 1974)		Family 3 (Sharpe et al., 1975)			Family 4 (This report)		
Sex	M	M	F	M	M	M	M	F	M	F	M
Ocular manifestations											
Age when first noticed (y)	?	?	?	2	Early infancy	Early adoles- cence	8	Child- hood	4	2 weeks	1
Lateral gaze paralysis	+	+	+	+	+	+	+	+	+	+	+
Optokinetic nystagmus	?	?	?	?	?	—	—	?	?	—	—
Vestibular stimulation	?	?	?	?	?	—	—	?	?	—	—
Convergence	?	?	?	?	?	+	+	+	+	+	+
Vertical movements	±	±	±	±	±	+	+	+	+	+	+
Doll's eye movements	?	?	?	?	?	—	—	—	—	—	—
Nystagmus	+	+	+	+	+	+	+	+	+	—	—
Facial contractions	—	—	—	?	?	Myo- kymia	—	—	—	+	+
Head oscillations	+	+	+	?	?	+	+	?	?	—	—
Skeletal manifestations											
Age when first noticed (y)	10	2	2	4	4	10	10	8	4	1/2	1
Scoliosis pattern	Lower thoracic curve to right			Same as family 1		Severe thoracic convex to left to right			convex to left	Thoracolumbar convex to left and kyphosis	
Associated abnormalities	Mental retardation, depressed pharyngeal reflexes on left, uvula deviated to right, head tremor			—		Head tilt, self improving			Haematological abnormalities, apparently coincidental		
Parental consanguinity	—			—		—			+		
Other family members affected	Father, mild kyphosis			—		One brother, pendular nystagmus			Mother and 2 maternal cousins, scoliosis		
Parent's country of origin	Greece			Greece		China			Israel		
No of unaffected sibs	4			0		6			0		

recessive mode of inheritance, as suggested in the aforementioned report (Sharpe *et al.*, 1975). However, the presence of two maternal cousins with early onset idiopathic scoliosis, born to unrelated parents, and the mild structural scoliosis detected in the mother cast doubt on this assumption. Autosomal dominant or multifactorial inheritance, as usually implicated in familial idiopathic scoliosis (Roseborough and Wynne-Davies, 1973), may be operative in this family also. The ocular findings could be a coincidental genetic disease transmitted via a different gene. The present data are not sufficient to determine the pathogenesis of this syndrome. Additional neuro-ophthalmological surveys of patients with idiopathic infantile scoliosis may help to clarify the question of whether a syndrome of conjugate gaze paralysis and congenital scoliosis does exist, or whether the few families reported with this combination, including the one in this report, merely represent coincidences.

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