

An autosomal dominant multiple pterygium syndrome

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SUMMARY Three sibs and their mother with features of a multiple pterygium syndrome are reported. Inheritance in this family is consistent with autosomal dominant inheritance with great variation in severity between affected subjects. The importance of examining other family members closely in cases of multiple pterygium is emphasised.

Pterygium syndromes have been described since 1880 but have proved difficult to classify. In recent years there has been renewed interest in the limb pterygium syndromes, together with further refinement in definition and classification.¹ The features of multiple pterygium syndrome^{2,3} include webbing of the neck and popliteal and antecubital fossae, with associated scoliosis, syndactyly, camptodactyly, and short stature. A family, consisting of three sibs and their mother, is reported where the most severely affected member has features consistent with this multiple pterygium syndrome. Other family members have some features of the multiple pterygium syndrome in a less severe form and resemble the syndrome of multiple pterygia, ptosis, and skeletal abnormalities described by Frias *et al*,⁴ but with the additional features of short stature and mental retardation.

Case reports

CASE 1

Case 1, the proband (III.1, fig 1), a 24 year old male, requested genetic counselling because of his scoliosis. He was the first of three children born to unrelated parents. Pregnancy, delivery, and early development were normal. He was fully active and was of normal stature until the age of 10 years when a routine medical examination revealed scoliosis. This required surgery at the age of 14. Subsequently he has remained well and symptom free. Examination (figs 2 and 3) showed a short young man (159 cm, <3rd centile). His intelligence appeared low normal although it has not been formally assessed. He had slightly nasal speech, a short neck, ptosis, and low

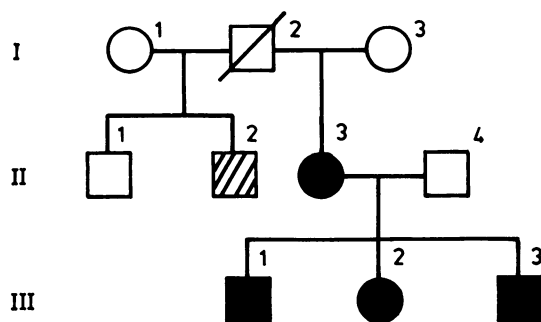


FIG 1 Family pedigree.

set, posteriorly rotated ears. The fourth and fifth fingers of both hands showed camptodactyly and absent flexion creases, with bilateral transverse palmar creases (fig 4). The chest was broad with low set nipples. Radiology (figs 5 and 6) confirmed the presence of a severe dorsolumbar scoliosis with several hemivertebrae at the apex of the curvature and block vertebrae at L4 and 5. There was fusion of C1 and C2 vertebrae (fig 7) with hypoplasia of the anterior arch of the atlas. The ulnar styloid was poorly developed at both wrists and there was fusion of the lunare and triquetrum bones. In the pelvis both hips were rather centrally placed with a valgus deformity of the upper femora. There was hypoplasia of the right first sacral segment.

CASE 2

Case 2 (III.2), the sister of the proband, was the result of the second pregnancy during which the mother took phenobarbitone and phenytoin for idiopathic epilepsy. III.2 was noted at birth to have some syndactyly and restriction of movement of the

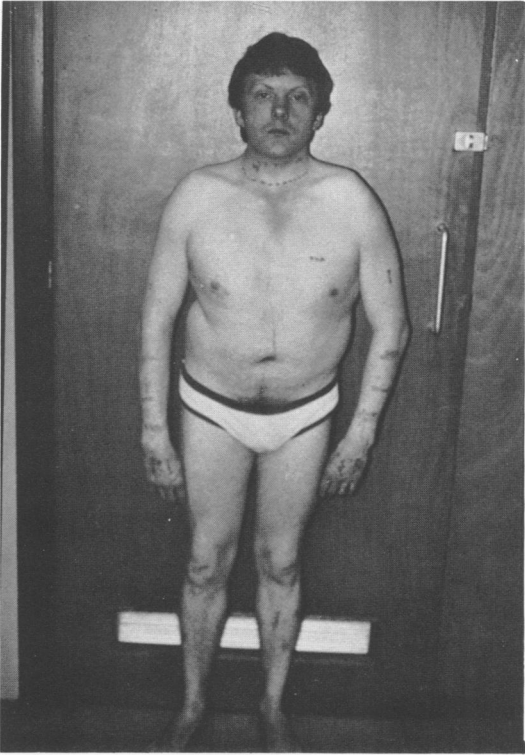


FIG 2 Case 1. Note ptosis, short neck, short stature, and low set nipples.

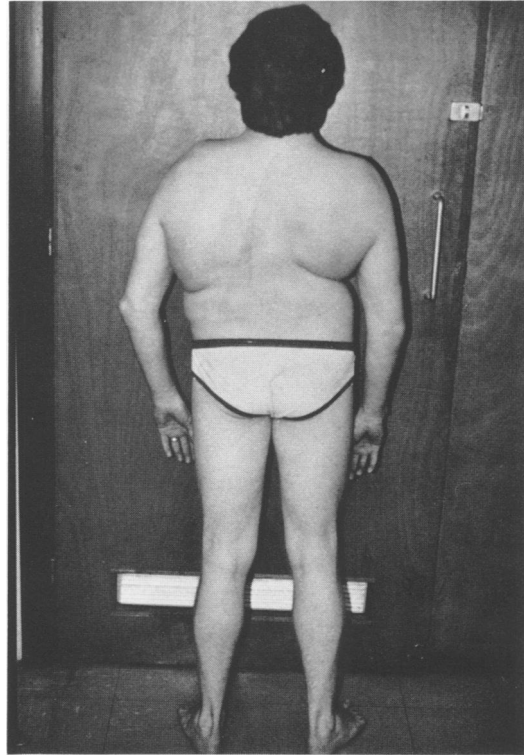


FIG 3 Case 1 showing scoliosis.

third and fourth fingers of the left hand. These improved with exercise. At the age of three years neck webbing was noted. She developed a scoliosis which, by the age of eight, had acquired a curve of 50° when fusion and plate fixation was performed. Abnormalities of the radioulnar joints were also noted at this time. She was always smaller than her peers and more so in puberty. Sexual development was normal with menarche at 11 years. On examination at 22 years she was a woman of apparently low normal intelligence, height 150 cm (<3rd centile), head circumference on the 10th centile, with a short webbed neck, downward slanting palpebral fissures, ptosis, low set, posteriorly rotated ears, a high palate, and nasal speech (figs 8 and 9). There were flexion deformities of all fingers of her left hand and the fourth and fifth fingers on the right. The shoulder movements were normal in spite of some minor axillary webbing. Supination was limited. She was not examined radiologically.

CASE 3

Case 3, III.3, the younger brother of the proband, was a small for gestational age baby, weighing 2.6 kg (3rd centile) at term. The pregnancy was uneventful apart from his mother's continued medication with phenobarbitone and phenytoin at the same (unknown) dose as before. Neonatally he was difficult to feed, and limitation of movement in his hands and fingers was noted. At the age of eight months he presented with bilateral inguinal herniae and was noted to have a scoliosis, abnormal ears, epicanthic folds, and possible neck webbing. He was able to sit unsupported. He walked at two and a half years and by this time his scoliosis had a curve of 22° , and multiple hemivertebrae had been noted. By the age of five there was definite axillary and neck webbing, radioulnar subluxation, and fixed flexion deformities of 15° at the hips and 20° at the knees with pterygia. At eight years he had measurably impaired respiratory function and began to develop urinary

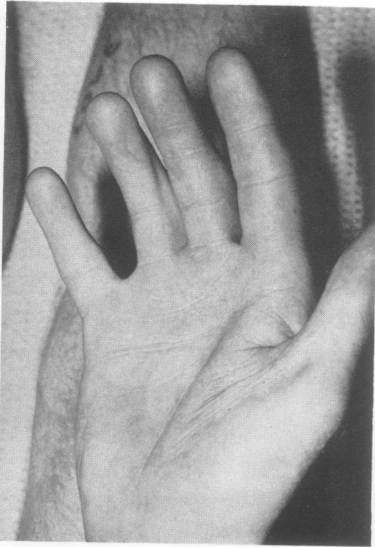


FIG 4 *Hand of case 1. Note absent flexion creases on fourth and fifth fingers, transverse palmar crease, and camptodactyly.*



FIG 6 *Case 1. Note block vertebrae at L4 and 5 and hypoplasia of the first sacral segment.*



FIG 5 *Case 1 showing hemivertebrae and scoliosis.*



FIG 7 *Case 1. Note fusion of C1 and C2.*



FIG 8 *Case 2 showing ptosis, antimongoloid slant of the eyes, short neck, and axillary webbing on the right.*



FIG 9 *Case 2. Note low set, posteriorly rotated ears.*

incontinence. A myelogram revealed tethering of the cord in the lower lumbar region which was released. Following this, at the age of eight and a half years, he had a Harrington rod inserted and spinal fusion for his scoliosis which by this time had a curve of 70°. He was assessed formally as being educationally subnormal in addition to his physical handicaps.

Examination at the age of 14 revealed a very short boy, with a height well below the 3rd centile and a head circumference on the 25th centile and with

very indistinct nasal speech. He had a short neck with marked webbing, downward slanting palpebral fissures, marked ptosis, low set, posteriorly rotated ears, and a broad palate (figs 10 and 11). In addition there was axillary, antecubital, and popliteal webbing (figs 12 and 13). There was mild soft tissue syndactyly of the first to fourth fingers of both hands and single palmar creases with absent flexion creases on some fingers (fig 14). He was prepubertal. Radiological investigation confirmed severe scoliosis with multiple hemivertebrae at the apex of the



FIG 10 Case 3 showing ptosis, expressionless face, and short webbed neck.



FIG 11 Case 3. Note low set, posteriorly rotated ears.

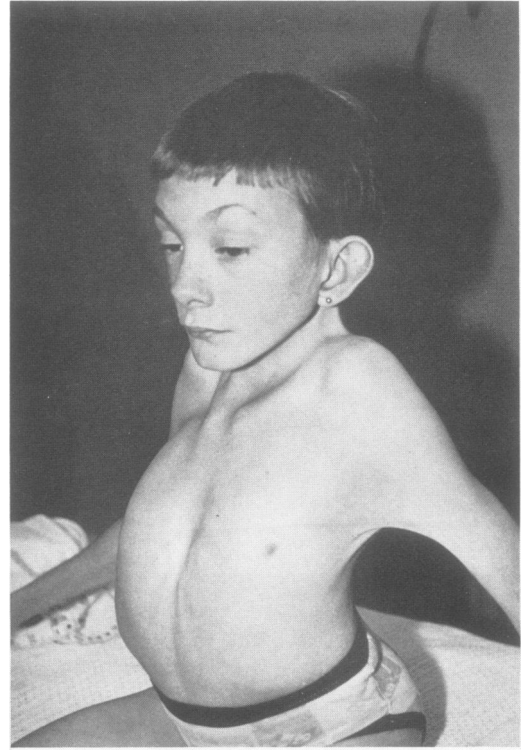


FIG 12 Case 3 showing axillary webbing and scoliosis.

CASE 4

Case 4 (II.3), the mother of the above cases, was a woman of normal stature and intelligence, but with slightly nasal speech. There was no evidence clinically of scoliosis, but she had ptosis, low set, posteriorly rotated ears, a high palate, and a short neck (figs 16 and 17). She had transverse palmar creases and flexion deformity at the proximal interphalangeal joints in both hands together with camptodactyly of the fourth and fifth fingers. Radiological examination showed congenital abnormality of C1 and 2 with fusion of the posterior elements. The anterior arch of the atlas was hypoplastic and appeared fused with the irregular shaped dens. There were also congenital block vertebrae at T10 and 11 (fig 18). X rays of the hands were unremarkable.

A brother (II.2) of case 4 (II.3) was said to have the "family hands" but declined to be seen. The father (II.4) of cases 1, 2, and 3 was examined and found to be completely normal.

curve and spina bifida occulta of the lumbar region. The cervical spine showed fusion of C1, 2, and 3 (fig 15) and a hypoplastic anterior arch of C1. In the proximal row of carpal bones there was fusion of the scaphoid and trapezium.

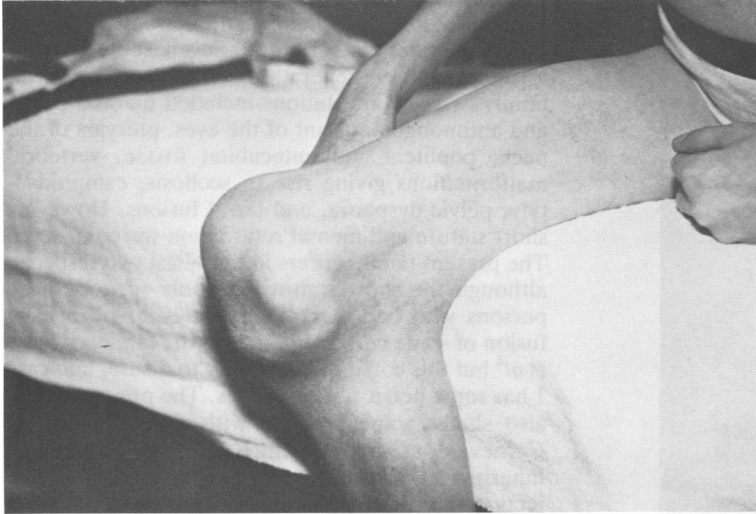


FIG 13 Case 3 showing popliteal webbing.



FIG 14 Case 3. Note absent flexion creases, camptodactyly, and syndactyly.



FIG 15 Case 3. Note fusion of C1, 2, and 3.

Discussion

This family shows variable expression in a dominantly inherited multiple pterygium syndrome. Cases 2 and 3 were exposed to prenatal phenobarbital and phenytoin. The features common to the mother and all affected children are ptosis, low set, posteriorly rotated ears, a functional palate abnor-

mality producing nasal speech, short neck, camptodactyly, abnormal palmar and finger creases, and vertebral abnormalities. In addition, members of this kindred show varying degrees of webbing at various joints. The clinical features of case 3, including the low birth weight with mild camptodactyly progressing to severe pterygia of neck, axillae, and antecubital and popliteal fossae, odd



FIG 16 Case 4. Note ptosis and short neck.

facies with ptosis, palatal abnormality, short stature, mental retardation, and vertebral abnormalities, are very striking and resemble the severe sporadic cases described by Hall *et al.*¹ These authors noted that of 49 cases reviewed, 17 were sporadic and, in general, these tended to be more severely affected. Intra-familial variation between sibs was noted in familial cases.

Frias *et al.*⁴ reported a family with many features of the multiple pterygium syndrome but with autosomal dominant inheritance. Seven subjects were affected in three generations of a black American family. The manifestations included marked ptosis and antimongoloid slant of the eyes, pterygia of the neck, popliteal and antecubital fossae, vertebral malformations giving rise to scoliosis, camptodactyly, pelvic dysplasia, and tarsal fusions. However, short stature and mental retardation were not seen. The present family differs in these last two respects, although the short stature was only seen in those persons who had a scoliosis. Cases 1 and 3 have fusion of some carpal bones as in the family of Frias *et al.*⁴ but this could be secondary to disuse, and case 1 has some pelvic abnormalities. The present family also shares some features with that reported by Carnevale *et al.*,⁵ in which X linked dominant inheritance was inferred. The seven affected subjects in their family had ptosis, webbing of the neck, axillae, and popliteal fossae, camptodactyly, fused vertebrae, and scoliosis. However, severe scoliosis associated with hemivertebrae was not seen.

The most mildly affected persons in this family might be confused with distal arthrogryposis type IIB^{6,7} where joint contractures are associated with ptosis. However, in this family, while there is camptodactyly, there is no deviation of the fingers, all affected subjects have some vertebral abnormalities, and there is no trismus.

Because case 3 most closely resembles autosomal recessive multiple pterygium syndrome, but with autosomal dominant inheritance, it is interesting to

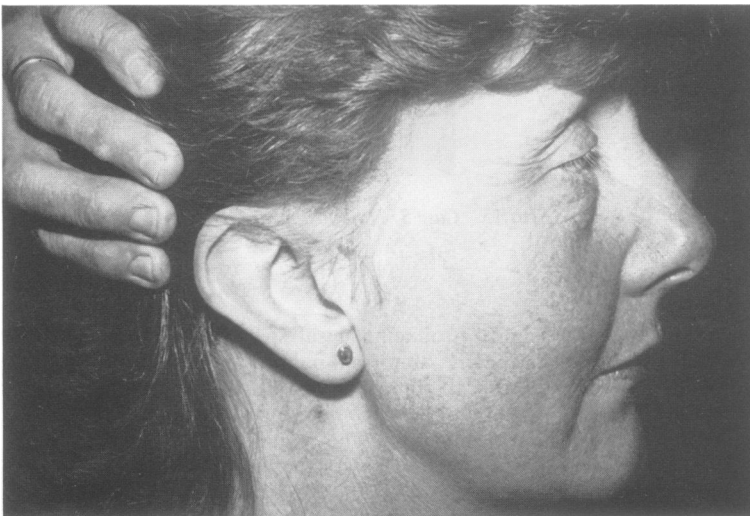


FIG 17 Case 4. Note low set, posteriorly rotated ears.



FIG 18 Case 4. Note block vertebrae at T10 and 11.

speculate whether some isolated cases of multiple pterygium syndrome might not have the same condition. It is obviously important in such a

situation to examine both parents closely for any minor manifestations. Such examination should include a search for minor camptodactyly, syndactyly, and ptosis, and spinal x ray for asymptomatic congenital abnormalities. It is possible that fetal immobility induced by phenobarbitone and phenytoin may have played some part in the more severe expression of the phenotype in cases 2 and 3 than in 1 and 4.

References

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