Short reports

Four sibs with dislocated elbows, bowed tibiae, scoliosis, deafness, cataract, microcephaly, and mental retardation: a new MCA/MR syndrome

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Abstract

We report four sibs with an MCA/MR syndrome whose parents were first cousins. The sibs had mental retardation, microcephaly, hearing problems, cataract, and multiple osseous malformations, such as dislocated elbows, bowed tibiae, and scoliosis. Review of published reports and the use of the London Dysmorphology Database suggest that this family presents a new syndrome.

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When isolated communities have a custom of marriage to a close relative it favours the manifestation of rare genetic diseases or the description of new ones. Here we report four sibs from a consanguineous union with dislocated elbows, bowed tibiae, scoliosis, deafness, cataract, microcephaly, and mental retardation. To our knowledge this is the first report of such an association.

Case reports

The sibs, one boy and three girls, children of healthy, first cousin Lebanese parents, were referred to us for a dysmorphology diagnosis. When the first affected child was born, the mother was aged 22 years and the father 34 years. There was no medical follow up during the pregnancies as the family was very poor, but no toxic exposures or unusual events were noted. Delivery at term by cephalic presentation was performed at home for the four reported sibs. Birth weight, length, and head circumference (OFC) were not available but no obvious gross abnormality was noticed by the parents. The family also consisted of four other healthy children, one boy and three girls. All were free of all the abnormalities described here. The mother reported a miscarriage and the loss of a baby boy at 16 months of age owing to pulmonary complications.

CASE 1

Case 1 is the third child of the family. Deformity of limbs had been noticed from birth. He was first examined when he was 22 years old. He was quite thin and walked with a scissor gait. He was mildly mentally retarded and had a noticeable speech articulation problem, most probably secondary to his hearing problems. On physical examination, his weight was 55 kg (25th centile), height 179 cm (75th centile), and OFC 51.7 cm (<3rd centile). There was microcephaly and prominent ears, but no other facial abnormality was noticed. The upper limbs were apparently short with a limitation of extension and supination. The lower limbs were bowed with severe genu valgum and bilateral wasting of calf muscles secondary to surgical repair of his genu valgum malformation (fig 1). Examination of the external genitalia showed a left undescended testicle. Ophthalmological evaluation was normal. Audiometry showed a mild to moderate hearing loss with a mean sensory loss around of 40 db bilaterally. The evoked potentials were in line with the audiometry.

On physical examination, arm span was 150 cm, total upper limb length 67 cm (25th centile), forearm length 20 cm (<3rd centile), hand length 18 cm (30th centile), total lower limb length 103 cm (60th centile), upper leg

Figure 1 (A) Photograph of case 1 at 22 years of age. Note the bowed lower limbs with severe genu valgum. (B) Note the apparently dislocated elbow.

Figure 2 (A) X ray showing the congenital bilateral posterointernal luxation of the elbow. (B) X ray of the hands showing the carpal fusions on the left hand and the mild shortening of the fourth metacarpals. (C) X ray of the left lower limb. Note the bowed tibiae.

length 50.5 cm (97th centile), with an upper to lower segment ratio of 0.77 cm.

Radiological examination of the skeleton showed a moderate kyphoscoliosis, congenital bilateral posterointernal luxation of the elbow, bilateral radial head hypoplasia, a trapezium scaphoid, a triquetrum-lunate fusion, mild shortening of the fourth metacarpals on the left hand, bowed tibiae, bilateral hallux valgus, brachymetatarsy, synostosis between the scaphoid and the cuneiform, calcaneum valgum, and small talus (fig 2).

Abdominal ultrasound and echocardiography were unremarkable. Complete blood count, haemoglobin electrophoresis, blood glucose, serum electrolytes, urea, calcium, magnesium, phosphate, hormonal evaluation, urine analysis, amino acid studies in plasma and urine, and liver and thyroid function studies were all within normal limits. Chromosome study of lymphocytes with high resolution G and R banding showed a normal 46,XY karyotype.

From birth to the time of examination, recurrent episodes of coughing and dyspnoea secondary to a tracheomalacia were reported.

CASE 2

Case 2, aged 20 years, was seen on the same occasion as her brother, case 1. On examination, her weight was 46 kg (15th centile), height 167 cm (75th centile), and OFC 51.3 cm (<3rd centile). Her physical appearance was quite similar to her affected brother (fig 3), with the exception of the lower limbs which seemed to be less severely affected. Menstrua-

tion was normal. Audiometry and evoked potentials correlated with a moderate hearing loss with a mean sensory loss of around 55 db bilaterally. Ophthalmological evaluation showed bilateral cataracts leading to visual impairment. On physical examination, arm

Figure 3 Photograph of case 2 at 20 years of age.

Figure 4 Photograph of case 3 at 13½ years of age. Note the prominent kyphoscoliosis.

span was 147 cm, total arm length 64 cm (15th centile), forearm length 19 cm (<3rd centile), hand length 17 cm (15th centile), total lower limb length 94 cm (70th centile), upper leg length 48 cm (97th centile), with an upper to lower segment ratio of 0.81 cm.

Total body radiographs were identical to case 1, but a subdislocation with dysplasia of the right hip was present, the tibiae were less severely affected, and no abnormalities of the hands were seen. Chromosomes were normal 46,XX by G and R banding. She was mildly mentally retarded.

CASE 3

Case 3 was 13½ years old at the time of examination. Her weight was 40.5 kg (15th centile), height 155 cm (25th centile), and OFC 50.5 cm (<3rd centile). She had a similar physical appearance to her affected sibs, in addition to ptosis of the left eyelid and a significant kyphoscoliosis (fig 4). Her menses started three months ago. On physical examination, arm span was 140 cm, total arm length 63 cm (40th centile), forearm length 19.5 cm (<3rd centile), hand length 16.5 cm (20th cen-

Figure 5 Photograph of case 4 at 12 years of age. Note the striking resemblance to her other affected sibs with the presence of bilateral ptosis of the eyelids.

tile), total lower limb length 92.5 cm (75th centile), upper leg length 45 cm (95th centile), with an upper to lower segment ratio of 0.71 cm.

Laboratory examinations and cardiac and abdominal investigations were unremarkable. Bilateral cataracts and considerable visual impairment were present on ophthalmological examination. Radiological findings were similar to those of her older affected sister, but with a more pronounced scoliosis. The karyotype was 46,XX. Mental retardation was present.

CASE 4

Case 4, the youngest affected child of the family, was 12 years old at the time of examination. Her weight was 36 kg (40th centile), height 164 cm (>97th centile), and OFC 49.7 cm (<3rd centile). Physical, laboratory, and radiological findings were similar to those of her oldest affected sister, but with the presence of bilateral ptosis of the eyelids (fig 5). There was no cataract. She was not menstruating. On physical examination, arm span was 143 cm, total arm length 63 cm (60th centile), forearm length 19 cm (<3rd centile), hand length 16.5 cm (30th centile), total lower limb length 93.5 cm (95th centile), upper leg length 45.5 cm (95th centile), with an upper to lower segment ratio of 0.79 cm.

The standard karyotype showed a normal 46,XX chromosome constitution. Mental retardation was also present.

Discussion

The most conspicuous findings in the affected sibs reported here were dislocated elbows,

Table 1 A comparison of the clinical features of the patients

	Case 1	Case 2	Case 3	Case 4
Sex	M	F	F	F
Microcephaly	+	+	+	+
Cataract	-	+	+	-
Ptosis of eyelids	-	-	+/-	+
Impaired hearing	++	+	+	+
Scoliosis	+	+	++	+
Dislocated elbow	+	+	+	+
Radiographic hand abnormalities	+	-	-	-
Bowed tibiae	++	+	+	+
Radiographic foot abnormalities	+	-	-	-
Mental retardation	+	+	+	+

bowed tibiae, scoliosis, deafness, microcephaly, and mental retardation (table 1).

Bowed tibiae occur in nearly 70 known different malformation syndromes.¹ Of these, 12 also have elbow dislocation. Since the patients discussed in this paper are of normal stature, all of these syndromes could be ruled out because of their association with short stature. However, one of them, the otopalatodigital (OPD) syndrome, has many manifestations which overlap the condition reported here, such as deafness, dislocated elbow, bowed tibia, carpal fusion, and mental retardation.² However, the absence of the characteristic face with cleft palate, hypertelorism, supraorbital ridges, and antimongoloid slant present in the OPD syndrome and the different mode of inheritance are distinguishing traits.

We then compared the sibs with entities that share mental retardation and joint instability. Our patients have several manifestations in common with Larsen syndrome, namely scoliosis, dislocated elbow, cataract, and deafness. However, the phenotype of patients with Larsen syndrome is quite different from our probands and the radiographic abnormalities described here have not been reported in Larsen syndrome.³ Martsolf syndrome consists of microcephaly, cataract, scoliosis, mental retardation, hirsutism, short stature, and hypogonadism.⁴ As the last three features were not present in our sibs this syndrome could also be ruled out. Furthermore the osseous abnormalities reported here are different from the ones reported in Martsolf syndrome. Finally, Liberfarb *et al*⁵ described a patient with mental retardation, microcephaly, deafness, scoliosis, and dislocated elbow. However, there was also tapetoretinal degeneration and short stature with short limbs, absent in our sibs.

Although carpal fusions were present only in one of the affected sibs reported here, we checked in our differential diagnosis all the disorders associated with carpal fusion that share clinical features with our patients,⁶ such as

dyschondrosteosis (MIM 127300) and frontometaphyseal dysplasia (MIM 305620). These were ruled out as well because of their different phenotype.

Owing to the difficulty of access to older published reports, we used the London Dysmorphology Database with search traits bowed bones, elbow dislocation, mental retardation with or without cataract/deafness. This search did not yield any diagnosis.

The pertinent findings in these four patients, bowed tibiae, dislocated elbow, scoliosis, hearing problems, cataract, microcephaly, and mental retardation, have, to our knowledge, never been reported before as a syndrome. The observed difference in severity of some of the features between the affected sibs, such as bowing of the tibiae, deafness, mental retardation, and the presence or absence of cataract, might be secondary to the intrafamilial heterogeneity of this syndrome. This difference may also be the consequence of sex limited expressivity, explaining the presence of more pronounced abnormal features in the male proband. Finally, the presence of four affected sibs who are the offspring of a consanguineous marriage indicates autosomal recessive inheritance as the most likely mode of inheritance.

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