Two brothers with the Marden-Walker syndrome: case report and review

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SUMMARY Two brothers with blepharophimosis, congenital joint contractures, and mental retardation characteristic of the Marden-Walker syndrome are described. This sib pair strengthens the case for autosomal recessive inheritance of the syndrome.

In 1966, Marden and Walker¹ writing from Minneapolis described a female infant with blepharophimosis and joint contractures. She died at 3 months of age. There have been subsequent reports but, apart from a pair of first cousins, only of single cases. Hitherto there have been no reports of affected sibs.

We describe here the clinical features of two brothers with the Marden-Walker syndrome. The parents are healthy and unrelated, but both are educationally subnormal (ESN). The mother has had two normal children by different men; we describe the only two children from her present marriage (fig 1).

Case reports

CASE 1

This boy (III.5) was born at term on 25.9.78, after an uneventful pregnancy, by lower segment caesarean section for fetal distress. Birthweight was 2·9 kg.

The odd facies was noted at birth (fig 2) and also a left inguinal hernia. At 13 months old the following observations were made: height 74·8 cm (10th centile); weight 8·275 kg (below the third centile); head circumference 45·7 cm (below the 50th centile). He had a tall forehead, immobile facies, depressed nasal bridge, upturned nose, blepharophimosis with widely spaced eyes (inner canthal distance 3·2 cm; >97th centile), and epicanthic folds. Micrognathia, a high arched palate, low set simple ears, and a minor degree of pectus excavatum. There was a left inguinal herniotomy scar. The palmar creases and dermatoglyphs were normal. There were no heart murmurs and the genitalia were normal.

There were fixed contractures at elbows and knees: right elbow, 35°; left elbow, 25°; right knee, 15°; left knee, 10°. There was also some tightness around the shoulder joints and also tightness of hip flexors.

Developmentally he was performing at the 1 month old level at 13 months chronological age.

Routine investigations were normal. Radiology, electrocardiogram, EMI scan, and ultrasound scan of the kidneys showed no abnormality. Electromyography showed no spontaneous activity and no myotonic discharges. A normal record was obtained from tibialis anterior, but there was an increased proportion of spiky polyphasic potentials of normal amplitude from vastus medialis and deltoid. Chromosome analysis showed a normal male karyotype with...
large satellites on chromosome 22. This was also present in the unaffected mother and so was presumably a familial polymorphism.

**CASE 2**
This boy (III.4) was born at 34 weeks’ gestation on 18.1.73. Birthweight was 1.8 kg. When examined at 6 years 10 months old his height was 113.7 cm (10th centile), weight 19.5 kg (10th centile), and head circumference 56.0 cm (>97th centile).

He has strikingly similar facies to his brother (fig 3). He had bilateral inguinal herniotomy scars. The genitalia were normal. The palmar creases and dermatoglyphs were normal.

He ran and jumped with a stooped posture and had tightness around the shoulder joints and hip flexors; elbows: right, 15°, left 15°; extension supination: right, 25°, left, nil; pronation: right, 25°, left, 10°; knees: (both) extension to neutral.

Routine investigations and electrocardiogram were normal. Skeletal survey showed abnormalities at the elbows: “no dislocation, but there is an abnormality of development of the proximal radial metaphysis with abnormal tilt of the radial heads”.

Chromosome analysis showed a normal male karyotype with large satellites on chromosome 22, similar to those previously found in his brother and mother.

Formal developmental testing at 6 years showed he was functioning at the 4-year-old level [ESN(M)]. However, in language he was only functioning at the 24 month level.
Discussion

The Marden-Walker syndrome\(^1\) is characterised by blepharophimosis (short narrow palpebral fissures) and congenital contractures. These affect the knees, hips, elbows, and ankles and remain stable or slightly improve with time. There is no myotonia, thus differentiating the condition from the Schwartz-Jampel syndrome.\(^2\) The blepharophimosis is associated with an immobile facies, micrognathia, and low set ears.

Nine cases (two females and seven males, including our family) have been described in detail, and three others, those of Ealing,\(^3\) Gethis,\(^4\) and Passarge,\(^5\) have been briefly reported. Two of the children died in infancy, and the oldest surviving case (our case 2) is now nearly 7 years old. The mean birthweight was 2.54 kg (range 2.08 to 2.86 kg) and the children have tended to fail to thrive, with weight and height—2 SD below the mean, although head circumference remains about the mean. All nine cases have been mentally retarded with delayed milestones and marked delay in language development (no speech had been acquired by 5 or nearly 7 years, although hearing was normal, in the two longest survivors). Younessian and Ammann\(^6\) in 1964 described a further case, but here the diagnosis is, we think, uncertain.

Cleft palate has been observed in two cases (table) and a high arched palate in four others. In Marden and Walker’s original case an abnormal connection between the superior and inferior vena cava was found at necropsy. Cardiac lesions in other cases include dextrocardia, ejection systolic murmur, and in the case of Fitch et al.,\(^7\) the heart was clinically normal but with a RBBB (right bundle branch block) on the electrocardiogram.

Genitourinary abnormalities have occurred in five of the nine patients. These were microcystic disease of the right kidney,\(^1\) hypospadias,\(^8\) undescended testis,\(^9\) and inguinal hernia (our family). Two of the children (table,\(^10\) and our case 2) have anomalies of the radial head; one of these\(^10\) also had camptodactyly. One child\(^7\) had hypertrichosis and a left preauricular tag. The case of Abe et al.\(^11\) was recognised coincidentally after investigation of recurrent vomiting because of the Zollinger-Ellison syndrome (multiple gastric ulcers associated with hypergastrinaemia).

INVESTIGATIONS

Electromyography, performed in four cases, has given a slightly myopathic picture, with patchy small amplitude, short duration motor unit potentials. Muscle biopsy in three cases showed nonspecific changes. An abnormal electroencephalogram was found in two cases.\(^1\)\(^10\) The EMI scan was normal in our case 1, and the brain was macroscopically normal in Marden and Walker’s original case.

An AEG in the case of Fitch et al.\(^7\) showed reduced size of the cerebellum and brain stem. Microcystic disease of the kidneys was found at necropsy in that case: IVP on four subsequent cases has been normal.

Chromosomes have been reportedly normal in seven cases, while our cases both had large satellites on chromosome 22, which were also present in their mother. Dermatoglyphs have been unhelpful.

INHERITANCE

Our cases are the only sib pair so far reported. Five cases, three boys and two girls, have been sporadic. The evidence for autosomal recessive inheritance previously rested on the male first cousins (related both on the maternal and paternal side) described by Temtamy et al.\(^9\) who were both the offspring of a consanguineous marriage. The family described here strengthens the case for autosomal recessive inheritance of the Marden-Walker syndrome.

We thank Professor Otto Wolff and Professor C O Carter for permission to report these cases.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Sex</th>
<th>Mental retardation</th>
<th>Blepharophimosis</th>
<th>Contractures</th>
<th>Cleft palate</th>
<th>Heart</th>
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<tbody>
<tr>
<td>Marden and Walker(^1)</td>
<td>F</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Abnormal sup VC/inf VC junction</td>
<td>Microcystic kidneys; died left preauricular tag, hypertrichosis</td>
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<tr>
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<td>RBBB</td>
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<td>M</td>
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TABLE Marden-Walker syndrome: diagnostic features

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References

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