The 3-M syndrome

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SUMMARY Five patients from four families, including two male sibs, are reported with clinical and radiological features of the 3-M syndrome.

In 1975, five authors published a report of four children with low birthweight, short stature, and dysmorphic features. They named the syndrome after the initials of the first three (sic!), hence the 3-M syndrome. More recently a report of a further six children has more firmly established the dysmorphic features. The purpose of this paper is to add five further children, including sibs, to the literature in the hope that the condition will be recognised more easily by clinicians.

Case reports

FAMILY 1 (PATIENTS 1 AND 2)
The two affected males in a sibship of five are the product of non-consanguineous, unaffected Indian parents. The father is 160·0 cm and mother is 172·7 cm tall. The other sibs have normal stature and there is no family history of note. Birth weight could not be determined, but the height and weight (patient 1, height 123·5 cm at 16·5 years; patient 2, height 128 cm at 22 years) are below the 3rd centile. On clinical examination (fig 1) both brothers have a broad forehead and a triangular facial outline. Their cheeks slope sharply down to end in a prominent square chin. Considered as a whole, the original description of ‘hatchet face’ would be appropriate to these brothers. The other unusual features are the presence of ‘pouty’ lips, and the heavy facial contours are further accentuated by the presence of a broad fleshy nose. The eyes are normally placed as are the morphologically normal ears. Examination of the trunk revealed both boys to have square shoulders and a short neck with prominent trapezi. They had prominent heels and limitation of extension at the elbows. Both had glandular hypoplasias. The boys were of average intelligence.

Chromosome analysis (G banded) showed a 46,XY karyotype.

Radiographs (figs 2 and 3)
Radiographs showed narrowing of the long bones with diaphyseal over-constriction. The cortices were of normal thickness and there appeared to be medullary narrowing, giving rise to apparent increased bone density. The vertebral bodies were tall and there was a reduction in their AP diameter. The transverse processes were pronounced and over-modelled. Patient 2 demonstrated spina bifida of S1. The thorax was broad and of increased volume. The ribs were slender and horizontal. At
PATIENT 3

Patient 3 is the fourth child of unrelated unaffected parents. His three sibs are normal. Delivery was by lower segment Caesarian section for transverse lie. He weighed 1.7 kg at birth but was of 30 weeks’ gestation and hence had an appropriate weight for his gestational age. On the neonatal unit he fed poorly, gained weight slowly, and developed convulsions. Although these have been well controlled, his motor milestones have been delayed. He crawled at one year, sat at 18 months, and started to walk between 3 and 4 years. The head has always been large relative to body size and the anterior fontanelle was open at 2.5 years. Bilateral inguinal hernias were repaired. His intelligence quotient, measured when he was 13 years old, was between 60 and 70. The following dysmorphic features were noted at 13 years of age (fig 4). There was dolichocephaly (head circumference on 50th centile), a broad forehead, triangular shaped face, pouty, fleshy lips, and a square chin. His short stature was proportionate and below the 3rd centile. He had a square build, short neck, and a pronounced lumbar lordosis. Prominent heels had been noted since birth.

Neurological examination revealed him to have a spastic gait, brisk reflexes, but down-going plantar responses. A CT scan showed dilated ventricles suggestive of communicating hydrocephalus. In view of the delayed milestones and low birthweight, it was concluded that the dilated ventricular system may have been secondary to neonatal intraventricular haemorrhage.
Radiographs
There was dolichocephaly of the skull (fig 5) and the vault was large, particularly in relationship to the facial bones. The anterior fontanelle was widely open. The pituitary fossa showed an anterior elongation. There was bilateral irregularity of the articular surfaces of the trochlear and capitellum epiphyses at the elbows (fig 6). The diaphyses of the long bones were slender and there was some metaphyseal flaring with normal cortical thickness and some reduction in the medullary cavity (fig 7).

The vertebral bodies of the lumbar spine were tall with a slight reduction in their AP diameters. The spinal canal was wide. There was a vertical talus deformity on both sides giving rise to unusual prominence of the calcanea and heel pads (fig 8). The thorax was unusually broad, especially in its upper part, and the posterior ends of the ribs showed a horizontal orientation.

PATIENT 4 (FIG 9)
Patient 4 is the fifth child of non-consanguineous Iranian parents. Two of the previous sibs were very small at birth and died in early infancy, but we have no further information on these children. The proband was the product of a normal term pregnancy. Immediately after delivery she was noted to be very short (length 38 cm) with a relatively large head and was initially considered to have achondroplasia.

When first seen at the age of 2·5 years her height was 69·7 cm (<3rd centile). She was noted to have a relatively large head (circumference 51 cm, >90th centile), a triangular shaped face with prominent lips and a sunken nasal bridge, a small chest with a rather distended abdomen, marked lumbar lordosis,
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short limbs with prominent heels, and hyper-extensible joints. Intelligence was normal. Investigations showed a normal 46,XX karyotype and normal growth hormone secretion. At the age of 10·5 years her height was 108·5 cm (20 cm below the 3rd centile) and there had been very little change in her physical appearance.

**FIG 8** Lateral view of both feet of patient 3.

**FIG 9** Patient 4.

**FIG 10** AP radiograph of both tibiae and fibulae of patient 4 at 3 years.

**Radiographs**

AP radiographs of both tibiae and fibulae at 3 years (fig 10) showed overmodelling of the long bones with diaphyseal over-constriction and metaphyseal flaring. The cortices were of normal thickness. A skull radiograph showed dolichocephaly.

**Patient 5**

Patient 5 is the first child born to unrelated Cypriot parents. Her birth weight at term was 1·9 kg when she was noted to have a disproportionately large head, mid-facial hypoplasia, and short limbs. A diagnosis of achondroplasia was contemplated but
The x-rays did not confirm this. At 1·4 years of age she was proportionately short (height 68 cm, <3rd centile), had a relatively large head (46·5 cm, 50th centile), a small face (fig 11), and prominent heels. There was minor clinodactyly of the fifth fingers but no limb asymmetry. Development was normal.

**Radiographs**

The long bones were slender but showed apparent metaphyseal flaring (fig 12). The vertebral bodies were tall with reduced AP diameters in the dorso-lumbar spine. The ribs were slender and horizontal.

**Discussion**

The 3-M syndrome is established as a clinically recognisable entity, the main features of which are: low birth weight, proportionate dwarfism, hatchet shaped face, relatively large head, prominent mouth and lips, short broad neck, prominent trapezii, deformed sternum, often with a transverse groove below the rib cage, winged scapulae, and prominent heels. Although the head appears large, it is usually on the 50th centile. Other reported features have included short fifth fingers and hyperextensible joints. To these can be added hypospadias, found in both male sibs in this report, and delayed closure of the anterior fontanelle. Low birth weight might not be essential for the diagnosis as it was not present in one of the cases reported here.

The radiological features comprise slender long bones with diaphyseal constriction and over-modelling. The cortex is of normal thickness giving rise to an apparent increase in bone density.

In the spine, especially in the lumbar region, the vertebral bodies are tall and reduced in their AP and transverse diameters. This becomes more apparent with increasing age. Spina bifida occulta was present in three of our five patients. The thorax is broad with horizontally orientated and slender ribs.

In the pelvis the iliac wings are narrow and the femoral necks short. Bone maturation is usually retarded. The inheritance pattern has been suggested as being autosomal recessive2 3 and the description of two further sibs in one family (patients 1 and 2), together with the history of possibly affected sibs in case 4, confirms this.

The differential diagnosis is with other forms of primordial dwarfism, particularly Russell-Silver syndrome. This is well reviewed by Spranger.4

**References**


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