A girl with the Weaver syndrome

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SUMMARY A female with the Weaver syndrome is reported. In addition to the characteristic manifestations of overgrowth and advanced bone age, the facies were typical, with a broad forehead, hypertelorism, a long philtrum, micrognathia, and large ears. Like most other patients with Weaver syndrome, she was developmentally delayed, hypertonic, and had a hoarse voice. Other clinical features included prominent finger pads, narrow hyperconvex nails, small and narrow chest, unilateral dislocated distal ulna, and abnormal thoracic vertebrae.

There is still limited information about the clinical course in the Weaver syndrome, and the recurrence risk remains uncertain. There have been reports of eight cases in males[1-7] and only one unequivocal case in a girl.[8] We present another female with the syndrome.

Case report

A three year three month old girl was admitted for assessment of developmental delay and dysmorphic facies. She was born in Greece, the only child of healthy, unrelated Greek parents (father aged 35 and mother aged 31 years) at 32 weeks' gestation, weighing 2·45 kg (75th to 90th centile). The pregnancy was normal apart from pre-eclampsia in the last 10 days. Fetal movements were normal. Polyhydramnios was noted at delivery. At birth she was noted to have a broad forehead, hypertelorism, flat nasal bridge, large ears, long philtrum, micrognathia, loose skin, and camptodactyly (fig 1).

At nine days she had pneumonia treated with antibiotics and oxygen. She was discharged at five weeks, but continued to have rapid, shallow, noisy breathing due to upper airway obstruction. At two months she had a further bout of pneumonia with cardiac failure. At three and a half months laryngomalacia was diagnosed at laryngoscopy. Chromosome karyotype (46,XX), serum thyroxine (T4), sweat test, and an examination of the urine for mucopolysaccharides were normal. At four months, she was referred to another hospital where, in addition to the above dysmorphic features, it was observed that she also had a small anterior fontanelle, large hands and feet with unusual creases, excessive skin, and curved femora. Her breathing was still noisy. Tone and deep tendon reflexes were increased. A right convergent strabismus was present. An *x* ray of the left wrist revealed a bone age of six to nine months (chronological age four months). Thyroid function tests (T3, T4, TSH) were normal. An umbilical hernia was present which disappeared at six months. At two years four months she was reviewed at the same hospital and her overall developmental level was between six and nine months. A contracture of the right elbow was noted. Bone age (the left wrist) estimated by the TW2 method[9] was 5·6 years at a chronological age of 2·3 years.

Since then, problems have included slow feeding and developmental delay. When recently seen at three years three months she could sit unaided but walked only with support and had only a few words of speech. She was a large child (table). The cry was low pitched, hoarse, and grunting. She had a broad forehead, hypertelorism, flat nasal bridge, mild micrognathia, large ears, peg shaped premolar teeth, a high arched palate, and strabismus (fig 2). There were prominent finger pads and narrow hyperconvex nails. The chest appeared small and narrow with Harrison's sulci. There was generalised hypertonia, hyperreflexia, and mild right sided weakness. There was a mild kyphosis. The right knee could only be extended to 90°, the left to 110°, and there was limitation of extension at the right elbow. The distal ends of the femora appeared widened, but on *x* ray the changes were equivocal. An *x* ray confirmed suspected dislocation of the right distal ulna. Spine *x* rays revealed a mild thoracolumbar kyphosis and an abnormal rounded shape of the thoracic vertebral bodies. The bone age (right wrist) using the TW2 method was 5·8 years (chronological age 3·2 years). A computerised brain scan showed an arachnoid cyst in the right middle fossa

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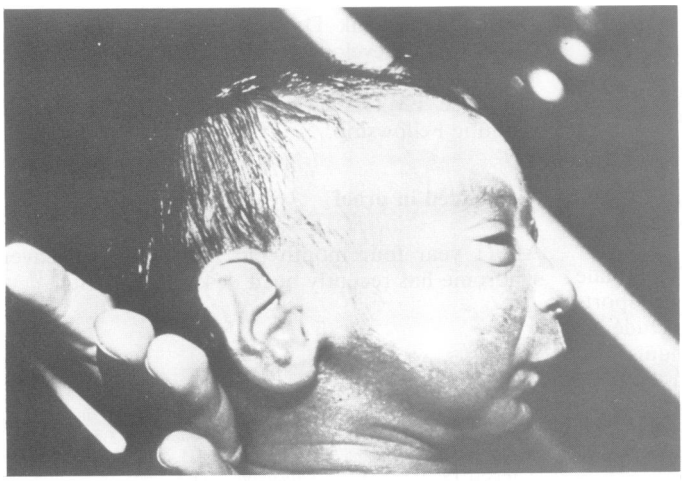
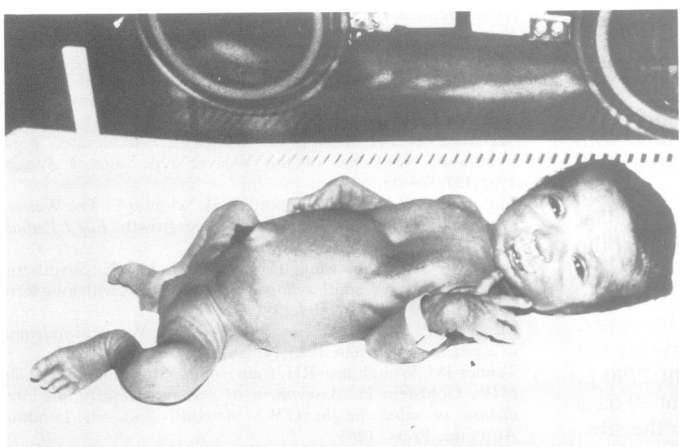


(a)



(b)

FIG 1 *(a) Patient as a neonate. Note large ears, long philtrum, and micrognathia. The resemblance to the patient described by Weisswichert et al*[5] *is striking. (b) Patient as a neonate showing broad forehead, flat nasal bridge, loose skin, and camptodactyly, best seen on right hand.*

TABLE *Growth measurements.*

Age	*Weight (kg)*	*Height (cm)*	*Head circumference (cm)*
Birth*	2·45 (+1·6 SD)	—	—
3 mth†	4·0 (50th centile)	60 (+2·7 SD)	37 (+1·3 SD)
4 mth†	4·8 (50th centile)	—	39 (+1·3 SD)
3 y 3 mth	18·5 (+2·0 SD)	110 (+3·8 SD)	52·4 (+2·0 SD)

*32 weeks' gestation.
†SD calculated correcting for gestational age (according to standards for height and weight from birth to five years. British Children 1970: Tanner JM, Whitehouse RH).

and moderate dilatation of the lateral ventricles (more marked on the left), consistent with cerebral atrophy.

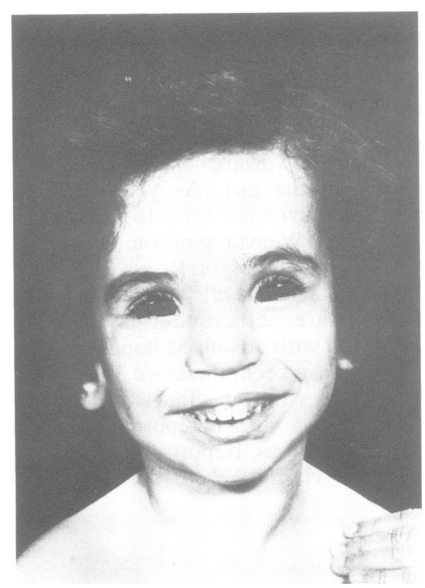


FIG 2 *Patient aged 3·2 years.*

Discussion

Our patient has typical features of Weaver syndrome, as well as some less common manifestations including respiratory difficulties and thoracic and vertebral deformities.[10] Although bone age was advanced it apparently did not alter between 2·3 and 3·2 years. However, this apparent stasis may be seen normally and does not necessarily imply true failure of maturation.

The syndrome was first described in two male infants by Weaver *et al* in 1974.[1] Subsequent reports have been mainly of sporadic cases and include six males[2–7] and only one female.[8] Roussounis and Crawford[11] described sibs (a girl and a boy) as having the Weaver syndrome but we, with other authors,[7 10] consider that there is insufficient evidence to confirm their diagnosis. Jalaguier *et al*[12] described a girl and her brother who they believed demonstrated overlap of the Weaver syndrome with the Marshall-Smith syndrome. In the latter, in addition to advanced bone age, failure to thrive and death in infancy are common, and the facies are characterised by small facial bones, a prominent clavarium, a low nasal bridge, and a short nose with anteverted nostrils. Abnormally shaped middle phalanges of the fingers are also seen. Features common to both syndromes include camptodactyly, herniae, a long philtrum, and large ears. Fitch compared the two syndromes and concluded that they are separate.[10 13] She believed the two sibs described by Jalaguier *et al*[12] had the Weaver syndrome. However, against the diagnosis of the Weaver syndrome are the small size of the female sib at birth (weight 2790 g, length 49 cm), her failure to thrive (weight at 30 days 2700 g), the generalised hypotonia in both the sibs, and their death in early infancy. Both had an unusual appearance of the eyes, described as 'ptosis' in the boy and downward slanting 'limited' palpebral fissures in the girl. As yet, we believe there is insufficient evidence for autosomal recessive inheritance in the Weaver syndrome. As the eye manifestations in the sibs of Roussounis and Crawford[11] and of Jalaguier *et al*[12] are similar and hypotonia is also a feature, perhaps they have a separate disorder associated with advanced bone age.

There have been, therefore, only two definite cases of Weaver syndrome in girls. The reason for the male preponderance in reported cases is uncertain and may be fortuitous. Reports of further cases are clearly needed to clarify these issues.

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Note added in proof

An 11 year four month old female with Weaver syndrome has recently been described by Hall.[14]

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