Unknown syndrome: abnormal facies, hypothyroidism, and severe retardation: a second patient

SUMMARY In the November 1987 issue of this journal, Young and Simpson¹ presented a female infant with abnormal facies (microcephaly, blepharophimosis, small, low set, posteriorly rotated ears, bulbous nose, carp shaped mouth, and micrognathia), congenital heart abnormalities (large atrial and ventricular septal defects), congenital hypothyroidism, and severe global retardation.

We have observed a male newborn with a similar pattern of malformations (figs 1 and 2).

History

Prenatal. No cigarettes or alcohol. No medication. Hydramnios at five months.

Birth. Caesarean section (hydramnios and postmaturity of 42 weeks). Required resuscitation. Apgar scores 1 at one

minute, 4 at 10 minutes. Despite intensive therapy death occurred after 12 hours.

Family. First child of healthy unrelated parents. Spontaneous first trimester abortion in first pregnancy. Father aged 34 years, mother 32 years.

Clinical examination

Clinical postmortem findings. Weight 2600 g (3rd centile), length 46.5 cm (3rd centile), head circumference 35 cm (25th centile). Sloping forehead, prominent occiput, large posterior fontanelle, high nasal bridge with bulbous nasal tip, small palpebral fissures in normal position, thin upper lip, low set ears with prominent antihelix, marked microretrognathia, small tongue, cleft soft palate, bilateral simian crease, camptodactyly of fourth and fifth fingers, absence of distal interphalangeal creases, rockerbottom feet, lumbar hyperlordosis, bilateral cryptorchidism.

Internal findings. No internal malformations except for a mobile caecocolon and absence of thyroid. No ectopic thyroid tissue. No gross malformations of the brain; enlargement of the aqueduct of Sylvius and fourth ventricle.

FIG 1 AP view of the dead neonate.

FIG 2 Lateral face. Note the sloping forehead, high nasal bridge, and marked microretrognathia.

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Karyotype. Normal G banded male karyotype on cord blood and skin biopsy. Normal parental karyotypes.

Discussion

This male neonate presents a number of striking similarities with the unknown syndrome presented by Young and Simpson.¹ Among these similarities the most important seem to be the facial appearance with bulbous nose and microretrognathia and the hypothyroidism. The only major discordant finding is the absence of a cardiac anomaly in the present patient. Complete necropsy did not reveal other important internal malformations.

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Reference

- 1 Young ID, Simpson K. Unknown syndrome: abnormal facies, congenital heart defects, hypothyroidism, and severe retardation. *J Med Genet* 1987;24:715-6.

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A further patient with the lethal type of Larsen syndrome

SUMMARY We present a female infant with multiple joint dislocations, flat facies, cleft soft palate, redundant neck skin, pulmonary hypoplasia, and skeletal abnormalities.

History

Prenatal. No medication, alcohol, or cigarettes. Normal liquor volume. Poor fetal movements.

Birth. Normal vaginal delivery at 42 weeks. Apnoeic after birth. No response to resuscitative measures and died at 30 minutes.

Family. Both parents healthy; 40 year old mother and unrelated 41 year old father. Two previous pregnancies had ended in spontaneous abortion at eight weeks and fetal death at 22 weeks. Necropsy in the latter case did not reveal any abnormality. The parents had a total of seven healthy children by previous partners.

Clinical examination

External (fig 1). Weight 2550 g (3rd to 10th centile), length 45 cm (3rd centile), OFC 32 cm (3rd centile). Flat occiput, large posterior fontanelle and very narrow, diamond shaped anterior fontanelle. Low set ears, flat nasal bridge, and cleft soft palate. Short, broad neck owing to an excess of subcutaneous tissue. Cervical kyphosis. Dislocation of both hips and knees and talipes equinovarus deformity of the feet. Rhizomelic shortening of upper limbs. Bilateral single palmar creases.

Necropsy. Severely hypoplastic lungs, weight 13 g and 11 g (normal 25 g), small spherical brain weighing 309 g with formation of microgyri in the frontal lobes. Fusion of frontal and parietal bones.

Radiology (fig 2). Hypoplasia of the vertebral bodies from T2 to T8. Severe hypoplasia of the fibulae, especially proximally.

Discussion

This patient has similar features to the two cases reported previously by Chen *et al.*¹ The Larsen syndrome² of multiple congenital dislocations associated with characteristic facial abnormality appears to arise as a result of a generalised mesenchymal disorder³ and collagen fibre abnormalities have been reported. This is a heterogeneous

FIG 1 Postmortem view of the infant showing joint dislocations, unusual facies, and redundant neck skin.