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A lethal presentation of de novo deletion 7q

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SUMMARY Deletion of 7q32→qter is a well defined syndrome which usually arises de novo. The proband we report was the result of an uncomplicated 36 week first pregnancy of non-consanguineous Oriental parents. The male infant died shortly after birth. Chromosome studies of peripheral blood and umbilical cord revealed 46,XY,del(7), apparently (q32→qter). The parents' karyotypes were normal. The observed facial structural abnormalities and hydrocephalus rather than microcephaly are in sharp contrast to the clinically described syndrome.^{1,2} The lethal components, absence of suprarenal glands and hydranencephaly, suggest either an unknown con-

founder factor or a more proximal deletion with an alternative interpretation of 7q-(q23.1→q36.1) rather than the apparent breakpoint at 7q32.

Although relatively few cases have been reported, partial monosomy of 7q appears to be a well defined syndrome which usually arises de novo.¹⁻³ Young *et al*⁴ reviewed published reports and added new cases of terminal and interstitial deletions, bringing the total number of reported cases to 38. The clinical features found in more than 50% of the patients with terminal deletions of 7q are mental and growth retardation, microcephaly, low birth weight, eye anomalies, flat, broad nasal bridge, bulbous nasal tip, ear malformations, abnormal palm and sole creases, prominent forehead, and genital anomalies in males. Many of these features are also seen in patients with interstitial deletions of 7q which have been reported less frequently. While the proband

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we report has some of the features of 7q monosomy, he is remarkable in that he had hydrocephalus rather than microcephaly and also hydranencephaly and adrenal agenesis which resulted in perinatal death. The syndrome has not been observed in studies of spontaneous abortions^{5 6} and usually does not result in early death.⁴

Case report

The proband was the product of an uncomplicated first pregnancy of non-consanguineous Oriental parents. The mother was 29 years old and the father 30 years old. The proband was delivered by Caesarean section at 36 weeks' gestation because of breech presentation with possible prolapsed cord. The male infant weighed 1590 g with a head circumference of 30.5 cm. The Apgar scores were 1 at one minute and 0 at five minutes. Attempts to resuscitate the infant failed. The anatomical malformations noted at delivery were hydrocephalus, anophthalmia, absence of the nasal septum with one nostril, depressed nasal bridge, small, long, sharply pointed nose, midline cleft palate, widened philtrum, small mouth, webbed neck, small penis, undescended testes, imperforate anus, and left club foot.

NECROPSY FINDINGS

At necropsy, the body of the newborn Oriental baby boy of 36 weeks' gestation weighed 1620 g (<3rd centile) and measured 37 cm from crown to heel (<3rd centile) and 26 cm from crown to rump.

External examination showed severe craniofacial abnormalities (fig 1) including hydrocephalus with prominent forehead and a occipitofrontal circumference of 30.5 cm, horizontal palpebral fissures, bilateral anophthalmos, elongated, narrow nose, flat nasal bridge, agenesis of the nasal septum, completely cleft palate, small mouth, wide nasal philtrum, and low set, deformed ears. In addition, webbed neck, bilaterally undescended testes, and left club foot were noted (fig 2).

Examination of the body cavities showed normal gross anatomical findings with the exception of agenesis of both adrenal glands. The skull sutures were widely open and the fontanelles were enlarged. The cerebral hemispheres were replaced by a unilocular, transparent, thin sac filled with clear fluid that flowed up at rupture (fig 3). The basal ganglia, brain stem, and cerebellum were formed. The falx cerebri was absent but otherwise the dura were not remarkable. No pituitary was noted.

Histological findings of the viscera were within normal limits except for the lungs which showed

FIG 1 Craniofacial appearance of proband at necropsy.

FIG 2 Whole body appearance of proband at necropsy.

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mild acute intra-alveolar haemorrhage and aspiration pneumonia.

CYTOGENETIC STUDIES

Peripheral blood and umbilical cord cells from the proband were obtained for chromosome studies. With G banding, cells from both sources showed a consistent apparently terminal deletion of 7q distal to band q32. However, an alternate interpretation which cannot be excluded is that the abnormal chromosome 7 is the result of an interstitial deletion of q23.1→q36.1. Chromosome studies of peripheral blood cells from both parents showed normal chromosomes.

Discussion

The proband we report has some findings not previously reported in subjects with monosomy 7q. The adrenal agenesis is probably secondary to aplasia of the pituitary. These anomalies are usually associated with abnormalities of the brain and skull.⁷ The lethal features suggest an unknown confounding factor. However, since hydranencephaly is a rare finding, it seems more plausible to associate it with the chromosome abnormality. Therefore, the interpretation of the

FIG 4 Partial karyotype of chromosomes 7 from the proband and the parents. Because of bends in the chromosomes, two pairs are shown for mother and child.

deletion as interstitial rather than terminal is more attractive. Of 17 reported cases of interstitial deletions of 7q, six lacked bands 7q11→q21 or q22, seven were monosomic for 7q21→q31 or q32, and four were missing 7q31→q34.⁴ If the present case is interpreted as an interstitial deletion, it would represent loss of more genetic material than the other reported interstitial deletions which might contribute to increased lethality.

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FIG 3 Intracranial findings on opening of skull. Note the ruptured, thin walled sac replacing cerebral hemispheres: the cerebellum and brain stem are in situ.