De novo interstitial deletion in the long arm of chromosome 9: a new chromosome syndrome

SUMMARY An infant with an interstitial deletion 46,XY,del(9)(pter→q22::q32→qter) is described. Clinical features included abnormal craniofacies with hypotelorism, narrow palpebral fissures, sclerocornea, deep vertical groove, and supraorbital ridge hypoplasia. There was unilateral preaxial polydactyly and toe syndactyly. Generalised hirsutism was noted. The infant had surgery for duodenal atresia but died at the age of 3 months. Unilateral renal dysplasia and accessory spleens were found at necropsy.

Deletions involving the long arm of chromosome 9 are rare. We are aware of only five such published cases. One was a deletion of the euchromatic region in a mentally subnormal patient. In another, the deletion was associated with fragments without precise identification of the deleted segment in a severely malformed male infant. Wisniewski et al reported a deletion of the secondary constriction, together with a small amount of adjacent euchromatin, in a girl with developmental retardation and multiple abnormalities. A similar deletion was reported by Turleau et al in an 8-year-old boy with different clinical anomalies. The same report also described a second deletion in a 5-month-old boy with a very peculiar craniofacial dysmorphism, and the deletion involved was in the euchromatic region: del(9)(q32q34).

In this paper, we describe a male infant with multiple congenital abnormalities and an interstitial deletion of a different euchromatic segment in the chromosome 9 long arm.

Case report

This Mexican-American male was the product of an uncomplicated 34-week gestation of a 21-year-old, G5, P1, A3 mother and a 30-year-old father. Presentation was vertex and delivery uncomplicated. Apgar scores were 1 at one minute and 5 at five minutes. Abdominal distension with respiratory distress prompted the transfer to the newborn intensive care unit at Valley Children's Hospital shortly after birth. His birthweight was 1915 g (25th centile), length 45 cm (25th centile), and head circumference 30.5 cm (25th centile).

Initial physical examination was remarkable for numerous dysmorphic findings (fig 1a). There was marked generalised hirsutism (fig 1b). Examination of the craniofacies revealed downward slanting palpebral fissures measuring 1.5 cm bilaterally (<3rd centile). The inner canthal distance was 1.75 cm and interpupillary distance was 3.5 cm. The corneas were hazy bilaterally and there was a dense sclerocornea of the left eye at the 9 o'clock position which persisted throughout the child's life. There were no colobomata and the retinal examination was normal. There was a deep vertical groove in the forehead and bilateral supraorbital ridge hypoplasia. The nasal bridge was depressed and there were bilateral lower canthal folds. The ears were 3 cm bilaterally with tenting of the superior helix on the right. Auditory canals were narrow. The philtrum was long and full. No cardiac murmurs were heard. Genitalia were normal.

Multiple abnormalities of the extremities were noted. The right hand had pedunculated preaxial polydactyly with only a small fragment of bone seen radiographically (fig 2a). The feet showed total 2/3 syndactyly on the right and complete 1/2 and 4/5 syndactyly on the left (fig 2b).

Skeletal radiographs showed multiple bony dysmorphic findings. The clavicles were angulated.

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Case reports

FIG 2  Note (a) polydactyly on the right hand and (b) syndactyly on both feet.

FIG 3  Radiographs showing (a) angulated clavicles and asymmetrical thorax and (b) marked widening of synchondrosis between the exoccipital and supraoccipital bones and orbital hypotelorism.

inferiorly and the ribs were unusually contoured and fluted (fig 3a). The thorax was asymmetrical. There were no vertebral abnormalities noted. Skull films showed marked widening of the synchondrosis between the exoccipital and supraoccipital bones (fig 3b). Orbital hypotelorism was evident.

Clinical and radiological evidence of bowel obstruction was progressive and led to laparotomy at 12 hours of age. Duodenal atresia, malrotation, and a Meckel's diverticulum were noted. A duodenostomy was performed and the infant was maintained on parenteral hyperalimentation because of persistent symptoms of partial bowel obstruction. Oral feedings were finally tolerated at 5 weeks of age. Hyperbilirubinaemia and staphylococcus aureus sepsis were successfully treated and the child was discharged home at 7 weeks of age.

Readmission was necessitated by poor feeding and recurrent abdominal distension. He underwent laparotomy for lysis of adhesions and performance of a gastrostomy. Feedings were, however, not tolerated. The child's neurological status, which was abnormal from the time of birth, deteriorated. He had mild hypertonicity and clinical seizures became evident. An electroencephalogram showed generalised dysrhythmia. Computerised tomography of the brain showed no structural abnormalities. Recurrent apnoeic spells ensued and the infant died at 3 months of age.

Necropsy examination revealed a multilobulated spleen with five additional accessory spleens, the largest measuring 1 cm in diameter. Hydroureter was present bilaterally. The right kidney was small and dysplastic.

CYTOGENETIC STUDIES
Both peripheral blood and skin fibroblast cells were used in the chromosome analysis. The patient had a normal count of 46 chromosomes including X and Y in all the cells examined. However, upon karyotyping of G banded metaphase spreads, it was found that, while all the other chromosomes were normal, one of the chromosomes 9 had a deletion in its long arm. Combining this with the studies from Q, C, and R bandings, it was determined that the deletion was interstitial and involved the euchromatic region between q22 and q32 (fig 4). The proband's

FIG 4  Ideogram of chromosome 9 (Paris Conference, 1971). Arrows indicate breakpoints in band region 9q22 and 9q32. The segment lying between them was completely deleted. The chromosome pair are demonstrated by Q, G, R, and C banding; the deleted chromosome 9 is on the right.
karyotype was therefore designated 46,XY,del(9) (pter→q22;q32→qter).

Both parents were subsequently studied and found to have normal karyotypes. The deleted chromosome 9 in the proband was also identified as being of maternal origin since its enlarged heterochromatin (C band region) corresponded to that in one of the mother's chromosomes 9. This suggests that the breakage, giving rise to a deletion, took place during oogenesis.

Deletion mapping of the genes for ABO, adenylase kinase 1, and galactose-1-phosphate uridyl transferase was performed, but assays failed to localise any of these loci to the deleted segment.

Discussion

The present case is believed to be the second report of a chromosome long arm deletion consisting of only the euchromatic region. Since none of the other chromosomes was found to be involved in the aberration, this case is regarded as a bona fide 9q deletion syndrome. The clinical features present in the patient can thus be attributed to partial monosomy for the deleted segment. The phenotype seen in our case does not correspond to those reported previously, since different regions of the chromosome 9 were involved in each of the other cases. The findings in the extremities and the marked generalised hirsutism should aid in the clinical recognition of other similarly affected infants.

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References


A malformed baby with two separate de novo translocations

SUMMARY A case of two separate apparently balanced de novo reciprocal translocations 46,XX,t(2;4)(p25;q21), t(10;18)(p15;q12.2) in an infant girl with multiple malformations is reported.

Case report

The proband was the second child of a father aged 24 and a mother aged 25. She was born at 38 weeks' gestation, weight 2.06 kg, length 44.5 cm (both less than the 3rd centile), and head circumference 33.5 cm (25th centile). She had rather 'pixie' facies, a relatively large cranial vault, and malformed ears. No other malformations were detected. She had a weak cry and functional palatal incompetence, with considerable feeding difficulties. At 2 months, a

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