systolic murmur was noted but there was no evidence of heart failure. At 41 months, her weight and length were well below the 3rd centile, the head circumference continuing along the 25th. She was developmentally retarded, did not smile or fix or follow with her eyes, and head control was poor. She was found dead in her cot at 41 months. At necropsy, a 1 cm secundum type atrial septal defect, a bicornuate uterus with a double cervix, and a septate upper third of the vagina were found. No gross or histological abnormalities of the brain were noted apart from rather prominent gyri. The thymus was small (1.2 g) but histologically normal.

Metaphase preparations (GTG) on lymphocyte cultures consistently showed translocations involving chromosomes 2, 4, 10, and 18 (figure). The karyotype is interpreted as 46,XX,t(2;4)(p25;q21),t(10;18) (p15;q12-2). The parents’ chromosomes were normal.

Discussion

Single apparently balanced reciprocal translocations are not uncommon, but the coincidence of two unrelated apparently balanced reciprocal translocations in one person is extremely rare. In previous reports, some have1-3 and some have not4 5 been associated with phenotypic abnormality. The phenotypic abnormality often associated with a single reciprocal translocation may be the result of a submicroscopic loss of chromosome material, or a gene function disturbance owing to a position effect.6 Where the phenotype is normal, the translocation is presumably indeed balanced, with no ill effect of the chromosomal shift. We may suppose the same principles apply to the double reciprocal translocation.

We thank Drs A G Dempster and B B Berkeley, who did the necropsy examination.

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References


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A second patient with partial deletion of the short arm of chromosome 3: karyotype 46,XY,del(3)(p25)

SUMMARY A child with monosomy for the distal part of the short arm of chromosome 3 is presented. Altered features include prenatal onset growth deficiency, postaxial polydactyly, ptosis, ear anomalies, and a triangular facial appearance. In addition to generalised delay in psychomotor development, specific problems in visual attention were present. Comparison with the previously reported case suggests that the phenotype observed constitutes a clinically recognisable pattern of malformation.

The purpose of this report is to present a patient with monosomy for the distal segment of the short arm of chromosome 3. One child with a similar chromosomal abnormality has been previously reported.1

Case report

Features of this child are depicted in fig 1. The patient was born after a 40 week gestation remarkable for decreased fetal activity. The mother smoked 20 cigarettes per day. Delivery was via caesarian section for frank breech presentation. Birth length, weight, and head circumference were 43.75 cm, 2552 g, and 32 cm, respectively. All are less than the third centile for 40 weeks’ gestation. Craniofacial alterations included a small (1.5 x 1.5 cm) anterior fontanelle, overriding cranial sutures, a triangular face, micrognathia, short (1.6 cm) palpebral fissures.

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marked bilateral ptosis, a prominent nasal bridge, underdeveloped nasal alae, a long (1.0 cm) simple philtrum, and unusual ears which measured 3.3 and 3.2 cm. In addition, the child had an umbilical hernia, right cryptorchidism, limited mobility in his major joints, and skin dimples over the coccyx, both shoulders, and both elbows. The left fifth finger lacked a crease over the proximal interphalangeal joint. A rudimentary digit which was inserted at this position had been removed at birth. Dermal ridge patterns consisted of five arches and five ulnar loops. The infant had a very soft, hoarse voice.

Chest x-ray and electrocardiogram obtained to evaluate a soft grade 2/6 systolic ejection murmur were normal. On brainstem audiology, waves I to V were normal at 60 dBHL. No responses were obtained at lesser frequencies. The results were compatible with a mild to moderate hearing loss at the cochlear level.

Bilateral inguinal hernias were repaired at 5 weeks of age. At 5 months of age the child continued to be growth retarded. Delayed bone age was noted on radiographs obtained to evaluate hip structure (absent proximal femoral ossification centres). Social and motor milestones were slightly delayed; however, the infant had very poor visual fixation and tracking abilities. Visual evoked responses were normal. Operative repair of the ptosis was accomplished with bilateral frontalis slings. During surgery both nasolacrimal ducts were probed to relieve obstruction. The optic discs appeared somewhat pale. Each macula was noted to have an unusual wrinkled appearance. Visual responsiveness improved minimally after surgery.

The mother was 29 and the father 32 years of age at the time of the infant's birth. One previous pregnancy ended at 2 months' gestation with a spontaneous abortion, probably related to the presence of an intrauterine device.

Analysis of G banded chromosomes obtained from lymphocyte cultures detected a deletion of the distal portion of the short arm on one chromosome 3 (fig 2). Since the G banded chromosomes of both parents were normal, the patient's deletion was not the product of malsegregation of a balanced parental reciprocal translocation. Both G banded and R banded preparations suggested the presence of chromatin beyond band p24 of the deleted chromosome. The breakpoint appeared to lie within band p25 but the preparations were not considered adequate to identify the sub-band region.

Discussion

Features of the patient described here and the patient reported by Verjaal and De Neef are set out in the table. Band p25 was the breakpoint in both cases. The presence of a similar pattern of malformations in unrelated subjects with identical chromosomal anomalies confirms that the two are aetiologically related.

Follow-up information on the previously reported patient indicated that at the age of 5 years the child was growth deficient and severely retarded. He could sit, but was unable to walk or communicate. Visual responsiveness was markedly decreased; only light perception was present. The patient described here appears to be less severely affected from the standpoint of psychomotor development.
the severe ptosis, however, has made only a slight difference in the child's visual responsiveness.

Comparison of the two cases indicates that monosomy 3p forms a clinically recognisable pattern of malformation which should be considered in the face of prenatal onset growth deficiency, small ears, ptosis, and postaxial polydactyly.

The authors wish to thank Dr J J De Nef for generously providing follow-up information on the previously reported child, and Marian Gallagher for her assistance in the preparation of the manuscript.

Addendum

Since this article was submitted for publication, we have become aware of two further cases with identical deletions of chromosome 3. The children, both females, aged 11 and 3 years, also had severe growth and mental deficiency, microcephaly, ptosis, micrognathia, and altered ear structure. The findings further support the hypothesis that monosomy 3 (p25) has a distinct clinical phenotype.

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Chronic renal disease, myotonic dystrophy, and gonadoblastoma in XY gonadal dysgenesis

SUMMARY A patient with XY gonadal dysgenesis and gonadoblastoma showed myotonic dystrophy and chronic renal disease of unknown aetiology. The coexistence of renal disease and XY gonadal dysgenesis in this and two other subjects suggests a presently obscure aetiological relationship between the phenomena.

XY gonadal dysgenesis is a genetically heterogeneous group of disorders, the most common form being an X linked recessive or male limited autosomal dominant disorder in which phenotypic females have bilateral streak gonads and fail to undergo normal secondary sexual development. The pathogenesis is uncertain and H-Y antigen may or may not be present. Gonadoblastomas or dysgerminomas have been reported in 20 to 30% of cases.

Blanchet et al reported a patient who, in addition to XY gonadal dysgenesis, showed renal failure resulting from "interstitial nephritis". While the patient was receiving immunosuppressive therapy, a gonadoblastoma was discovered after renal transplantation. However, the authors did not attribute the development of neoplasia to immunosuppression. Harkins et al also observed renal failure of unknown origin. Similarly, we have observed renal failure in a patient with XY gonadal dysgenesis who not only had gonadoblastoma but also myotonic dystrophy, an autosomal dominant trait.

Case report

The proband was born to a 35-year-old father and a 32-year-old mother. The patient, her father, and her two brothers were born to a 36-year-old mother and her husband.

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