

associated with a male karyotype including an abnormal X chromosome was reported by Bernstein *et al.*⁵ The abnormal X was interpreted as a duplication of p21→pter. In addition to sex reversal, H-Y antigen was found to be virtually absent. This finding was interpreted as interference with a putative regulatory element on the X chromosome.

The recent tentative localisation⁹ of the H-Y antigen suppressor gene distal to Xp22 would perhaps explain why the sexual development in Bernstein's patient with a distal duplication was severely affected, while our patient, with a more proximal duplication, had a male phenotype; however, unfortunately, H-Y antigen studies were not carried out in our patient.

Anomalous segregation of the Xg^a allele in Bernstein's patient might suggest that the Xg locus was involved in the inactivation process, but recombination at meiosis was also a possibility. Since both our proband and his brothers were Xg(a-) and the mother was Xg(a+), the findings in our patient do not seem to help in elucidating this problem. Furthermore, there was no evidence from BrdU incorporation for inactivation of short arm material on the X chromosome in the proband.

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References

- Therman E, Patau K. Abnormal X chromosome in man: origin, behavior and effects. *Humangenetik* 1974;25:1-16.
- Davidenkova EF, Verlinskaja DK, Mashkova MV. Structural aberrations of the X chromosome in man. *Hum Genet* 1978;41:269-79.
- Sacchi N, Dalpra L, Kehyayan E. A duplication-deficiency X chromosome in a girl with severe mental retardation. *Hum Genet* 1980;54:279-81.
- Steinbach P, Horstmann W, Scholz W. Tandem duplication dup(X) (q13q22) in a male proband inherited from the mother showing mosaicism of X-inactivation. *Hum Genet* 1980;54:309-13.
- Bernstein R, Jenkin T, Dawson B, *et al.* Female phenotype and multiple abnormalities in sibs with a Y chromosome and partial X chromosome duplication: H-Y antigen and Xg blood group findings. *J Med Genet* 1980;17:291-300.
- Laurent C, Biemont MC, Dutrillaux B. Sur quatre nouveaux cas de translocation du chromosome X chez l'homme. *Humangenetik* 1975;26:35-46.
- Hagemeyer A, Hoovers J, Smit FME, Bootsma D. Replication pattern of the X chromosomes in three X/autosomal translocations. *Cytogenet Cell Genet* 1977;18:333-48.
- Bühler EM, Jurik LP, Voyame M, Bühler UK. Presumptive evidence of two active X chromosomes in somatic cells of a human female. *Nature* 1977;265:142-4.
- Wolf U, Fraccaro M, Mayerova A, Hecht T, Marashio P, Hameister H. A gene controlling H-Y antigen on the X chromosome. *Hum Genet* 1980;54:149-54.

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A complex chromosome rearrangement resulting in trisomy 15q22→qter

SUMMARY A black infant with malformations was found to have trisomy 15q22→qter. The mother had a complex chromosomal rearrangement involving three chromosomes (5, 13, and 15). A comparison with previously published cases of trisomy for distal 15q suggests a pattern of clinical findings including retardation in growth and development, microcephaly, asymmetrical facies, prominent occiput, anti-mongoloid slant of the palpebral fissures, micrognathia, prominent nose, and congenital heart disease.

Partial trisomy for the distal third to half of the long arm of chromosome 15 has been observed rarely. In the four previously reported families,¹⁻⁴ the affected children were the result of maternal malsegregation of balanced translocations involving two chromosomes. We report an affected child resulting from the maternal malsegregation of a complex chromosome rearrangement involving three chromosomes, 5, 13, and 15.

Case report

The proband, a newborn black male, was the 1820 g product of an uncomplicated term pregnancy. He was born to a 28-year-old gravida 3, para 0, abortif 2 mother. There was no history of smoking nor alcohol or drug abuse. Labour was spontaneous and delivery was vaginal with mid-forceps assistance. The infant was meconium-stained and subsequently received

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FIG 1 *The patient at the age of 6 months.*

oxygen therapy but never required mechanical ventilation. Apgar scores of 1 and 3 were assigned at 1 and 5 minutes, respectively. He remained in the nursery for 3 weeks and was discharged on nasogastric feedings. The baby was readmitted at 7 weeks of age for irritability, symptoms of upper respiratory infection, possible congestive heart failure, and failure to gain weight.

Physical examination showed a small, cyanotic, unusual appearing infant with multiple dysmorphic features (fig 1), which included length and weight markedly below the third centile; asymmetrical

facies; sparse hair; large anterior fontanelle; severe microcephaly; prominent occiput; receding forehead; hypertelorism; microphthalmia; corneal clouding; low set, posteriorly rotated ears; right-sided preauricular pit; micrognathia; high arched palate, prominent upper lip; widely spaced nipples; short sternum; grade 4/6 holosystolic murmur; hepatosplenomegaly; flexion deformities of both elbows; micromelia; arachnodactyly; 3rd and 4th fingers of the same length; partial syndactyly of the 3rd and 4th fingers; bilateral simian creases; hypoplasia of all interphalangeal creases; flexion contractures of the proximal interphalangeal joints; fisting with adduction deformity of the thumb and radial sway of the fingers; syndactyly of the 2nd to 4th toes; the 2nd and 5th toes overlap the 3rd and 4th toes, respectively, on the right; the 2nd toe overlaps the 3rd toe on the left; metatarsus adductus and cryptorchidism with both testes palpable in the inguinal canal. Laboratory data were unremarkable. Chest x-ray showed cardiomegaly with increased pulmonary vasculature. Sector scan of the heart

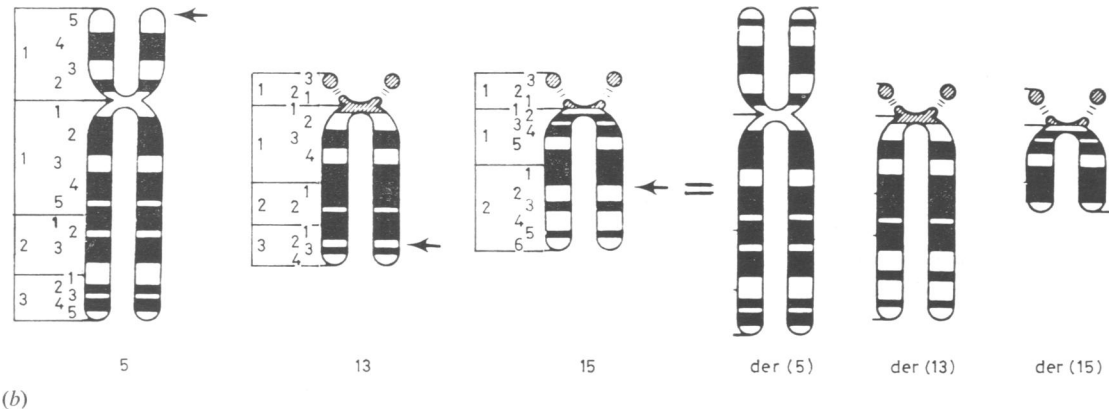
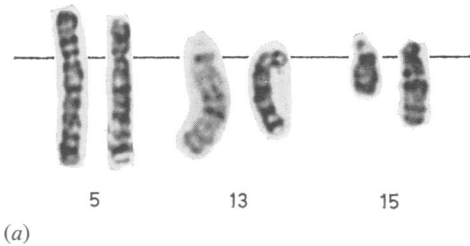


FIG 2 (a) *Partial karyotype of the mother with the derived chromosome on the left;* (b) *diagrammatic illustration of the complex rearrangement. Breakpoints are indicated by arrows.*

was compatible with an A-V canal and possible subaortic stenosis. Radiographic studies showed mild gastro-oesophageal reflux and a small hiatal hernia. Intravenous pyelogram and voiding cystourethrogram were normal.

The infant was discharged on digoxin and was continued on nasogastric feedings. Further cardiac evaluation is planned when the baby has attained a weight of $4\frac{1}{2}$ kg.

He was seen at follow-up at 6 months of age. Weight, height, and head circumference were 4050 g, 58 cm, and 32.5 cm, respectively, all still markedly below the third centile. He had attained none of the expected developmental milestones and was still maintained on tube feedings since his suck was too weak to deliver adequate calories orally. The baby has been seen in the emergency room on several occasions for recurrent bouts of otitis media and upper respiratory infections but has not required readmission to hospital.

CYTOGENETIC STUDIES

Chromosome preparations were obtained from short term phytohaemagglutinin-stimulated lymphocytes. Cells were analysed using GTG banding. The initial analysis of the proband's karyotype revealed two abnormalities, 5p+ and 13q+. The karyotype of the father was normal. The mother's analysis revealed a complex chromosome rearrangement involving chromosomes 5, 13, and 15, as illustrated in fig 2, and was interpreted as 46,XX,t(5;15;13)(p15;q22.00;q32). The proband would be interpreted as 46,XY,-5,-13,+der(5),+der(13),t(5;15;13)(p15;q22.00;q32)mat. Thus, he is trisomic for 15q22→qter and it is assumed he is also monosomic for the telomeric region of 5p.

Discussion

Complex chromosomal rearrangements occur rarely, as recently reviewed by Pai *et al.*⁵ In those cases where derivative chromosomes come from one parent, only maternally derived abnormalities have been described. This report is consistent with this observation.

The clinical features of patients with trisomy for distal 15q are compared in the table. Only those findings reported in three or more of the five published cases are included. The similarities noted suggest a pattern of common features that may result in an established chromosomal syndrome as more cases are accumulated.

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References

- Fujimoto A, Towner JW, Ebbin AJ, Kahlstrom EJ, Wilson NG. Inherited partial duplication of chromosome 15. *J Med Genet* 1974;11:287-91.

TABLE Clinical features in the reported cases of distal 15q trisomy

Clinical features	Case 1 ¹	Case 2 ²	Case 3 ³	Case 4 ⁴	Case 5 ⁴	Present report
Duplicated region	q22→qter	q21·2→qter	q15→qter	q21→qter	q21→qter	q22→qter
Sex	M	M	F	M	F	M
Birthweight (g)	2980	3650	2900			1820
Psychomotor retardation	+	+	+	+	+	+
Growth retardation	+	+	+	-		+
Microcephaly	+	+	+	-		+
Asymmetrical facies	+	+	+	+		+
Prominent occiput	+	+	+	+		+
Short neck		+	+	+		-
Antimongoloid palpebral fissures	+	+	+	+		+
Micrognathia	+	+	+	+		+
Prominent nose		+	+	+		+
Abnormal ears	+	+	+	+		+
High arched palate		+	+	+		+
Long upper lip		+	+	+		+
Distinct philtrum		+	+	-		+
Congenital heart disease	-	+	+	+	+	+
Simian creases	-		-	+	+	+
Abnormality of fingers/toes	+		+	+		+
Repeated respiratory difficulty	+	+	+			+
Hypertonia			+	+	+	-

- ² Turleau C, de Grouchy J, Chavin-Colin F, Roubin M. Trisomie 15q distale. *Ann Genet (Paris)* 1977;20:214-6.
- ³ Zabel B, Baumann W. Trisomie partielle pour la partie distale du bras long du chromosome 15 par translocation X/15 maternelle. *Ann Genet (Paris)* 1977;20:285-9.
- ⁴ Tzancheva M, Krachounova M, Damjanova Z. Two familial cases with trisomy 15q dist due to a rcp(5;15) (p14;q21). *Hum Genet* 1981;56:275-7.
- ⁵ Pai GS, Thomas GH, Mahoney W, Migeon BR. Complex chromosome rearrangements. Report of a new case and literature review. *Clin Genet* 1980;18:436-44.

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Familial pericentric inversion of chromosome 13 resulting in duplication 13q22→qter

SUMMARY A 10-year-old male with a recombinant (13)dup q chromosome is reported. The recombinant chromosome originated from a maternal pericentric inversion which was present in two of his four normal sibs. A segregation analysis of 60 pregnancies from which one of the parents was a carrier of inv(13) showed a significant predominance of males among the viable offspring.

Cases with duplication of a distal 13q segment have led to the detection of familial pericentric inversions

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of chromosome 13. De novo rearrangements between the homologous chromosomes 13 seem to be rare.¹ Another case of duplication 13q (distal) originating from a maternal pericentric inversion is presented here.

Case report

The proband, a male, was born in 1969, the fifth child of healthy non-consanguineous parents. At the time of birth his mother was 37 and his father 38 years old. The other four children were normal. There was no family history of abortions, birth defects, or mental retardation (fig 1).

At the age of 10 years his height was 113 cm, below the 3rd centile. He had severe psychomotor retardation, spastic diplegia of the legs, and myoclonic and akinetic seizures. The facial appearance was characteristic of partial trisomy for the distal segment of 13q (fig 2). The thumbs and big toes

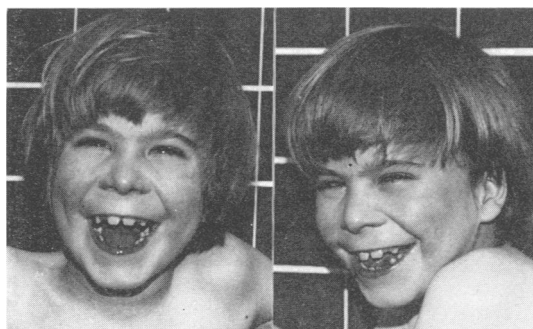


FIG 2 Proband at 10 years of age.

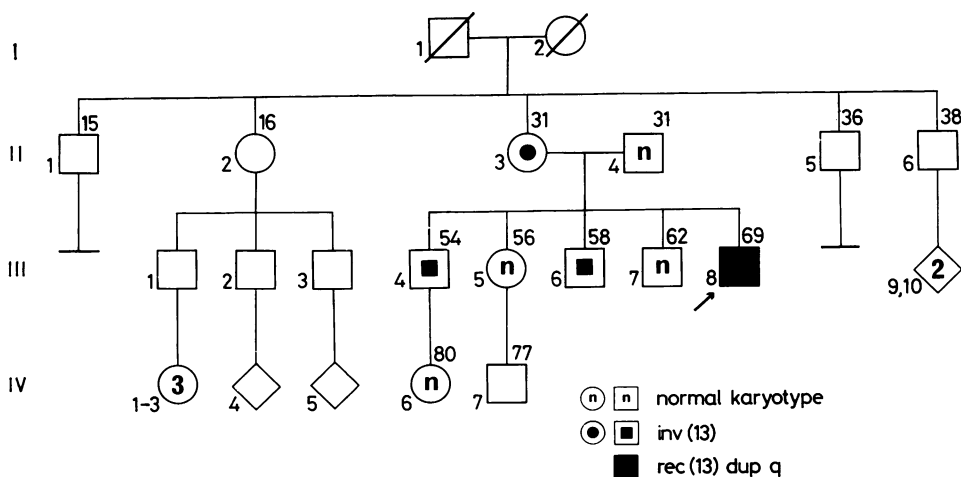


FIG 1 Family pedigree including years of birth.