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Severe mental retardation in six generations of a large South African family carrying a translocation t(6;10)(q27;q25·2)

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SUMMARY Partial monosomy 10q25·2→qter, detected in a newborn baby with multiple congenital abnormalities, was found to be derived from a balanced maternal translocation t(6;10)(q27;q25·2). The pedigree of six generations of the family is presented. In an extensive cytogenetic study of this family, the chromosome complements of 57 subjects, potentially capable of carrying some form of this translocation, were analysed. A total of 14 male carriers (four obligatory) and 14 female carriers (three obligatory) of this translocation was found. Partial trisomy 10q25·2→qter, associated with severe mental retardation, occurred in nine cases, eight males and one female. Two of these eight males were detected prenatally and subsequently therapeutically aborted. The phenotypes of the family members with partial trisomy 10q25·2→qter are compared to each other and to those reported in publications. No further cases of partial monosomy 10q25·2→qter were encountered. A review of published reports of partial monosomy and partial trisomy 10qter is given. The apparent absence of infertility, the occurrence of many first trimester miscarriages, and the marked sex ratio are discussed.

The application of improved culture and staining techniques has enabled the study of longer chromosomes and, consequently, very small aberrations in the detailed banding pattern of each chromosome can be more easily detected. As partial monosomy and partial trisomy of specific regions of the chromosomes are associated with characteristic phenotypic abnormalities, an accurate determination of the breakpoints facilitates the classification of new clinical syndromes.

Francke[1] recorded the first case of partial trisomy for the distal two-thirds of the long arm of chromosome 10 in a female baby whose mother was found to carry a balanced translocation t(10;15). Partial trisomy for the distal third of the long arm (10q22→qter) was first reported by Laurent *et al*[2] in a female baby and also in her male first cousin. A balanced familial translocation t(1;10)(q44;q22) was traced back to their maternal grandfather. Yunis and Sanchez[3] proposed that the specific phenotype of their patient, who was partially trisomic for 10q24→qter, be recognised as a new syndrome. Subsequently there have been published reports of partial trisomy 10q22→qter,[4] partial trisomy 10q23→qter,[5] partial trisomy 10q24→qter,[6–18] partial trisomy 10q24·2→q25·3,[19] and partial trisomy 10q25→qter.[17 20 21]

The partial trisomy 10q syndrome has been delineated by Smith[22] as trisomy for 10q24→qter. Both pre- and postnatal growth retardation occurred in the majority of cases. The characteristic phenotype has unique craniofacial features, including microcephaly, a flat face with a large forehead and high arched eyebrows, short palpebral fissures, microphthalmia, a broad and depressed nasal bridge, a bow shaped mouth with prominent upper lip, cleft palate, and malformed, posteriorly rotated ears. Limb, heart, and renal malformations, in addition to severe mental retardation, cause many such subjects to be bedridden and unable to communicate.

The clinical characteristics of partial trisomy 10q24→qter and partial trisomy 10q25→qter have more recently been separately described by Schinzel,[23] after reviewing 24 and 11 cases respectively. It appears that subjects in the latter group, although also severely mentally retarded, have a

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comparatively normal birth weight and lack major heart, renal, and palatal malformations and can thus survive to an adult age.

It has, however, not yet been possible to delineate a syndrome for partial monosomy 10q, as a constant phenotype has still not emerged from the nine reported cases described. Partial monosomy 10q23→qter,[24] partial monosomy 10q25→qter,[25–27] and partial monosomy 10q26→qter[28–32] have been reported.

In the large pedigree presented in this article, the region 10q25·2→qter has been found to be partially trisomic in nine subjects. The clinical features of six of these are presented and compared. This region was found to be partially monosomic in only one case, the proband.

Case report of the proband

The index patient was referred for multiple congenital abnormalities and indeterminate sex. The baby was born by Caesarian section at 36 weeks' gestation because of breech presentation. At the time of birth, the healthy and unrelated father and mother were 25 and 23 years old respectively. The mother had had one previous pregnancy which ended spontaneously in a first trimester miscarriage.

The birth weight was 2440 g and the head circumference was 32 cm. Asphyxia neonatorum was present. The baby had scaphocephaly and a small anterior fontanelle. Examination revealed a wide, prominent nose bridge, a slight upward slant of the lateral canthi, a highly arched palate, micrognathia, low set, big, abnormally shaped ears, and a short broad neck (fig 1). The nipples were widely spaced. A cardiac murmur and signs of respiratory distress were present. The hands were broad with low placed thumbs and long, broad fingers. The hands were held in flexion and ulnar deviation. There was bilateral clinodactyly. A simian crease was present on the right palm. The lower limb abnormalities included talipes calcaneovarus and congenital hip dislocation. The urogenital tract showed labioscrotal folds, a phallus, perineal hypospadias, and an anteriorly displaced anal opening.

The patient died 15 days after birth. Necropsy findings confirmed the presence of a heart defect, a small ventricular septal defect. The gonads, found intra-abdominally, were a normal testis in the left internal inguinal aperture and a small nodule of testicular tissue in the right pelvic area. A small structure, possibly a rudimentary uterus, was found posterior to the bladder. This was histologically identified as fibromuscular tissue with tubules of undefined origin. Only one ectopic, dysplastic kidney was present; this was situated on the right side of the pelvis.

Cytogenetic analysis of the family

Standard procedures were used for the cultivation of blood lymphocytes, skin fibroblasts, gonadal tissue, and amniotic fluid. Methotrexate was used to improve the quality and length of the chromosomes in the lymphocyte cultures. The chromosomal DNA was denatured by trypsin or heat or both and subsequently stained with Giemsa[33] or quinacrine[34] stains. Banding analysis and breakpoint determination were done according to the Paris Conference[35] and the ISCN.[36]

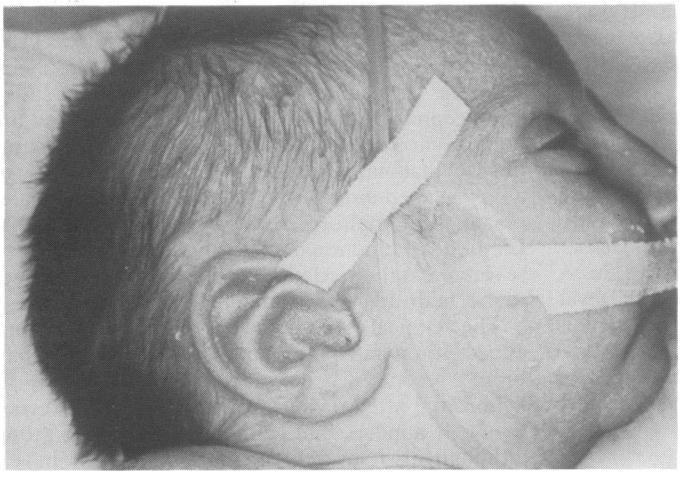

FIG 1 *Proband (V.35) at birth.*

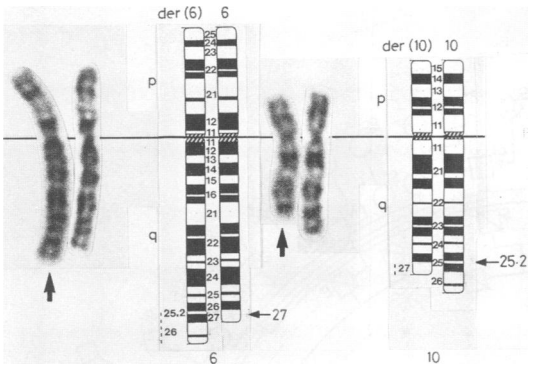

FIG 2 *G banded chromosomes 6 and 10 involved in the familial reciprocal translocation t(6;10)(q27;q25·2). Large arrows indicate derivative chromosomes. Small arrows indicate breakpoints on the diagrammatic representations of these chromosomes.*

In the proband, a 46,XY,der(10),t(6;10)(q27;25·2) chromosome complement (breakpoints shown in fig 2) was found in the lymphocytes and in the left gonad. The chromosome analysis of the mother of the proband revealed a balanced reciprocal translocation (breakpoints shown in fig 2): 46,XX,t(6;10)(q27;q25·2). The father's karyotype was normal.

The large pedigree, including six generations of this family, is presented in fig 3. The results of the chromosome analyses of 56 family members are given in table 1. The proband was the only case with partial monosomy 10q25·2→qter. Two (table 1, V.36 and V.37) of the eight cases of partial trisomy 10q25·2→qter were found prenatally in two subsequent pregnancies of the mother of the proband; these pregnancies were both terminated at 20 weeks. A balanced translocation t(6;10)(q27;q25·2) was found in 21 subjects (10 males and 11 females); another seven deceased persons (table 1, I.5, II.1, II.10, III.1, III.5, III.21, and IV.11) were assumed to be obligate carriers. Twenty-six subjects had a normal karyotype: 11 were 46,XY and 15 were 46,XX.

TABLE 1 *Chromosome analysis of the pedigree.*

Chromosome complement	*No of cases*	*Pedigree No*
46,XY	11	III.13–14, III.20, IV.19–21, IV.65, IV.69, IV.71, V.3, VI.4
46,XX	15	III.4, III.19, IV.5, IV.24–25, IV.60–64, IV.66, V.20, V.26, V.30, V.38, VI.1
46,XY,t(6;10)(q27;q25·2)	10	III.23, III.30–31, IV.10, IV.54, IV.58, IV.72–73, V.2, V.23
46,XX,t(6;10)(q27;q25·2)	11	IV.1, IV.57, IV.59, IV.67–68, IV.70, V.1, V.18–19, V.31, VI.2
46,XY,der(6),t(6;10)(q27;q25·2)	7	IV.56, V.17, V.22, V.27, V.36–37, VI.3
46,XX,der(6),t(6;10)(q27;q25·2)	1	V.21
46,XY,der(10),t(6;10)(q27;q25·2)	1	V.35
Total	56	

Table 2 shows the chromosome complement of the offspring of 21 carriers. Of the 53 phenotypically normal persons born to male and female carriers, 27 had a balanced karyotype and 26 had normal chromosomes. In the group where the father was the carrier, it was found that 50% of the offspring had a balanced karyotype and 35% of the offspring had a normal karyotype. In the group where the mother was the carrier, these values were 28% and 48%, respectively. In the group of 12 phenotypically abnormal subjects, there was one case of partial monosomy 10q25·2→qter, nine cases of partial trisomy 10q25·2→qter, and two congenitally abnormal females, who died neonatally before the initiation of this study. An institutionalised male (fig 3, III.29), born with the phenotypic features of partial trisomy 10q, died without a cytogenetic evaluation; he has been included in the above nine cases. A child with partial trisomy 10q was born to four of the 11 carrier fathers and to three of the 10 carrier mothers; a fourth carrier mother (the mother of the proband) had two such pregnancies teminated. The number of miscarriages recorded for male and female carriers was similar, 10 and nine respectively; a reliable figure could not be accurately assessed for the earlier generations.

Male carriers had 24 male and 16 female children. Female carriers had 15 male and 10 female children. It is interesting to note that, in each case, the male to female ratio is 3:2. The significance thereof will be dealt with in the discussion.

An amniocentesis was carried out in seven cases where one of the parents was a carrier of the t(6;10)(q27;q25·2) translocation. The results of the chromosome analyses of the amniotic fluids are as follows: three normal females (V.30, V.38, and VI.1), two carrier females (V.31 and VI.2), and two males with partial trisomy 10q (V.36 and V.37). These findings were confirmed in the skin fibroblasts of the fetus after a therapeutic termination in the last two cases, and in the blood lymphocytes after birth in three of the first five cases. The recently evaluated pregnancies V.38 and VI.2 have not yet reached term; follow up studies will be carried out postnatally.

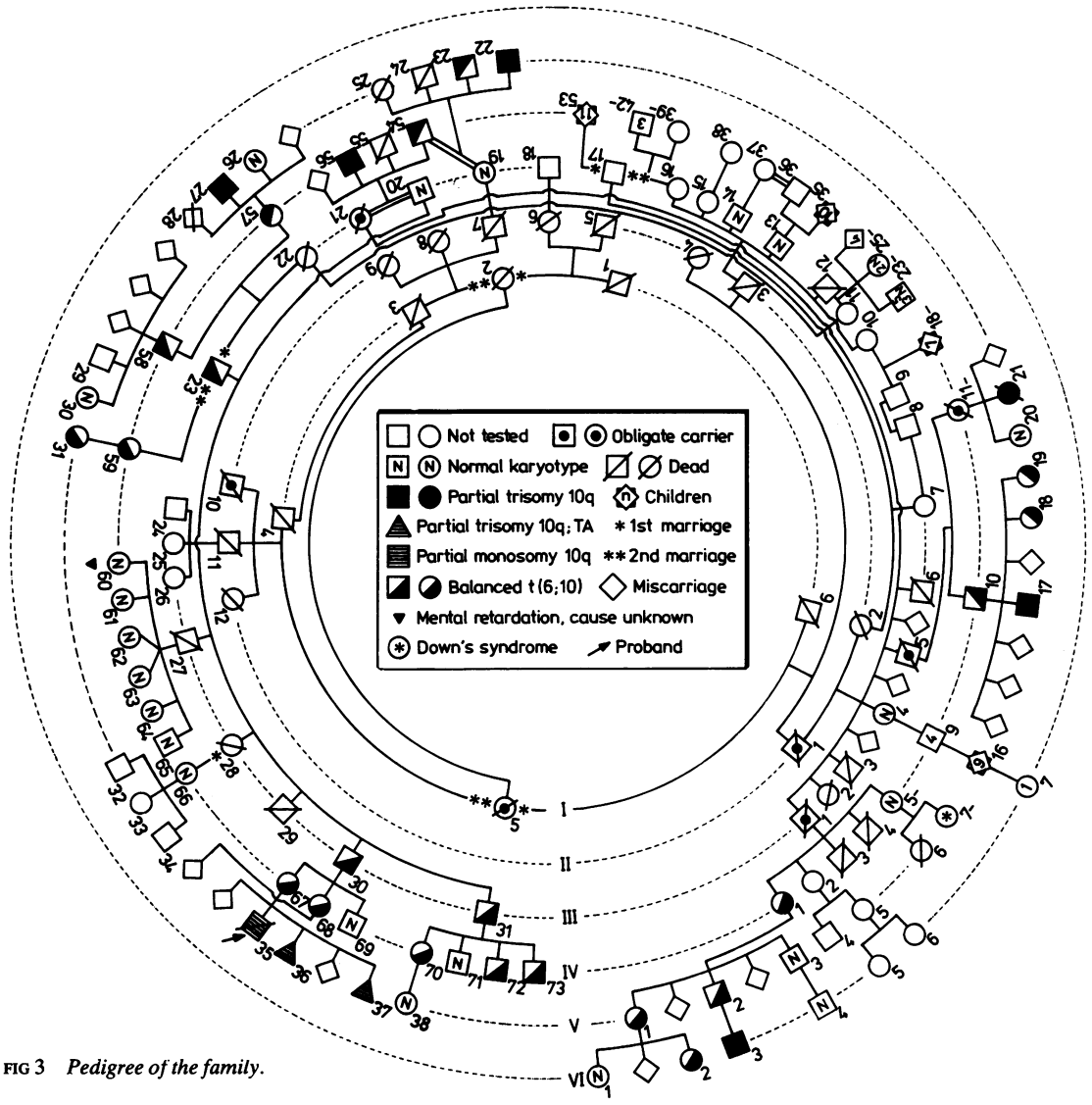

FIG 3 *Pedigree of the family.*

TABLE 2 *Chromosome complement of the offspring of the carriers.*

Karyotype	*Offspring of 11 male carriers*		*Offspring of 10 female carriers*		*Totals*	
	46,XY	*46,XX*	*46,XY*	*46,XX*		
Normal	10	4	6	6	26	53
Balanced	10	10	4	3	27	
Partial trisomy 10q	4		4	1	9	12
Partial monosomy 10q			1		1	
Congenital abnormality: not identified		2			2	
Miscarriages	10		9		19	

Case reports of family members with partial trisomy 10q

CASE 1

IV.56 is the third child of normal, consanguineous parents. After an uneventful pregnancy, he was born at term by normal vertex delivery. His birth weight is unknown. His father and his mother were 38 and 37 years old, respectively, at the time of his birth.

When he was evaluated for the first time at the age of 33 years, he presented with the following clinical features (fig 4): normal weight (57 kg), growth retardation (height 160 cm), severe mental retardation, a relatively large head (head circumference 55 cm), brachycephaly, a large high forehead, long facies, narrow palpebral fissures, mongoloid slanting eyes, hypertelorism (inner canthal measurement 4 cm, outer canthal measurement 11 cm), a prominent nasal bridge, prognathism, large ears, drooping shoulders, severe kyphoscoliosis, thoracic dysplasia, long thin fingers, and a valgus deformity of the feet. Since the age of 30 years, he has become progressively deaf.

CASE 2

V.22 is the oldest child of normal, consanguineous parents. After an uneventful pregnancy, he was born at term by normal vertex delivery; the birth weight was 3100 g. His father and mother were 22 and 21 years old, respectively, at the time of his birth.

At the age of 19 years he presented with the following features (fig 5): weight 44 kg, growth retardation (height 157 cm), severe mental retardation, a relatively large head (head circumference 54 cm), brachycephaly, oval shaped facies, arched eyebrows, mongoloid slanting eyes, hypertelorism (inner canthal measurement 4 cm, outer canthal measurement 12 cm), a prominent nasal bridge, severe kyphoscoliosis, thoracic dysplasia, a ventricular septal defect type murmur over the left precordial area, long thin fingers with clubbing and peripheral cyanosis, bilateral camptodactyly of the fifth fingers, and a valgus deformity of the feet. His heart lesion has not been investigated.

CASE 3

V.21 is the second child of normal parents. After an uneventful pregnancy, she was born at term by normal vertex delivery; her birth weight is unknown. The father and mother were 34 and 28 years old, respectively, at the time of the birth. As a baby she was hypotonic.

At the age of 13 years she was admitted to a mental institution where she presented with the following clinical features (fig 6): severe mental retardation, a relatively large head, brachycephaly, a large high forehead, long flat facies, fine arched eyebrows, narrow palpebral fissures, a prominent nasal bridge, retrognathia, a high arched palate, large ears, drooping shoulders, scoliosis, thoracic dysplasia, long thin fingers, camptodactyly of the

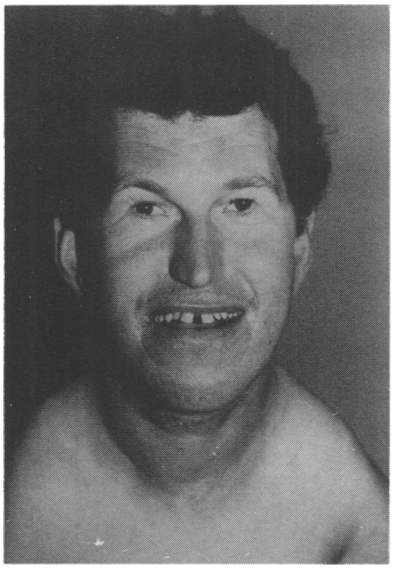

FIG 4 *Case 1 (IV.56) at the age of 33 years.*

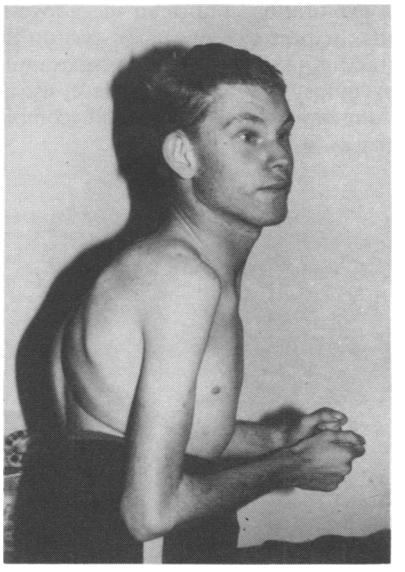

FIG 5 *Case 2 (V.22) at the age of 19 years.*

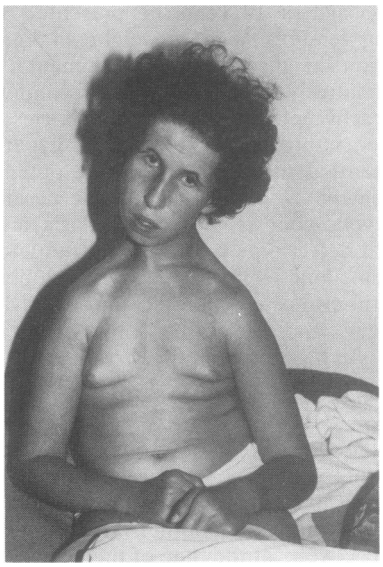

FIG 6 *Case 3 (V.21) at the age of 13 years.*

second finger of the right hand and the fifth finger bilaterally, hypoplastic dermal ridges, ulnar deviation of the hands, a valgus deformity of the feet and a wide space between the first and second toes (fig 7).

At the age of 15 years she was investigated for a possible renal mass. A renal angiogram demonstrated a horseshoe shaped kidney with multiple renal arteries supplying both sides of the kidney. Surgical exploration confirmed the above findings, as well as the presence of a large cyst on the upper pole of the right kidney. Histological examination of a kidney biopsy revealed multiple cysts. She died shortly afterwards of postoperative complications. No necropsy was done.

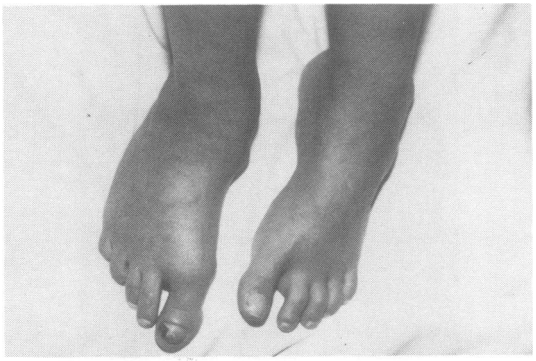

FIG 7 *Case 3 (V.21) showing abnormalities of the feet.*

CASE 4

VI.27 is the second child of normal parents. After an uneventful pregnancy he was born at term by forceps delivery; his birth weight was 3200 g. His father and mother were 30 and 24 years old, respectively, at the time of his birth. He presented with an undescended testis on the right side and had surgical repair of two inguinal hernias. He was admitted to a mental institution at the age of 20 months.

When he was evaluated at the age of 15 years, he was still inarticulate. He presented with growth retardation (height 132 cm), weight 30 kg, severe mental retardation, a relatively big head (fig 8), brachycephaly, a large high forehead, oval facies, narrow palpebral fissures, bilateral epicanthic folds, mongoloid slanting eyes, hypertelorism (inner canthal measurement 4 cm, outer canthal measurement 12 cm), a flat nasal bridge, a short nose, a long philtrum, a bow shaped mouth, a high arched palate, low set ears, a short neck, kyphosis of the lumbar vertebrae, long thin fingers, a simian crease on the right palm, hypoplastic dermal ridges, and overlapping of the second and third toes. A radiological examination of the spine, pelvis, and hands was performed. The lumbar kyphosis was confirmed and bilateral coxa valga and a generalised decrease in density were revealed, as well as a delay in skeletal maturation. The pisiform bones were absent bilaterally.

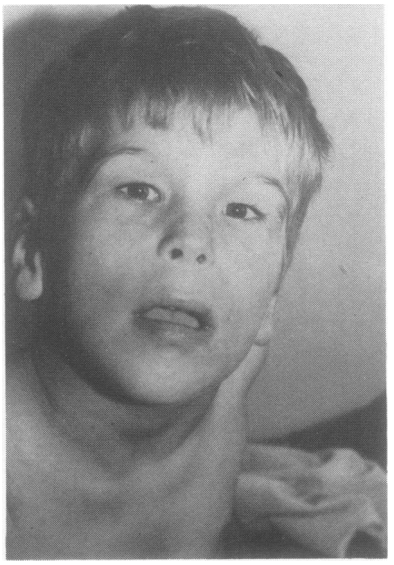

FIG 8 *Case 4 (VI.27) at the age of 15 years.*

CASE 5

VI.3 is the only child of normal parents. After an uneventful pregnancy he was born at term by Caesarian section because of cephalopelvic disproportion; he weighed approximately 4000 g. Both parents were 26 years old at the time of his birth. He presented as a strange looking baby (fig 9), with hypotonia, brachycephaly, a third fontanelle, narrow palpebral fissures, mongoloid slanting eyes, bilateral epicanthic folds, hypertelorism, a flat nasal bridge, an accessory nipple on the left side of the thorax, a pilonidal sinus, and a systolic heart murmur. On heart catheterisation he was shown to have a preductal aortic coarctation, a ventricular septal defect, and a patent ductus arteriosus. The coarctation was surgically repaired at the age of 4 months.

At the age of 4 years he presented with the following clinical features: weight 15·6 kg, normal length (99 cm), severe mental retardation, a relatively large head (head circumference 52 cm), brachycephaly, a large high forehead, an oval flat facies, narrow palpebral fissures, bilateral epicanthic folds, mongoloid slanting eyes, hypertelorism (inner canthal measurement 4 cm, outer canthal measurement 12 cm), a short nose, a long philtrum, a bow shaped mouth, large ears, a short neck, a wide space between the first and second toes, and overlapping of the second and third toes, bilaterally.

CASE 6

VI.39 was a male fetus terminated at 20 weeks' gestation after a partial trisomy 10q25·2→qter chromosome constitution had been detected in the amniotic fluid. This was the fifth pregnancy of the mother of the proband; her third pregnancy had been terminated at 20 weeks' gestation for the same reason.

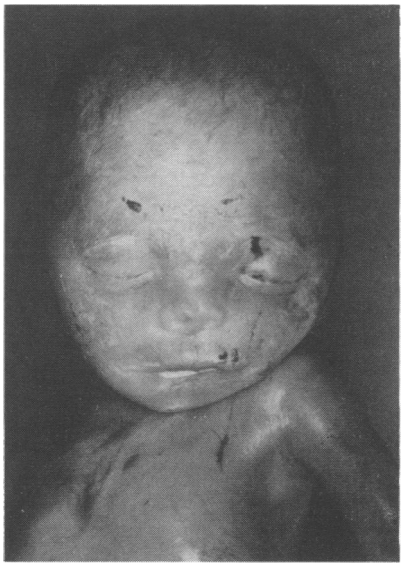

FIG 10 *Case 6 (VI.39) at 20 weeks' gestation.*

The fetus (fig 10) presented with a relatively large head, brachycephaly, a large forehead, flat oval facies, antimongoloid slanting eyes, hypertelorism, a flat nasal bridge, a short nose, a long philtrum, micrognathia, and a short neck. No other abnormalities could be detected clinically. No necropsy was performed.

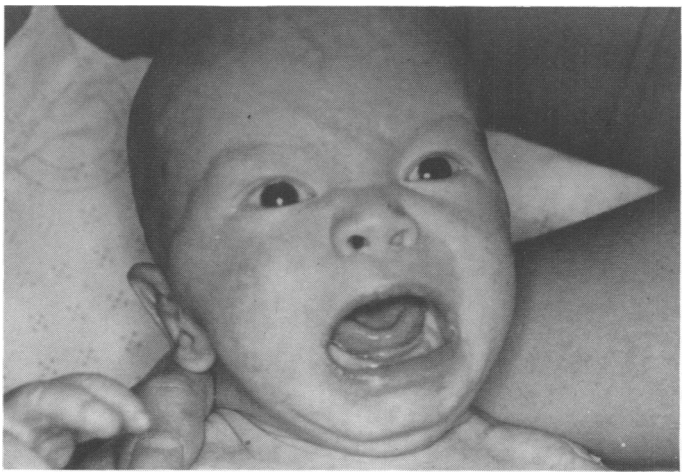

FIG 9 *Case 5 (VI.3) at birth.*

Discussion

Aurias *et al*[37] reported an excess of telomeric breakpoints in all cases of translocations ascertained through offspring with an unbalanced reciprocal translocation, especially in cases of 2:2 segregation (as in the present study). They also found an excess of breakpoints in 10q.

Among the phenotypically normal subjects in the present study, there was a fairly equal distribution of balanced carriers and chromosomally normal offspring, as is theoretically expected; a significant excess of balanced carriers has, however, often been reported.[38]

In the present study, an altered sex ratio (three males:two females) was observed among the offspring of both male and female carrier parents. Among the offspring with a partial trisomy 10q25·2→qter, a very marked sex difference was found (eight males:one female). A preponderance of affected males has previously been reported.[15] These sex ratios and the occurrence of first trimester miscarriages recorded in the pedigree indicate that certain unbalanced chromosome complements are less compatible with life than others. The single case of partial monosomy 10q25·2→qter in this study indicates very strongly the reduced viability of fetuses with this deletion (the proband died 15 days after birth). This factor may contribute significantly to the number of miscarriages recorded. Male fetuses with partial trisomy 10q25·2→qter appear to have a selective advantage for survival over their female counterparts and the non-viability of female fetuses with this abnormality could account for some of the miscarriages.

Petrosky and Borgaonkar[38] reviewed 327 pedigrees, including those involving translocations of 6q and 10q. They recorded a high fetal loss rate for both male and female carriers of 10q translocations and also for female carriers of 6q translocations. In addition to the size of the chromosome imbalance produced, loss or duplication of critical loci may be involved in the production of some chromosome complements which are incompatible with fetal survival.

Glutamic oxaloacetic transaminase (the enzyme which catalyses the reversible conversion of aspartate and α-ketoglutarate to oxaloacetate and glutamate) plays a significant role in maintaining nitrogen balance in metabolism. By electrophoresis it has been possible to demonstrate two forms of human glutamic oxaloacetic transaminase (GOT), the mitochondrial and the cytoplasmic forms. Creagen *et al*[39] have shown that they are coded for by separate loci. The structural gene coding for cytoplasmic GOT has been assigned to chromosome 10 and localised to 10q24→qter[39–43] using interspecific somatic cell hybrids and also by gene dosage studies. More recently, this gene has been localised to 10q24→q25,[44] 10q24,[45 46] and 10q26·1 (or 10q25·3).[47] Similar studies on the affected members of this pedigree would help to localise the position of the gene.

Dysmorphic features found in all or most of the six cases of partial trisomy 10q25·2→qter presented in table 3 include growth retardation, severe mental retardation, a relatively large head, brachycephaly, a large high forehead, narrow

TABLE 3 *Comparison of clinical features of present six cases of partial trisomy 10q25·2→qter.*

Clinical features	*Case 1*	*Case 2*	*Case 3*	*Case 4*	*Case 5*	*Case 6*
Mental retardation	+	+	+	+	+	
Aggressive behaviour	+		+		+	
Growth retardation:						
Height <3%	+	+		+	−	
Weight <3%	−	+	−	+	−	
Head circumference <3%	−	−		−	−	
Brachycephaly	+	+	+	+	+	+
Large high forehead	+	−	+	+	+	+
Long facies	+	−	+	−	−	−
Oval facies	−	+	−	+	+	+
Flat facies	−	−	+	−	+	+
Fine arched eyebrows	−	+	+	−	−	−
Narrow palpebral fissures	+	−	+	+	+	−
Epicanthus	−	−	−	+	+	−
Mongoloid slanting eyes	+	+	−	+	+	−
Hypertelorism	+	+		+	+	+
Prominent nasal bridge	+	+	+	−	−	−
Short nose	−	−	−	+	+	−
Long philtrum	−	−	−	+	+	+
Bow shaped mouth	−	−	−	+	+	−
Micro/retrognathia	−	−	+	−	−	+
Low set ears	−	−	−	+	−	
Big ears	+	−	+	−	+	
Short neck	−	−	−	+	+	+
Drooping shoulders	+	−	+	−	−	−
Kyphoscoliosis	+	+	+	+	−	−
Dysplasia of thorax	+	+	+	−	−	−
Long thin fingers	+	+	+	+	−	−
Camptodactyly	−	+	+	−	−	−
Simian crease	−	−	−	+	−	−
Hypoplastic dermal ridges	−	−	+	+	−	−
Increased space between 1st and 2nd toes	−	−	+	−	+	−
Pes planovarus/valgus	+	+	+	−	−	−
Overlapping toes	−	−	−	+	+	−
Congenital heart disease	−	+	−	−	+	
Renal abnormalities			+			
Hypotonia			+		+	
Inguinal hernia				+		
Cryptorchidism				+		
High arched palate			+	+	−	
Ulnar deviation of hands			+			
Delayed bone maturation				+		

TABLE 4 *Comparison of clinical features of cases with monosomy 10qter grouped according to breakpoints.*

	Chieri et al[24]	*Lewandowski et al*[25]	*Mulcahy et al*[27]	*Wegner et al*[26]	*This report*	*Turleau et al*[28]	*Taysi et al*[29]	*Evans-Jones et al*[30]	*Shapiro et al*[32]	*Shapiro et al*[32]	*Shapiro et al*[32]	*Zatterale et al*[31]
Deleted chromosomal segment	q23→ qter	q25→ qter	q25→ qter	q25·2 →qter	q25·2 →qter	q26→ qter	q26→ qter	q26→ qter	q26→ qter	q26→ qter	q26→ qter	q26.1→ qter
Age of patient	10/12	7 y	11 wk	Newborn (died d9)	Newborn (died d15)	11 y	Newborn (died d23)	20/12	3/12	2/12		16/12
Sex	F	F	M	F	Ambiguous	F	F	M	F	F	F	M
Birth weight (g)	2700	2594	3010	1770	2440	1900	2290	2700	2466	3458	3373	2800
Gestation (wk)	Term	?	39	36	36	37	Term	Term	35	?	Term	?
Growth retardation	+	+	−	+	+	+	+	−	+	+	+	+
Asphyxia neonatorum or RDS	+	+	+	+	+	+	+	−	+		+	−
Mental retardation	+	+	?	?	?	+	?	+	+	+	+	+
Microcephaly	+	+	−	+	+	+	+	−	+	+		−
Hypertelorism	+	−	+	+		+	−	+				+
Strabismus	+	+	−	?	?	+	?	+			+	−
Prominent nasal bridge	+	+	+	?	+	+	+	−				+
Small nose/anteverted nostrils	−	+	+	−	−	−	+	−		+		?
Large ears		−	+	?	+	+		−				+
Malformed/low set ears	+	+	+	+	+	−	+	+		+		+
Palpebral fissures	Long, narrow						Deep set, short		Narrow			Deep set
Upward slant		+			+							
Downward slant			+	+								
Horizontal	+					+						+
Short neck	+	+	+		+	−	+					+
Clinodactyly	−	−	+	−	+	+						+
Congenital heart defect	−	+	+	+	+	−	+	−	−	+	+	−
Cloaca	−	+	−	+	Anal displace-ment	−	−					
Cryptorchidism			+		+			+				+

palpebral fissures, mongoloid slanting eyes, hypertelorism, kyphoscoliosis, and long tapering fingers.

The present cases differed from seven reported cases of partial trisomy 10q25→qter[17 20 21] by the absence of microcephaly, microphthalmia, ptosis of the eyelids, cleft palate, and dislocation of the hips.

The present cases differ from the partial trisomy 10q syndrome, that is, partial trisomy 10q24→qter,[22 23] in that there was a normal birth weight, but absence of microcephaly, microphthalmia, cleft palate, ptosis of the upper eyelids, anteverted nostrils, malformed ears, pectus excavatum, clenched overlapping fingers, and rockerbottom feet. Four of the present cases had mongoloid slanting eyes; antimongoloid slants were found in published reports. Only two of the present cases had clinical heart defects and kidney abnormalities were confirmed in only one case. Additional features found in this group are drooping shoulders (two cases) and progressive deafness (case 1); the latter could not be investigated.

Decreased bone maturation and 11 pairs of ribs are described in the partial trisomy 10q syndrome, but, unfortunately, all the present cases could not be radiologically investigated. The clinical cyanotic congenital heart lesion of case 2 could not be investigated. No IQ estimations could be done.

Most of the features considered to be characteristic of the partial trisomy 10q syndrome[23] appear to be associated with partial trisomy of 10q25→qter. A partial trisomy of the region 10q22→q24 may not contribute significantly to the phenotype.[15 21]

Variations of certain features between the present familial cases and other published cases may be due to loss of telomeric material on the other chromosome involved in the translocation.[9] No resemblance could, however, be found between the present six cases and those patients with deletions of the long arm of chromosome 6.[48] Yunis and Lewandowski[15] found that there was a general tendency for 10q to translocate to a telomeric region of another chromosome with minimal or no reciprocal loss of genetic material. This could explain the similarity of persons with the partial trisomy 10q syndrome and hence aid the clinical diagnosis of this syndrome.

There are nine reports of a partial deletion of the distal part of the long arm of chromosome 10. The clinical features of these cases are presented in table 4. In four cases, the breakpoint occurred in 10q25 and asphyxia neonatorum, abnormal palpebral fissures, low set, malformed ears, and a congenital heart defect were present in all. The two female patients had cloaca type defects and the two male patients had cryptorchidism.

Although asphyxia neonatorum, microcephaly, growth retardation, a prominent nasal bridge, and low set, malformed ears seemed to be the most common abnormalities, more cases need to be described to ascertain whether these features will eventually delineate the partial monosomy 10q syndrome.

Conclusion

From the pedigree it can be concluded that the fertility of male and female subjects carrying a balanced translocation t(6;10) has not been adversely affected. There were more phenotypically normal offspring than phenotypically abnormal offspring. In the former group, there were similar numbers of karyotypically normal subjects and balanced carriers. The most common unbalanced chromosome abnormality among the offspring was found to be partial trisomy 10q25·2→qter associated with severe mental retardation; eight of the nine cases were males. Offspring with partial monosomy 10q25·2→qter did not survive. Spontaneous miscarriages were often recorded. Genetic counselling and the facility of amniocentesis or chorionic villi sampling are of great importance in such pedigrees for the prenatal detection of phenotypically abnormal offspring.

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