Human Heredity *23:* 568–585 (1973)

An (11;21) Translocation in Four Generations with Chromosome 11 Abnormalities in the Offspring

A Clinical, Cytogenetical, and Gene Marker Study[1]

PETREA JACOBSEN, M. HAUGE, K. HENNINGSEN, N. HOBOLTH, MARGARETA MIKKELSEN and J. PHILIP

Brejning Institute for Research in Mental Retardation, Cytogenetic Department, Børkop; Institute of Clinical Genetics, University of Odense, Odense; Blood Group Department, University Institute of Forensic Medicine, Copenhagen; Paediatric Department, Kolding Hospital, Kolding; Cytogenetic Department, John F. Kennedy Institute, Glostrup, and Chromosome Laboratory, Department of Obstetrics and Gynecology, Rigshospitalet, University of Copenhagen, Copenhagen

Abstract. A family in which a translocation t(11; 21) (q23;q22) was segregating through three generations was studied clinically and cytogenetically. Individuals monosomic for the distal part of the long arm of chromosome No. 11 showed severe malformations and retardation. A patient trisomic for this part of chromosome No. 11 was mentally retarded but less severely affected. Marker gene studies could exclude the location of several blood group loci at the distal part of the long arm of chromosome No. 11, but did not give any positive evidence of linkage to this part.

Key Words
Congenital malformations
Chromosome translocation
Marker loci assignment

Fluorescence and Giemsa banding techniques have made it possible to identify all human chromosomes and to determine breakpoints in rearrangements. With fluorescence technique, we could identify a translocation involving chromosomes No. 11 and 21. The translocation chromosomes were segregating in the family.

The family was ascertained through an infant with malformations (case 1). The child had a 46,XX,11q- karyotype.

Family History

The proposita was born in 1968. Nine months later, a paternal second cousin with the same type of malformations was born. The family was then evaluated and the chromosomes examined. A translocation between the long arm of a C group chromosome and the long arm of a G group chromosome was segregating. When banding technique was introduced, the translocation type was identified as (11;21)(q23;q22).

[1] This work was supported in part by the Danish Medical Research Council and the Danish National Board of Social Welfare, Department of Mental Retardation.

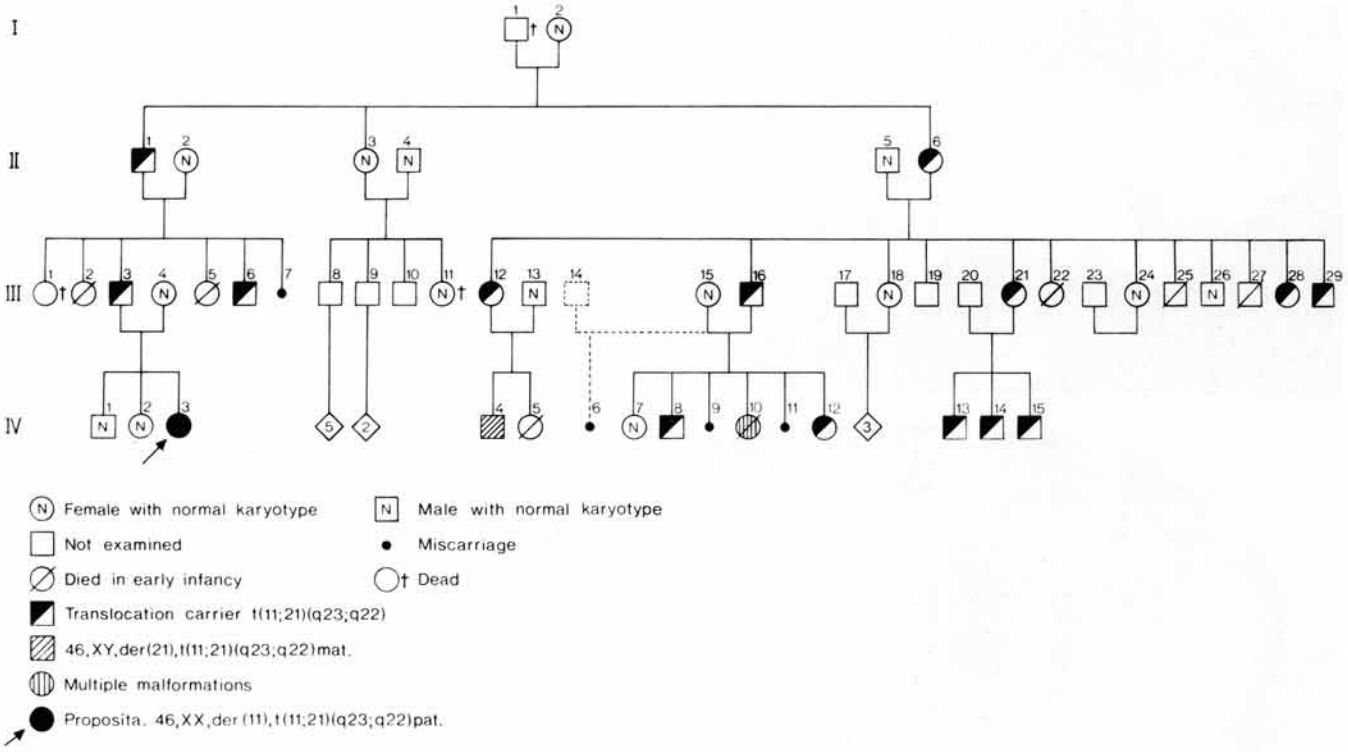

Fig. 1. Pedigree of the family.

Fig. 2. Case 1. *a* At the age of 5 weeks. Note narrow cranium with keel-formed forehead, hypertelorism and broad-bridged nose. *b* Note slanting forehead, low hairline, low-set malformed ears, ulnar deviation of second finger, and hammer toe.

The pedigree of the family is given in figure 1 and a more detailed description of the family in the Appendix.

Case Histories

Case 1.

The proposita (individual IV–3 in the pedigree) was born in July, 1968, five weeks before term after an uneventful pregnancy; birth weight 2,000 g, length 46 cm. Her mother was 24 years and the father 25 years at the time of her birth. The patient is the youngest of three children. The elder brother, sister, and mother are healthy. The father is disabled because of a traffic accident.

At birth the child was oedematous with respiratory distress for which reason she was treated in an incubator with oxygen. Because of failure to thrive, the patient was transferred to a paediatric department at the age of five weeks.

At that time (fig. 2a, b) her weight was 2,320 g, her length 48 cm. The cranium was narrowed from side to side and the frontal region was formed like a keel. The occipito-frontal circumference was 32 cm. The hair-line was low posteriorly. Ocular findings included epicanthus, hypertelorism and mongoloid slant of the palpebral fissures. The nose was broadbridged. The upper lip was short and the chin receding. The ears were low-set and slightly malformed with an indicated double helix. The palate was high arched and narrowed.

Stethoscopy of the heart revealed a strong systolic murmur, best heard along the left sternal border. The extremities were hypertonic with brisk deep reflexes and indicated foot clonus. The feet were held in an equinovarus position, and the big toes were hammer-shaped. The hands were in a clenched fist position, and the second finger showed ulnar deviation. The right hand was broad, the left was normal. The fingers were short, the fourth and fifth finger being relatively shorter than the others. The fifth finger was curved on both sides. Simian creases were present bilaterally.

The child continuously failed to thrive, and physical and mental development was retarded. She was discharged from the hospital at the age of 4 months and was cared for at home. At the age of 14 months, her development was estimated to correspond with that of a 4-month-old child. She was able to keep her head upright without support, could not sit alone without support, she could reach out for things passed to her. The patient died at home at the age of 19 months. Autopsy was not performed.

Laboratory investigations. Haemoglobin, erythrocytes, leucocytes, and differential counts were normal. In the urine neither protein nor glucose were found and the sediment was normal. Phenylpyruvic reaction was negative.

ECG was normal.

Slightly increased activity of all lactate dehydrogenase (LDH) isoenzymes were found. Galactose-1-phosphaturidyltransferase was normal. Serum electrophoresis was normal. Qualitative cellulose-acetate electrophoresis of urinary acid mucopolysaccharides revealed a normal pattern.

For blood, serum and enzyme types, see table II.

Radiographic examination. The cranium was narrowed from side to side. Left hand and wrist were normal for the age, so was the spine. Hip and pelvis roentgenograms showed no abnormalities. Radiographic examination of the thorax showed enlargement of the heart.

Cardiac catheterization performed at Queen Louise's Children's hospital (Copenhagen) showed an atrial septum defect. According to oxygen analysis, it was not conjugated with any shunt. Furthermore, an interventricular defect with a left-right shunt was found. In the right ventricle a significant elevated tension was diagnosed.

Ophthalmoscopic examination was normal.

Case 2.

A girl (individual IV–10 in the pedigree) was born in April, 1969, when the mother was 23 years and the father 29 years. She was number three of three living sibs. The mother, who is healthy, had a spontaneous abortion before the birth of the first child and a therapeutic abortion on psychiatric indication after the birth of the second child. The sister and brother are healthy. The pregnancy was complicated with hydramnios. The child was born

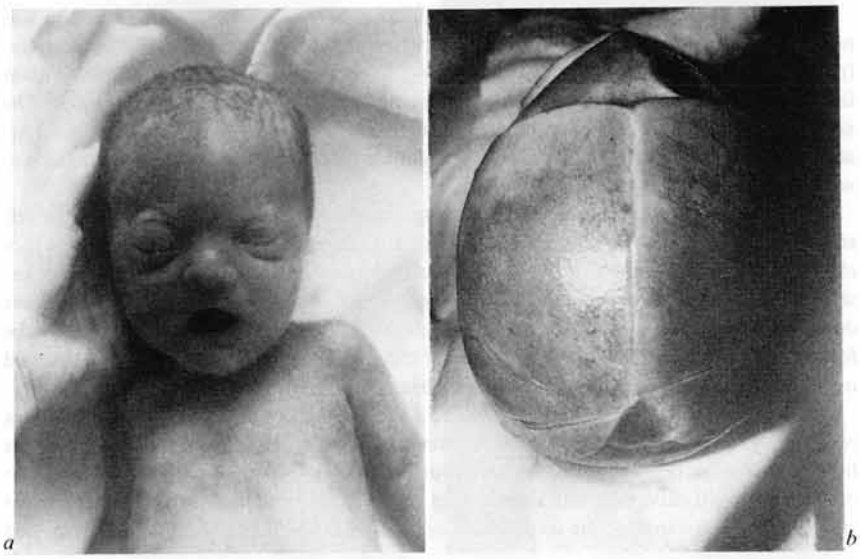

Fig. 3. Case 2. *a* After death. Note keel-formed forehead, broad-bridged neos, and epicanthus. *b* Post-mortem photo of calvarium, showing acute angle of frontal bone.

at term with head presentation; birth weight was 1,700 g, length 43 cm, head circumference 30.5 cm. The child was flabby, slow at crying, and had a peculiar appearance. She was therefore transferred to a paediatric department in the first day of life. She expired, 28 h old, after repeated attacks of cyanosis. The child was phenotypically exactly like case 1 (fig. 3a, b).

For appearance and pathological findings, see table I.

Case 3.

A boy (individual IV–4 in the pedigree) was born in January, 1960, three weeks before term after an uneventful pregnancy. Birth was uncomplicated; birth weight 2,250 g, length 50 cm. The parents were 31 years old at the time of the child's birth, and he was the first born. A younger sister died at five days old. There were no abortions.

At birth the appearance of the child was normal; at the age of three weeks he had a single attack of cyanosis. Because of feeding difficulties and failure to thrive, he was hospitalized the first 3 months of life. He was restless; physical and mental development was retarded. He sat without support at the age of 10 months, could walk at 2 years of age, and began to talk at 2½–3 years old. He was toilet-trained at the age of 2½ years. At the

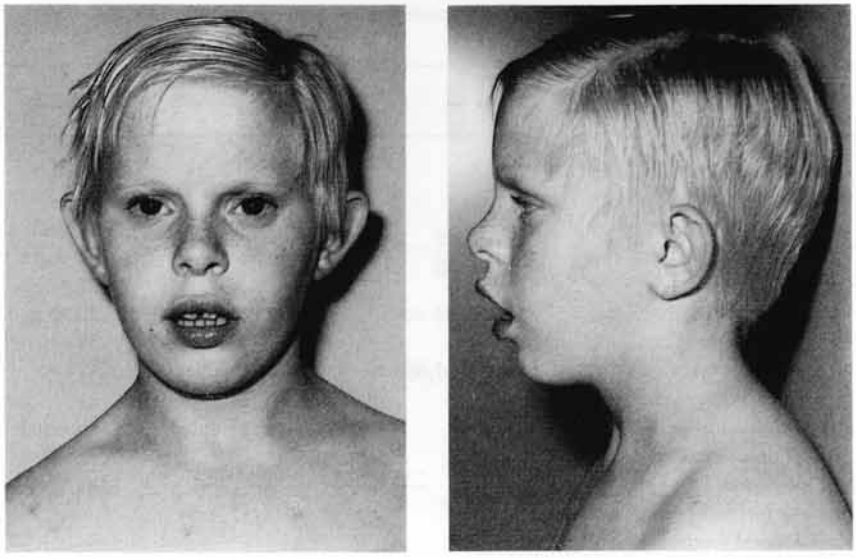

Fig. 4. Case 3 at the age of 11½ years.

age of 7 years, he continued to talk in a babyish manner in short sentences. Furthermore he stutters. During childhood he had numerous periods of illness with colds, pneumonia, and otitis.

An intelligence test was performed when he was 7 years old; his concentration span was short and his IQ was 65. At the age of 7½ years he attended a special school for the mentally retarded. He made little progress, still has a short concentration span, is childish and dependent on others. He reacts violently towards all that is new, getting aggressive and crying when something upsets him.

Clinical investigation at the age of 11½ years (fig. 4a, b) revealed a boy with an appearance of slight mental retardation, coarse facial appearance, a high prominent forehead, an asymmetrical face and flopping, low-set, sparsely modelled, backward placed ears.

His height was 137 cm, weight 36 kg; armspan was 134 cm; maximum head circumference was 53½ cm, cephalic index 0.76. The nose was small with anteverted nostrils. Extensive dental caries were present, teeth were very irregular, and there was a high arched palate. Clinical neurological investigation showed no abnormalities except for slight predominance of the reflexes on the left side. The hands were broad with tapering fingers. The fifth finger was short on both sides and the left fifth finger curved. The feet were small with broad distance between the first and second toe on the right side. The fifth toe was short on both sides. There were marked pedes plani. The skin showed extensive prurigo Besnier. The external genitals were normal.

Table 1. Summary of anamnestic and pathological findings in the cases described

	Case 1	Case 2	Case 3
Index number	IV–3	IV–10	IV–4
Sex	F	F	M
Maternal age at birth of child	24 years	23 years	31 years
Paternal age at birth of child	25 years	29 years	31 years
Gestational length	35 weeks	40 weeks	37 weeks
Birth weight; length	2,000 g; 46 cm	1,700 g; 43 cm	2,250 g; 50 cm
Neonatal problems	cyanosis, dyspnea	cyanotic attacks, died 28 h old	—
Physical development	retarded	'small for date'	retarded
Mental development	retarded	—	retarded
Microcephalia	+	+	—
Narrow forehead	+	+	—
Keel-formed frontal region	+	+	—
Broad-bridged nose	+	+	—
Epicanthus	+	+	—
Mongoloid slant	+	+	—
Receding chin	+	+	—
Low-set ears	+	+	+
Loose skin folds at the back of the neck	—	+	—
Ulnar deviation of 2nd finger	+/+	—	—
Simian crease	+/+	+/+	—
First toe is a hammer toe	+/+	—	—
Congenital heart disease	asd + vsd pulmonary hypertension	cor univentriculare, truncus arteriosus comm., hypoplasia atrii sin.	—
Renal defect	?	ren dupl. utr., hydronephrosis sin.	—
Chromosome analysis	46,XX,der(11)pat	post-mortem culture failed	46,XY,der(21)mat

Laboratory investigations. Haemoglobin, ESR, and serum creatinine showed normal values. No protein was found in the urine, and the sediment was normal. ECG was normal. EEG showed diffuse fast activity, 4–7 Hz, and sharp waves with uncertain predominance in the right temporo-occipital region. Electrophoresis of serum proteins

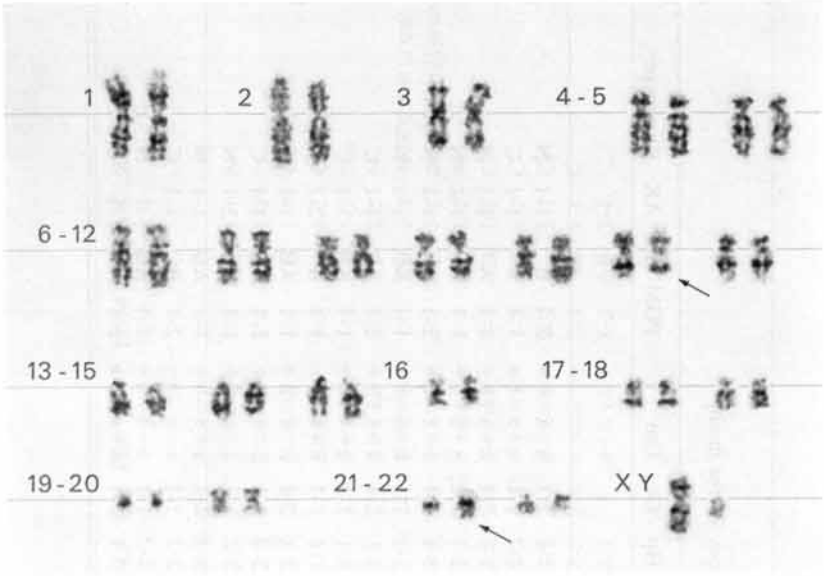

Fig. 5. Giemsa band karyotype from a male carrier (III–6). The translocation chromosomes are indicated by arrow.

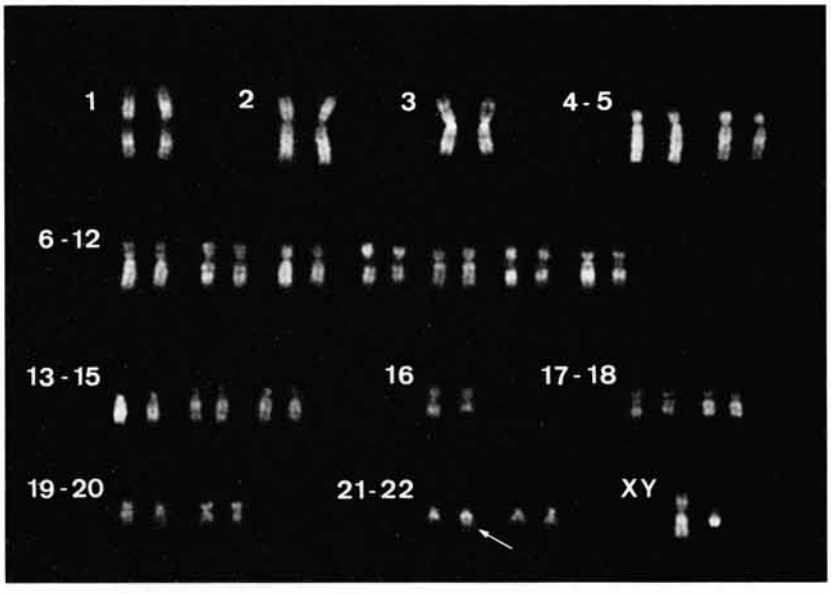

Fig. 6. Fluorescence karyotype from case 3. The der(21) chromosome is indicated by arrow.

Table II. Blood, serum, and enzyme types for the family

Pedigree No.		ABO	MNSs	Rhesus					P	K	Kp(a)	Fy(a)	Hp	Gc	Gm	PGM	AcP[1]	AK	Karyotype[2]
				C	C^w	D	E	c											
I.	2	A_1	NS—s+	—		—	—	+	+	+	—	—	2–1	2–1	a—x—b+	2–1	B	1–1	N
II.	1	A_1B	MNS—s+		+	+	—	+	+	—		+	2–2	2–1	a+x+b+	1–1	B	1–1	C
	2	A_1	MS+s+	+	—	+	—	+	+	—	—	+	2–1	2–1	a+x+b+	1–1	A	1–1	N
	3	A_1	MNS—s+	+	—	+	—	+	+	+	(+)	—	2–1	2–2?	a+x+b+	1–1	B	1–1	N
	4	A_2	NS—s+	+	—	+	—	+	+	—		—	2–1	1–1	a+x—b+	2–1	B	1–1	N
	5	A_1	MNS+s—	+	—	+	—	+	+	—	(+)	+	2–2	1–1	a—x—b+	1–1	BC	1–1	N
	6	A_1	MNS+s+		+	+	—	+	—	+	(+)	+	2–1	2–1	a+x+b+	2–1	AB	1–1	C
III.	3	A_1B	MS—s+	+	—	+	—	+	+	—		—	2–1	1–1	a+x+b+	1–1	AB	1–1	C
	4	A_1	MNS+s+	—		—	—	+	+	+	—	+	1–1	1–1	a+x+b—	1–1	B	2–1	N
	6	B	MNS—	+	—	+	—	+	+	—		+	2–1	2–1	a—x—b+	1–1	AB	1–1	C
	12	A_1	MNS+s+	—		—	—	+	+	+	—	+	2–2	2–1	a—x—b+	1–1	AC	1–1	C
	13	O	MNS+s+	+	—	+	—	—	+	—	—	+	2–2	1–1	a—x—b+	1–1	B	2–1	N
	15	O	MNS—s+	+	—	+	—	+	+	—	—	+	2–2	2–1	a+x—b+	1–1	AB	1–1	N
	16	A_1	NS+s+	—		—	—	+	+	—	—	+	2–2	2–1	a—x—b+	2–1	BC	1–1	C
	18	A_2	NS+s+	+	+	+	—	—	+	+	—	+	2–2	1–1	a—x—b+	1–1	AC	1–1	N
	21	A_1	MS+s—	+	+	+	—	—	+	+	—	+	2–1	2–1	a+x+b+	2–1	AB	1–1	C

Table II. (Continued)

Pedigree No.		ABO	MNSs	Rhesus					P	K	Kp(a)	Fy(a)	Hp	Gc	Gm	PGM	AcP[1]	AK	Karyotype[2]
				C	C^w	D	E	c											
	24	A_2	NS+s+	—		—	—	+	+	+	—	+	2–1	1–1	a—x—b+	1–1	BC	1–1	N
	26	A_1	MNS+s+	+	—	+	—	+	+	+		+	2–2	1–1	a—x—b+	2–1	BC	1–1	N
	28	A_2	MS+s—	—		—	—	+	+	+	(+)	+	2–1	2–1	a—x—b+	1–1	AC	1–1	C
	29	A_1	MNS+s—	—		—	—	+	+	+	(+)	+	2–1	1–1	a—x—b+	1–1	BC	1–1	C
IV.	1	A_1B	MNS+s+	+	—	+	—	+	+	+		+	1–1	1–1	a+x+b(+)	1–1	AB	1–1	N
	2	A_1	MNS+s+	+	—	+	—	+	—	+	—	+	1–1	1–1	a+x—b+	1–1	AB	1–1	N
	3[3]	A_1B	MNS+s+	—		—	—	+	+	+		+	?	1–1	a+x+b—	1–1	AB	1–1	46,XX,der(11)pat
	4[4]	A_2	MS+s—	+	—	+	—	+	+	—	—	+	2–2	2–1	a—x—b+	1–1	BC	1–1	46,XY,der(21)mat
	7	A_2	MNS+s+	—		—	—	+	+	—	—	+	2–2	2–1	a—x—b+	1–1	B	1–1	N
	8	A_1	NS+s+	—		—	—	+	+	—	—	+	2–2	2–1	a+x—b+	2–1	AB	1–1	C
	12	A_2	MNS+s+	—		—	—	+	—	—		+	?	1–1?		1–1	AC	1–1	C
	13	A_1B	MS+s+	+	—	+	—	+	+	—		—	2–1	2–2	a—x—b+	2–2	A	1–1	C
	14	A_1	MS+s+	+	—	+	+	+	—	+		+	2–2	2–1	a—x—b+	2–1	AB	1–1	C
	15	A_1	MS+s+		+	+	+	+	+	—		—	2–1	?	a+x+b+	1–1	AB	1–1	C

[1] AcP = Red cell acid phosphatase.
[2] N = Normal karyotype; C = 46,XX or XY,t(11;21)(q23;q22).
[3] Proband
[4] case 3.

including immunoelectrophoresis of the γ-globulins showed normal values. LDH isoenzymes were normal.

Cytogenetic Studies

Chromosome analysis was performed on lymphocytes cultured for 2 or 3 days under addition of phytohaemagglutinin. Conventional Giemsa-stained slides from the proposita, case 1, showed a 46,XX,Cq- karyotype. In her father a translocation between a C group and a G group chromosome was identified. Extensive autoradiographic studies with ^{3}H-thymidine, with the method described by FRØLAND [1965], in the proposita and her father did not allow identification of the C or the G group chromosomes involved in the translocation. In case 2 the post-mortem culture failed.

After introduction of banding methods, the family was studied either by fluorescence with a modification of the method described by CASPERSSON *et al.* [1970] or with Giemsa banding with the method routinely used at the Kennedy Institute [MIKKELSEN and DYGGVE, 1973]. The proposita, case 1, was dead at that time and could not be reexamined with banding methods. In the father of the proposita and 13 other family members, a balanced translocation between the long arm of chromosome No. 11 and the long arm of chromosome No. 21 was found (fig. 5). The breakpoints were at 11 q23 and 21 q22; karyotypes being 46,XX or XY,t(11;21)(q23;q22). In case 3, a partial trisomy for the long arm of chromosome 11 was found; the karyotype was 46,XY,der(21) (fig. 6). The banding methods applied did not allow to decide with certainty if the translocation was reciprocal or simple. It appeared as a simple transmission of the distal part of the long arm of chromosome 11 onto the terminal end of chromosome 21. 15 other family members had normal karyotypes. The ratio of normal karyotypes:translocation carriers among the offspring of female carriers was 3:8, among males, 4:6.

Anthropological and Serological Studies of the Family

Data on the distribution of blood and serum groups and enzyme systems are given in table II and on dermatoglyphics in table III.

In 26 family members including both carriers, normal individuals, and case 3, the following examinations were carried out: Agar-gel electrophoresis and immunoelectrophoresis of serum proteins and also serum LDH isoenzyme activity. In all cases normal values were found. (We are indebted to Dr. KNUD JENSEN, University Hospital, Odense, Clinical Chemical Department, for these studies.)

Table III. Dermatoglyphics

	Fingers thumb						Palms
	1	2	3	4	5		
Case 1 (IV–3)							
Right	W	W	W	W	W	TRC = 136?	11.0.7.3–0.0.0.0.0–t′ 13, at′d 59°
Left	W	W	W	W	W		9.0.5′.1–0.V.0.0.V–t′ 11, at′d 63°
Simian line on both hands							
Case 3 (IV–4)							
Right	U	U	U	W	U	TRC = 178	7.5′′.5′′.3–L^{r}.0.0.0.L–t 13, atd 42°
Left	U	U	U	W	U		7.5′′.5′.3–0.0.0.0.L–t 13, atd 45°
No simian line							
Father to case 1 (III–3)							
Right	W	W^{sm}	U	W^{sm}	U	TRC = 169	11.7.7.3–0.0.0.0.v– t 13, atd 38°
Left	U	U	U	U	U		11.X.7.3–0.0.0.0.0– t 13, atd 38°
No simian line							
Mother to case 1 (III–4)							
Right	W	W	W	W	W	TRC = 152	11.x.7.3–Comp.0.0.0.0– t 13, t′′ 11, at′′d 75°
Left	W	W	W	W	W		9.7.5′′.2–M/A^{c}.0.0.0.L– t′ 11/12, at′d 45°
No simian line							
Brother to case 1 (IV–1)							
Right	U^{cp}	W	W	W	W	TRC = 169	11.9.7.3–0.0.0.L.0– t′ 13, at′d 46°
Left	U	W	W	W	W		11.9.7.3–0.0.0.V.0– t 13, atd 40°
No simian line							
Sister to case 1 (IV–2)							
Right	U	W	W	W	W^{sm}	TRC = 144	9.x.5′.3/11–0.L^{r}.0.0.0– t 13, atd 45°
Left	W	W	W	W	W^{sm}		10.x.6.2–V.0.0.0.0– t 12, atd 42°
No simian line							

Discussion

The clinical picture of IV–3, who lacked the distal part of chromosome No. 11, showed considerably more severe abnormalities than IV–4, who was

trisomic for the same part of chromosome No. 11. It must be assumed that case 2, who was clinically identical to case 1, had the same chromosomal aberration. It seems that the deletion of a chromosome has more deleterious effect than the trisomic state for the same part of the chromosome in question.

Only few chromosome abnormalities concerning No. 11 have been described. ROTT *et al.* [1972] described a family with a C11/D13 translocation. The propositus, who was partially trisomic for the long arm of chromosome No. 11, showed low birth weight and severe congenital malformations including congenital heart failure, lack of subcutaneous fatty tissues, epicanthic folds, hypertelorism, low-set ears with preauricular dimples, broad flat nose, micrognathia, muscular hypotonia, and psychomotor retardation. He died at the age of 10 months. FRANCKE [1972] described a girl trisomic for the distal third of the long arm of chromosome No. 11. The child showed micrognathia, macroglossia, complete cleft palate, dislocated hips, atrial septal defect, agenesis corporis callosi, one kidney, and one fallopian tube. She died at the age of 5 weeks.

These two cases showed a more severe clinical condition than our trisomic case presumably because the amount of extra material of the long arm of chromosome 11 was greater. No cases of deletion of the long arm of chromosome No. 11 were described until now.

The balanced translocation was found in two siblings in generation II and, as their mother (I–2) had a normal karyotype, it must be assumed that the father (I–1) carried the translocation.

This family is interesting because besides normal and carrier karyotypes, both partial monosomic and partial trisomic individuals were found. The unbalanced individuals represent both types of adjacent–1 segregation. Also, two children in generation III (III–1 and III–22), who died in early infancy, may have had an unbalanced karyotype as retardation and malformations were recorded. Poor economic and social conditions in this generation may have contributed to the great infant mortality observed also in children where nothing is known about malformations or mental and physical retardation.

The ratio of normal and carrier karyotype found in this family, 7:14, differs from the expected 1:1 ratio, but not significantly. There is a remarkably small number of known abortions and there are no signs of decreased fertility in this family, as has been observed in other translocation families. The transmission to an unbalanced child was maternal as well as paternal, and no sex difference was found in the segregation ratio.

The information which this family may give with respect to the chromosomal assignment of the loci of serological markers has been analysed. Conclusive negative evidence is provided by the individual IV–3 who lacks the distal part of the long arm of one chromosome No. 11; as this person is heterozygous at the ABO, MNS, and red cell acid phosphatase loci, it is excluded that these loci are sited here. Furthermore, individual IV–4 shows partial trisomy involving the same distal segment of chromosome No. 11, transmitted from the mother who also contributed her normal chromosome No. 11 to IV–4. As this child has received only one of the two different alleles identified at the mother's ABO, MNS, red cell acid phosphatase, and Kell loci, the location of these loci on the distal part of the long arm of chromosome No. 11 is likewise excluded.

The two visibly abnormal chromosomes in the carriers, No. 11 and 21, may serve as chromosome markers in an analysis of possible linkage between these and the serological markers. No information is provided concerning the P and AK systems, and no positive evidence of linkage is found for the other markers investigated. Finally, if lack of a small part of chromosome No. 11 and/or 21 is assumed in the carriers, it is of relevance to note that heterozygosity at most of the marker loci (except P, Kell, Duffy, and AK) has been observed in one or more of the carriers.

The finding of a normal karyotype in the amniotic fluid cells when the girl IV–12 was examined prenatally, while a 46,XX, (11; 21) translocation was found after birth, stresses once more the necessity of fluorescence or HL-A antigen studies to exclude that maternal cells have been cultured.

References

Caspersson, T.; Zech, L., and Johansson, C.: Differential binding of alkylating fluorochromes in human chromosomes. Exp. Cell Res. *60:* 315–319 (1970).

Francke, U.: Quinacrine mustard fluorescence of human chromosomes: characterization of unusual translocations. Amer. J. hum. Genet. *24:* 189–213 (1972).

Frøland, A.: Photographic recording and dye staining of chromosomes for autoradiography and morphology. Stain Technol. *40:* 42–43 (1965).

Mikkelsen, M. and Dyggve, H.: (6;15) translocation with loss of chromosome material in the patient and various chromosome aberrations in family members. Humangenetik *18:* 195–202 (1973).

Rott, H.-D.; Schwanitz, G.; Grosse, K.-P., and Alexandrow, G.: C11/D13-translocation in four generations. Humangenetik *14:* 300–305 (1972).

Appendix

Description of the family including cytogenetical findings

Index No.		Sex	Born	General remarks	Chromosomal findings
I.	1	M	1880	died 1961	not examined
	2	F	1884	healthy, no abortion	46,XX
II.	1	M	1911	healthy	46,XY,t(11;21)(q23;q22)pat
	2	F	1920	healthy, 6 pregnancies	46,XX
	3	F	1913	healthy, 4 pregnancies	46,XX
	4	M	1908	husband to No. 3	46,XY
	5	M	1915	husband to No. 6, healthy	46,XY
	6	F	1918	twelve pregnancies, no abortion	46,XX,t(11;21)(q23;q22)pat
III.	1	F	1939	Pregnancy uneventful, spontaneous delivery 2 weeks before term; physical and mental development retarded. At the age of 8 years referred to an institution for mentally retarded. She was small for age, 115 cm tall and looked normal, except for a very long and narrow head, a café-au-lait spot as large as the palm of a hand in front of the right side of the thorax, and a 2×4-cm teleangiectasia on the left side of the cheek and neck. UK (Bühler-Hetzer) 42. She died at the age of 29 years of a stemcell leukemia. Autopsy showed atrophy of the cerebral cortex; no malformations recorded.	not examined
	2	F	1940	birth weight 3,100 g, length 49 cm; looked normal, except for ecchymoses of feet and legs; she died at home, 11 months old, of pneumonia	not examined
	3	M	1943	disabled on account of motor accident; previously healthy; father to the proband	46,XY,t(11;21)(q23;q22)pat
	4	F	1944	mother to the proband; healthy	46,XX
	5	F	1947	died at the age of 3 months, presumably of gastroenteritis; no further information available	not examined
	6	M	1948	healthy	46,XY,t(11;21)(q23;q22)pat

Appendix (Continued)

Index No.	Sex	Born	General remarks	Chromosomal findings
7	?	1951	abortion M II–III	
8	M	1933	healthy, married, with three living children, one stillbirth, and one abortion	not examined
9	M	1940	healthy, married, with two children	not examined
10	M	1946	healthy	not examined
11	F	1948	hydrocephalus congenita, idiotia; at the age of 13 years referred to an institution for mentally retarded; died 1971	46,XX
12	F	1939	healthy, mother of case 3	46,XX,t(11;21) (q23;q22)mat
13	M	1929	healthy, husband to No. 12	46,XY
14	M	?	illegitimate connection III–15	not examined
15	F	1946	healthy	46,XX
16	M	1940	healthy, father of case 2	46,XY,t(11;21) (q23;q22)mat
17	M	?	husband to No. 18	not examined
18	F	1941	healthy; three normal children	46,XX
19	M	1944	healthy	examination refused
20	M	1946	husband to No. 21	examination refused
21	F	1946	healthy	46,XX,t(11;21) (q23;q22)mat
22	F	1947	died of bronchitis capillaris at the age of 7 months; retarded development and imbecile appearance were recorded (head was big and square; she could not support it)	not examined
23	M	?	husband to No. 24	not examined
24	F	1949	healthy	46,XX
25	M	1950	Uncomplicated birth at home, birth weight 3,500 g. Because of failure to thrive, he was referred to the hospital at the age of 7 weeks; weight was then 3,900 g; died of bronchopneumonia at the age of 4 months. No malformations registered.	not examined
26	M	1952	healthy, has attended a special school (slightly retarded)	46,XY

Appendix (Continued)

Index No.		Sex	Born	General remarks	Chromosomal findings
	27	M	1953	Birth at home, breech presentation, birth weight 3,400 g, length 51 cm. Because of weakness, the child was referred to hospital, where it died, 3 days old (intracranial haemorrhage); no record of malformations.	not examined
	28	F	1955	healthy	46,XX,t(11;21)(q23;q22)mat
	29	M	1958	healthy	46,XY,t(11;21)(q23;q22)mat
IV.	1	M	1965	healthy	46,XY
	2	F	1967	healthy	46,XX
	3	F	1968	proposita, case 1	46,XX,der(11)pat
	4	M	1960	case 3	46,XY,der(21)mat
	5	F	1962	Born at term in hospital, breech presentation, birth weight 2,500 g, length 50 cm, no malformations. After increasing weakness and jaundice, the child expired, 5 days old.	not examined
	6	?	1963	spontaneous abortion M IV	not examined
	7	F	1964	healthy	46,XX
	8	M	1966	healthy	46,XY,t(11;21)(q23;q22)pat
	9	?	1966	therapeutic abortion	not examined
	10	F	1969	case 2	post-mortem culture failed
	11	F	1971	spontaneous abortion M III	46,XX
	12	F	1973	Amniocentesis in 15th week of pregnancy; cultured cells showed a normal female karyotype. A healthy female was born 4 weeks before term; birth weight 2,800 g, length 51 cm, head circumference 34.5 cm; showed no malformations, but simian crease on both hands. Chromosome analysis after birth showed carrier karyotype.	46,XX,t(11;21)(q23;q22)pat
	13	M	1966	healthy	46,XY,t(11;21)(q23;q22)mat

Appendix (Continued)

Index No.	Sex	Born	General remarks	Chromosomal findings
14	M	1968	healthy	46,XY,t(11;21) (q23;q22)mat
15	M	1969	healthy	46,XY,t(11;21) (q23;q22)mat

Request reprints from: PETREA JACOBSEN, Brejning Institute for Research in Mental Retardation, Cytogenetic Dept., *DK–7080 Børkop* (Denmark)