

An Inherited 1;G Translocation*

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A child with multiple congenital anomalies and retardation was found to have a translocation involving chromosome No. 1 and a chromosome of the G group. The affected child has a minute centric fragment of unknown origin in addition to the 1;G translocation. Although the translocation is found throughout 4 generations, the child described here is the only known instance of fetal abnormality in this family. To our knowledge there are only three other reports of a translocation between chromosome No. 1 and a G chromosome (Kontras *et al*, 1966; Maganias *et al*, 1967; Wilson, 1969). In two of these families the translocation was transmitted from mother to child. In this family the translocation is transmitted from both male

and female carriers. The patient's phenotype does not correspond to any currently catalogued chromosomal syndrome and is not similar to the physical features of other individuals with 1;G translocation.

Case Report

The patient (EB030869) (Fig. 1) is a white female infant born at term to a primiparous 25-year-old mother and a 29-year-old father. There is no history of consanguinity or irradiation in pregnancy. The mother took an oral anti-emetic for nausea and sulphonamide for a urinary tract infection during her first trimester; otherwise, the pregnancy was unremarkable. The infant, although full-term at birth, weighed only 2240 g (4 lb 15 oz) and was 47 cm (18½ in.) in length.

Physical examination at 2½ months revealed a small, hypertonic infant with a vigorous cry. The weight was 2807 g (6 lbs 3 oz), the length 51 cm (20 in.), the head circumference 34 cm (13½ in.), and the chest circumference 30 cm (11½ in.). The child had a round head, an

Received 18 December 1970.

* This work was supported in part by Children's Bureau Grant no. 322.

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FIG. 1. The proposita at 2½ months of age.

anterior fontanelle 3 × 3 cm, and sparse pale-blond hair. There was hypertelorism (inter-canthal distance 2.75 cm), but no epicanthi, strabismus, or slanted palpebral fissures. Both pupils were ectopically placed. The ears were low with poorly formed helices and rotated backwards. There was a haemangioma over the broad and malformed nose. The mouth was small and the palate showed a complete midline cleft. The neck was short. The chest and abdomen were unremarkable. Both clitoral prepuce and labia minora appeared enlarged for age. There were dimples over the elbows. The hands were tightly fistled with contractures of the right index and 3rd fingers, and ulnar clinodactyly of the right 3rd finger. There was also clinodactyly of the second toe bilaterally. The Moro reflex was present; the suck was fair; and the deep tendon reflexes were equal and brisk. Developmental examination at 5½ months of age revealed that the child was functioning at about a one-month level. Radiographs of the skull, chest, hands, feet, long bones, and pelvis were all normal. Bone age was normal.

Laboratory values were as follows: haemoglobin 9.5 g%; leucocytes 6500/mm³ with a normal differential and adequate thrombocytes; urinalysis normal; urine culture negative for growth; and normal blood chemistry values for urea nitrogen, potassium, sodium, albumin, globulin, total bilirubin, calcium, inorganic phosphate, alkaline phosphatase, and protein-bound iodine.

The infant gained weight poorly and tube feeding was necessary. At six months of age the infant developed vomiting and diarrhoea. Due to an excessive intake of sodium chloride, she developed hypernatraemia, convulsions, and, in spite of dialysis, expired.

The only significant post-mortem findings were cerebral oedema attributable to the hypernatraemia, and bronchopneumonia. Examination of the thoracic and abdominal viscera revealed no congenital malformation.

Chromosome Analysis. Chromosome analyses of the proposita were obtained from peripheral blood cultures, fibroblast (skin) culture, and bone marrow direct preparation and culture. The results of these analyses are summarized in Table I. All the cells show a missing

No. 1 chromosome and a missing G chromosome (Fig. 2). Interpreted as representing a 1;G translocation are two chromosomes: a large submetacentric chromosome with long arm similar to a No. 1 and an additional chromosome in the D-group. Most cells from all tissues analysed, including the direct bone marrow preparation (32 of 35 cells), show an additional centric fragment. This fragment is smaller than a G chromosome and constant in size. Two such fragments are found in a small proportion of karyotypes from cultures *in vitro* from bone marrow and skin.

Autoradiographic studies yielded 50 analysable cells from the blood culture. The atypical chromosomes are essentially unlabeled, consistent with a 1;G translocation. Autoradiography was of no aid in identifying the origin of the centric fragment. Sex chromatin from buccal smears is positive.

The infant's karyotype is interpreted as 46,XX,t(1?p-;Gq+)/47,XX,t(1?p-;Gq+),mar+ (Chicago Conference nomenclature, 1966). For simplicity a reciprocal translocation between a No. 1 and a G chromosome is assumed, although an insertion of a portion of the arm of No. 1 into the long arm of the G chromosome is also consistent with the cytogenetic results. We do not know the origin of the centric fragment.

Family Studies. It was possible to examine two generations antedating the proposita (Fig. 3). All these family members were phenotypically normal. A minimal number of 10 cells was analysed in each instance. Sex chromatin from buccal smears is consistent with phenotypic sex in all instances. Karyotypes from the father, paternal grandfather, two great aunts, a great uncle, and two second cousins are found to have the 1;G translocation which is apparently identical with that of the proposita, except that the centric fragment is not present (see Fig. 2). The 1;G translocation is assumed also to be present in one of the great grandparents since 4 of their children are known to be translocation carriers; thus, the translocation is transmitted through at least 3 generations.

Further inspection of the family pedigree (Fig. 3)

TABLE I
CHROMOSOMAL ANALYSES FROM THE PROPOSITA AND HER PARENTS

Tissue	Culture Period	Percentage of Cells			No. of Cells Analysed	Analysis
		0 Fragment	1 Fragment	2 Fragment		
<i>Proposita</i>						
Blood	48 hr	14	86	—	22	46, XX, t(1?p-; Gq+)/47, XX, t(1?p-; Gq+), mar+
Blood	48 hr	3	97	—	36	All cells had 1;G translocation
Marrow	0	8	92	—	35	
Marrow	17 day	30	13	57	30	
Skin	22 day	15	62	23	13	
<i>Mother</i>						
Blood	72 hr	—	—	—	10	46, XX (apparently normal)
<i>Father</i>						
Blood	72 hr	—	—	—	32	46, XY, t(1?p-; Gq+) All cells had 1;G translocation

* A minimal number of 10 cells was analysed in each instance.

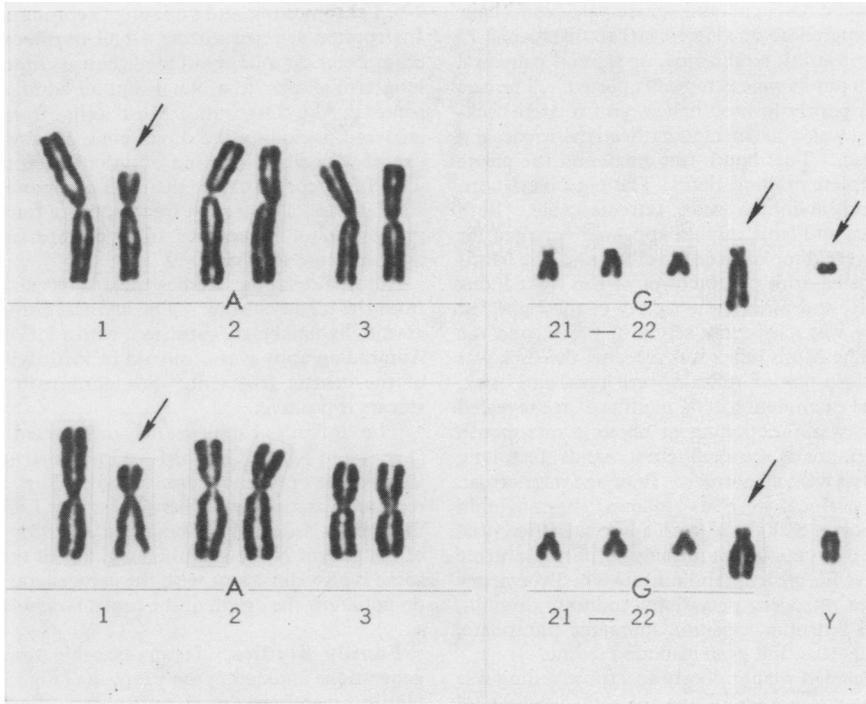


FIG. 2. Partial karyotype from the probanda showing 1;G translocation and a centric fragment (top). Partial karyotype from the father showing the 1;G translocation and the Y chromosome (bottom).

demonstrates that the translocation was transmitted by both male and female carriers, who have both normal and carrier offspring. One of the carriers (III.3) had reduced fertility of unexplained cause; however, the frequency of abortions in this family does not appear to be unusually high and there are no other instances of congenital abnormalities or mental retardation.

Dermatoglyphic analysis. The dermatoglyphic patterns of the probanda and her parents are summarized in Table II. The dermatoglyphs of the probanda are generally unremarkable except for hypoplastic ridges and an elevated distal axial triradius due to hypothenar patterns. The father showed this latter feature in the left hand. The mother's lowered total ridge count of 29 (average female 127, SD 53) is interesting but unrelated to the cytogenetic abnormality in the family.

Discussion

The present family shows a 1;G translocation in 4 generations. An affected child in the 4th generation shows a centric fragment in addition to the translocation. The chromosomal constitution is assumed to be unbalanced in this child since an extra centromere is present. The origin of the fragment is unknown and the appearance of the child is not typical for any known chromosomal syndrome. We assume that the fragment is responsible for the clinical findings in the child; however, this is, in fact, unknown since additional centric fragments or small acrocentric or metacentric chromosomes have now been reported in phenotypically normal individuals (Smith *et al*, 1965; Pfeiffer, Diekman, and Buchner, 1967; Ricci, Ventimiglia, and Preto, 1968).

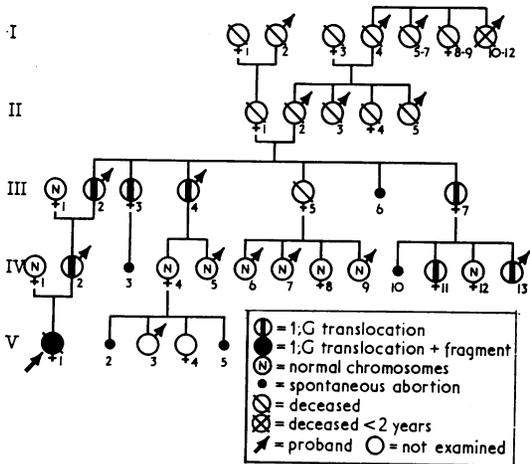


FIG. 3. Family pedigree.

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TABLE II
DERMATOGLYPH PATTERNS

	Digits					Total Digital Ridge Count	atd Angle	Palmar Formula
	I	II	III	IV	V			
<i>Proposita</i>								
Right	U	U	U	W	W	—	—	-. t, t ^r . L ^r /L ^u . - L
Left	U	U	U	W	W	—	—	-. t ^r . L ^r /L ^u . O. -
<i>Mother</i>								
Right	A	A	A	U	A	29	43°	9.7.5".3.t.A ^u /A ^c .O.O.O.L/O
Left	A	A	U	U	U		40°	9.7.5".5'.t.A ^u .O.O.O.L
<i>Father</i>								
Right	W	U	U	W	W	164	41°	8.5"/6.5".5'.t.L ^r .L ^r .V.L.L
Left	U	U	U	W	W		50°	7.5".5".4.t,t'.L ^r /L ^u .L ^r .O.L.L

The other three reports of 1;G translocations have not been associated with an extra centric fragment or the clinical phenotype of the *proposita* in this family.

A child described by Maganias *et al* (1967) showed features of Turner's syndrome and retardation, and was found to have two translocation chromosomes involving No. 1 and G, morphologically similar to those of the balanced carriers in our family. The father's karyotype was normal. The mother had 46 chromosomes; however, one chromosome of the G group was thought to have elongated short arms. The morphology of this marker chromosome, however, was not similar to either translocation chromosome in the child.

In a study of recurrent abortion, Wilson (1969) found an apparently balanced 1;G carrier mother who had 4 spontaneous abortions and two normal children, one of whom carried the 1;G translocation. Wilson speculated that the carrier state might be responsible for the abortions.

Kontras *et al* (1966) reported a family in which maternal transmission of a balanced 1;G translocation was demonstrated through 4 generations. The G-group chromosome involved in this family study was evidently No. 21 since four children were affected with Down's syndrome. Two were karyotyped and found to have 47 chromosomes, including 4 G-group chromosomes and both translocation chromosomes. The increased incidence of spontaneous abortions in carrier mothers further suggested that the family was at greater risk for unbalanced progeny.

Summary

An infant with multiple congenital anomalies,

retardation, and karyotypic findings of a 1;G translocation and a centric fragment of unknown origin is described. The translocation is present in 4 generations of the family. Although 8 family members are carriers of the translocation, there is no apparent excess of fetal deaths or congenital abnormalities in the family. It is possible that the centric fragment is responsible for the abnormalities found in this child and that the fragment has only a coincidental relationship with the translocation.

Three families with 1;G translocations previously reported show no instance of phenotypic resemblance to our patient and have not been associated with a centric fragment.

The authors wish to thank Mrs Talma Dawson and Mr Paul Brager for technical assistance, Mr Paul Brager for the dermatoglyphic analysis, and Drs Kirchdoerfer, Graves, and Hovsepian for referring the patient to us.

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