A Familial Survey of a B/C Chromosome Translocation[1)]

By

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(With 6 Text-figures and 2 Tables)

Several different cases of familial transmissions involving chromosome translocations have been referred to in current human cytogenetic literature. Two cases of a B/C translocation are accessible in the literature, one by Edwards *et al.* (1962) and another by Mann *et al.* (1965).

While working with chromosome studies of patients with serum hepatitis, a B/C translocation was found by chance in a female patient who was hospitalized for a viral disease, as well as in one of her two sons. She had in her past clinical career two successive spontaneous abortions. Preliminary accounts of this chromosomal aberration have been given by Makino *et al.* (1965).

In hopes of obtaining further information on the familial transmission of this particular abnormality, a chromosomal survey was continued by us among the relatives of both paternal and maternal families. The present paper reports the results of this survey as concerns the transmission pattern of the abnormal chromosome, its origin and nature and its genetic significance in relation to spontaneous abortion.

Material and Methods: Our preliminary report described that the propositus was a phenotypically and mentally normal woman, aged 36 years (Makino *et al.* 1965). However, further detailed clinical examinations have made it clear that she carried some minor phenotypic abnormalities, as evidenced by a high arched palate, hypertelorism, a slight epicanthal fold, a flat nose and the shortness of the 5th fingers. She was 160.5 cm tall, weighed 60 kg and had a 162.5 cm arm span, and was characterized by a remarkable eunuchoid body proportion. She cast two successive spontaneous abortions in March and June, 1958. The abortions took place on the 5th and 8th week of gestation, respectively. She delivered two male infants on November 4, 1963 and on February 3, 1965. The younger son was physically as well as mentally normal, while the elder son suffered from left facial paralysis and small abdominal hemangioma (Makino *et al.* 1965). Further physical examinations detected that the elder son carried a high arched palate, a flat nose, hyperflexibility of fingers, unusually short 5th fingers and abnormally protruded heels. He measured 99.5 cm

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in height, 17 kg in weight and 98.0 cm in arm span.

Immediately after the second delivery, the propositus received an operation and two thirds of her uterus were removed. At operation blood transfusion was performed due to inevitable atonic bleeding of the uterus. About one month later, she suffered from serum hepatitis, and attended the hospital.

The pedigree of the propositus is shown in Figure 3. Twenty seven persons in this family were subjected to the chromosomal study. Chromosome studies were exclusively carried out on the basis of short-term leucocyte cultures derived from the venous blood from 27 individuals as mentioned above. Chromosome slides were made according to the air-drying method of Moorhead *et al.* (1960) with a slight modification. For examination of sex chromatin body, buccal mucosal smears stained with orcein were prepared from the propositus, and 200 cells with well flattened nuclei were scanned.

Dermatoglyphic analyses of the palms and soles were performed in some detail in the propositus, her husband, her two sibs and her sister. The hands of a paternal aunt of the propositus were roughly checked for dermatoglyphy.

In addition, some immunological and biochemical studies were carried out in the propositus and her elder son and younger sister by Miki.

Clinical examinations were done by Kajii, Oikawa, Kuroki and the cytological work was made by Aya, Kuroki and Makino.

Results

The results of zygosity tests as given in Table 1 indicated that the propositus is the mother of the child carrying the B/C translocation.

Chromosome studies revealed 46 chromosomes in the cells of the propositus and her elder son, while there was a consistent existence of an unusually large submetacentric element which was slightly larger than the autosome no. 1 of the normal complement. After karyotype analyses in several excellent metaphasic cells it became evident that two chromosomes were lacking in the complement, one from group-B and the other from group-C. In addition to the large submetacentric chromosome mentioned above, another unusual element was present: it is well defined by its centromere lying at an almost medianly inserted position, and corresponds in length to the autosomes 13–15 (Figs. 1–2).

The most probable interpretation for the origin of these two unusual elements is that a reciprocal translocation might have occurred between the long arm of one of group-B chromosomes and the long arm of one of group-C chromosomes. The two abnormal elements were tentatively designated as heteromorphic partners of no. 4 and of no. 7 autosomes.

The chromosomes of the remaining 25 persons including the propositus' husband and their younger son showed no visible deviation from the normal diploid complement of either a female (46, XX) or a male type (46, XY) within the scope of our observations, except the feature that the propositus' husband and his two sons had an unusually long Y chromosome which apparently corresponded in length to no. 18 chromosomes (Figs. 2, 4, 5).

In the propositus, the sex chromatin was positive in 19.5 per cent of 200 cells observed.

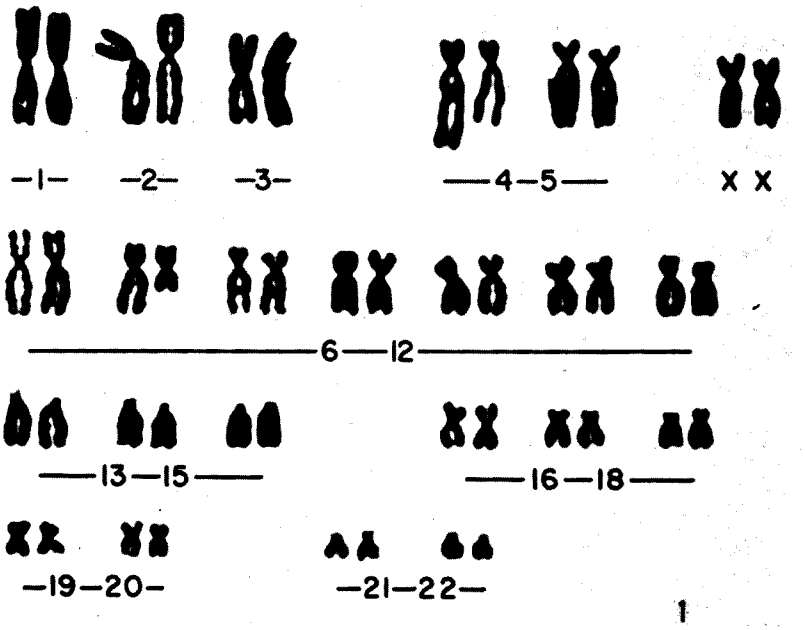

Fig. 1. Karyotype analysis of the propositus, a 36-year-old woman, showing a B/C translcoation.

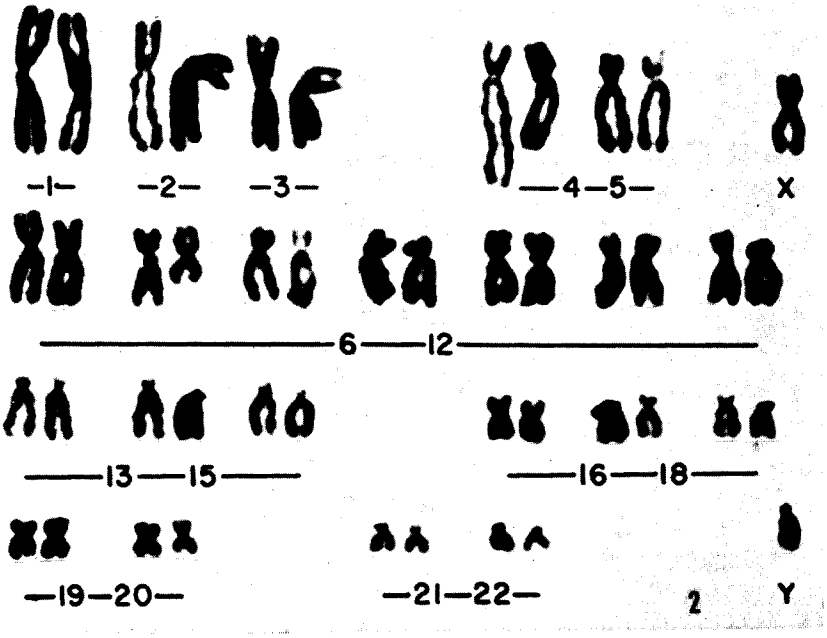

Fig. 2. Karyotype of the elder son of the propositus, showing a B/C translocation.

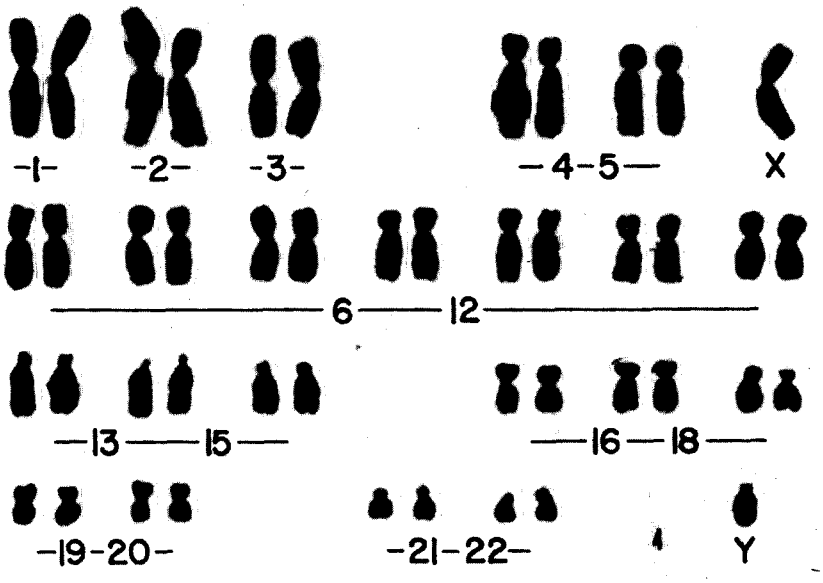

Fig. 4. Chromosomes of the husband of the propositus, showing a normal karyotype.

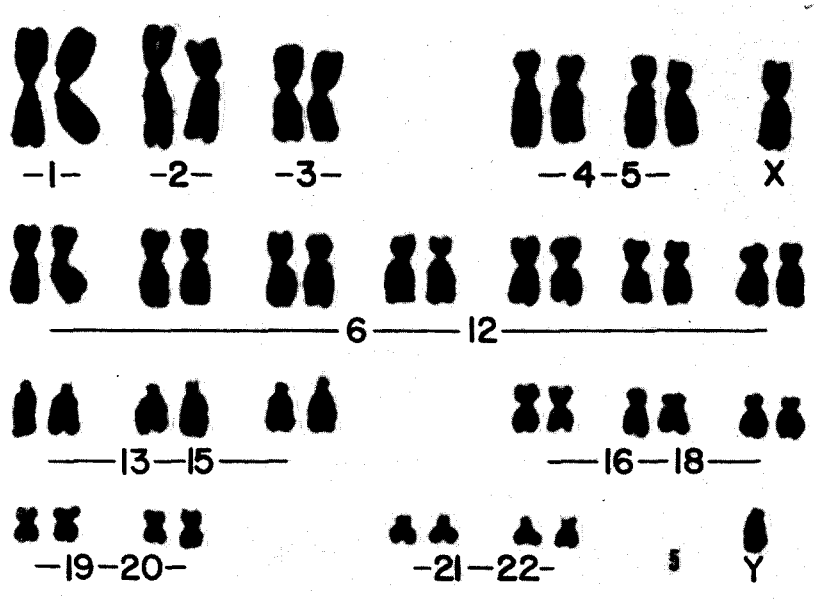

Fig. 5. Chromosomes of the young son of the propositus, showing a normal karyotype.

The dermatoglyphic features observed in the propositus, her husband, her two sons, her sister and her aunt are shown in Figure 6, and their finger tip ridge counts are summarized in Table 2.

Table 1. Blood and serum types

Subjects	Blood types									Serum types		Secretor types
	ABO	MNSs	Rh	Kell	Kp^a	Kp^b	Fy^a	Jk^a	Lu^a	Gc	Hp	Le^a
Propositus	A	NsNs	ccDEE	kk	−	+	+	−	−	2-1	2-2	+
Propositus' elder son	A	MSNs	ccDEE	kk	−	+	+	+	−	1-1	2-1	−
Propositus' younger sister	A	MsMs	ccDEE	kk	−	+	+	+	−	2-1	2-2	+

Table 2. Dermatoglyphic patterns

Case	Sex	Left					Right					Total ridge count	Loop in third interdigital area	
		V	IV	III	II	I	I	II	III	IV	V		Lt.	Rt.
a (Aunt)	♀	W	UL	UL	RL	W	UL	W	UL	W	UL	?	0	0
b (Propositus)	♀	UL	UL	UL	UL	UL	UL	UL	UL	UL	UL	60	0	+
c (Sister)	♀	UL	UL	UL	UL	UL	UL	UL	UL	UL	UL	86	0	0
d (Elder son)	♂	UL	UL	UL	UL	UL	UL	UL	UL	UL	UL	108	0	+
e (Younger son)	♂	UL	UL	RL	A	A	UL	UL	UL	UL	UL	16	0	+
f (Husband)	♂	UL	UL	UL	RL	UL	UL	RL	UL	UL	UL	114	0	+

A=arch. UL=ulnar loop. RL=radial loop. W=whorl. +=pattern present.

Discussion

The translocation shown by the two persons in the present familial survey was found to be the one occurring reciprocally between the long arm of one of B chromosomes and the long arm of one of C chromosomes. Referring to the fact that the propositus had two living births preceded by two successive spontaneous abortions, it seems very likely that the B/C translocation here concerned may have participated to a certain extent in the miscarriage.

Several instances of the familial translocations have been referred to in recent literature: for example, an A/A translocation reported by Summitt (1966),

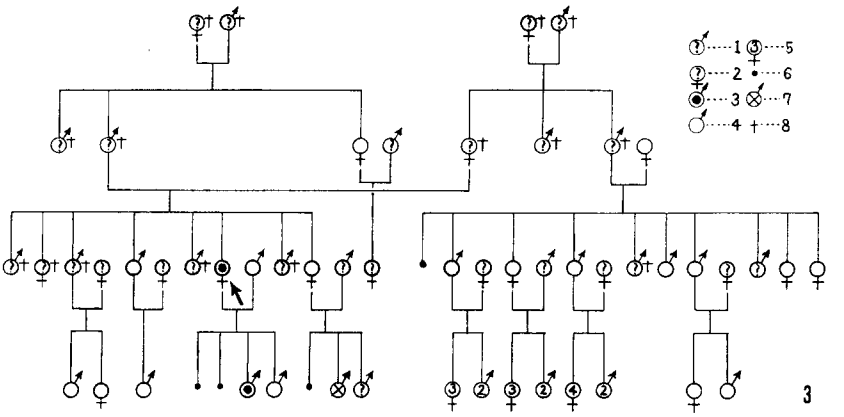

Fig. 3. Pedigree of the family under study, showing transmission of a B/C translocation. The propositus is indicated by an arrow. 1. Untested male, 2. Untested female, 3. Balanced translocation, 4. No translocation, 5. Three sisters, 6. Miscarriage, 7. Stillborn, 8. Dead.

of the left and right hands

Axial triradius			Thenar pattern		Hypothenar pattern		Simian line		a-b ridge count			Others
Lt.	Rt.	Mean	Lt.	Rt.	Lt.	Rt.	Lt.	Rt.	Lt.	Rt.	Mean	
?	?	?	0	0	0	0	0	+	?	?	?	
50	48	49.0	0	0	0	Lr	0	0	35	36	35.5	
36	41	38.5	0	0	0	0	0	+	35	31	33.0	
45	45	45.0	0	0	0	Lu	+	+	36	29	32.5	
49	48	48.5	+	+	0	0	0	0	32	32	32.0	
44	51	49.5	0	0	0	0	0	0	38	38	38.0	absent triradii c

O=pattern absent. Lr=loop radial. Lu=loop ulnar. Lt=left. Rt=right.

an A/B translocation by Walzer *et al.* (1966), a B/B translocation by Shaw *et al.* (1965), a B/C translocation by Edwards *et al.* (1965), a C/E translocation by Punnett *et al.* (1966), Mann *et al.* (1965), and a C/C translocation by Lindsten *et al.* (1965), Walker and Harris (1962), Jacobsen *et al.* (1963), and Dekaban (1966). The patients with reciprocal translocations in the above reported cases were mostly phenotypically normal and could survive as carriers of the translocation. Even a duplication of parts of an autosome due to partial trisomy occurring in a person

seems to be compatible with life, albeit not without severe defects. Monosomy or partial disomy of the autosome seems to be incompatible with live birth.

If the C group chromosome involved in the translocation of the present cases would not be the X, it can be stated that the propositus carries a balanced autosomal translocation. This assumption would be encouraged to some extent by relatively normal phenotype, positive sex chromatin and normal gestations, because there are reports showing that balanced autosomal translocation heterozygotes are not

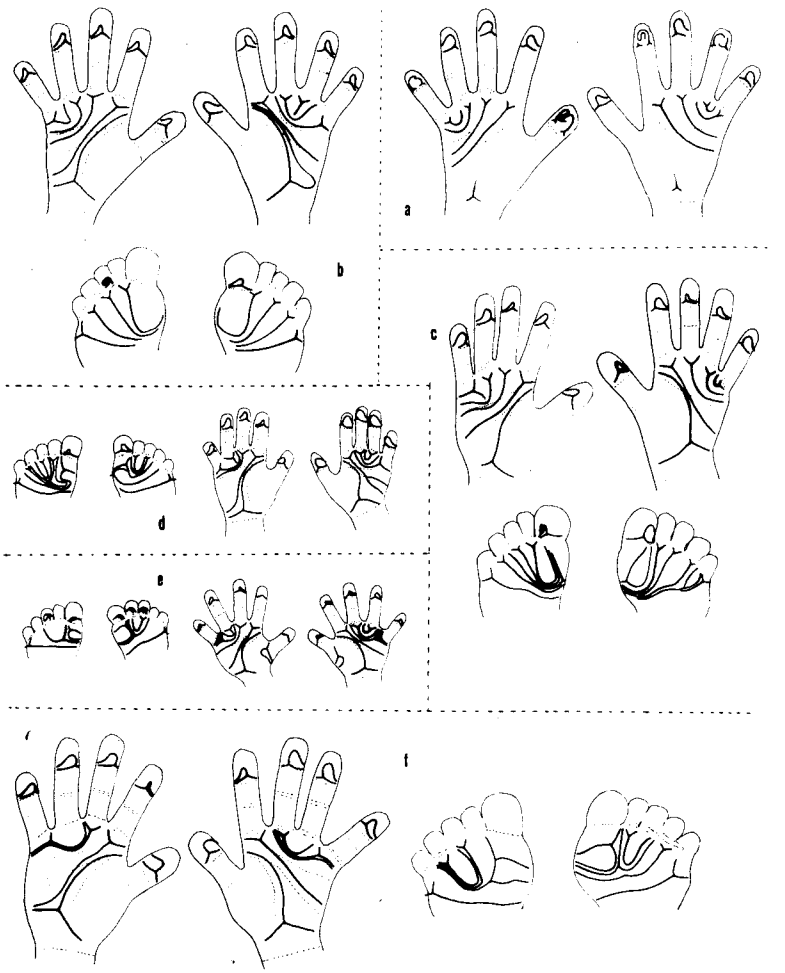

Fig. 6. Dermatoglyphics of the palms and soles of some propositus' relatives. a, Paternal aunt of the propositus. b, Propositus. c, Sister of the propositus. d and e, Elder son and younger son of the propositus. f, Husband of the propositus.

always infertile (Böök *et al.* 1961, Moorhead *et al.* 1961, Clarke *et al.* 1964, Court Brown *et al.* 1964, Yunis *et al.* 1964).

It has been shown that the birth of a Down's syndrome child is frequently preceded by abortions and that the monosomic zygote for chromosome 21 as expected in translocation mongol families is interpreted as having a lethal effect (Polani *et al.* 1960, Zellweger and Mikamo 1961). Schmid (1962) found a new translocation heterozygote occurring in one of 21-22 chromosomes in a phenotypically normal male whose wife had lost two children. The same chromosome abnormality was also found to occur in his father. Walker and Harris (1962) discovered many miscarriages in a large pedigree involving a familial translocation between two large acrocentrics.

Recent literature refers to some reports of familial translocations which are implicated as a cause of abortions (Jacobsen *et al.* 1963, Punnett *et al.* 1966, Summitt 1966, Walzer *et al.* 1966, and some others).

Information is available to show that, normal, monosomic, trisomic and polyploid chromosome constitutions are common in spontaneously aborted specimens (Delhanty *et al.* 1961, Penrose and Delhanty 1961, Carr 1963, Hall and Källén 1964, Thiede and Salm 1964, Kelly *et al.* 1965, Szulman 1965, Trujillo *et al.* 1966), whereas the anomaly involving chromosome translocation has been very rarely reported (the Geneva Conference). It seems very probable that the chromosome translocation of certain types might be associated with intrauterine death and abortion, or with the failure of implantation due to its lethal or allied effect.

To date, the value of cytogenetic studies on abortuses has been greatly increased, and chromosome anomalies as an etiological cause of spontaneous abortion have been subjects of attractive attention in both biological and medical fields in many countries.

Dermatoglyphic pattern of the finger tips did not show any significant difference among the propositus, her elder son and sister. An arch-pattern was detected in the I and II fingers of the left hand of her younger son, while the other member of this family showed no such pattern. The whorl pattern as observed in the aunt was rare in occurrence in the members of this family.

Summary

A 36-year-old woman with some minor phenotypic anomalies who was hospitalized for serum hepatitis, was found to have a chromosomally balanced B/C reciprocal translocation. Her sex chromatin observed in buccal smears was positive. The propositus cast two spontaneous abortions in the past. Twenty seven familial members were chromosomally studied. It was found that the elder son of the propositus carrying some phenotypic anomalies was the carrier of a balanced B/C translocation, while the remaining members showed no deviation from a normal chromosome complement.

Some dermatoglyphic, immunological and biochemical data were given for the propositus and her relatives.

Acknowledgements

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