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ALESSANDRA CARNEVALE, and LUIS DE LOS COBOS*

Genetics Service, Hospital Infantil, IMAN
Insurgentes Sur 3700-C, Mexico 22, DF

* Present address: Department of Biochemistry, Section of Genetics, Universidad de los Andes, School of Medicine Mérida, Venezuela.

An Inherited Small Extra Chromosome:

A Mother with 46,XX,t(17;22)
(p1;q1) and a Son with 47,XY,
+ der(22) mat

Summary. A boy with multiple congenital anomalies was found to have a small extra chromosome. This small chromosome was interpreted as a der(22)mat because his mother was a balanced carrier with 46,XX,t(17;22)(p1;q1) chromosomes. It is hoped that with the use of the banding techniques many karyotypes will be revaluated and reinterpreted. The mother's karyotype was erroneously interpreted earlier as a 21/22 translocation.

A small extra chromosome has been linked to two specific syndromes. Schachenmann *et al* (1965), Weber, Dooley, and Sparkes (1970), and Gerald *et al* (1968) described anal atresia, vertical colobomata of the iris, bilateral preauricular fistulas, and other congenital defects in a condition called 'the cat eye syndrome'. Abbo and Zellweger (1970) pro-

posed a syndrome under the noncommittal name 'the syndrome of the (supernumerary) metacentric chromosome' with characteristics including severe mental retardation, irritability and even destructiveness, muscular hypotonia, retinal coloboma, and other constitutional stigmata. We reported (Borgaonkar, Schimke, and Thomas, 1971b) on five unrelated patients with a small metacentric extra chromosome and pointed out that it is difficult to assess the clinical significance of a karyotype containing a small extra chromosome member. In two of these patients no serious clinical problems were noted whereas in the remaining three the multiple congenital abnormalities were neither striking nor fitting the descriptions of the above two syndromes. Since there are several possible mechanisms by which the extra chromosome material can arise it is possible that the extra chromosome has a different origin in each case.

In the present report the source of the small extra chromosome is known since the mother carried both products of a 17/22 translocation. It is rare that an inherited small chromosome product of a translocation can be documented.

Case Report

C. C. (JHH 131 89 28), a white male, born on 27 May 1967, was the product of an uneventful second pregnancy. Development was rather unremarkable; he had walked at 16 months, his teeth were normal, and he spoke a few words. Genitalia were normal and no abnormalities

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FIG. 1. Front and side view of the patient's face at 5½ years of age.

FIG. 2. Karyotype of the patient prepared by standard staining techniques showing 47 chromosomes including the small der(22)mat chromosome.

of eyes, ears, heart, or lungs were noted. Examination at 29 months showed that the height was 100 cm (97th centile); weight 3178 g; head circumference was 48.5 cm (below third centile); span was 92 cm; lower segment was 38 cm. Subsequent examination at 42, 50, and 69 months revealed consistent growth. Radiology at 42 months of age showed a normal bone age; however bones were unusually thin. The skull was dolichocephalic and the neurocranium probably small. The physical appearance (Fig. 1) was unusual with a narrow head and face which bore resemblance to the patient described by Bühler and colleagues (1972).

Psychological Examination (Dr Carol R. Zussman) at 63 months showed that the child was functioning in the educable-retarded range. IQ tests (WISC scale) gave a verbal IQ of 74, performance IQ of 63, and a full scale IQ of 66.

Family History. The father and mother were 31 and 30 years of age, respectively, at the time of the patient's birth. The first pregnancy, complicated by moderate hydramnios, terminated in an intrauterine

fetal death of a male infant at approximately 35 week's gestation, the baby being macerated but noted to have an extra digit. Microscopic examination showed no histologically recognizable features and degenerative changes were seen. No testes were palpable in the scrotum. Low placed ears and micrognathia were found. The couple have, since the birth of the patient, adopted a girl. The maternal grandfather and grandmother were 43 and 40 years of age, respectively, at the time of birth of the mother of the patient.

Chromosome Findings

In both blood and skin fibroblast cultures the patient was found to have 47 chromosomes which included a small chromosome (Fig. 2). The father of the patient and both the maternal grandparents were found to have apparently normal chromosome constitutions. The mother of the patient, however, had 46 chromosomes including two abnormal chromosomes (Fig. 3). Satellites were visible on one arm of the small chromosome which is interpreted

FIG. 3. Karyotype of the mother prepared by the Giemsa-banding method showing the 46,XX,t(17;22)(p1;q1) chromosome constitution.

(Fig. 4) as a deleted chromosome 22 (22q-). One chromosome 17 had elongated short arms. This is interpreted as a translocation of the long arm of chromosome 22 onto the short arm of a No. 17 chromosome: t(17;22)(p1;q1) (Paris Conference, 1971).

This karyotype was, previous to the use of the banding technique, interpreted as a balanced 21/22 translocation. One of the chromosomes 18, although noticeably shorter, was misplaced there and was in fact a G autosome. The translocated chromosome 17 was interpreted as either a 16 or an F-group chromosome. In other words the variability found in the E- and F-groups was considered to be within normal limits. A futile search was also undertaken to locate satellites on the other arm of the small chromosome. Another analysis on the mother and child showed a 17/G translocation (Farber, 1969).

Giemsa- and quinacrine-banding techniques led to the interpretation that in the mother the long

arm of chromosome 22 (which has a non-specific G- and Q-banding pattern) had been translocated onto the short arm of chromosome 17 (Fig. 3). Whether it is a reciprocal translocation, ie, whether any segment of the short arm of chromosome 17 has been translocated to the remaining long arm of chromosome 22, cannot be determined.

Dermatoglyphic Data

The details are provided in Table I. The dermatoglyphic patterns of the fingers, palm, and sole in the patient are unremarkable in comparison with the parents except that the patient has a simian crease on the right palm. The Hopkins score of the patient was -4.10, in the non-Down's syndrome range (Borgaonkar *et al*, 1971a).

Comment

Before the use of the newer banding techniques in the study of this family, we had interpreted the

FIG. 4. Partial photograph showing the satellites at one end of the small chromosome in the mother of the patient.

TABLE I
DERMATOGLYPHIC DATA

Sole Patterns		Palmar Patterns							Fingers					
Hallucal	Big Toe	Triradius	Hypothenar	Simian Crease	Interdigital Area				1	2	3	4	5	
					I	II	III	IV						
<i>Propositus</i>														
L R	W W	W W	t t	— L ^r	— +	— —	— —	L ^d L ^d	— —	L ^u L ^u	L ^u L ^r	L ^u W	L ^u W	L ^u L ^u
<i>Mother of propositus</i>														
L R	W W	L ^f L ^f	t' —	L ^d A	— —	— —	— —	— —	— —	L ^u W	L ^u L ^r	L ^u L ^u	L ^u W	L ^u L ^u
<i>Father of propositus</i>														
L R	W L ^d	L ^f L ^f	t t	L ^d L ^d	— —	— —	— —	L ^d L ^d	L ^u L ^u	L ^r L ^u	L ^u L ^u	L ^u L ^u	L ^u L ^u	L ^u L ^u

mother's karyotype to be one of 21/22 translocation. We had placed one of the G autosomes in the 17-18 group and the larger 17 was incorrectly interpreted as a 21/22 translocation metacentric chromosome. The small chromosome was interpreted as the smaller product of a reciprocal 21/22 translocation referred to here as der (22) mat (Paris Conference, 1971).

Familial metacentric extra chromosomes with satellites at both ends have been reported previously (Pfeiffer, Diekmann, and Buchner, 1967; Armendarces *et al*, 1969). Borges and Wald (1963) reported satellites on only one end in a father and one offspring.

The phenotype of the patient is, in our opinion, not characteristic of either of the two syndromes described previously with a small extra chromosome (Schachenmann *et al*, 1965; Gerald *et al*, 1968; Abbo and Zellweger, 1970; Weber *et al*, 1970). However, he does resemble the patients described by Bühler *et al* (1972). These patients have partial trisomy 22, ie, all of chromosome 22 except the distal segment of the long arm was present in triplicate. Karyotypically the patients may be similar to our patient and the differences between the two may be due to inherent phenotypic variation and to differences in deleted segments.

Macintyre, Walden, and Hempel (1971) have reported a translocation which appears to be similar to that found in the present family. Their patient also had an extra small chromosome which was considered as an example of tertiary trisomy. In their family also the transmission of this small chromosome was through the mother and due to non-disjunction.

Cohen and Putnam (1972) recently reported an 18p- syndrome patient whose karyotype was presumptive of a 'monosomy G.' In fact, the patient

had the long arms of a chromosome 21 translocated onto chromosome 18.

With the advent of new techniques it is plausible that many karyotypes will be re-evaluated and reinterpreted. Some of the correctly interpreted chromosome rearrangements, if found in several, or even many members of large kindreds can be helpful in gene assignment studies (Borgaonkar *et al*, 1973) and even in the sporadic cases the translocation chromosomes can be used in chromosome mapping studies by the cell hybridization approach.

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DIGAMBER S. BORGAONKAR, VICTOR A. MCKUSICK,
and PHILLIP A. FARBER

*Division of Medical Genetics, Department of
Medicine, The Johns Hopkins University School
of Medicine, Baltimore, Maryland 21205 and
Cytogenetics Laboratory, Department of Pathology,
Geisinger Medical Center Danville, Pennsylvania
17821, USA*

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Segregating Reciprocal (4;21) (q21;q21) Translocation with Proposita Trisomic for Parts of 4q and 21

Summary. The segregation of a balanced reciprocal (4;21)(q21;q21) translocation is described. The family was ascertained through a clinically abnormal proposita with an unbalanced karyotype 47,XX,+der(21),t(4;21)(q21;q21)mat. The proposita was trisomic for regions 4q2, 4q3, 21p, and 21q1. Symptoms that might be attributed to the partial trisomy for parts of 4q were narrow bird face with slanting forehead, prominent nasal bridge and small mandible, downward pointing corners of the mouth, deformed ears, palpebral ptosis, and bushy eyebrows. Similar symptoms occur in other trisomy and deletion syndromes.

Several different procedures can be used to produce banding patterns in mammalian chromosomes (Paris Conference, 1971). The application of these methods often permits the precise identification and description of chromosomal rearrangements such as translocations. It thus becomes feasible, for

example, to determine which segments occur in triplicate in unbalanced translocation heterozygotes. The object of the present report is to describe the segregation of a balanced human reciprocal translocation in a family. Clinical signs in the unbalanced proposita may be attributed to trisomy for parts of 4q and 21.

Case Report

The proposita was the parents' only child. She was born at term in August 1970 after an uncomplicated pregnancy and delivery. She weighed 2810 g and was 48 cm long. Her head circumference was 31 cm at birth. One day after birth she was admitted to a paediatric ward because of respiratory difficulties.

Physical examination revealed her to be a malformed microcephalic infant (Fig. 1). She had a bird face with slanting forehead, prominent nasal bridge, narrow and high palate, and micrognathia. Her face was narrow with narrow palpebral fissures. She had slight epicanthal folds and deformed ears. Her fingers and toes were short and square. The thumbs were small and widely separated from the second fingers, as were the first and second toes. She had transverse plantar creases. Her muscles were hypotonic. There was a large umbilical hernia, pectus excavatum, and slight pes equinovarus in both feet. The external genitalia were normal and no abnormalities were detected in the genito-urinary or cardiovascular systems.

She was examined at regular intervals and showed retarded somatic and psychomotor development. She rolled over at 8 months, crawled at 13 months, and sat at 16 months, but at 28 months she still could not stand or walk without support. At 28 months she weighed 7340 g