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INTERSTITIAL DELETION 3p ASSOCIATED WITH t(3p−;18q+) TRANSLOCATION

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Summary A girl with growth and mental retardation, ventricular dilatation, hypoplastic brain, and other minor anomalies was found to have a 46,XX,t(3p−;18q+) karyotype. G-, Q-, and R-band analyses and measurements of chromosome length revealed a partial deletion del(3)(p13p21), in addition to the translocation. Her karyotype was 46,XX,del(*3*), t(*3*;18) (3qter→3p13::18q23→18qter;18pter→18q23::3p21→3pter) according to the Paris and Stockholm Conference nomenclature.

INTRODUCTION

Several cases of partial trisomy of no. 3 chromosome have so far been reported. Partial monosomy, however, is extremely rare.

In the present communication, a girl with interstitial deletion 3p is described. As far as the authors are aware of, the case represents the first of the kind. The patient also represents an example of deletion simultaneously induced with reciprocal translocation.

CASE REPORT

The patient, a girl, was born at term after uneventful pregnancy. She was the first child of unrelated parents, both being 22 years old. There was no history of congenital anomalies in the family. The weight and length at birth were 2,600 g and 48 cm, respectively. She was very slow in both gaining and development. At 21 months, her weight was 5,700 g which corresponded to that of an infant at 3 months of age. On the other hand, height (70 cm), both head (44 cm) and chest (41 cm) circumference were within normal limits. She began to crawl at the age of 18 months and to walk with support at the age of 22 months. At the age of 3 years she was able to walk without support. By 3 years and 2 months of age, she spoke a few words. The first tooth erupted at 11 months of age. Her appearance was not unusual. However, physical examinations revealed various minor anomalies. They included hypertelorism, downward slant of palpebral fissures, saddle

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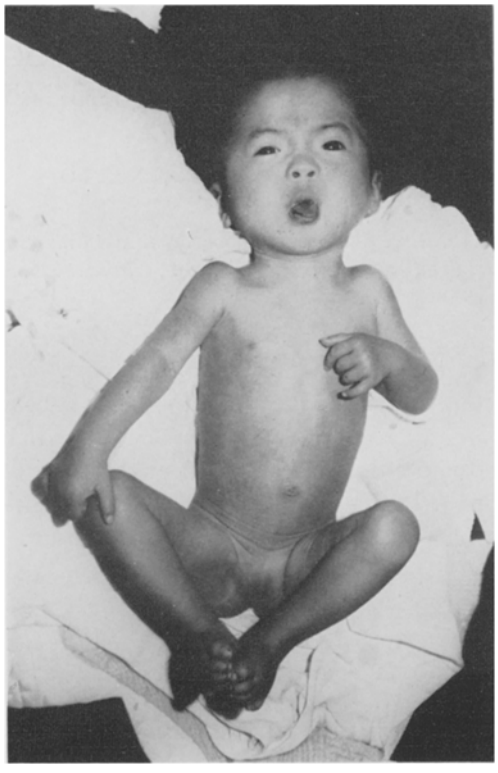

Fig. 1. The patient at 1 3/4 years of age.

nose, low set ears, high arched palate, narrow nasal cavity, and clinodactyly. Extremities were thin and the feet were flattened bilaterally. Both third and fifth toes overlapped on the fourth bilaterally (Fig. 1).

Growth hormone stimulation tests by insulin and arginine revealed low response, however, the levels of thyroxin, protein bound iodine and ACTH were within normal limits.

Pneumoencephalography revealed ventricular enlargement (Evan's ratio 0.35; Schievsman's ratio 2.77) and hypoplastic brain. No abnormalities were found in ECG, PCG, EEG, and fundscopy. Bone age corresponded to chronological age.

Developmental test was done at the age of 21 months according to the method of Tsumori and Inage. Her development corresponded to that of an 11-month-old infant (DQ=52).

Dermatoglyphics: Dermatoglyphic findings were as follows: right fingers: I ulnar loop; II arch; III whorl; IV ulnar loop and V whorl, left: I ulnar loop; II arch; III ulnar loop; IV whorl and V whorl. There was an incomplete simian crease on the right. Axial triradii were distally located on both palms (*atd* angles: R 63° and L 60°).

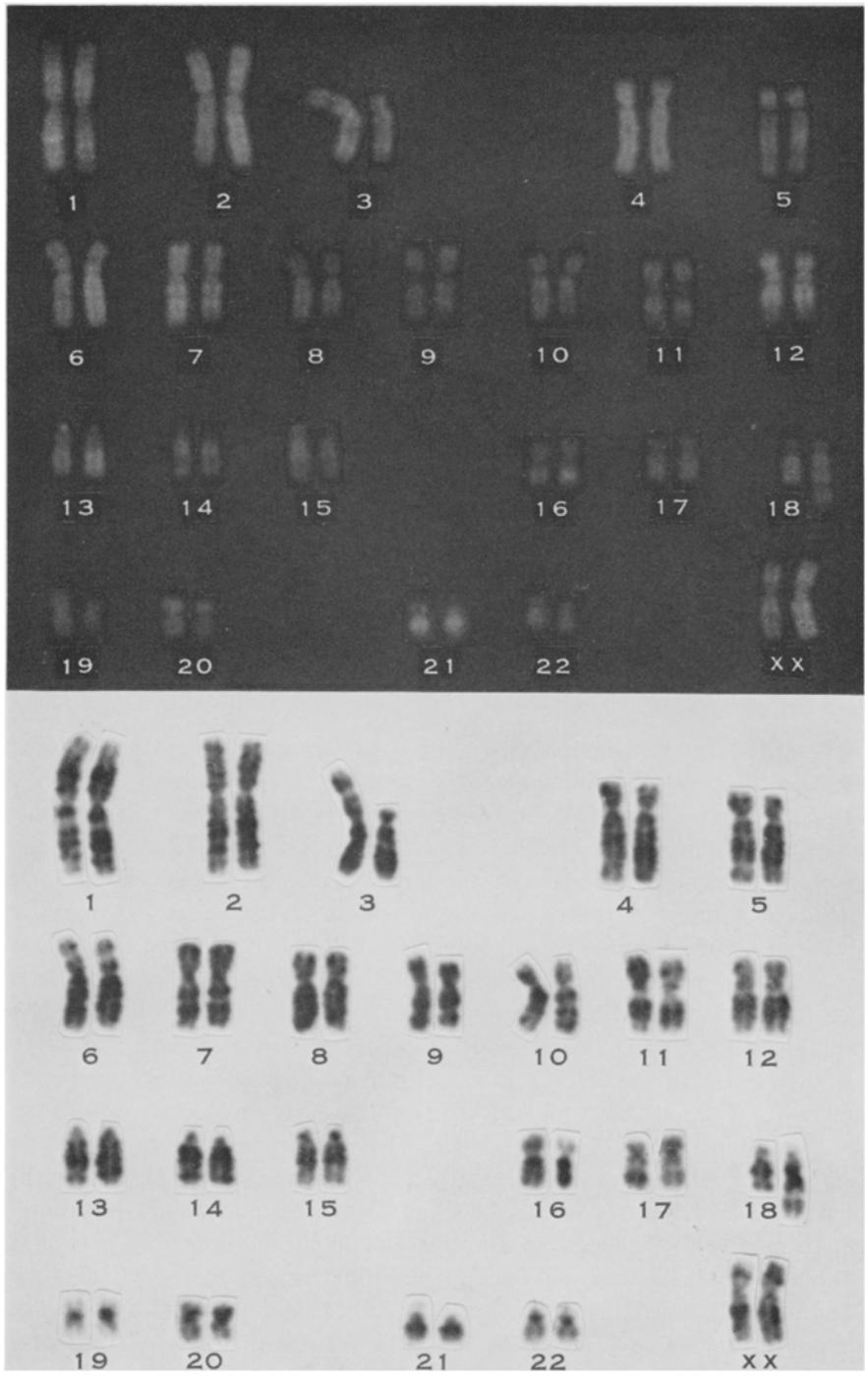

Fig. 2. Q banded (top) and G banded (bottom) karyotypes from the patient. Showing partial deletion associated with translocation, t(3 ; 18) (3qter→ 3p13 : : 18q23→18qter ; 18pter→18q23 : : 3p21→3pter).

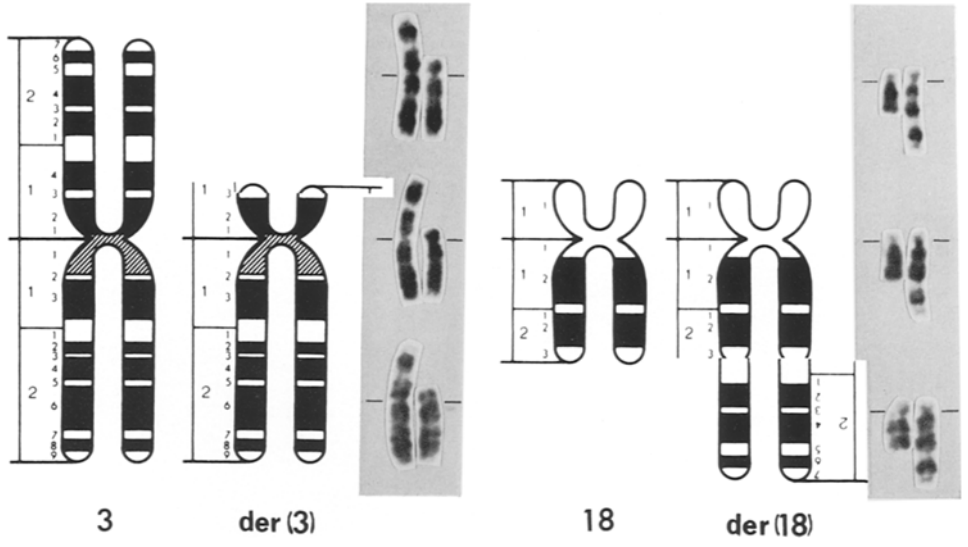

Fig. 3. Partial karyotypes of the patient and schematic representation of them.

CYTOGENETIC FINDINGS

Cytogenetic studies were carried out by the standard lymphocyte-culture technique. G-, Q-, and R-staining methods were those described by Sumner *et al.* (1971), Caspersson *et al.* (1970), and Sehested (1974). The patient had 46 chromosomes with a translocation between one of no. 3 and a no. 18 chromosome, *i.e.*, t(3p−;18q+) (Figs. 2 and 3). At the first glance, the translocation appeared reciprocal in nature. However, close examination revealed that the length of the der(18) (18q+ chromosome) was slightly shorter than that expected from the length of a no. 18 chromosome with minimal deletion plus a segment of distal 3p translocated to it. As to the no. 18 chromosome, the break point was in the q23 band. Two different break points were identified in the no. 3 chromosome. In the der(3), it was at p13, and in the der(18), it was at p21, *i.e.*, a small segment including p14 was missing. Formula for both derivative chromosome were, 3qter→3p13::18q23→18qter and 18pter→18q23::3p21→3pter. To determine the length of deleted segment, measurements of the derivative chromosomes were made using photographic prints (final enlargement × 4,000) of G-banded metaphases. Results were expressed relative to the length of a normal no. 18 chromosome and were shown in the Table 1. If there were no deletion, the difference in the length of a normal no. 3 and der(3) should equal to that of a der(18) and a normal no. 18, *i.e.*, the column D in the Table 1 should be 0. However, there is a small but consistent difference between the two. Based on the *F*- and *t*-tests the results were significant ($p<0.025$ and $p<0.001$, respectively). The deleted segment corresponded to about

Table 1. Results of chromosome measurements in 20 metaphases from the patient.[a]

Cells	Chromosome measured			
	A No. 3	B der(3)	C der(18)	D[b]
1	2.24	1.40	1.68	0.10
2	2.60	1.59	1.83	0.18
3	2.55	1.59	1.67	0.21
4	2.50	1.59	1.67	0.24
5	2.45	1.59	1.77	0.09
6	2.39	1.41	1.62	0.36
7	2.30	1.50	1.59	0.21
8	2.39	1.50	1.70	0.19
9	2.21	1.40	1.46	0.35
10	2.43	1.45	1.60	0.38
11	2.57	1.68	1.81	0.08
12	2.65	1.76	1.77	0.12
13	2.64	1.73	1.84	0.07
14	2.34	1.44	1.72	0.18
15	2.69	1.72	1.92	0.05
16	2.31	1.55	1.67	0.09
17	2.74	1.71	1.82	0.21
18	2.38	1.48	1.66	0.24
19	2.86	1.71	1.87	0.28
20	2.58	1.55	1.69	0.34
Mean	2.49	1.57	1.72	0.20
S.D.	0.176	0.113	0.108	0.101

[a] Results were expressed relative to the length of a normal no. 18.
[b] D=A−B−(C−1). Represents length of deleted segment from a no. 3 chromosome (1=length of a normal no. 18).

8% of the length of a normal no. 3 chromosome. The karyotype of the patient may be formulated as 46,XX,del(*3*),t(*3*;18) (3qter→3p13::18q23→18qter; 18pter→18q23::3p21→3pter). Both parents showed a normal karyotype.

DISCUSSION

Scince the advent of banding techniques, there have been fifteen reports describing partial trisomy or monosomy involving the short arm of no. 3 chromosome, the latter included ring chromosomes (Table 2). The most of these reports dealt with either cases of partial trisomy or recombinant type abnormality. In only two cases was simple 3p monosomy described (Fineman *et al.*, 1978; Verjaal and Nef, 1978). The monosomic segment was from 3p25 to 3pter in both cases. In the present case, the monosomic segment included band p14 as well as a part of p13 and/or p21, *i.e.*, the segment distal to band p22 was not involved.

Table 2. References on the cases with 3p trisomy and monosomy.

Author	Karyotype	Trisomy	Monosomy
Allerdice *et al.* (1975)	46, XX or XY, rec(3), dup q, inv(3) (p25q21) pat or mat	3q21→qter	3p25→ter
Ballesta and Vehi (1974)	46, XY, der(4), t(3;4) (p23;p16) mat	3p23→pter	4p16
Boue *et al.* (1974)	46, XX, rec(3), dup q, inv(3) (p25q21) pat	3q21→qter	3p25→ter
Fineman *et al.* (1978)	46, XY, rec(3), dup q, inv(3) (p25q13) mat	3q21→qter	3q25→ter
	46, XX, rec(3), dup q, inv(3) (p25q25) pat	3q25→qter	3p25→ter
	46, XX, del(3) (p25)	—	3q25→ter
Fitch (1978)	46, XY, der(3), t(3;6) (p24;q22) mat	6q23→qter	3p24→ter
Kawashima and Maruyama (1979)	46, XX, rec(3), dup q, inv(3) (p25q21) mat	3q21→qter	3p25→ter
Parloir *et al.* (1979)	46, XY, der(18), t(3;18) (p25;q23) mat	3p25→pter	18q23
Rethoré *et al.* (1972)	46, XY, inv? ins(7;3) (q31;p21p26)mat	3p21→p26	—
Sachdeva *et al.* (1974)	46, XY, der(12), t(3;12) (p?23;q?24) mat	3p?23→pter	12q?24
Say *et al.* (1976)	46, XX or XY, der(15), t(3;15) (p23;p12) mat	3p24→pter	15p13
Schinzel *et al.* (1978)	46, XY, der(4), t(3;4) (p23;q35) mat	3p23→pter	4q35
Surana *et al.* (1977)	46, XY, der(22), t(3;22) (p2;q13) pat	3p2→pter	22q13
Verjaal and Nef (1978)	46, XY, del(3) (p25)	—	3p25→ter
Witkowski *et al.* (1978)	46, XY, r(3)	—	not stated
Yunis (1978)	46, XY, der(22), t(3;22) (p21.2;q13.3) pat	3p21.2→pter	22q13.3→q13.5

A family with multiple cases of interstitial 3p trisomy was reported by Rethoré *et al.* (1972). The trisomic segment was from 3p21 to 3p26 and therefore was not overlapped with the monosomic segment in the present case. If trisomic cases involving the same segment as our case are reported, it will be interesting to see whether counter-type symptoms appear.

Fried *et al.* (1978) reported the first example of deletion which presumably occurred simultaneously with reciprocal translocation. As far as the authors are aware of, the present case represents the second of such abnormality. It appears to be advisable to exert maximum effort to detect possible small deletion when *de novo* "balanced" translocation is observed in a patient who is phenotypically abnormal.

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