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A CASE OF DISTAL 4q TRISOMY DUE TO FAMILIAL (4;5)(q31; p15) TRANSLOCATION

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Summary A boy with multiple anomalies including atresia of the esophagus, ventricular septal defect, horseshoe kidney and some minor anomalies is described. His karyotype was 46,XY, der(5), t(4;5)(q31;p15)pat, *i.e.*, he was partially trisomic for a distal segment of long arm of no. 4.

INTRODUCTION

The use of various banding techniques has made it possible to establish a number of new chromosomal syndromes (Lewandowski and Yunis, 1975; Nakagome, 1975). Distal 4q- trisomy syndrome represents one of the kinds.

In the present report, a male infant with multiple congenital malformations is described. The patient was trisomic for a distal segment of 4q(q31→qter) due to paternal balanced translocation.

CASE REPORT

The propositus, a boy, was born at 42 weeks of gestation and weighed 2,380 g. The amount of amniotic fluid appeared normal. The head circumference was 33.5 cm and length 46 cm both being within normal limits. He scored 4 on the Apgar's score. Both cyanosis and dyspnea lasted since then. He started to vomit pale green mucus mixed with bubbles. X-ray examinations revealed congenital atresia of esophagus. The diagnosis of aspiration pneumonia and ventricular septal defect (VSD) was also made.

Abnormalities noticed at birth included muscle hypotonia, unusual facial appearance, hypertelorism, low set and malformed ears and preauricular skin tag at left, wide set nipples, bilateral simian creases, overlapping fingers, bilateral retentio testis, and the deviated fourth toes from the third toes (Fig. 1). The patient received

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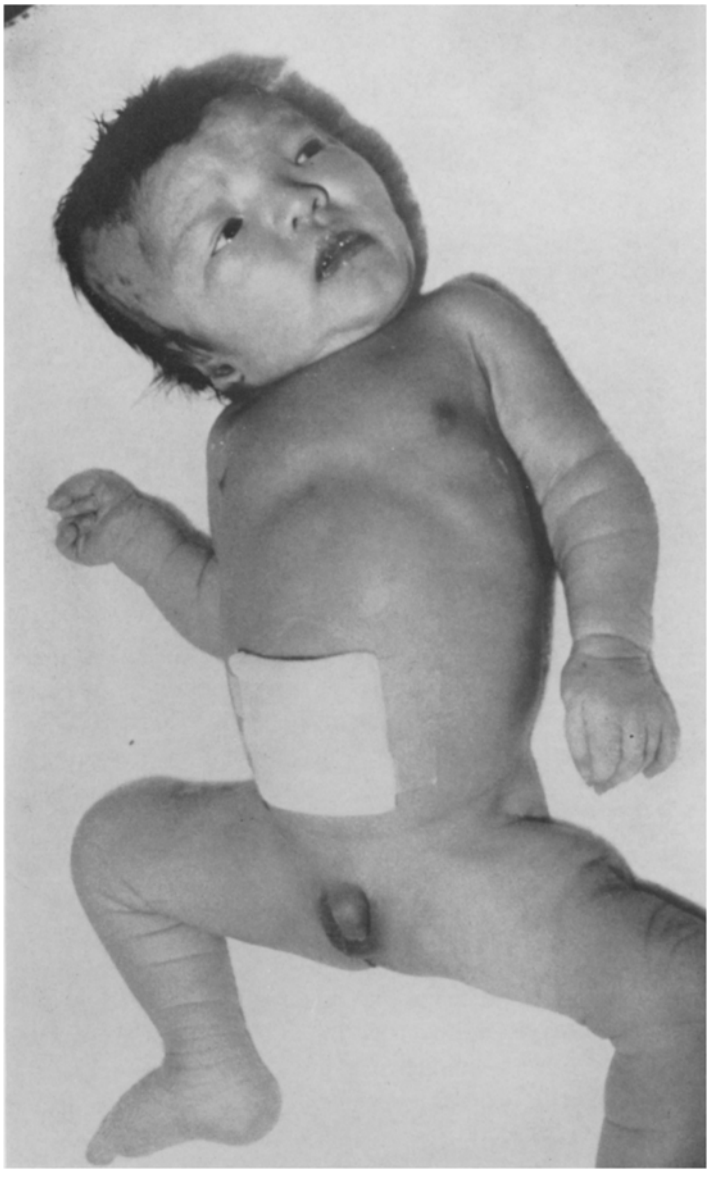

Fig. 1. The propositus at 10 days of age.

gastrostomy at 20 days of age. He died of pneumonia at 76 days of age.

The autopsy disclosed congenital atresia of the esophagus associated with esophagotracheal fistula (C-Type of Gross Classification), VSD, the horseshoe kidney, incomplete pulmonary lobes, and bilateral retentio testis abdominalis. Histological examination of kidney showed normal features.

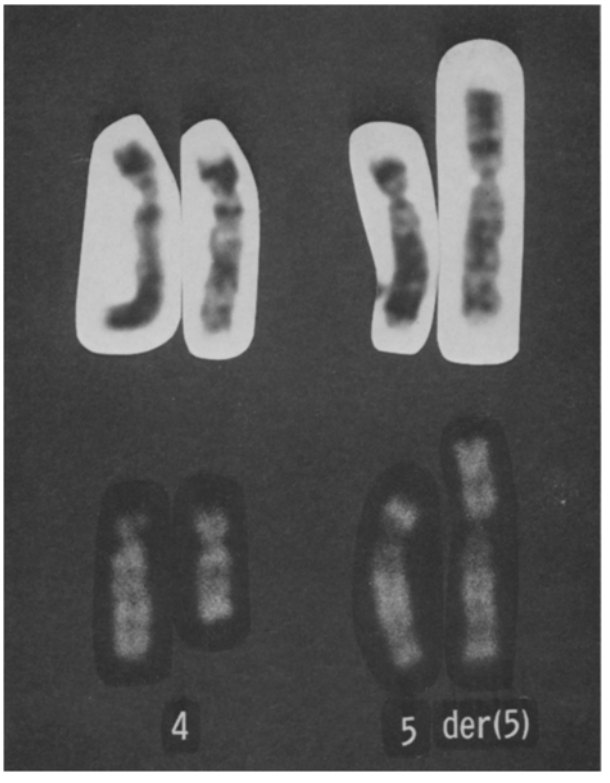

Fig. 2. Partial karyotypes of propositus (G-band, top) and his father (Q-band, bottom).

CYTOGENETIC STUDIES

The propositus and his parents were examined by the standard leukocyte-culture technique. Slides were aged for 7 to 10 days and treated by the modified trypsin Giemsa technique (Nakagome *et al.*, 1973). In all karyotypes of the propositus, there was a marked increase in the length of the short arm of one of the no. 5 pair, the karyotype being 46,XY, 5p+.

In the karyotype of the phenotypically normal father a balanced 4/5 translocation was observed. Metaphases were examined further by both Q- (Caspersson *et al.*, 1970) and LBA-techniques (Nakagome *et al.*, 1977; Oka *et al.*, 1977). The points of breakages in chromosomes 4 and 5 were at bands q31 and p15 respectively (Figs. 2 and 3). Hence, his karyotype could be written: 46,XY, t(4;5) (4pter→4q31::5p15→5pter; 5qter→5p15::4q31→4qter).

The 5p+ chromosome of the propositus represents, in fact, the der(5) transmitted from his carrier father. He was trisomic for the distal segment of 4q (from

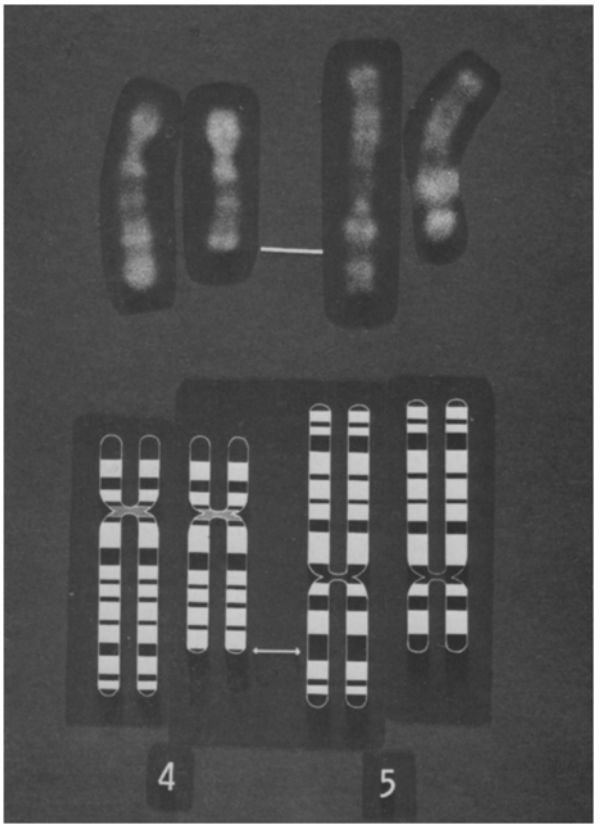

Fig. 3. Partial karyotype of father (LBA-technique, top) and schematic representation of it (bottom).

q31 to qter), and monosomic for a very small segment of 5p15. G-band pattern of the propositus was consistent with this interpretation. The propositus' karyotype was designated as: 46,XY, der(5), t(4;5) (q31; p15)pat, based on Paris Conference System (Paris Conference, 1971).

His mother had a normal karyotype.

DISCUSSION

There have been twenty reported cases of trisomy for the distal part of long arm of no. 4 chromosome (Francke, 1972; Surana and Conen, 1972; de la Chapelle *et al.*, 1973; Schwingshackl und Ganner, 1973; Warren *et al.*, 1973; Fonatsch and Flatz, 1974; Knörr-Gärtner *et al.*, 1974; Schrott *et al.*, 1974; Baccichetti *et al.*, 1975; Dutrillaux *et al.*, 1975; Vogel *et al.*, 1975; Biederman and Bowen, 1976; Cervenka *et al.*, 1976; Issa *et al.*, 1976; Sparkes *et al.*, 1977). The trisomic segment ranged

Table 1. Clinical features of partial trisomy 4q.

	Published cases	Present case
Psychomotor retardation	13/13	?
Microcephaly	12/15	−
Ocular abnormality	10/11	−
Hypertelorism	8/11	+
Depressed or wide nose bridge	10/13	−
Low set and/or malformed ears	16/16	+
Malformed digits	11/13	+
Malformed toes	5/9	+
Simian crease	8/12	+
Congenital heart disease	8/14	+
Abnormalities of urogenital system	8/14	+
Undescended testis (male)	8/8	+
Hypotonia	5/13	+
Hypertonia	4/13	−

from 4qter to 4q32, 4q31, 4q28, 4q27, 4q25 or 4q21. This difference might, in part, be responsible to the variation of clinical pictures observed among reported cases.

Common features in all of published cases included psychomotor retardation of various degree, abnormalities of ocular and/or palpebral fissures, low set and/or malformed ears, undescended testis in males and low birth weight. Microcephaly, hypertelorism, malformed digits and toes were also frequently observed (about 80% of examined cases). Congenital abnormalities of the heart and urogenital system were described in 8 out of 14 cases. Changes in muscle tone of variable degree have been described: hypotonicity in 5 of 13 cases and hypertonicity in 4 of 13 (Table 1).

The present case shows almost all of these features. In addition, he had congenital atresia of the esophagus, and incomplete pulmonary lobes.

Schwingshackl and Ganner (1973) reported a case of a partial 4q trisomy from paternal 4/5 translocation. The patient showed features of cri du chat syndrome. In the present case, the partial trisomy of 4q and monosomy of 5p (5p15→5pter) was transmitted from his carrier father with 4/5 translocation. However, he did not show the clinical features of cri du chat syndrome such as cat-like crying, microcephaly, round face, micrognathia, and antimongoloid slanting.

Recently, a new type of banding technique, LBA, was developed. It was shown that the technique was very useful in the study of chromosome variants in man (Nakagome *et al.*, 1977; Oka *et al.*, 1977). In LBA-banded chromosomes, late replicating segments showed intense fluorescence most of which corresponded to Q-bands. In the present study, the technique proved itself to be very useful in the determination of break points in structurally abnormal chromosomes. Individual bands were more clearly represented than those in Q-banded chromosomes.

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REFERENCES

Baccichetti, C., Tenconi, R., Anglani, F., and Zacchello, F. 1975. Trisomy 4q32-4qter due to a maternal 4/21 translocation. *J. Med. Genet.* **12**: 425–427.

Biederman, B. and Bowen, P. 1976. Partial trisomy 4q due to familial 2/4 translocation. *Hum. Genet.* **33**: 147–153.

Caspersson, T., Zench, L., and Johansson, C. 1970. Analysis of the human metaphase chromosome set by aid of DNA-binding fluorescent agents. *Exp. Cell Res.* **62**: 490–492.

Cervenka, J., Djavadi, G. R., and Gorlin, R. J. 1976. Partial trisomy 4q syndrome: Case report and review. *Hum. Genet.* **34**: 1–7.

de la Chapelle, A., Koivisto, M., and Schröder, J. 1973. Segregation reciprocal (4;21) (q21;q21) translocation with proposita trisomic for part of 4q and 21. *J. Med. Genet.* **10**: 384–389.

Dutrillaux, B., Laurent, C., Forabosco, A., Nosl, B., Suerinc, E., Biemot, M, -C., and Cotton, J, -B. 1975. La trisomie 4q partielle. A propos de trois observations. *Ann. Génét.* **18**: 21–27.

Fonatsch, C. and Flatz, S. D. 1974. Partial trisomy 4q and partial monosomy 18q as a consequence of a paternal balanced translocation. *Humangenetik* **25**: 227–233.

Francke, U. 1972. Quinacrine mustard fluorescence of human chromosome: Characterization of unusual translocation. *Amer. J. Hum. Genet.* **24**: 189–213.

Issa, M., Potter, A. M., and Blank, C. E. 1976. Multiple congenital defects associated with trisomy for long arm of No. 4. *J. Med. Genet.* **13**: 326–329.

Knörr-Gärtner, H., Knärr, K., and Hass, B. 1974. Familiäre Translokation t(4q−; 18q+) mit verschiedenartign unbalancierten Nachkommen. *Humangenetik* **21**: 315–321.

Lewandowski, R. C. and Yunis, J. J. 1975. New chromosomal syndromes. *Amer. J. Dis. Child.* **129**: 515–529.

Nakagome, Y. 1975. Annotation: "New" chromosomal abnormality syndromes. *Cong. Anom.* **15**: 139–149 (in Japanese).

Nakagome, Y., Iinuma, K., and Taniguchi, K. 1973. Points of exchange in a human NO. 5 ring chromosome. *Cytogenet. Cell Genet.* **12**: 35–39.

Nakagome, Y., Oka, S., and Matsunaga, E. 1977. LBA technique in the detection of chromosome variants. II. Chromosomes Except for Those with Q Variants. *Hum. Genet.* **38**: 307–314.

Oka, S., Nakagome, Y., Matsunaga, E., and Arima, M. 1977. LBA technique in the detection of chromosome variants. I. Chromosomes with known sites of Q variants. *Hum. Genet.* **39**: 31–37.

Paris Conference (1971): Standardization in human cytogenetics. Birth Defects. [Orig. Art. Ser., Vol. 8, No. 7, Nat. Fdtn. New York, 1972.

Schrott, H. G., Sakaguchi, S., Francke, U., Luzzatti, L., and Fialkow, P. J. 1974. Translocation t(4q−: 13q+), in three generations resulting in partial trisomy of the long arm of chromosome 4 in the fourth generation. *J. Med. Genet.* **11**: 201–205.

Schwingshackl, A. und Ganner, E. 1973. Partielle B-Trisomie bei Cri du Chat Syndrom. *Pädia. Pädolo.* **8**: 362–371.

Sparkes, R. S., Francke, U., Muller, H., and Toomey, K. 1977. Partial 4q replication due to inherited der(20), t(4;20) (q25; q13) mat. *Ann. Génét.* **20**: 31–35.

Surana, R. B. and Conen, P. E. 1972. Partial trisomy 4 resuting from a 4/18 reciprocal translocation. *Ann. Génét.* **15**: 191–194.

Vogel, W., Siebers, J. W., Gunkel, J. und Noel, B. 1975. Uneinheitlicher Phänotyp bei Partialtrisomie 4q. *Humangenetik* **28**: 103–112.

Warren, R. J., Monkus, E. and Tamer, A. 1973. Partial trisomy of the long arm of chromosome 4. *Amer. J. Hum. Genet.* **25**: 84A.