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Partial trisomy 13q22→qter and monosomy 18q21→qter as a result of familial translocation

S Čekada, S Kilvain, B Brajenović-Milić[1], L Brečević[2], E Kirinčić-Paučić and J Franulović

Department of Pediatrics, University of Rijeka, Children's Hospital "Kantrida", Rijeka; Department of Biology[1], School of Medicine, University of Rijeka, Croatia; Institute of Medical Genetics[2], University of Zürich, Zürich, Switzerland

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We report on a patient with a partial trisomy of chromosome 13q22→qter and partial monosomy of chromosome 18q21→qter showing distinct malformations. The phenotype of this unbalanced karyotype has not been previously described. The proband had a craniofacial dysmorphism, neck pterygium, closed fists with overlapping fingers, cutaneous appendix of the left fist, equinovarus and postaxial hexadactyly of the feet, atrial septum defect, unilateral cryptorchidism and hypertrophic pyloric stenosis. Using fluorescence *in situ* hybridization (FISH) the father's karyotype 46,XY.ish t(13;18)(13pter→13q22::18q21→18qter; 18pter→18q21::13q22→13qter) and the child's 46,XY.ish der(18)(18pter→18q21::13q22→13qter)pat were established. The mother's karyotype was normal. A risk of unbalanced offspring in carriers of a balanced reciprocal translocation depends on the length and genetic constitution of the exchanged segments. Risk figures should come only from empirical data. A phenotypically normal child with a balanced or normal karyotype could be born in the case of alternate segregation. Amniocentesis should therefore be recommended in any further pregnancy. □ *FISH, karyotype, malformations, prenatal diagnosis*

S Kilvain, Department of Paediatrics, University of Rijeka, Children's Hospital "Kantrida", 51 000 Rijeka, Istarska 43, Croatia

Reciprocal translocation constitutes the most frequent type of chromosomal aberration in humans (1). Carriers of such aberrations may have a high risk of producing live-born infants with an unbalanced karyotype. Here we report on a patient with multiple malformations caused by partial trisomy 13q22→qter and monosomy 18q21→qter, which was paternal in origin. To our knowledge such a karyotype and its phenotype have not previously been described. However, the patient's phenotype can be compared with previously described cases of partial trisomy 13q and monosomy 18q in spite of different break points, especially on chromosome 18 (2–4).

Case report

The male proband is the first child born to phenotypically healthy, non-consanguineous young parents. This was the mother's first pregnancy, and it followed a normal course until the 33rd week of gestation when she developed eclampsia and delivery was performed by Caesarean section. Foetal ultrasonography was performed at the 15th week of gestation and nuchal translucency of 9 mm was detected. No other ultrasonographic markers for chromosomal abnormalities were observed. At 15 + 5 wk of gestation a maternal serum screening test for Down's syndrome and neural tube defects was performed and showed a low risk for both (1:11 596 and 1:4799, respectively). Down's syndrome risk was calculated regarded to gestational age (15 + 5 wk), maternal age at delivery (24.1 y), maternal serum alpha-foetoprotein (1.19 MoM) and free β-human chorionic gonadotropin (0.65 MoM). This test has been used only for Down's syndrome and neural tube defects risks, but not for the other aneuploidies. No further invasive prenatal diagnostic procedures were performed. The proband's birthweight was 2240 g (75th centile), length 46 cm (75th centile) and head circumference 31.4 cm (75th centile). The Apgar scores were 6 and 7 at the first and fifth minute respectively. Multiple malformations noted at birth included: craniofacial dysmorphism (protruded forehead, deep set eyes, unilateral microphtalmos with cataract, bilateral epicanthic fold, wide and flat nasal bridge, low set ears, micrognathia and long philtrum), high arched palate, neck pterygium, elongated thorax, closed fists with overlapping of fingers, cutaneous appendix of the left fist, equinovarus and postaxial hexadactyly of the feet (Figs 1–3) and unilateral cryptorchidism. Further anomalies (atrial septum defect, different size kidneys, cortical atrophy of the brain, enlargement of the lateral

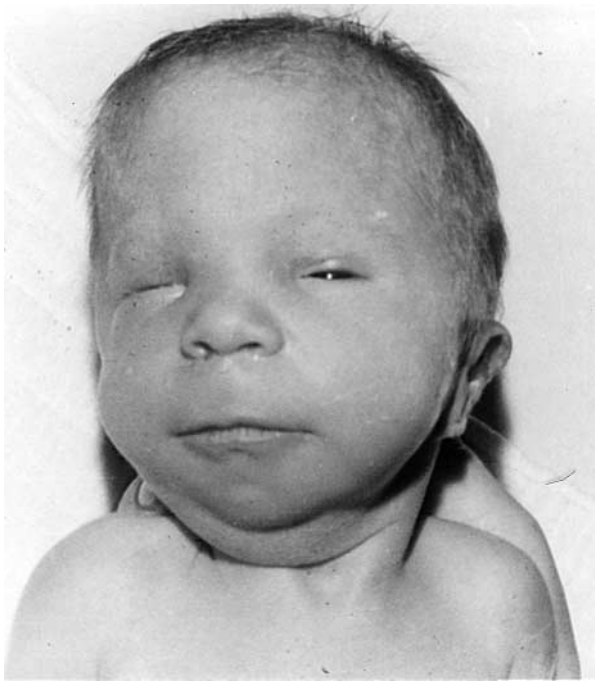

Fig. 1. The patient at 1 mo of age. Note the craniofacial dysmorphism and neck pterygium.

ventricles and pontocerebelar cistern, and gastroesophageal reflux) were detected by multiple imaging procedures. Hypertrophic pyloric stenosis was resolved surgically at the second month of age. Seizures accompanied by apnoea appeared at the fifth month of age. EEG showed multifocal changes in electrical activity of the brain, with a general tendency to a hypsarrhythmia pattern.

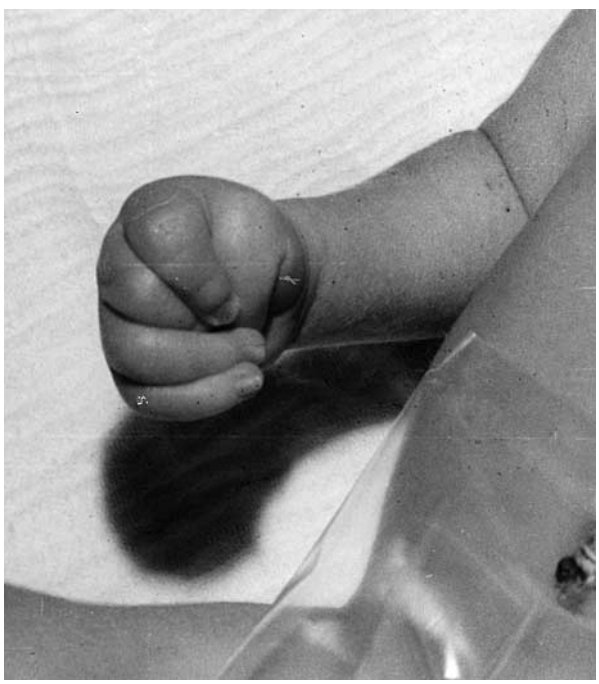

Fig. 2. The patient's closed fists with overlapping fingers.

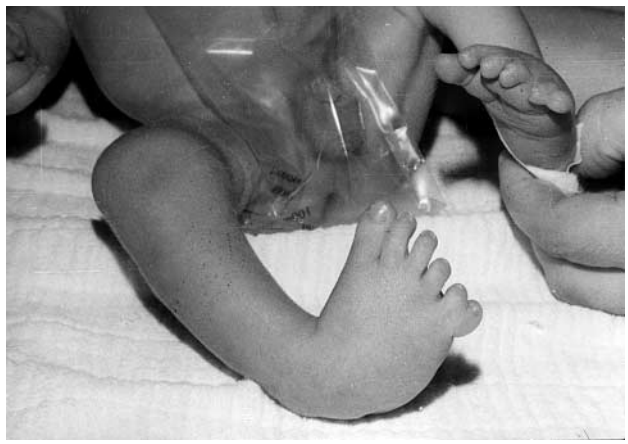

Fig. 3. Equinovarus and hexadactyly of the patient's feet.

Methods

Chromosome preparations from the patient and his parents were obtained from 72 h lymphocyte cultures. Karyotypes were provided after GTG-banding. Fluorescence *in situ* hybridization (FISH) was performed on lymphocyte specimens using whole chromosome painting probe for chromosomes 13 and 18: dual-colour painting with a library 13-green; biotin-labelled/detected via avidin-FITC and a chromosome 18-red;

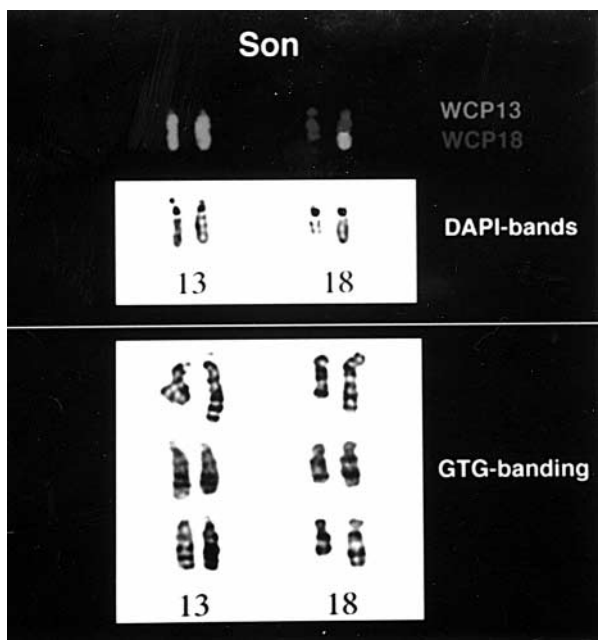

Fig. 4. Unbalanced karyotype of the child (GTG-banding; FISH).

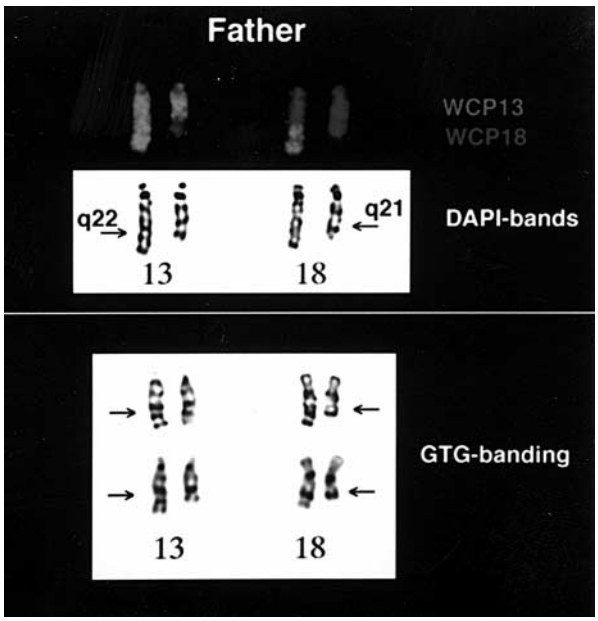

Fig. 5. Reciprocal translocation of the father (GTG-banding; FISH).

digoxigenin-labelled/detected via anti-digoxigenin-rhodamine, Fab fragments (Figs 4 and 5).

Results

Cytogenetic analysis (GTG-banding) in the patient revealed a trisomy 13q22→qter and monosomy 18q21→qter caused by balanced translocation (13q22; 18q21) presented in the proband's father. Application of the FISH techniques enabled us to confirmed the aberration, thus the patient's karyotype was 46,XY.ish der(18)(18pter→18q21::13q22→13qter)pat and the father's 46,XY.ish t(13; 18)(13pter→13q22::18q21→18qter; 18pter→18q21::13q22→13qter).

Discussion

Reciprocal translocation (*de novo* or inherited from a parent) occurs with a frequency of 1 in every 500 live-born infants (5). One of the most frequent breakage sites within chromosome 13 is the region between q14 and q21 (3). Duplication of 13q including the regions q2 and q3 and monosomy 18q lead to a characteristic syndromes (3, 6, 7). In our proband there is an influence of both partial trisomy 13q22→qter and monosomy 18q21→qter, and it is useful to compare its features with previously described cases of partial trisomy 13q and monosomy 18q in spite of their having different break points (Table 1).

Low maternal serum alpha-foetoprotein levels (MSAFP) may be associated not only with Down's syndrome, but with trisomy 13 or 18 (8). In contrast, Ou et al. found elevated MSAFP in partial trisomy 13q but not in complete trisomy 13 (9). Chen et al. reported *de novo* deletion of 18q22.2→qter associated with elevated levels of maternal serum free-βhCG (6). In our case maternal serum screening test for Down's syndrome and neural tube defects showed the decreased risk for both. We tend to believe that identification of a structurally unbalanced karyotype through a maternal screening test for Down's syndrome could be more or

Table 1. Comparison of clinical findings of the proband and two patients with partial trisomy 13 and partial monosomy 18.

Findings	Present case	Eggermann et al. (3)	Yu et al. (4)
Karyotype	46,XY der(18)(18pter-18q21::13q22-13qter)pat	46,XX, der(18)(18pter-18q23::13q14.3-13qter)	46,XX, -18,+der(18)t(13; 18) (13qter-13q22::18q23-18pter)pat
High forehead	+	+	−
Epicanthus	+	+	−
Hypertelorism	+	−	+
Corneal opacification	−	−	+
Cataract of the eye	+	−	−
Microptalmos	+	−	−
Long philtrum	+	+	−
Thin upper lip	−	+	−
High arched palate	+	−	+
Micrognathia	+	+	−
Neck pterygium	+	−	−
Elongated thorax	+	−	−
Polydactyly of hands/feet	+	−	+
Overlapping fingers	+	−	−
Rocker bottom feet	−	+	+
Pes equinovarus bil.	+	−	−
CNS anomalies	+	−	−
Atrial septum defect	+	+	−
Pulmon. valve absence	−	−	+
Pylorospasm	+	+	−
Cryptorchidism	+	−	−

less accidental. The association of increased nuchal translucency and foetal aneuploidy has been well-documented (10, 11, 12). However, detection of abnormal nuchal fold thickening associated with other ultrasonographic findings, such as polydactyly, congenital heart defect and CNS abnormalities, should serve as useful guideposts in prenatal ultrasound in addition to maternal serum screening in pregnancy with foetal partial trisomy 13q and partial monosomy 18q. The risk of carriers of a balanced reciprocal translocation having unbalanced offspring depends on the length and genetic constitution of the exchanged segment (13). Risk figures should only come from empirical data (13). A phenotypically normal child with a balanced or normal karyotype would be born in the case of alternate segregation. Thus amniocentesis should be recommended for any further pregnancy.

References

1. Schinzel A. Catalogue of unbalanced chromosome aberation in man. Berlin: Walter de Gruyter, 1984: 10
2. Schinzel A. Human cytogenetic database. In: Baraitser M, Winter R, editors. Oxford Medical Database Series. Oxford: Oxford University Press, 1997
3. Eggermann T, Engels H, Heidrich-Kaul C, Moderau I, Schwanitz G. Molecular investigation of the paternal origin of a de novo unbalanced translocation 13/18. Hum Genet 1997; 99: 521–2
4. Yu J, Wu JM, Lin SJ, Tzeng CC. Congenital isolated absence of pulmonary valve in a neonate with partial trisomy 13q. Chung-Hua Min Kuo HsiaoErh Ko i Hsueh Hui Tsa Chih 1995; 36: 214–6
5. Hall JG. Chromosomal Clinical abnormalities. In: Nelson WE, editor. Textbook of pediatrics. 15th ed. Philadelphia: WB Saunders Co., 1996: 317–8
6. Chen CP, Chern SR, Liu FF, et al. Prenatal diagnosis of a deletion of 18q in a fetus associated with multiple marker screen positive results. Prenat Diagn 1997; 17: 571–6
7. Dowton SB, Hing AV, Sheen-Kaniecki V, Watson MS. Chromosome 18q22.2-qter deletion and a congenital anomaly syndrome with multiple vertebral segmentation defects. J Med Genet 1997; 34: 414–7
8. Merkatz IR, Nitowski HM, Macri JN, Johnson WE. An association between low maternal serum alfa-fetoprotein and fetal chromosomal abnormalities. Am J Obstet Gynecol 1984; 148: 886–91
9. Ou CY, Hsu TY, Chang JC, Chang SY. Partial trisomy 13 [46,XY,dup(13)(q14-13)]: a case report. Chang-Keng-I-Hsueh 1998; 21: 82–5
10. Benacerraf BR, Neuberg D, Bromley B, Frigoletto FD. Sonographic scoring index for prenatal detection of chromosomal abnormalities. J Ultrasound Med 1992; 11: 449–58
11. Nicolaides KH, Azar G, Byrne D, Mansur C, Marks K. Fetal nuchal translucency: ultrasound screening for chromosomal defects in first trimester of pregnancy. Br Med J 1992; 304: 867–9
12. Vintzileos AM, Egan JFX. Adjusting the risk for trisomy 21 on the basis of second-trimester ultrasonography. Am J Obstet Gynecol 1995; 172: 837–43
13. Plomp AS, Engelen JJM, Albrechts JCM, de Die-Smulders CEM, Hamers AJH. Two cases of partial trisomy 8p and partial monosomy 21q in a family with a reciprocal translocation (8; 21)(p21.1; q22.3). J Med Genet 1998; 35: 604–7

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