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Case Report

CHROMOSOME 1q TERMINAL DELETION RESULTING FROM *DE NOVO* TRANSLOCATION WITH AN ACROCENTRIC CHROMOSOME

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Summary Distal deletion of chromosome 1q has been reported in nearly 30 patients, all being associated with a deletion ranging from the 1q42 or q43 band to 1qter region. Here, we describe a girl with 1q terminal deletion resulting from an unbalanced *de novo* translocation t(1;D or G)(q44; p11), as revealed by the presence of a satellited feature and an NOR-stained region at the tip of 1q. We suggest that most of the phenotypic abnormalities seen in patients with 1q distal deletion are attributable to the monosomy for band 1q44.

Key Words chromosome 1q, terminal deletion, *de novo* unbalanced translocation, NOR-staining

INTRODUCTION

Deletion of the distal long arm of chromosome 1 causes a characteristic combination of multiple phenotypic abnormalities, including psychomotor retardation, dismorphic craniofacial features, and neurologic signs (Mankinen *et al.*, 1976; Johnson *et al.*, 1985; Murayama *et al.*, 1991; Ioan *et al.*, 1992). To date, nearly 30 cases of distal 1q deletion have been reported. In the majority of cases the deletion was of *de novo* origin, and only 4 cases were due to an inversion or translocations derived from one of the parents (Juberg *et al.*, 1981; Golabi *et al.*, 1982; Speevak *et al.*, 1985). The deleted regions on 1q in the reported cases have ranged

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from 1q42 or 1q43 to 1qter. We report here a patient with a terminal deletion of 1q, resulting from an unbalanced translocation with an acrocentric chromosome, the breakpoint being at band q44.

We propose that the monosomy for band 1q44 alone is sufficient to account for most of the phenotypic abnormalities seen in patients with 1q distal deletion.

CLINICAL REPORT

The patient, a female, was the only child born to a 40-year-old father and 39-year-old mother, both healthy and unrelated. She was delivered at 41 weeks of gestation by Cesarean section in view of hypoxia, following artificial fertilization with a combination of ovulation stimulation and Pacol differential sperm sedimentation. Her birth weight was 2,560 g (−1.5 SD), length 45.5 cm (−2.2 SD), head circumference 31.6 cm (−1.2 SD), and chest circumference 31 cm (−0.9 SD). Hypoglycemia and hyponatremia were noted. At 2 months of age, she weighed 4,050 g (−1.2 SD), height 52.2 cm (−2.7 SD), head circumference 34.5 cm (−3.5 SD), and chest circumference 37.2 cm (−1.3 SD). Physical examination revealed multiple craniofacial abnormalities: brachymicrocephaly, frontal prominence, upslanting palpebral fissures, a broad nose, raised cheek bones, low-set ears, large deformed auricles, micrognathia, a cupid bow mouth, a short neck, and a hammer foot. Radiological examination revealed spina bifida. Cephalic CT and MRI showed agenesis of the corpus callosum. She also had a patent ductus arteriosus and tricuspid regurgitation. Now aged 4 years (Fig. 1), she weighs 12.1 kg (−2.1 SD) and height 89 cm (−3.3 SD). She shows psychomotor retardation, speech delay and general hypotonia. No seizures have occurred.

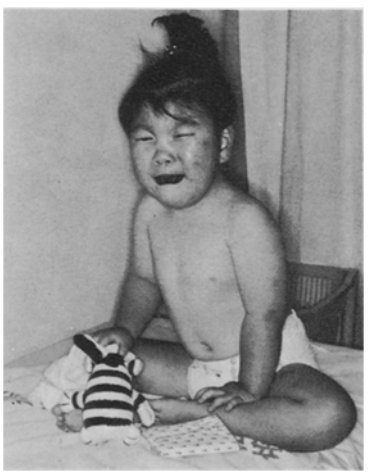

Fig. 1. The patient at age 4 years, showing multiple craniofacial abnormalities.

CYTOGENETIC FINDINGS

QFQ and GTG banding chromosome analyses on 50 metaphases of cultured peripheral blood lymphocytes demonstrated an unusual chromosome 1 showing a satellite-like structure on the terminal end of the long arm (Fig. 2). NOR-staining, performed according to the method by Howell and Black (1980), revealed a distinct Ag-NOR signal at the terminal end of 1q (Fig. 2), an indication that the unusual chromosome 1 was the product of translocation with an acrocentric (D or G group) chromosome. The satellited chromosome 1 was found in all the metaphases analyzed, and no other abnormal chromosomes were detected. In order to determine precisely the translocation breakpoint of chromosome 1, high-resolution G-banded chromosomes at the 550–850 band stages were analyzed using methotrexate synchronization (Yunis *et al.*, 1978) or ethidium bromide pretreatment (Ikeuchi, 1984). A representative partial karyotype is shown in Fig. 3. In the translocated chromosome, the G-positive sub-band 1q42.2 and band 1q43 were retained. This indicates that the breakpoint on the chromosome is either at band q44 or at the border between q43 and q44. Her karyotype was thus designated as 46,XX,−1,+der(1)t(1;D or G)(q44;p11). Her parents showed normal karyotypes.

Attempts were made to identify the acrocentric chromosome involved in the translocation and its parental origin. The results, however, were unfruitful, because the heteromorphic characteristics on the region of distal 1q, as revealed by Q- and NOR-staining methods, were also found in some acrocentrics in both parents (data not shown).

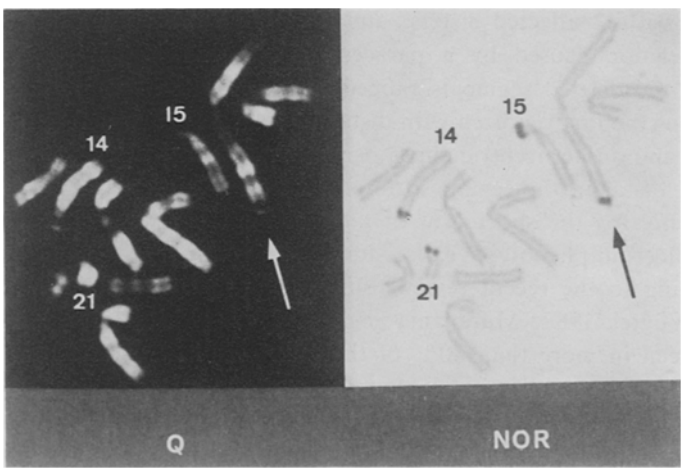

Fig. 2. Sequential Q- and NOR-stained chromosomes. The arrows point to the signal on the der(1) chromosome.

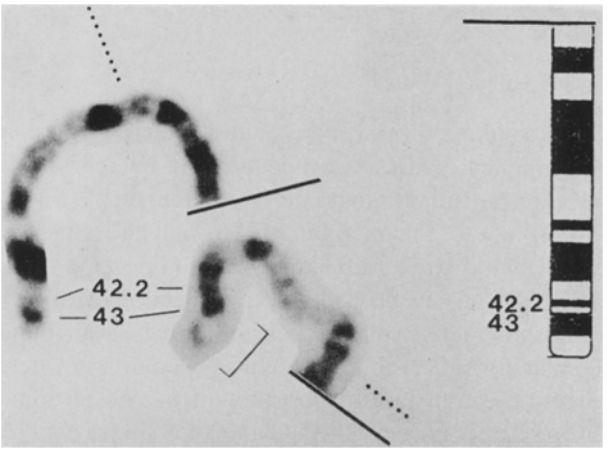

Fig. 3. A pair of high resolution G-banded chromosomes 1 from the patient. The left is a normal chromosome 1, and the right a derivative chromosome 1. Dotted lines show the site of centromeres. Bracket shows the translocated segment including a satellite. On the far right is a schematic diagram showing the distal two-thirds of 1q.

DISCUSSION

There have been some 30 reported patients with a distal deletion of chromosome 1q (Murayama *et al.*, 1991; Ioan *et al.*, 1992). Most of them were due to *de novo* deletion, and only 4 cases were derived from familial balanced chromosome abnormalities: Juberg *et al.* (1981) reported a male infant due to a balanced translocation t(1;16)(q43;q24)mat, Golabi *et al.* (1982) showed t(1;12)(q43;p13) in 3 generations with 2 affected sisters, and Speevak *et al.* (1985) reported a case of distal 1q deletion caused by a paracentric inversion inv(1)(p42q44)mat. In all these cases, the deleted segments ranged from band 1q42 or 1q43 to 1qter. Our patient is thus the first reported with distal 1q deletion resulting from a translocation between 1q and an acrocentric chromosome, and with the translocation breakpoint (1q44) most distal in the region so far reported. The patient is assumed to have partial trisomy for the short arm of an acrocentric chromosome, but this would have little effect on phenotypic expression.

According to the recent reviews summarizing cases from the literature (Meinecke and Vögtel, 1987; Murayama *et al.*, 1991; Ioan *et al.*, 1992), the phenotypic anomalies seen in more than 80% of the patients with 1q distal deletion include: growth and mental retardation, corpus callosum hypoplasia, speech delay, microcephaly, upslanting palpebral fissures, epicanthal folds, short broad nose, low-set abnormal ears, downcurved mouth, micrognathia, short neck, genital anomalies, abnormal feet, general hypotonia, and seizures. Most of these clinical features were present in the patient we described, except for genital anomaly, epicanthal

folds, and seizures. Congenital heart disease, as present in our case, is seen in about one-third of patients (Meinecke and Vögtel, 1987; Tolkendorf *et al.*, 1989). On this basis, we suggest that the loss of band 1q44 alone is responsible for most of the clinical features in patients with distal chromosome 1q deletion.

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REFERENCES

Golabi M, Ito M, Hadley D (1982): Double neural tube defects in two siblings; new features of chromosome 1 deletion syndrome-1q43. Am J Hum Genet **34**: 125A

Howell WM, Black DA (1980): Controlled silver-staining of nucleous organizer regions with a protective colloidal developer: a 1-step method. Experientia **36**: 1014–1015

Ikeuchi T (1984): Inhibitory effect of ethidium bromide on mitotic chromosome condensation and its application to high-resolution chromosome banding. Cytogenet Cell Genet **38**: 56–61

Ioan DM, Maximilian C, Kleczkowska A, Fryns JP (1992): Distal deletion of the long arm of chromosome number 1(q43→qter) associated with severe mental retardation and a nonspecific dysmorphic syndrome. Ann Génét **35**: 167–169

Johnson VP, Heck LJ, Carter GA, Flom JO (1985): Deletion of the distal long arm of chromosome 1: a definable syndrome. Am J Med Genet **22**: 685–694

Juberg RC, Haney NR, Stallard R (1981): New deletion syndrome: 1q43. Am J Hum Genet **33**: 455–463

Mankinen CB, Sears JW, Alvarez VR (1976): Terminal (1)(q43) long arm deletion of chromosome no. 1 in a three-year-old female. In: Bergsma D, Schimke RN (eds). Cytogenetics, environment and malformation syndromes. New York: Alan R. Liss, Inc. for the National Foundation-March of Dimes. Birth Defects, Orig Art Ser XII(5): 131–136

Meinecke P, Vögtel D (1987): A specific syndrome due to deletion of the distal long arm of chromosome 1. Am J Med Genet **28**: 371–376

Murayama K, Greenwood RS, Rao KW, Aylsworth AS (1991): Neurological aspects of del(1q) syndrome. Am J Med Genet **40**: 488–492

Speevak M, Hunter AGW, Hughes H, Cox DM (1985): A familial paracentric inv(1)(q42q44) resulting in a child with a del(1)(q42) karyotype. Ann Génét **28**: 177–180

Tolkendorf E, Hinkel GK, Gabriel A (1989): A new case of deletion 1q42 syndrome. Clin Genet **35**: 289–292

Yunis JJ, Sawyer JR, Ball DW (1978): The characterization of high-resolution G-banded chromosome of man. Chromosoma **67**: 293–307