Letter to the Editor

Molecular Analysis of a Translocation (6;11)(p21;q25) in a Girl With Jacobsen Syndrome

To the Editor:

More than 70 patients with Jacobsen syndrome have been described [Penny et al., 1995; Pivnick et al., 1996; Ono et al., 1996]. The Jacobsen syndrome comprises mild to moderate psychomotor retardation, trigonocephaly, minor facial anomalies, cardiac defects, and thrombocytopenia. The syndrome is caused by distal deletions of chromosome arm 11q, including 11q24.1. Until now, no clear correlation between genotype and phenotype could be established. Recently, Michaelis et al. [1998] showed that in most cases in which the breakpoint was distal to marker D11S924, the deleted chromosome was paternal in origin. We describe a patient with Jacobsen syndrome, due to a de novo translocation (6;11)(p21;q25).

The affected girl was born at 40 weeks of gestation to a 31-year-old father and a 30-year-old mother. The nonconsanguineous parents and an older sibling were healthy. The pregnancy was uneventful, but delivery was by Cesarean section because of a breech presentation. Birth weight was 2,710 g (50th centile) and Apgar scores were 6, 8, and 10 at 1, 5, and 10 minutes, respectively.

Neonatally there were feeding difficulties and hypoglycemia. At physical examination a systolic cardiac murmur and enlargement of liver and spleen were found. Facial abnormalities consisted of slight frontal bossing, bitemporal narrowness, capillary hemangioma on the forehead, broad nasal bridge, dystopia canthorum, downward slant of palpebral fissures, convergent strabismus, long philtrum, small upper lip, broad mouth with down-turned corners, broad alveolar ridges, high palate, simple formed helices, simian creases, and proximal-placed thumbs (Fig. 1). Cardiac sonography showed a severe ventricular- and atrial septal defect and a patent ductus arteriosus. A computed tomography scan of the head showed slight enlargement of the Sylvian fissure and increased extracerebral spinal fluid. The urogenital tract was sonographically normal. On laboratory examination a thrombocytopenia was noted (38 × 10^9/l). The other hematological values were normal, and therefore a bone marrow aspiration was not performed. Results of ex-

Fig. 1. The proposita at age 7 months. Note frontal bossing, bitemporal narrowness, capillary hemangioma on the forehead, broad nasal bridge, dystopia canthorum, downward slant of the palpebral fissures, strabismus, small upper lip, and broad mouth.

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Extensive metabolic investigations and serological tests for infectious causes were normal.

Chromosome analysis demonstrated an apparently balanced translocation between chromosomes 6 and 11. The Jacobsen syndrome was suspected, therefore a fluorescence in situ hybridization study was performed with probes for the short arm of chromosome 6 (cCI6-15 on 6p21.31; cCI6-47 on 6p21.2) [Saito et al., 1992], centromere specific probe D6Z1 (Cytocell Ltd., Oxfordshire, UK), and a subtelomeric probe for the long arm of chromosome 11 (probe P1-23388) [Vocero-Akbani et al., 1996]. The breakpoint in chromosome 6 was between the 6p markers used. The subtelomeric probe for chromosome 11q was only present on the normal 11, not on the der(6) chromosome. Subsequently, the following polymerase chain reaction primers for microsatellite repeat polymorphism were used: D11S968, S11S1309, D11S969, D11S1320, D11S912, D11S934, D11S933, D11S1353, D11S925, D11S924, and D11S1356. This polymerase chain reaction-based analysis enabled us to define the extent of the paternally derived deletion between markers D11S1328 (deleted) and D11S1353 (not deleted) (Fig. 2). Chromosomes of both parents were normal.

At age 7 months the patient was admitted for cardiac evaluation. At that time, weight was 5.2 kg (<3rd centile) and length 62 cm (<3rd centile). She was alert, but physical activity, including feeding, was limited because of her cardiac problems. Development was mildly delayed. The thrombocytopenia had improved spontaneously to 128 × 10^9/l. Catheterization and angiography of the heart were performed, and limited left-right shunting and severe pulmonary hypertension were found. Because of poor prognosis it was decided not to operate.

This is the second patient with Jacobsen syndrome and a de novo translocation involving chromosome band 11q24 [Van Hemel et al., 1992]. Therefore, in patients with a de novo translocation involving the distal part of chromosome 11q, especially in prenatal diagnosis, a careful search for signs of the Jacobsen syndrome should be performed.

REFERENCES


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