Two Siblings with Partial Trisomy 15 and Monosomy 21 Associated with Central Nervous System Anomalies

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A sister and a brother with 46, XX (46, XY), -21, + der (15) (q22.1; g22.1) mat were reported whose mother had a karyotype of 46, XX, t(15; 21)(q22.1; 22.1) and was phenotypically normal. Both sibs were mentally retarded and dysmorphic. Moreover, the sister had a holoprosencephaly with congenital hydrocephalus, and the brother showed congenital hydrocephalus.

About 40 cases of partial trisomy 15 have been reported (Fujimoto et al. 1990). Trisomy 15 for the pter-q22 segment is most common (Power et al. 1977). Although several studies have documented psychomotor retardation in connection with partial trisomy 15, data on brain involvement are scarce (Zannotti et al. 1980). As for monosomy 21, there have been a few cases of central nervous system anomalies. We report here two sibs with partial trisomy 15 and monosomy 21 associated with a central nervous system anomalies.

Case Reports

The pedigree of this family is shown in Fig. 1.

Case 1. The propositus (III-3) was a female born on June 28, 1984 as the second child in a sibship of five. The parents were non-consanguineous, and none of individuals with mental retardation and major malformations were in this family. The pregnancy was uneventful until pleural effusion, generalized edema and congenital hydrocephalus were detected by fetal echo examination in the 35th week of gestation. Caesarian section was elected at term, and the neonate was resuscitated by intubation because of dyspnea due to

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laryngeal edema. Thoracentesis removed 100 ml of pleural fluid. The birth weight was 2,750 g. Her head circumference was 36 cm, with marked edema of the head. She was noted to have a cleft palate and low-set ears (Fig. 2). At the age of one month, she had several apneic attacks due to an increase in the intracranial pressure, and her head circumference increased from 31 to 34 cm within 20 days. Although a ventriculo-peritoneal shunt was put in place, she died at the age of 2 months because of aspiration of milk.

A CT scan of the brain at 12 days of age showed holoprosencephaly with hydrocephalus (Fig. 3A).

Case 2. The patient (III-5) was a male born in August 25, 1990 as the fifth child. Hydrocephalus had been detected by fetal echo examination. He was born at term by spontaneous delivery and weighed 1,928 g. The Apgar score was 5(1') and 7(5'). Four hours later, frequent cyanotic attacks occurred. Oxygen supplementation and positioning

Fig. 1. Pedigree of the family.

Fig. 2. Facial features of the propositus (III-3).
therapy alleviated the attacks. His length was 44 cm, chest circumference was 25 cm and head circumference was 32 cm. Clinical examination revealed: the anterior fontanel 4 × 8 cm, flat nose bridge, low-set ears, micrognathia, cleft palate, bilateral cryptorchidism, right simian crease and equinovarus of the left foot. Mild systolic murmurs were heard along the left sternal border. The routine laboratory test values were within the normal limits. The lung and heart roentgenograms were normal. His psychomotor development at the age of 2 months was estimated to be equivalent to the normal level at 1 month of age. The CT at age 9 days revealed congenital hydrocephalus (Fig. 3B).

CYTOGENIC STUDIES

Lymphocytes of the mother were subjected to chromosome examination. G-banding technique and ethidium bromide-added high-resolution technique were performed. In all 20 inspected lymphocytes, a 46, XX, t(15; 21) (q22.1; 22.1) karyotype was present (Fig. 4A). The karyotype of the father was normal. The karyotype of the propositus (III-3) was 46, XX, −21, +der(15), t(15; 21)(q22.1; q22.1)mat, while that of the brother (III-5) was the same except for being XY (Fig. 4B). The parents did not consent to the cytogenic studies of the other siblings (III-2 and III-4).

DISCUSSION

In spite of the fact that patients with partial trisomy 15 commonly manifest delayed development, few cases have been reported to have central nervous system (CNS) anomalies. Pfeiffer and Kessel (1976) reported slight ventricular dilata-
tion suggested by echoencephalography, and Hongell and Iivanainen (1978) reported an enlargement of the left temporal horn by the pneumoencephalogram. The same karyotype as our cases was reported in two papers. Rethoré et al. (1973) reported two siblings without mentioning any CNS abnormalities. One of the two cases reported by Gregoire et al. (1981) had several convulsive episodes, but the pneumoencephalogram revealed no anomalies.

Phenotypic variation would be expected when a different segment of distal 15q is duplicated and monosomy of a different second chromosome is present (Fujimoto et al. 1990).

Although more than 40 cases of complete or partial monosomy 21 have been reported in the literature, only 11 cases, to our knowledge, involving CNS anomalies have been published. They included two cases of holoprosencephaly (Aronson et al. 1987; Estabrooks et al. 1990), two cases of the dilatation of ventricles (Wisniewski et al. 1983; Garzicic et al. 1988), three cases of the brain atrophy (Rethoré 1977; Rivera et al. 1983; Cuoco et al. 1990), and two cases of agenesis of corpus callosum (Holbek et al. 1974; Wisniewski et al. 1983). Two cases had both CNS anomaly and midline facial defects such as cleft palate, cleft lip and flat nasal bridge (Fryns et al. 1977; Wisniewski et al. 1983). Abe et al. (1990) reported a case with midline facial defects whose karyotype was 45, XX, −2, −21, + der(2) t(2; 21)(q3.3; q22.1), but they did not mentioned CNS anomalies. Published cases of partial monosomy 21 mentioning CNS anomalies are shown in

![Fig. 4. Partial karyotype using the high-resolution G banding technique. (A) Chromosomes of the mother (II-4) showed a reciprocal translocation between 15 and 21. (B) Partial trisomy 15pter-q22.1 and monosomy 21 in case III-5.](image-url)
Table 1. Partial monosomy 21 and central nervous system anomaly

<table>
<thead>
<tr>
<th>Author</th>
<th>Karyotype</th>
<th>CNS anomaly</th>
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<tbody>
<tr>
<td>Rethoré (1977)</td>
<td>44, XX, −5, −21. (Monosomy for pter-q21)</td>
<td>Brain atrophy</td>
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<tr>
<td>Rivera et al. (1983)</td>
<td>45, XX, −14, −21, +der(14), t(14; 21)(p12; q22) mat</td>
<td>Brain atrophy</td>
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<tr>
<td>Cuoco et al. (1990)</td>
<td>45, XX, −15, −21, +der(21), t(15; 21)(q13; q22.3)</td>
<td>Brain atrophy</td>
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<tr>
<td>Estabrooks et al. (1990)</td>
<td>46, XX, del(21)(q22.3)</td>
<td>Alobar holoprosencephaly</td>
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<tr>
<td>Present case (III-3)</td>
<td>46, XX, −21, +der(15), t(15; 21)(q22.1; q22.1) mat</td>
<td>Holoprosencephaly</td>
</tr>
<tr>
<td>Present case (III-5)</td>
<td>46, XY, −21, +der(15), t(15; 21)(q22.1; q22.1) mat</td>
<td>Hydrocephalus</td>
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Table 1. Although there may be some relationship between partial monosomy 21, specifically for 21(pter-q 22), and CNS anomalies, further observations are undoubtedly necessary to clarify these relationships. The band q 22.1 of chromosome 21 is an important region as the loci of both phosphoribosylglycinamide synthetase and superoxide dismutase 1 (Sinet et al. 1976; Chadefaux et al. 1984). Holoprosencephaly is one of the failure of the primary cerebral vesicle (telencephalon) to cleave and expand bilaterally, and it usually associates with midline facial defects (Menkes et al. 1990). Our two cases showing the same karyotype must have lost the same amount of genetic materials. There is interesting difference in the phenotypic expression that our first case had a lobar holoprosencephaly and cleft palate, while the second had only hydrocephalus and cleft palate.

References


