DISTAL 15q TRISOMY WITH DANDY-WALKER MALFORMATION IN A FEMALE INFANT

Atsushi IESHIMA,¹ Kenzo TAKESHITA,¹ Yukiyoishi SHIRASAKA,²
Yasuji NAKAO,² and Toshiro KISA²

¹*Division of Child Neurology, Tottori University School of Medicine, Yonago 683, Japan*

²*Department of Pediatrics, Shimane Prefectural Central
Hospital, Izumo 693, Japan*

Summary A female infant with distal 15q trisomy and terminal 12q monosomy is reported. This is the first oriental case. Facial dysmorphism in this case is similar to that of previous cases. Additional features are severe brain malformation including Dandy-Walker malformation and agenesis of the corpus callosum, and multiple limb anomalies. These features differed from those of previous cases with the trisomy 15q and may be due to terminal 12q monosomy.

INTRODUCTION

More than twenty cases with distal 15q trisomy have been reported so far (Fujimoto *et al.*, 1974; Pederson, 1976; Turleau *et al.*, 1977; Zabel and Baumann, 1977; Coco and Penchaszadeh, 1978; Tzancheva *et al.*, 1981; Gregoire *et al.*, 1981; Yip *et al.*, 1982; Zergollern *et al.*, 1982; Schnatterly *et al.*, 1984). The remarkable similarity in clinical features between them suggests that distal 15q trisomy is a clinically recognizable syndrome.

Brain anomalies and skeletal anomalies in cases with distal 15q trisomy have been rarely reported. We report here a female infant with distal 15q trisomy associated with Dandy-Walker syndrome and multiple limb anomalies.

CASE REPORT

The proband is the second product of healthy and unrelated 22-year-old mother and 41-year-old father. There is no family history of neurological diseases, abortions or stillbirths (Fig. 1). The patient was born at 39 weeks of gestation after an uneventful pregnancy with a breech delivery. Birth weight was 3,580 g, the length 50 cm, and the head circumference 39 cm. She was noted to have macrocephaly with flat occiput, narrow palpebral fissures, downward slanting of palpebral fissures,

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Fig. 1. The maternal pedigree of the family.

Fig. 2. Proposita at the age of 6 months.

broad nasal bridge, long philtrum, puffy cheek, high-arched palate, low-set ears with poorly formed helices and short neck. Furthermore, the following anomalies were also observed: short upper limbs; left preaxial poly-syndactyly; camptodactyly in bilateral hands; elongated third toes; bilateral simian creases (Fig. 2). There were no abnormalities of examination on both chest and abdomen. She had a weak cry and failed to thrive. The muscle tone was poor. Cranial CT scanning in Fig. 3 revealed the presence of posterior fossa cyst continuous with the fourth ventricle, the

Fig. 3. Cranial CT scanning at 1 month. Note the large cyst in posterior fossa, marked dilation of ventricular system, the agenesis of corpus callosum, enlarged Sylvian fissures, wide extracerebral space and hypoplasia of brain stem and frontal lobes. The metrizamide CT study revealed the communication between this huge cyst and ventricular dilatation.

cerebellar vermis agenesis, dilated third and lateral ventricles, agenesis of corpus callosum and wide sylvian fissures, which is compatible with Dandy-Walker malformation (Hart *et al.*, 1972). Arachnoid cyst of the posterior fossa was ruled out by the metrizamide CT study. Surgical shunting procedure was performed at 2 months of age. Cerebro-spinal fluid was normal. Ophthalmological examination, chest X-ray, electrocardiogram, echocardiogram and other laboratory findings were all normal.

Her physical growth was normal, but psychomotor development was retarded. She was able to follow objects by 4 months of age, but not to lift her head or roll over at age of 6 months. Auditory response was poor and hearing loss was suspected. She had several convulsive episodes beginning at 5 months of age, which were partly controlled by phenobarbital. Electroencephalograms showed no paroxysmal discharges.

At 9 months of age she died of bronchopneumonia and repeated convulsions. Autopsy was not available.

CYTOGENETICS

G- and R-banding analysis (Ieshima *et al.*, 1984) of peripheral blood metaphases from the proband revealed a 46,XX,12q+ karyotype (Fig. 4). The abnormal chromosome 12 was inherited from her mother, who was found to carry a balanced translocation t(12; 15) (q24.33; q22.3) (Fig. 1 and Fig. 4). Therefore, the karyotype of the proband was considered to be 46,XX, -12, +der (12), t(12; 15) (q24.33; q22.3)mat.

DISCUSSION

This is the first report of the case with distal 15q trisomy from among oriental people. Clinical features of previous 20 cases with 15q trisomy as well as our case are characterized as follows: mental retardation (19/19); growth retardation (13/19); microcephaly (10/19); congenital heart disease (11/20); convulsions (7/20); facial asymmetry (13/19); downward slanting of palpebral fissures (14/18); narrow palpebral fissures (9/15); prominent nose (14/19); long philtrum (13/20); micrognathia (11/18); high-arched palate (14/19); short neck (12/21); low-set ears (9/12). Limb anomalies including short limb or syndactyly have been observed only in 4 cases (Turleau *et al.*, 1977; Coco *et al.*, 1981; Tzandeva *et al.*, 1981; Zergollern *et al.*, 1982; Howard-Peebles *et al.*, 1982). Present case is severely affected with limb malformations: preaxial poly-syndactyly; camptodactyly; short upperlimbs; elongated toes. These limb malformations may be a characteristic of distal 15q trisomy.

As to brain anomalies in distal 15q trisomy, cited only in 4 cases, hydrocephalus is observed in 2 cases at autopsy, but not described in detail (Pederson, 1976; Zergollern *et al.*, 1981; Tzancheva *et al.*, 1981). Our case had severe brain anomalies including hydrocephalus, Dandy-Walker cyst, agenesis of corpus callosum and

Fig. 4. a: G-banded karyotype of the probanda (upper). b: G-banded (G) and R-banded (R) karyotype of the mother (lower).

hypoplasia of temporal operculum. Dandy-Walker malformation is frequently associated with other malformations (Hart *et al.*, 1972), and rarely observed in some cases with chromosome abnormalities such as trisomy 9, trisomy 8p and trisomy 5p (Kunz, 1980). Etiology of Dandy-Walker malformation remains unknown, but there are probably variable causes. We stress that some of chromosome abnormalities are one of the causes in Dandy-Walker syndrome.

In our case terminal deletion 12q as well as distal trisomy 15q were present. The effects of the terminal deletion 12q appears to be neglectable because clinical features in our case are mostly compatible with those in previous cases. However, since any cases with monosomy 12q have not been reported so far, it is possible that the terminal 12q monosomy might have contributed to the causal genesis of severe brain anomalies and limb malformations in our case.

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