

## An unusual case of monosomy 18p: minor malformations with speech delay

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An unusual case of monosomy 18p with molecular cytogenetic characterization of 18;21 whole arm translocation who had mild speech delay and normal motor development is presented.

A 3.5-year-old boy with complaints of speech delay, open mouth and drooling saliva was the child of a 33-year-old healthy mother and 35-year-old nonconsanguineous father with unremarkable prenatal history. Beside delayed speech, hyperactive movements, flat nasal bridge, prominent ears, micrognathia, hypotonia, and overriding of left 3<sup>rd</sup> the on 2<sup>nd</sup> toe were present. Cytogenetic studies revealed de novo 45,XY del (18) t(18;21)-21 karyotype, which was confirmed by fluorescence in situ hybridization (FISH).

**Key words:** monosomy 18p, t(18;21), FISH study, normal motor development.

Monosomy of the entire short arm of chromosome 18, acrocentric whole arm translocation, is one of the most frequent autosomal deletions observed. The entity was first reported by de Grouchy et al.<sup>1</sup> in 1963 and since then more than 100 cases have been published<sup>2</sup>. Clinical phenotype of monosomy 18p varies widely but usually comprises growth and mental deficiencies, hypotonia, ptosis, epicanthal folds, low nasal bridge, rounded facies, micrognathia, large protruding ears, short neck, pectus excavatum and small hands and feet<sup>3,4</sup>. Cerebral malformations include agenesis of corpus callosum, hydrocephaly and prosencephaly type defects. Most of the cases in recent years are prenatally diagnosed because of abnormal sonographic findings followed by amniocentesis, frequently in the second trimester of the pregnancy<sup>5</sup>.

The cytogenetic studies of the cases are mostly due to de novo deletions. In some cases the monosomy 18p results from a whole arm translocation between chromosome 18 and other chromosomes; in most cases the other chromosome involved is an acrocentric chromosome. In such cases, the chromosome number is 45, with a derivative chromosome [der (D/G;18) (q18;q18)] replacing a normal D/G and a normal 18<sup>6-8</sup>.

Here we report an unusual case of monosomy 18p ascertained by molecular cytogenetic studies, together with clinical findings. This case had near normal neurodevelopment and slight speech delay.

### Case Report

A 3.5-year-old boy was first seen in our clinic for slight speech delay compared to his peers, open mouth and drooling saliva. He was the single child of a 33-year-old healthy mother and 35-year-old nonconsanguineous father. The pedigree did not reveal any inherited mental or motor disorder. The perinatal history was unremarkable. The case was born by cesarean section for breech presentation, with a birth weight of 3,000 g. His head control was achieved in the 2<sup>nd</sup> month, unsupported sitting at the 8<sup>th</sup> month and walking at the 18<sup>th</sup> month. He could speak no more than a few words.

His weight was 15 kg (50<sup>th</sup> percentile) and height 96 cm (25<sup>th</sup> percentile) at admittance to our clinic and his physical examination showed a peculiar appearance with flat nasal bridge, prominent ears, micrognathia, mandibular hypotonia, overriding of 2<sup>nd</sup> and 3<sup>rd</sup> toes of left foot, and mild kyphosis and hyperactivity.

His abdominal and pelvic ultrasonographic examinations, echocardiography, chest and vertebral X-rays, computed tomography and magnetic resonance imaging of the cranium were normal. The Denver Development Screening Test (DDST) indicated only the slight speech delay with normal fine motor development (Fig. 1).



Fig. 1. Note prominent ears, micrognathia, and mandibular hypotonia.

#### *Cytogenetic and Molecular Cytogenetic Studies*

Chromosomal analysis was performed with high resolution G-banding technique according to standard procedures. Karyotype revealed 45,XY, der (18) t(18;21) (p11.2;q21.1)-21 chorosomal constitution in all cells without mosaicism (Fig. 2), and this was confirmed by fluorescence in situ hybridization (FISH).

Fluorescence in situ hybridization was carried out with biotin-labeled painted probes which were prepared for chromosomes 18 and 21, counterstained with propidium iodide and diaminophenylindole (DAPI) (Fig. 3). The karyotypes of both parents were normal.

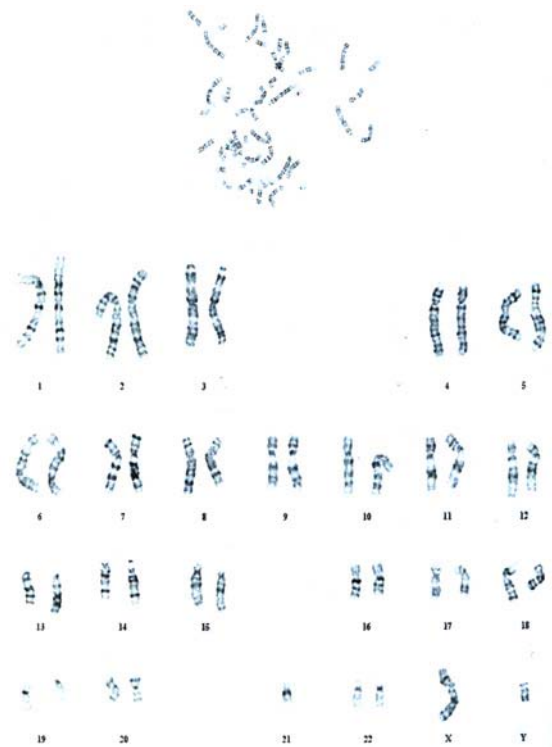


Fig. 2. Karyotyping.

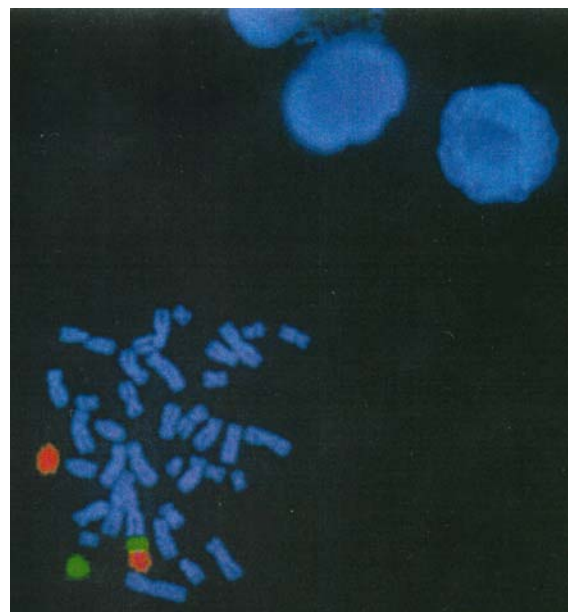


Fig. 3. Fluorescence in situ hybridization with biotin-labeled painted probes.

## Discussion

The clinical phenotypes of monosomy 18p vary widely. The male to female ratio is 0.71, while mean birth weight is approximately 3,000 g. Parental mean ages are usually between 30-35 years in reported cases. The dysmorphic features of the neonate may not be evident but phenotypic findings may become typical at about three years of age<sup>9</sup>. However, most of the recent reports are diagnosed in the second trimester of the pregnancy due to abnormal ultrasonographic findings and cytogenetic studies of amniotic fluid<sup>5</sup>.

The peculiar appearance of our case with flat nasal bridge, prominent ears, micrognathia, mandibular muscle hypotonia, overriding of 2<sup>nd</sup> and 3<sup>rd</sup> toes of the left foot and mild kyphosis have been described in previous reports of similar cases<sup>2,3,10</sup>.

The most important congenital malformation is holoprosencephaly, which is present in at least 10% of the cases. Holoprosencephaly may result in varying degrees of mental and motor retardation<sup>11,12</sup>. In the absence of holoprosencephaly, moderate-to-severe mental retardation with disproportionately delayed language and normal or borderline intelligence have occasionally been observed<sup>13</sup>. In our case, mental retardation was not evident. His DDST revealed only slight speech delay with normal fine and coarse motor development, which is not often seen. Rarely, monosomy 18p cases were reported in the medical literature as having normal intelligence<sup>9</sup>.

We aimed to call to the attention of physicians this unusual case of monosomy 18p, with near normal neurologic development and only delayed language. The minor dysmorphic features of newborns should be carefully evaluated and chromosomal abnormality should be ruled out.

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