Clinical features in patients with segmental aneuploidy often vary depending on the size of the chromosomal segment involved. Deletions of the distal segment of chromosome 2p are rare. Subtelomeric deletions of short arm of chromosome 2 have been demonstrated in few cases with developmental delay, mental retardation, facial dysmorphism and hypotonia. Monosomy 2p is usually observed as a part of complex syndromes among probands of balanced reciprocal translocation carriers. Patients with dup4q syndrome have variable clinical features, which are both related to the size of duplicated segment of the 4q and specific associated monosomy. Clinical findings of our patient were compatible with those previously reported in dup4q and del2p patients. Herein are presented the clinical and cytogenetic findings in a 4-year-old female with an unbalanced karyotype 46,XX,der(2)t(2;4)(p25.1;q31.3)pat. Clinical phenotypes of 2p;4q translocation cases are variable, because the involved breakpoints vary case-by-case. We also compare similarity of the clinical features of our proband and other patients carrying either duplication of the distal part of 4q and patients carrying a deletion of distal part of 2p as described in the literature. To our knowledge, this is the first case of partial trisomy 4q accompanied with partial monosomy 2p.

Key words: partial monosomy 2p, partial trisomy 4q, translocation, fluorescence in situ hybridization

Introduction

Clinical features in patients with segmental aneuploidy often vary depending on the size of the chromosomal segment involved. Deletions of the distal segment of chromosome 2p are rare. Subtelomeric deletions of short arm of chromosome 2 have been demonstrated in few cases with developmental delay, mental retardation, facial dysmorphism and hypotonia. Monosomy 2p is usually observed as a part of complex chromosomal syndrome among probands of balanced reciprocal translocation carriers, like in our case. Partial trisomy of the long arm of chromosome 4, usually resulting from familial translocation segregation, has been described in a number of patients. Clinically partial trisomy 4q is manifested by mental retardation, clinodactyly, facial dysmorphism, short neck and hypotonia. Patients with dup4q syndrome have variable clinical features, which are both related to the size and gene content of duplicated segment and specific associated monosomy. Comparing the phenotypes of all previously published cases, many differences between them can be found and the reason might be due to concomitant partial autosomal monosomy. Although partial trisomy 4q and partial monosomy 2p vary in their phenotypes, they also have many common features. Herein are presented the clinical and cytogenetic findings in a 4-year-old female with karyotype 46,XX,der(2)t(2;4)(p25.1;q31.3)pat. We also compare similarity of the clinical features of our proband and other patients carrying solely duplication of the distal part of 4q and a deletion of distal part of 2p as described in the literature.

Case Report

The proband is a 4-year-old female referred for genetic evaluation because of poor verbal articulation. The girl is the first-born of young, healthy non-consanguineous parents. After uneventful pregnancy she was delivered at term, at birth, length was 51 cm (75th centile), weight 3290 g (50th centile), and head circumference 35.5 cm.
cm (50\textsuperscript{th} centile). Hypotonia was observed at the age of 9 months. She took her first steps at 2 years and she is yet (4 year old) without sphincters control. Now weights 18.5 kg (95\textsuperscript{th} centile) and 98 cm tall (75\textsuperscript{th} centile). Distinctive facial dysmorphy is present: low hairline on the neck, hypertelorism, epicantal folds, strabismus, broad nasal bridge, low set ears, irregular teeth growth, small mandible, short neck. A disproportion between large neurocranium and small viscerocranium is present, thorax examination was insignificant. She has short fingers with clinodactyly. Her language is limited to a few words pronounced in syllables. Moderate psychomotor delay was observed (development level 36) with hyperactivity and restlessness. However, there was no growth delay. Family history revealed that the proband’s father had a mentally retarded sister, who was adopted and unavailable for cytogenetic study. This study was approved by the Ethics Committees of the University Hospital Center Osijek and School of Medicine, »J. J. Strossmayer« University in Osijek and the written informed consent was obtained from the parents of the girl.

**Cytogenetic and FISH Analysis**

Cytogenetic and fluorescence in situ hybridization (FISH) analysis were performed on cultured peripheral blood lymphocyte of the proband and her parents by standard methods\(^5\). Chromosome banding was performed by treatment with trypsin followed by staining with Giemsa to obtain a GTG banded pattern approximately at a resolution of 550 bands. The chromosome region specific probes for telomere 2p (VII2yRM2052), centromere 2 (D2Z1), locus specific probe Wolf-Hirschhorn Syndrome region 4p16.3 (LSI WHS) and telomere 4q (APMA224XH1) (Abbott/Vysis) were used for detection of suspected rearrangement by FISH.

Cytogenetics examination of GTG banded metaphases using Olympus BX61 microscope and Cytovision 3.93 software (Applied Imaging, England) showed an unbalanced karyotype with extra chromosome material at the short arm of the chromosome 2. Subsequent chromosomal analysis of the parents showed a balanced reciprocal translocation in the father; 46,XY,t(2;4)(p25.1;q31.3) (Figure 1). FISH with specific probes for chromosome regions: centromere 2, telomere 2, WHS and telomere 4q on metaphases showed that telomere 4q probe hybridized at the 4q and at the p arm of the derivate chromosome 2 (Figure 2), at the breakpoint 2p25.1 and 4q31.3. The karyotype of proband is then 46,XX,der(2)t(2;4) (p25.1;q31.3)pat.

**Discussion and Conclusion**

We described a proband with moderate mental retardation and dysmorphic features with an unbalanced...
translocation resulting, from paternal balanced reciprocal
translocation, in partial trisomy for 4q31.3®qter and
partial monosomy for 2p25.1®pter. Further family in-
vestigations revealed the balanced paternal reciprocal
translocation. A review of other cases identifies variable
features in common with pure del 2p16 and pure dup 4q
syndrome4,5. Those include: mental retardation, facial
dysmorphism, hypotonia, hyperactivity and speech delay.

The phenotypic features of our proband are summarized
and compared with previously reported cases of partial
trisomy 4q and partial monosomy 2p in Table 1. With ex-
ception of microcephaly, widely spaced nipples and con-
genital heart disease, our proband had most of the clinical
features associated with dup 4q syndrome. The variation
may be related to such variables as age, sex and different
size of chromosome segment involved in dup 4q syn-
drome, as well as the terminal loss of genetic material of
the second chromosome involved in such an unbalanced
translocation3. Our case does have most features in com-
mon with other cases of complete trisomy 4q. These in-
cluded delayed development, deep set eyes, strabismus,
hypertelorism, epicanticth folds, board nasal bridge, low
set ears, short neck, clinodactyly and mild mental retar-
dation. The involved breakpoints vary between the cases,
with consequently variation in phenotypes. Severe stig-
matisation has been observed in patients with a larger
degree of partial trisomy and in the patients with duplica-
tions spanning the distal part of 4q2. The patients with
duplicated fragment close to centromere or telomere had
mild abnormal phenotype while the segment from 4q27
to 4q31 seemed to be preferentially engaged in the tri-
somy 4q syndrome with severe clinical effects4. The
strongest association was found between reviewed terminal
2p aberrations and the presence of a wide range of de-
velopmental delay, from profoundly impaired, if larger size
of chromosome segment was involved in del 2p, to mild1.

Several features set this patient apart from those
with pure 2p deletion and pure dup 4q syndrome. These
features included an enlarged neurocranium, minor facial
dysmorphism, irregular teeth growth and lack of growth re-
 retardation.

Risk of unbalanced offspring in carriers of a balanced
reciprocal translocation depends on the length and ge-
netic constitution of exchanged segments7. In our family
both possible unbalanced karyotypes are probably viable,
as a deletion 4q31.3®qter has been reported in several
patients6 as well as the partial trisomy of the small termi-
nal part of 2p9,10. Our case represents the clinical mani-
festations of the combination of small region 2p deletion
and 4q duplication.

In conclusion, we reported a case with a karyotype
which was not published previously and establish a geno-
type-phenotype correlation. Reports of small regions of
duplication or deletion may contribute significantly to
the clarification of region specific phenotypes. It should
be useful then to compare clinically other subjects with
identical cytogenetic anomalies. Further case reports of
this nature would help in further delineating this chro-
mosomal abnormality.

| TABLE 1 | CLINICAL FEATURES OF PURE PARTIAL MONOSOMY 2p AND PURE PARTIAL TRISOMY OF 4q |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Short stature | + | – | – | – | – |
| Brachycephaly | + | – | – | + | – |
| Microcephaly | + | + | – | – | + |
| Facial dysmorphism | + | + | – | + | + |
| Strabismus | – | + | – | + | + |
| Epicantethc folds | – | + | – | + | + |
| Ears anomalies | + | + | – | + | – |
| Nose anomalies | – | – | + | – | + |
| Short neck | – | – | – | + | – |
| Clinodactyly | + | – | – | + | – |
| Poor verbal articulation | – | – | + | + | – |
| Hyperactivity | – | + | – | + | – |
| Mental retardation | + | – | + | + | + |
| Growth retardation | + | – | – | – | + |
| Hypotonia | – | + | – | + | – |

REFERENCE


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DJELOMIČNA MONOSOMIJA 2p I DJELOMIČNA TRISOMIJA 4p USLIJEĐEN OČEVE TRANSLOKACIJE t(2;4)(p25.1;q31.3)

SAŽETAK

Klinička slika pacijenta s djelomičnom aneuploidijom ovisi o veličini kromosomskog segmenta uključenog u translokaciju. Monosomija 2p često je dio složenih sindroma u potomaka nositelja uravnotežene recipročne translokacije. Pacijenti sa sindromom dup4q imaju promjenjivu kliničku sliku koja ovisi o veličini dupliciranog segmenta 4q i specifičnoj pridruženoj monosomiji. Klinička slika naših pacijenata podudara se s kliničkom slikom već objavljenih pacijenata s dup4q i del2p. Prikazani su klinički i citogenetički nalazi četvrogodišnje djevojčice sa nebalansiranim kariotipom 46, XX, der(2)(de(2;4)(p25.1;q31.3))pat. Fenotipovi slučajeva translokacije 2p;4q su promjenjivi jer točke loma variraju od pacijenta do pacijenta. Usporedili smo sličnost kliničkih nalaza naših pacijenata s ostalim pacijentima opisanim u literaturi koji imaju ili duplikaciju distalnog dijela 4q ili deleciju distalnog dijela 2p. Ovo je prva pacijentica s djelomičnom trisomijom 4q povezana s djelomičnom monosomijom 2p.