A case of partial trisomy 13 with features similar to 'C' Syndrome

Bulguları C sendromuna benzeyen parsiyel trizomi 13

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Abstract
We report a case of partial trisomy 13 with some distinct clinical findings which are similar to the features of 'C' syndrome including; trigonocephaly, microcephaly, frontal bossing, forehead and eyelid hemangioma, hypertelorism, upslanting palpebral fissures, apparently low-set ears, rethrognathia, highly arched palate, short neck, widely spaced nipples, foot deformity (spontaneous dorsiflexion of the hallux), failure to thrive, atrial septal defect and ventricular septal defect. Her karyotype was 46, XX, der(5) t(5;13)(p15.3;q14.2). In the family, a phenotypically normal father had balanced translocation between chromosome 5 and chromosome 13, and the proband has received the recombinant 5 from the father. The father karyotype was 46, XY, t(5;13)(p15.3;q14.2). Genetic counselling was given to the family for reproductive risks.

Key Words: **Chromosomes, human, pair 13; Genetic counselling; Trisomy; Translocation, genetic.**

Özet
Burada triganosefali, mikrosefali, frontal bossing, alın ve göz kapağında hemanjiom, hipertelorism, yukarı eğimli palpebral fissür, belirgin düşük yerleşimli kulaklar, retrognati, yüksek damak, kısa boyun, ayrık meme ucu, ayak deformitesi (ayak başparmağının spontan dorsifeleksiyonu), yutma güçlüğü, atrial septal defekt ve ventriküler septal defekt gibi 'C' sendromuna benzer bazı ayırt edici bulgulara sahip parsiyel trizomi 13 vakası sunulmuştur. Vakanın karyotipi 46, XX, der(5) t(5;13)(p15,3; q14,2) idi. Aileye yapılan kromozom analizinde, fenotipik olarak normal olan babada 5. ve 13. kromozom arasında dengeli translokasyon saptandı [46, XY, t(5;13)(p15,3; q14,2)] ve probandın babadan rekombinant 5.kromozomu alarak dengesiz karyotipe sahip olduğu anlaşıldı. Aileye ileride doğabilecek çocukları için genetik danışma verildi.

Anahtar Kelimeler: **13 nolu kromozom çifti; Genetik danışma; Genetik translokasyon; Trizomi.**

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Introduction

In 1969 Opitz et al. described a malformation syndrome in 2 sibs with trigonocephaly, called ''C syndrome of multiple congenital anomalies'' (1). Opitz trigonocephaly syndrome (OTS) is also used as a synonym. Other findings were upslanting palpebral fissures, convergent strabismus, epicanthal folds, depressed nasal bridge, small nose with upturned nares, macrostomia, multiple labiogingival frenula, thick alveolar ridges and highly arched palate, retrognathia, short neck, rhizomelic shortness, skin laxity, and additional internal anomalies such as pancreatic fibrosis. To date, more than 30 cases have been reported with a similar phenotype. Some of the cases reported had additional abnormalities such as medulloblastoma (2). Inheritance has been thought to be autosomally recessive although a number of cases with features similar to C syndrome have been reported with chromosomal abnormalities (3). Here, we report a case of partial trisomy 13 with features similar to C syndrome. This emphasizes the need for cytogenetic investigations of MCA/MR (multiple congenital anomaly/mental retardation) in order to provide accurate genetic counselling and prenatal diagnosis.

Case report

The kindred B.D is the last child of healthy non-consanguineous parents (Fig. 1, Pic. 1). When she was born, the father was 38 and the mother was 34 years old. The family had 3 first trimester spontaneous abortions due to unknown etiology and 2 neonatal deaths. Two neonatal deaths occured at 5 and 20 days, respectively before this child. Gestation was remarkable because of early membrane rupture. There was no exposure to toxins or known teratogens. The baby was delivered by normal spontaneous vaginal delivery at 36-37 weeks. The baby had cyanosis. The birth weight was 2700gr, height was 42cm (< 10th percentile) and occipitofrontal circumference was 30.5cm (<10th percentile).

We first examined the infant when she was 6 days old. She weighed 2320 g, and had a length of 42 cm and an occipitofrontal circumference (OFC) of 30.5 cm (all below the 10th centile). She had trigonocephaly, microcephaly, frontal bossing, forehead and eyelid hemangioma, hypoplastic orbital ridges, hypertelorism, upslanting palpebral fissures, broad nasal bridge, small nose with upturned nares, apparently low-set ears, rethrognathia, highly arched palate, short neck, widely spaced nipples, simian line in both hands, foot deformity including spontaneous dorsiflexion of the hallux and failure to thrive. Dermatoglyphic palm patterns were unremarkable.

Computed tomography of the brain showed corpus callosum dysgenesis. Transfontanel USG was normal and echocardiography revealed atrial septal defect ostium secundum, ventricular septal defect and pulmoner hypertention. Abdomen USG was normal. Her parents' physical findings were normal.

Cytogenetics. The GTG banded karyotype from peripheral blood of the child was 46, XX, der(5) t(5;13)(p15.3;q14.2) pat (Fig. 2a). This means that there was extra material on the p arm of chromosome 5. This extra segment is the part of the q arm of chromosome 13 between the band q14.2 and the terminal end of q arm. It resulted in the trisomy of the distal segment of 13 q between band q14.2 and the terminal end of the q arm. The father's and his sister's karyotype revealed balanced translocation between chromosome 13 and chromosome 5; 46, XY, t(5;13)(p15.3;q14.2) (Fig. 2b). The karyotype of the mother was normal.

Discussion

In the litretature, nearly 30 cases of presumed C syndrome have been reported (2). There are some striking common clinical findings: specific intraoral anomalies such as multiple labiogingival frenula, highly arched palate and broad alveolar ridges, that some authors consider diagnostic of C syndrome (4). However, there is evidence for clinical variability in the syndrome. Normal karyotype, parental consanguinity and normal parents with multiple affected offspring of equal sex ratio, autosomal recessive inheritance have been reported in the literature. However consanguinity was found in only 3 out of 25 cases (5,6,7). De Koster et al. proposed the possible inheritance of C syndrome might be caused by a cytogenetically undetectable microdeletion syndrome (8). Some cases with phenotype similar to 'C' syndrome are associated with chromosomal abnormalities. These include del(3p) (p12;?p14) (9), dup(3q) (pter ;q27) (5), dup and del(3q) (10), del(7p) (5), del(9p) (11), del(11q) (12), del(13q) (13), and dup(3q) (14), and partial trisomy and tetrasomy 13 (15).

McGaughran et al. (2000) reported a case who has trisomy of 3pter with C syndrome and her karyotype was 46,XX.ish der(5)t(3;5)(p26.3;p15.33)(3pter+)de novo (3). The case has translocation involving 5p similar to the current case's karyotype. Although, both of them share similar clinical

findings for C syndrome including; bitemporal narrowing, striking hemangioma of their forehead, apparently low-set ears, proximally placed thumbs, foot deformity, and cardiac defects, the case also have a partial trisomy 3p2 specific clinical findings distinct from our case.

Phadke et al. (2004) published a case with partial trisomy 13 had smilar clinical findings with our case including; trigonocephaly, upslant of eyes, postaxial polydactyly, smooth and long philtrum, apparently low-set ears with developmental delay. In addition the case had distinct karyotype [46, XY, rec(13), dup(13) (qter q22 :: cen qter)] from our case with additional findings including; a postaxial polydactly of all four limbs, unilateral renal agenesis and a pilonidal sinus but cardiac defects was absent in this case (16).

Bohring et al. (1999) presented 4 unrelated cases of a syndrome resembling Opitz trigonocephaly (C) syndrome. These cases have a prominent metopic suture, a characteristic haemangioma over the forehead and glabella, exophthalmos, hypertelorism and a cleft lip and palate in some cases The forehead is hirsute and the eyebrows prominent with synophrys. There are multiple joint contractures with a characteristic flexion deformity of the wrist associated with camptodactyly. Brain scanning showed enlargement of the fourth ventricle with a Dandy-Walker malformation in one case and agenesis of the corpus callosum in three cases. There was also delayed myelination. One case had an ASD. There was intrauterine growth retardation with failure to thrive and early demise in the majority of cases. Although differed from C syndrome and our case on the basis of intrauterine growth retardation, cleft lip/palate, exophthalmos, retinal involvement, flexion deformities of the upper limbs, dislocation of radial heads, and forehead hirsutism (17). The clinical features of our case are trigonocephaly, microcephaly, frontal bossing, forehead and eyelid hemangioma, hypoplastic orbital ridges, hypertelorism, upslanting palpebral fissures, broad nasal bridge, small nose with upturned nares, apparently low-set ears, rethrognathia, highly arched palate, short neck, widely spaced nipples, simian line in both hands, foot deformity (spontaneous dorsiflexion of the hallux), failure to thrive, atrial septal defect ostium secundum, ventricular septal defect and pulmoner hypertention, which are similar to the features of 'C' syndrome. Hypermobile joints, short fingers and toes with postaxial polydactyly, and cutaneous syndactyly up to the end of the proximal phalanges in the hands and complete between the 2nd, 3rd and 4th toes, and multiple alveolar frenula commonly seen in cases of 'C' syndrome were absent in the present case (1).

In this family, the phenotypically normal father had balanced translocation between chromosome 5 and chromosome 13, which resulted in recombinant 5 due to unbalanced chromosomal rearrangement during normal meiosis. Since the father is a carrier of balanced chromosomal rearrangement, there is an increased risk of having a child with chromosomal imbalance. Counselling for the risk of recurrence of malformed offspring and increased fetal loss is necessary once the carrier for such balanced chromosomal rearrangement is identified. However, the risk varies depending on the chromosome involved. Karyotyping of the parents and the siblings of such a translocation carrier is indicated to identify the carrier and offer parents genetic counselling and prenatal diagnosis. Prenatal cytogenetic analysis of chorionic villi or amniotic fluid can provide a diagnosis and help the family to avoid recurrences.

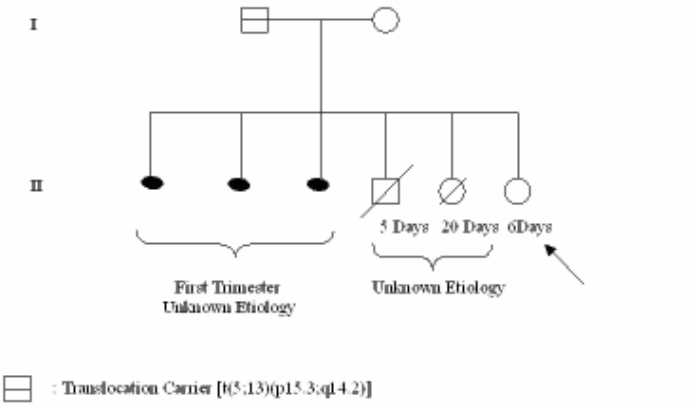
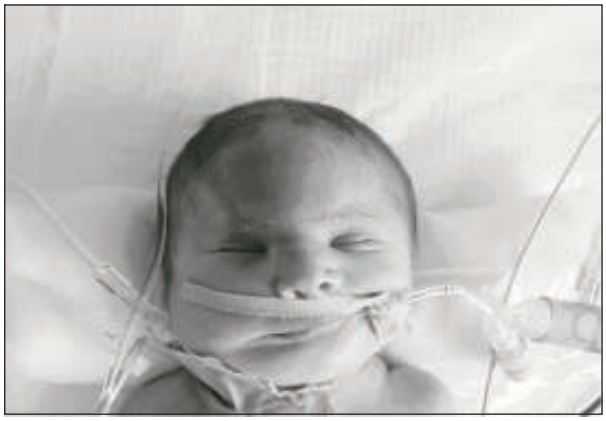


Figure 1. Patient's Family Pedigree



Picture 1. Dismorphic facial appearance, including trigonocephaly, prominent forehead with glabellar capillary hemangioma, a broad depressed nasal bridge, upslanted palpebral fissures, micrognathia, microcephaly and a short neck.

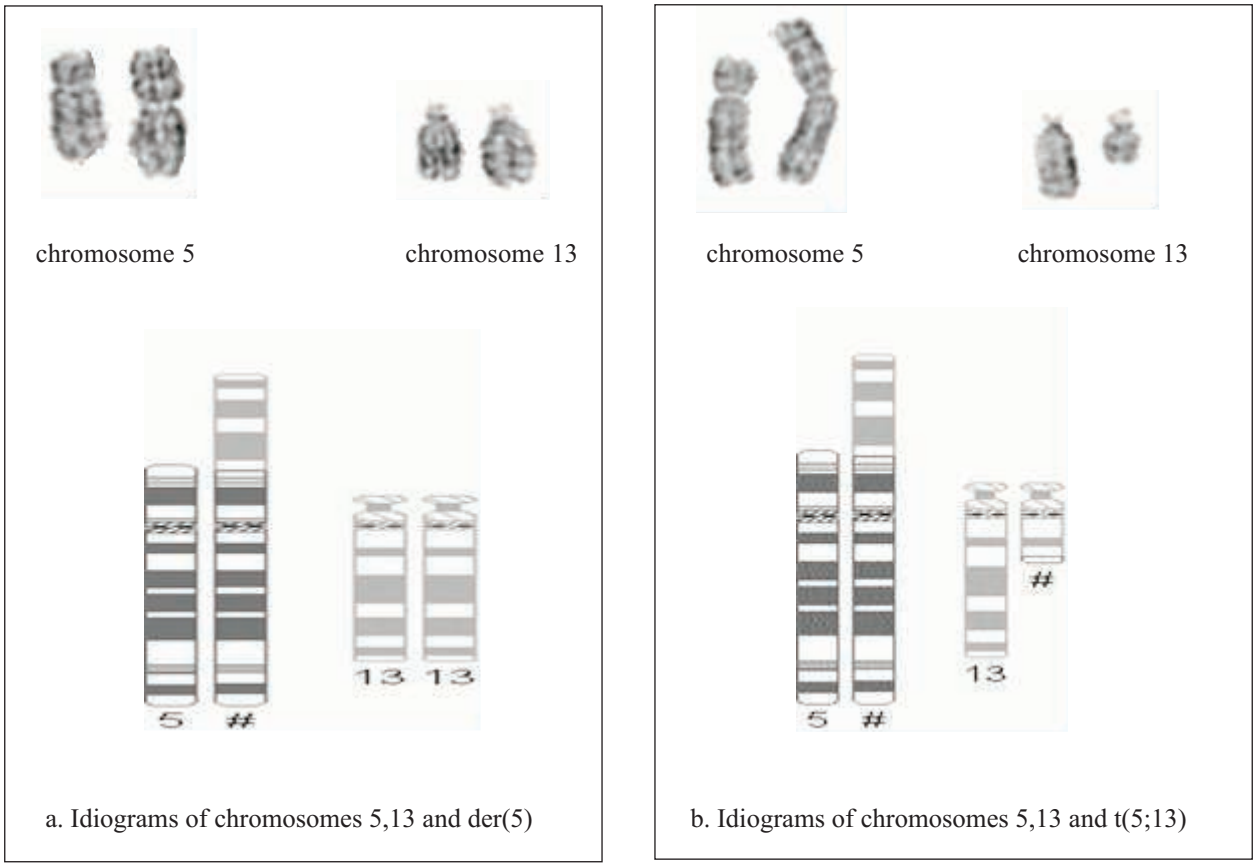


Figure 2. a. Child's partial karyotype showing duplication of p15.3-q14.1. Abnormal chromosome is on right side of the pair. The segment of q arm distal to the arrow is duplicated and is attached to the p arm. **b.** Father's and his sister's partial karyotypes showing balanced translocation between chromosome 13 and the chromosome 5. Abnormal chromosome is on right side of the pair. Arrows point to the breakpoints.

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