Prenatally diagnosed partial trisomy 3q case with an omphalocele and less severe phenotype

Prenatal tanısı konulmuş, omfalosel ve hafif fenotipik anormalliklere sahip kısmi trizomi 3q olgusu

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Abstract

Trisomy 3q is a very rarely reported chromosomal disorder. Duplication of part of the long arm of human chromosome 3 causes a distinct and severe syndrome that leads to multiple congenital abnormalities. A 27 year-old pregnant woman was admitted to our clinic at 17 weeks of gestation. Prenatal sonography identified a fetus with an omphalocele that contained the liver and bowel , mild ventriculomegaly and polyhydramnios. Amniocentesis revealed the karyotype of 46, XY, der (3) (3qter→3q21: : 3pter→3qter). The pregnancy was subsequently terminated. Postnatally, the proband showed midfacial hypoplasia, micrognathia, hypoplastic 12th ribs, omphalocele and prominent heels. We reported this partial trisomy 3q case because he had less marked malformations compared to other reported cases and also different features such as an omphalocele and hypoplastic 12th rib which have not been described previously in an isolated Trisomy 3q case with this karyotype.

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Özet

Trizomi 3q nadir görülen bir kromozom anomalisidir. İnsan 3. kromozomunun uzun kolunun bir kısmının duplikasyonu multipl kongenital anormalliklerle birlikte olan farklı ve ciddi bir sendroma yol açar. Yirmi-yedi yaşındaki gebe kadın mevcut gebeliğinin 17. haftasında polikliniğimize başvurdu. Fetusta yapılan prenatal ultrasonografide, karaciğer ve barsak içeren omfalosel, hafif ventrikülomegali ve polihidramnios tespit edildi. Yapılan amniyosentez sonucunda karyotip 46, XY, der (3) (3qter→3q21: :3pter→3qter) geldi. Ardından tıbbi terminasyon uygulandı. Terminasyon sonrası fetusta; midfasiyal hipoplazi, mikrognati, hipoplastik 12. kosta, omfalosel ve çıkıntılı topuklar tespit edildi. Biz bu olguyu, daha önce yayınlanmış izole Trizomi 3q olgularına göre daha hafif malformasyonlar içermesi ve ayrıca omfalosel ve hipoplastik 12. kosta gibi onlarda bulunmayan ek anomalilere sahip olması nedeniyle yayınladık.

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Anahtar kelimeler: Kısmi Trizomi 3q, omfalosel, amniyosentez

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Introduction

Trisomy 3q is a very rarely reported chromosomal disorder. The majority of cases have involved duplication of the segment 3q21-qter and, in most cases, these duplications are the result of unbalanced segregations of balanced parental translocation involving chromosome 3 (1).

Duplication of part of the long arm of human chromosome 3 causes a distinct and severe syndrome that leads to multiple congenital abnormalities. Some of the malformations include congenital heart defects (septal defects), renal malformations (polycystic kidneys or dysplasia), ocular malformations (strabismus, nystagmus, cataract, corneal opacities, colobomas of the iris, and anophthalmia), facial malformations (hypertrichosis, hypertelorism, anteverted nostrils, long philtrum, maxillary prognathism, downturned corners of the mouth, cleft palate, micrognathia) and limb anomalies (hypoplasia of the phalanges, camptodactyly and clinodactyly), malformed auricles, short/webbed neck, seizures and brain malformations (2).

Here we report a prenatally diagnosed partial Trisomy 3q (46, XY, der(3) (3qter→3q21::3pter→3qter) karyotype) case with an omphalocele (containing liver and bowel) and a less severe phenotype than the previously reported cases with such a large duplicated segment.

Case Report

A 27 year-old G3P1A1C0 pregnant woman was admitted to the Kahramanmaras Sutcu Imam University Obstetrics Outpatient Clinic for pregnancy follow-up. She had a first trimester pregnancy loss and pregnancy termination history due to diaphragmatic hernia, short extremities and Dandy-Walker malformation. The parents were relatives (first degree cousins). There was no positive family history. Prenatal sonography at 17 weeks revealed a 31x21 mm sized ompha-

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locele protruding out of the abdominal wall on the right side of the umbilical cord that contained the liver and bowel (Figure 1), mild ventriculomegaly and polyhydramnios. The couple was counseled and amniocentesis was performed after their written informed consent form had been obtained. Amniocytes were cultured in three independent culture flasks and then harvested. Chromosome analysis was performed at 550 band level and 46,XY,der(3)(3qter→3q21::3pter→3qter), partial trisomy 3q was detected. This trisomy includes the segment between q21 band to q terminal. The couple decided to terminate the pregnancy which was carried out at 21 weeks gestation. Postmortem examination revealed midfacial hypoplasia, micrognathia, hypoplastic 12th ribs, omphalocele and prominent heels (Figure 2). As the couple did not permit autopsy, prenatal ultrasound findings were confirmed with magnetic resonance imaging. Parental chromosome analysis was performed and maternal pericentric inversion of chromosome 3 (46, XX, inv (3) (p26q21)) was detected, while the father had normal (46, XY) karyotype.

Research ethics approval was obtained from the Ethics Committee of Kahramanmaras Sutcu Imam University and signed informed consent was obtained from the patient.

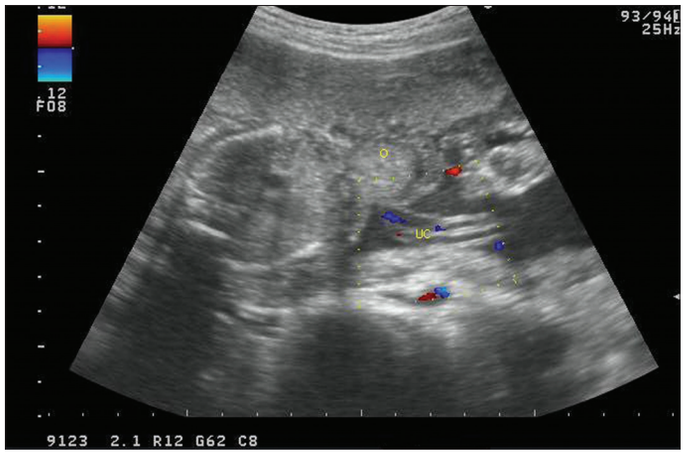

Figure 1. Ultrasonographic view of omphalocele (o: omphalocele, uc: umbilical cord)

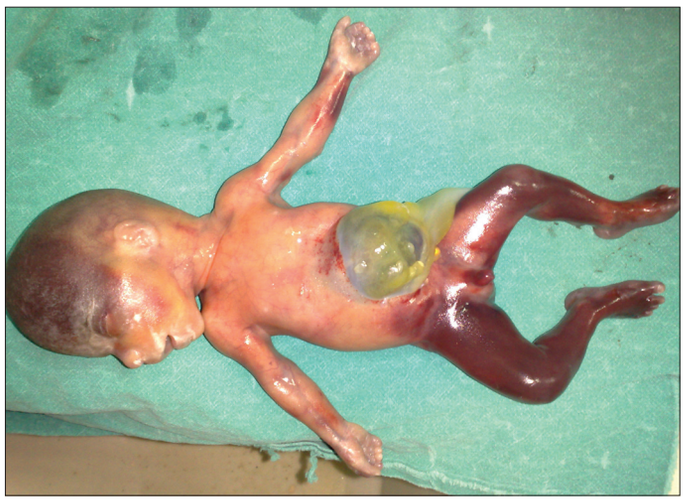

Figure 2. Anterior view of baby

Discussion

In the literature, to our knowledge, 94 patients with duplication of 3q have been reported. However, pure duplications are rare because most of the reported patients appear to carry unbalanced translocations. Also, recently mostly cases with more distal duplications-either single abnormalities or associated with a deletion of another chromosomal segment-have been described. Our case had 46, XY, der (3) (3qter→3q21::3pter→3qter) karyotype and we could only find 8 familial and 6 de novo cases with the same duplicated segment in the literature. The dysmorphic findings reported in these cases, and in partial Trisomy 3q cases with duplication of different segments, show significant differences from each other, as given in Table 1 (3-23). Compared to these cases, our patient manifested a less severe clinical picture, with some unusual characteristic features such as midfacial hypoplasia, hypoplastic 12th rib and prominent heels (Table 1). The case we present is a new example of familial cases.

Steinbach et al. described the most common abnormal features in these cases, such as statomotoric retardation, shortened life span, and multiple congenital anomalies (MCA) including abnormal head configuration, hypertrichosis, hypertelorism, ocular anomalies, anteverted nostrils, long philtrum, maxillary prognathia, down-turned corners of the mouth, highly arched or cleft plate, micrognathia, malformed auricles, short, webbed neck, clinodactyly, simian crease, talipes, and congenital heart disease (4). As shown in Table 1, micrognathia, short neck and eye anomalies were the most common findings among reported cases. Thoracic abnormality (absent ribs) was reported only by Steinbach et al (4) while our case had a hypoplastic 12th rib.

An omphalocele is a herniation of bowel, liver and other abdominal viscera into a membranous sac with the umbilical cord at its apex. The prevalence of omphalocele varies considerably, ranging from 0.8 to 3.9 per 10,000 births (23). Abnormal karyotypes have been reported in 10 to 40% (combined mean rate of 12%) of neonates with omphaloceles. Trisomy 18 and 13 are the most common associating chromosomal anomalies, followed in frequency by trisomy 21, 45, X (Turner syndrome) and triploidy (24). Usually, abnormal karyotype incidence increases when the liver is intracorporeal (25). Chen et al. (3) reported a case with duplication of 3q21→qter and deletion of 11q23→qter resulting from an unbalanced segregation of a maternal t (3;11) reciprocal translocation. At prenatal sonographic examination they demonstrated an omphalocele containing the liver (3). Yatsenko et al. (23) reported a case with karyotype of 46,XY,der (4)t(3;4)(q27.3;q32.3)mat, resulting in trisomy for 3q27.3→qter and monosomy for 4q32.3→qter. Their case had an omphalocele that contained part of the left hepatic lobe, stomach, and transverse colon. They also searched the literature to identify previously reported cases of partial trisomy 3q associated with omphalocele, and found that 26 of 93 cases presented with an omphalocele (23). In all of them, the area of duplication includes the region 3q27.3→qter. Yatsenko et al also attempted to specify which chromosomal region is responsible for omphalocele and searched previously reported 40 patients with monosomy of 4q. They found that none of them had omphalocele. As a result, they suggested that a dosage-sensitive locus on

Table 1. Comparison of clinical phenotype of our case with cases in the literature

	Literature	Our case
Head and neck	• Cleft lip, plate (Blumberg, 1980; Pires, 2005) • Broad and flat nasal bridge (Blumberg, 1980; Zafra de la Rosa, 2005; Gamerdinger, 2006; Gimelli, 2007) • Anteverted nostrils (Chiyo,1976; Fear,1979; Blumberg, 1980; Ismail, 1991; Gimelli, 2007) • Malformed ears (Blumberg, 1980; Ismail, 1991; de Azevedo Moreira, 2005; Carreira, 2009) • Downturned corners of the mouth and thin lips (Ismail, 1991; Zafra de la Rosa, 2005; Gamerdinger, 2006; Grossmann, 2009) • Micrognathia (Chiyo,1976; Fear,1979; Kondo,1979; Ismail,1991; Pires, 2005; Zafra de la Rosa, 2005) • Short neck (Chiyo,1976; Fear,1979; Kondo,1979; Ismail,1991; de Azevedo Moreira, 2005; Zafra de la Rosa, 2005; Gimelli, 2007) • Cystic hygroma (Pires, 2005) • Wide nasal bridge (Zafra de la Rosa, 2005; Grossmann, 2009) • Prominent philtrum (Zafra de la Rosa, 2005; Gamerdinger, 2006; Grossmann, 2009) • Prominent forehead (Gamerdinger, 2006)	Midfacial hypoplasia Micrognathia
Eye	• Coloboma of iris (Fryns, 1984) • Cataract (Mulcahy, 1979; Gustashaw, 1985) • Microphthalmia (Fear, 1979; Steinbach, 1981; Qureshi, 1994; de Azevedo Moreira, 2005) • Corneal opacities and other eye malformations (Blumberg, 1980; Qureshi, 1994; de Azevedo Moreira, 2005) • Congenital glaucoma (Kondo,1979; Blumberg, 1980) • Coloboma of optic nerve (Ayral, 1984) • Hypertelorism (Ismail, 1991; Zafra de la Rosa, 2005; Gamerdinger, 2006; Grossmann, 2009) • Epicanthic folds (Zafra de la Rosa, 2005; Grossmann, 2009)	Could't evaluated
Thorax	• Absent ribs (Steinbach, 1981)	Hypoplastic 12th rib
Skeletal system	• Thoracic hemivertebrae (Steinbach, 1981) • Narrow pelvis (Steinbach, 1981) • Dislocated elbow (Steinbach, 1981; Zafra de la Rosa, 2005) • Dislocated wrist (Steinbach, 1981) • Dislocated phalanx (Steinbach, 1981)	Normal X-rays
Extremities	• Clenched hands (Steinbach, 1981) • Abnormal dermatoglyphics (Steinbach, 1981) • Bifid thumb (Mulcahy, 1979; Steinbach, 1981) • Polydactyly (Fryns, 1979) • Syndactyly (Kondo, 1979; Zafra de la Rosa, 2005) • Fifth-finger clinodactyly (Chiyo, 1976; Fear,1979; Blumberg, 1980; Zafra de la Rosa, 2005; Gimelli, 2007) • Short limbs (Blumberg, 1980; Gimelli, 2007)	Prominent heels

	• Abnormal foot position (de Azevedo Moreira, 2005; Zafra de la Rosa, 2005; Carreira, 2009) • Brachydactyly (Grossmann, 2009) • Congenital hip dysplasia (Gamerdinger, 2006)	
Internal organ anomalies	• Cardiac anomalies (Chiyo, 1976; Fear, 1979; Steinbach, 1981; Pires, 2005; Zafra de la Rosa, 2005) • Polycystic kidney (de Azevedo Moreira, 2005) • Renal anomalies (Blumberg, 1980) • Renal cystic dysplasia (Blumberg, 1980) • Renal cortical cysts (Chiyo, 1976; Fear, 1979) • Unilateral renal agenesis (Blumberg, 1980) • Renal calcification (Ismail, 1991) • Adrenal neuroblastoma (Qureshi, 1994) • Malrotation (Blumberg, 1980) • Lung hypoplasia (Blumberg, 1980; Qureshi, 1994) • Omphalocele (Mulcahy, 1979; Chen, 1996; Yatsenko, 2003; Park, 2008)	Omphalocele (containing liver and bowel)
Central nervous system	• Dandy- Walker malformation (Chiyo, 1976; de Azevedo Moreira, 2005) • Cerebellar hypoplasia (Steinbach, 1979) • Arhinencephaly (Steinbach, 1979) • Hypoplasia of corpus callosum (Steinbach, 1979) • Microcephally (Blumberg, 1980) • Spina bifida (de Azevedo Moreira, 2005; Gimelli, 2007)	Ventriculomegaly
Genital system	• Hypospadias (Fryns, 1984) • Bicornuate uterus (Chiyo, 1979; Blumberg, 1980) • Streak ovaries (Blumberg, 1980) • Duplication of the vagina and cervix (Blumberg, 1980) • Ambiguous genitalia (Gimelli, 2007)	
Anal anomalies	• Anteriorly placed anus (Fryns, 1979) • Anal stenosis (Gustashaw, 1985)	

the distal 3q could be responsible from an omphalocele (23). Our case also has an omphalocele and no other chromosomal component other than a duplicated 3q segment.

In partial Trisomy 3q cases the abnormal genotypes are usually the result of parental abnormalities of chromosome 3. Reciprocal translocation is the most frequent parental chromosome anomaly. In our case, parental chromosome analysis demonstrated a maternal pericentric inversion of chromosome 3 (46, XX, inv (3) (p26q21)). Fear et al (8) demonstrated 5 (83%) maternal and 1 (17%) paternal structural anomalies in parents of 6 Trisomy 3q cases. Yatsenko et al. (23) demonstrated malsegregation of a parental balanced chromosomal rearrangement in 41 (64%) of 64 families, and the remaining (36%) were de novo. In cases with omphalocele, inheritance was maternal in 6 (%75) and paternal in 2 (25%) of 8 families. Pericentric inversions, unlike other balanced chromosomal variations, may cause deletion and duplication in conceptuses due to unbalanced cross-over in meiosis. These deletions or duplications may be either of a size detectable under the microscope as in our case, or be very small and may escape observation. Thus, if unbalanced chromosomal alterations have not been detected by conventional cytogenetic analyses in such cases, the recently developed array-CGH method should be recommended for scanning submicroscopic deletions and duplications.

In conclusion, we reported this partial trisomy 3q case because he had less marked malformations compared to other reported cases and also different features such as an omphalocele and hypoplastic 12th rib, which have not been described previously in an isolated Trisomy 3q case with 46, XY, der (3) (3qter→3q21::3pter→3qter) karyotype. For detection of etiology and determination of the risk in subsequent pregnancies, parental chromosomal analysis is mandatory in cases with this kind of structural chromosomal alt.

Conflict of interest

No conflict of interest is declared by authors.

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