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Distal trisomy 10q24 due to maternal 10;22 translocation, third case in the same family

Case report

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Abstract: Distal trisomy 10q is a well delineated but a rare syndrome with characteristic phenotypic features. We present clinical and cytogenetic data on a 7 day-old girl with distal 10q trisomy (10q24→qter), due to maternal t(10;22) reciprocal translocation. Her karyotype showed an unbalanced translocation between chromosomes 10 and 22, resulting in trisomy of the distal part of the long arm of chromosome 10q24.

Keywords: *Distal trisomy 10q • Facial dysmorphism • Congenital malformations • Familial reciprocal translocations*

1. Introduction

Carriers of balanced translocations can suffer from infertility and are at high risk of conceiving chromosomally abnormal pregnancies that may lead to recurrent spontaneous abortions or affected liveborns. Trisomy and monosomy of most chromosomes are fatal for a fetus during the prenatal development; on the other hand, partial trisomies or monosomies are encountered.

Distal trisomy 10q syndrome , a clinically well recognized syndrome, was reported in 1965 at first [1,2]. After that in 1974 and in 1979 Yunis and Sanches, Klep-de Pater et. al. dignosed the disease by its clinical features [3,4]. The disease was first recognized as "distal 10q Syndrome" by Taysi et al. in 1983. The most frequent cause of this syndrome is a balanced translocation in one parent [5,6]. Major features of this syndrome include microcephaly, flat and round face, small nose, depressed nasal bridge, deep set eyes with narrow palpebral fissures, high and large forehead, epicantal folds, blepharophimosis and blepharoptosis, downturned corners of the mouth, short neck, scoliosis, camptodactyly, Simian crease, feet deformity, deep plantar crease, renal, cardiac, genital and ocular abnormalities and inguinal hernies. Long term prognosis is poor and approximately half of the patients with distal trisomy 10q syndrome die in the first year of life due to heart defects or other congenital malformations [7,8].

Here we present an infant with distal trisomy 10q24 due to maternal 10;22 translocation, which is the third case in the same family. The chromosomal abnormalities in all cases resulted from a maternal balanced translocation involving chromosomes 10 and 22.

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2. Case report

A 7 day-old girl was referred to our department with a suspicion of Down Syndrome. The parents were healthy and non consanguineous. There was no history of recurrent miscarriages. She was born at term and her birth weight was 2.375 kg, height was 48 cm and head circumference was 34 cm. She was the second child of the family. Her elder brother was a healthy boy.

Dysmorphic features of the patient included microcephaly, microphtalmia, narrow eye openings, ptosis, blepharophimosis, upslanting palpebral fissures, arched eyebrows, hypertelorism, cleft palate, depressed nasal bridge, short neck, sloping shoulders, deep plantar crease, overlapping fingers and minimal pectus excavatum and umblical hernie. Echocardiography demonstrated mild pulmonary stenosis (PS), ventricular septal defect (VSD) and pulmonary hypertension. She had respiratory distress and her chest radiograph revealed acute bronchopneumonia. According to computerized tomography; there were multiple cystic lesions in her renal medullar area. Her external genitalia were normal.

During our study related to the preparation of the pedigree of the proband, we realized that this patient was relative with a family that consulted to our clinic in 1994 [9]. In that family, there was 2 affected infants and 6 balanced translocation carriers and our proband was the third trisomy 10q syndromic patient (Figure 1). Because of early deaths, the cause of death for V.5, 6, 9, 11 is not known.

After chromosomal analysis, we discovered that there was an unbalanced translocation resulting in trisomy of distal one third of the long arm of chromosome 10(q24→qter). Analysis of the parents revealed that there were a normal karyotype in father and a balanced reciprocal translocation between the long arm of chromosome 10 and short arm of chromosome 22 in mother (Figure 2). The mother's karyotype was found as 46,XX,t(10;22)(10q24;22p11) and the patient's karyotype was 46,XX,der (22)t(10;22)(10q24;22p11) (Figure 3).

Unfortunately, the baby died in a few days so that we couldn't apply other molecular technical analysis such as FISH analysis (Fluorescence in situ hybridization).

3. Discussion

Trisomy of the long arm in chromosome 10 has already been described in several patients [4,5]. Among them, most cases are resulted from an unbalanced

Figure 1. The pedigree of the family. Our proband is cousin with the other patients.

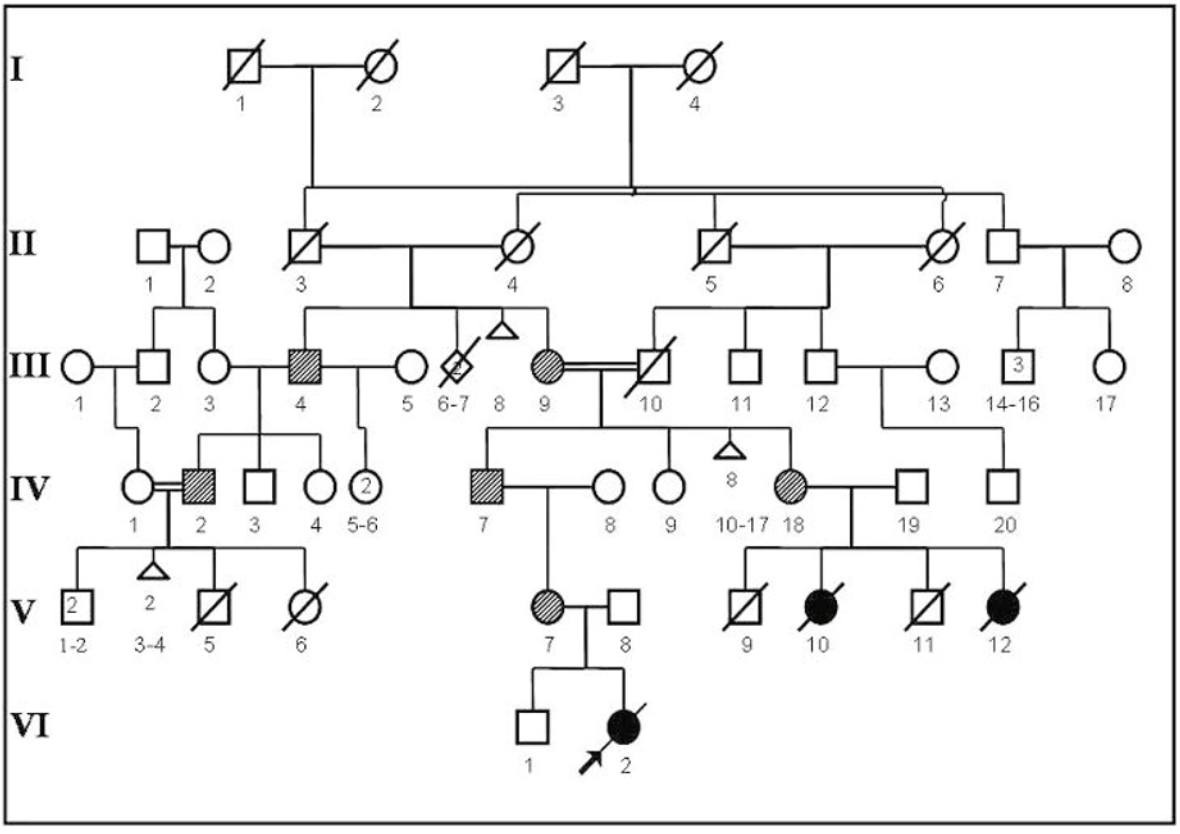


Figure 2. Ideogram of the balanced t(10;22). The arrows show the breakpoints on 10q24 and 22p11

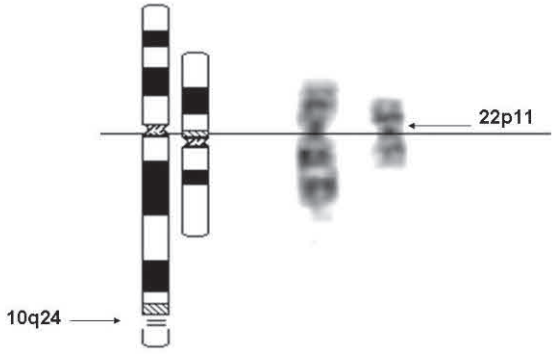
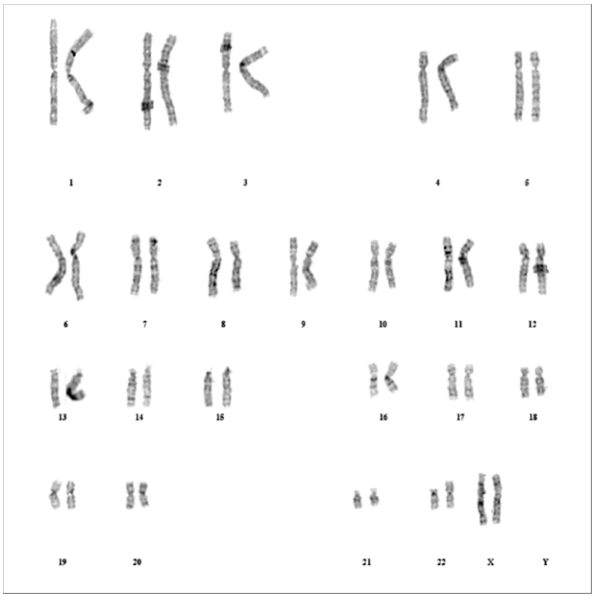


Figure 3.



product of a parental reciprocal translocation with another autosomal chromosome [10]. The disorder is characterized by growth retardation, mental retardation and hypotonia. Patients may also have craniofacial malformations, hands, feet and skeletal defects, heart, urogenital and pulmonary abnormalities [8].

Our proband has partial trisomy of the long arm of chromosome 10(q24→qter). There is a phenotypic similarity between our patient and cases of distal trisomy 10q24 described previously (Table 1). Similar to distal trisomy 10q cases, our patient's craniofacial dysmorphism includes microcephaly, microphtalmia, narrow eye openings, ptosis, blepharophimosis, upslanting palpebral fissures, arched eyebrows, hypertelorism, cleft palate, depressed nasal bridge, short neck. In addition she has cardiac defects such as ventricular septal defect (VSD), pulmonary stenosis (PS) and pulmonary hypertension and skeletal defects such as

Table 1. Comparison Between Distal Trisomy 10q Syndrome and Present Case

Trisomic Segment	Distal Trisomy 10q	Present Case
	10q24→ter	10q24→ter
General		
Growth retardation	+	+
Mental deficiency	+	Not available
Craniofacial		
Microcephaly	+	+
Microphtalmia	+	+
Epicantal folds	+	+
Round/flat face	+	+
Large forehead	+	+
Low set ears	+	+
Blepharophimozis	+	+
Ptosis	+	+
Broad nasal bridge	+	+
Bow shaped mouth	+	+
Cleft palate	+	+
Micrognathia	+	+
Overlapping fingers	-/+	+
Skeletal		
Camptodactyly	+	+
Syndactyly	+	-
Hypotonia	+	+
Deep plantar furrow	+	+
Simian creas	+	+
Others		
Cardiac malformation	+	+
Renal abnormalities	+	-
Hypospadias	+	-
Anal atresia	+	-
Inguinal hernie	-/+	-
Umblical Hernie	-/+	+

pectus excavatum. The only major difference was the absence of renal malformations except multiple cystic lesions in her renal meduller area and anal atresia in our patient.

The clinical findings of patients with partial trisomies for the middle and proximal segments of chromosome 10 are different from those of distal 10q trisomies [11,12]. Because of its clinical difference from trisomic syndromes of more proximal parts of the chromosome 10, Taysi et. al. suggested naming trisomy of the chromosomal region 10q24→10qter "distal 10q trisomy syndrome" [7,8].

The phenotype of individuals with trisomy of 10q24-qter is characterized by prenatal growth retardation,

severe developmental disability and anomalies of the eyes, heart, kidneys and lower limbs [8,13]. Chromosome band 10q24 is rich in genes involved in developmental and neurological disorders, tumorigenesis, hormone metabolism [11]. Trisomy 10q25-qter is less severe, typically without major congenital anomalies. There is pre-postnatal growth retardation, hypotonia, and variable degrees of cognitive disability [14]. Trisomy 10q26 is rarely reported, suggesting that the clinical features can be extremely mild. Indeed, subtelomeric duplications of 10q have been reported in phenotypically normal parents of children investigated for developmental delay or congenital anomalies [15].

After we studied on our proband's pedigree, we realized that 6 individuals were balanced translocation carriers. We had the information that there have been several abortions and early baby deaths. In the family there were 3 trisomy 10q syndromic patients. We found similar clinical findings which launched our proband to the other cases. In 1975, Fuenmayor mentioned about such a large trisomy 10q family with 2 affected cousins [16]. After performing a literature review, we come to the fact that this is the first case that subjects such a large family and 3 affected individuals.

Huo stated that the translocated 10q segments in most cases of 10q trisomy originate from father. Imprinting effect may exist in this chromosomal syndrome and cases originating from paternal reciprocal translocations being more competible with life [17]. Our patients were with distal 10q trisomy (10q24→qter), dependingupon maternal t(10;22) reciprocal translocation and had severe clinical features resulted in their death early in the neonatal period. The available literature on partial 10q trisomy does not indicate this imprinting effect and its relation to clinical severity and its survival.

Balanced reciprocal translocation carriers are almost phenotypically normal because there is no loss of genetic material. Translocations are usually diagnosed when a family member presents infertility, recurrent abortus or phenotypically abnormal offspring. After genetic counselling, the couples need to be followed up by ultrasonography during pregnancy and if necessary various prenatal test methods such as chorionic villus sampling, amniocentesis and umbilical cord blood collection can be used. The families should be led to try either preimplantation genetic diagnosis (PGD) or In Vitro Fertilization (IVF) methods to have successful pregnancies and healthy offspring.

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