PARTIAL TRISOMY 9 WITH t(9;21)(q22;q10) TRANSLOCATION DETECTED IN PRENATAL DIAGNOSIS

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SUMMARY

Trisomy 9p may occur due to either parental reciprocal translocation of chromosome 9 with other chromosomes or de-novo aberrations. Typical craniofacial features, intrauterine developmental delay, cleft lip-palate, micrognathia, cardiac abnormalities and congenital hip dislocation are findings which are expected to be seen in patients with partial trisomy 9pter->q22-32. With the triple testing of a 28-year-old G4P0A3 pregnant woman, performed during her fourth pregnancy, the risk of trisomy 18 was found to be increased. A cytogenetic analysis of the amniotic fluid was performed to establish prenatal diagnosis, and revealed the presence of three chromosome 9 and one chromosome 21. Thereupon, subsequent metaphase FISH analysis showed that one of three chromosome 9 was translocated with one of the chromosome 21 and this was considered to be partial trisomy 9 (pter->q22). As the parents have normal karyotype, this change in the fetus was considered to be de-novo. With the autopsy performed following the termination, the presence of agenesis of the corpus callosum and inlet VSD, which had been observed with previous the fetal USG was confirmed. This case will contribute to knowledge of the clinical evaluation of chromosomal abnormality including both 9p trisomy and chromosome 21 translocation, and also to genetic counseling for these patients.

Key words: *partial trisomy 9, prenatal diagnosis, translocation*

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PRENATAL TANIDA SAPTANAN t(9;21)(q22;q10) TRANSLOKASYONU OLAN PARSİYEL TRİZOMİ 9

ÖZET

Trizomi 9p, 9. kromozomun diğer kromozomlarla parental resiprokal translokasyonu ya da de-novo aberasyonlar sonucu meydana gelebilmektedir. Parsiyel trizomi 9pter->q22-32 'de ise tipik kraniofasiyal özellikler, intrauterin büyüme-gelişme geriliği, yarık damak-dudak, mikrognati, kardiyak anomaliler ve konjenital kalça çıkığı, görülmesi beklenen bulgulardır. Daha önce üç gebelik kaybı olan 28 yaşındaki hastanın, 4. gebeliğinde yapılan üçlü tarama testinde trizomi 18 riski artmış olarak saptandı. olguya prenatal tanı amacıyla sitogenetik analiz uygulandı. Sitogenetik analizde üç tane 9. kromozom ve bir tane 21. kromozom görülmesi üzerine, metafaz üzerinde yapılan FISH analizinde 3 tane 9. kromozomun bir tanesinin 21. kromozomlardan biri ile transloke olduğu görüldü ve parsiyel trizomi 9 (pter->q22) olarak değerlendirildi. Anne ve baba normal karyotip özelliğine sahip olduğu için fetüsteki değişim de-novo olarak değerlendirildi. Terminasyon sonrası otopside, daha önce yapılmış olan fetal USG'de gözlenen korpus kallosum agenezisi ve inlet VSD doğrulandı. Olgumuz, 9p trizomisinin, 21. kromozom translokasyonu ile birlikte görüldüğü kromozomal anomalinin klinik değerlendirilmesi ve prenatal genetik danışma açısından literatüre katkı sağlayacaktır.

Anahtar kelimeler: *parsiyel trizomi 9, prenatal tanı, translokasyon*

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INTRODUCTION

Trisomy 9p or duplication 9p syndrome was first reported in 1970 and the pattern of malformation was identified in 1975[1]. It is one of the most frequently observed chromosomal anomalies of live birth after classical aneuploidies. It may result after a parental reciprocal translocation or de-novo aberrations of chromosome 9 with other autosomal chromosomes[2]. According to Wilson et. al., the severity of clinical signs in trisomy 9p is associated with trisomy of chromosome length. The clinical symptoms caused by this syndrome are characterized in general with; hypoplazia of distal phalanges, delay in closing of the front fontanel and ocular hypertelorism. Retardation in growth-development is especially prevalent in postnatal stage. Puberty may be delayed and growth may continue until the middle of third decade. Mental retardation and serious delay in speaking can be observed. Cranio facial characteristics are micro-cephalia, hypertelorism, palpebral fissures being downward, deeply located eyes, apparent nose, edges of mouth pointing downwards, cup-like ears and these characteristics become more apparent with aging. Micrognathia, epicantal folds, short and mane like neck, syndactylia might be observed besides the anomalies related to extremities and skeletal system. While 5-10% of these cases suffer from heart defects, 5% suffer from cleft lip and/or palate, also hydrocephalia, agenesis of corpus callosum, renal malformations, micro-penis, cryptorchism cryptorchism, hypospadias, talipes equinovarus and congenital hip dislocation might be observed. 5-10% of the reported patients have died in early childhood [1,3,4].

Here we present a case which has applied with karyotype analysis indication in amnio-synthesis material because of a high risk of trisomy 18 in triple scanning test. Our purpose here is to analyze the cytogenetic and phenotypic findings in the case.

CASE REPORT

Amniocentesis was applied to a pregnant woman within the 19-20th week for prenatal diagnosis since trisomy 18 risk 1/130 was identified in the triple marker test of this patient in her 4th pregnancy, who was 28 years old and has had three miscarriages before. 20 cc of amnion fluid was sent to our Prenatal Diagnosis Laboratory. A cell culture was developed from the Amniocentesis material. Three flasks were used for the cell culture and cells were harvested in the 12th day for chromosomal analysis. The preparate banding was done using GTG banding technique. While one of the chromosome 21 could not be observed in metaphase plate karyotype analysis, a third extra chromosome was identified which resembled the structure of chromosome 9. Upon this discovery a FISH analysis was conducted with probes specific for 13, 18, 21, X, Y, CEP 9/9p21, 9q34/22q11(abl /bcr) and 12p13/21q22 (tel/aml1) regions(Figure. 1). On the other hand, blood samples were taken from the periferic blood of the mother and father of the fetus for chromosomal analysis.

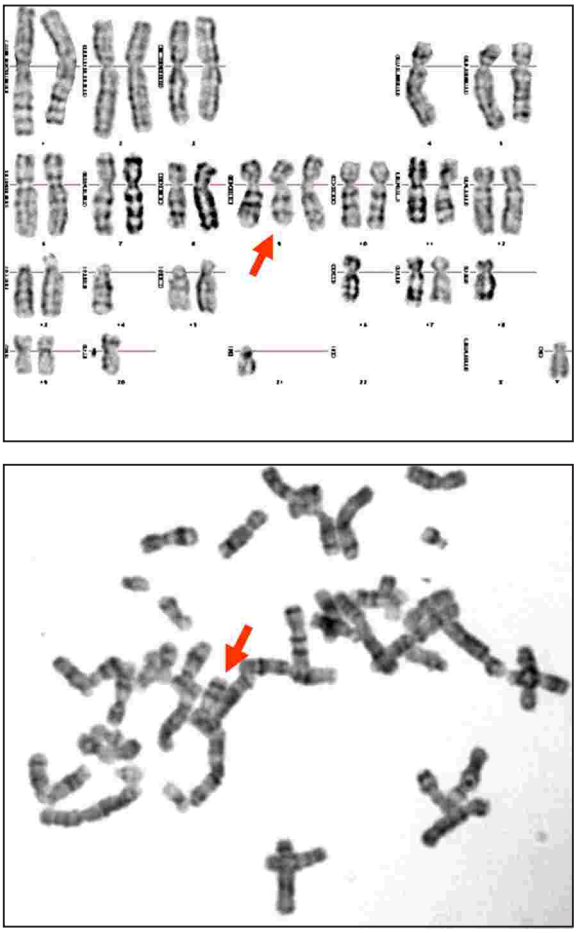

Figure 1: *Karyotype and metaphase images of case. Arrow marks indicate chromosome 21 translocated onto extra partial chromosome 9.*

Corpus callosum, lateral ventricule 12.1 mm, nasal bone hypoplazia (3.5mm), micrognathia and small inlet VSD in fetal echocardiography was identified in fecal USG. While in FISH analysis, anuploidy was not observed in chromosomes 13, 18, 21, 22, X and Y, three signals in each of centromer of chromosome 9 and 9p21 locus was observed and it was identified that

one of the chromosome 21 was translocated in metaphase and it was concluded that partial trisomy 9 (9pter_q22) existed. It was identified to be in Karyotype 46, XY, +der(9) t(9;21)(q22;q10),-21 pattern (Figure. 2). Since normal karyotype characteristics were observed in the mother and father, this variation in the fetus was assessed to be de-novo and detailed genetic consultation was given to the family. The pregnancy was terminated and agenesis of corpus callosum and inlet VSD observed in fetal USG was verified in the autopsy that followed the termination.

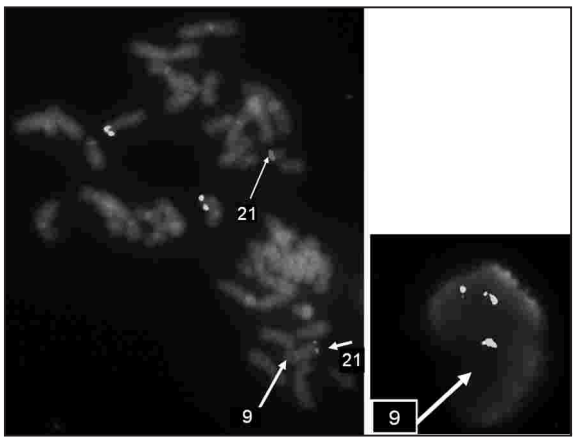

Figure 2: *FISH images of metaphase and interphase using t (12; 21) and Cep9/9p21 probes of the case. Red signals of chromosome 21 and green signals of chromosome 12 show in Figure 2A. Red signals of chromosome 9p21 and green signals of centromere of chromosome 9 show in Figure 2B.*

DISCUSSION

While the severity of clinical symptoms observed in Trisomy 9p syndrome is related to the size of the material that is tripled, mental retardation is observed in almost all patients. Partial trisomy 9pter->p21 is correlated to mild craniofacial characteristics and rarely with defects in skeletal system and internal organs. While Partial trisomy 9pter->p11 is related to typical craniofacial characteristics, Partial trisomy 9pter->q11-13 is related to defects of skeletal system and cardiac defects together with the typical craniofacial characteristics. Partial trisomy 9pter->q22-32 is related to typical craniofacial characteristics, intrauterin growth-development retardation, cleft lip-palate, micrognathia, cardiac anomalies and congenital hip dislocations. If the trisomic part is larger than 9pter->q31 or 32, clinical symptoms generally resemble trisomy 9 mosaic syndrome rather than the trisomy 9p syndrome[1]. In cases published up to this date, it was reported that central nervous system malformations can be observed in partial trisomy of chromosome 9. Smart et al. has reported enlargened ventricules of high level in an infant with Partial trisomy 9 (pter->q22.1)[5]. Chen and Shih have reported existence of enlarged cysterna magna and bilateral ventriculomegaly in a fetus with Partial trisomy 9 (pter->q22)[6] and von Kaisenberg et al. has reported Dandy-Walker malformation and cerebellar vermis hypoplazia in a fetus with Partial trisomy 9 (pter->q22.2)[7]. Chen et al. has shown the existence of corpus callosum dysgenesis, bilateral subependimal cysts and ventriculomegaly in a case with Partial trisomy 9 (9pter->q22.3)[8]. In the case presented here with it was shown that inlet VSD existed together with agenesis of corpus callosum in Partial trisomy 9pter->q22 with t(9;21)(q22;q10) translocation.

Partial trisomy 9 may develop as a result of parental reciprocal translocation or de-novo aberrations. In our case the detected derivative chromosomes that resembles partial trisomy 9 are rearrangement types that occur very rarely and such anomaly types are hard to find in the literature. In a case reported by Özer et al, 46,XY,-7,der(7)t(7;9)(q36;p12) pat. Karyotype has been determined and this case has been detected to have mental and motor retardation, microcephaly, bilateral undescended testicles and multiple minor malformations[4]. On the other hand our case is of 46,XY, -21, +der(9) t(9;21)(q22;q10) karyotype with a de-novo translocation that has occurred between 9 and 21 chromosomes. In terms of partial trisomy 9, our case covers the pter->q22.2 section of the chromosome. Since it has been terminated, only USG findings exist and the mental and motor symptoms could not be examined.

In conclusion, a cytogenetic prenatal diagnosis to be conducted in pregnant women with ultrasonographic anomalies that also include central nervous system malformations or with abnormal maternal serum markers is important for detection of unexpected chromosomal anomalies. To the extent of our knowledge our case is the first de-novo translocation case where the partial 9pter->q22 trisomy is observed together with chromosome 21 and will contribute to the literature as a phenotypic review of chromosomal anomaly and prenatal genetic study.

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