Case
Report

Prenatal Diagnosis of Trisomy 8 Mosaicism: A Case Report

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In this report we present a case of partial trisomy 8 referred to our clinic initially due to ultrasonographic finding of lateral ventricular dilatation. The detailed ultrasound scan at 26 weeks' gestation demonstrated agenesis of corpus callosum and bilateral hidronephrosis in fetus. Later amniocentesis and fetal blood sampling were performed. The case of mosaicisim for partial trisomy 8 was detected in cultured amniotic fluid cells. This karyotypic anomaly was subsequently confirmed by fetal blood sampling as well.

Key Words: Trisomy 8 mosaicism, Prenatal diagnosis, Ultrasound findings

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Introduction

Trisomy 8 is a very rare chromosomal abnormality that consists of complete and mosaic forms. Homogeneous and complete trisomy is extremely rare (estimated 0.1% of recognized pregnancies) and lethal disorder. In liveborns, trisomy 8 is almost always associated with mosaicism.[1] The frequency of mosaic trisomy is about 1:30000 in newborn children.[2] Since the level of mosaicism is not related with the clinical severity, the prenatal detection of trisomy 8 mosaicism can lead to genetic counseling problems.[3] When counseling these patients many issues remain unresolved such as the predictive value of karyotyping with respect to phenotype.[4] Acquired or constitutional chromosome 8 trisomy is often associated with myelodysplasia and acute monoblastic leukemia; however, it is not currently known that at which level the trisomy induces carcinogenesis.[5,6]

Case Report

A 20-year-old, gravida 1, para 0 woman was referred to our clinic at 26 weeks' gestation because of lateral ventricular dilatation. The pregnancy was properly dated and her medical, obstetric and social histories were unremarkable except that her husband was first degree relative.

Upon sonography, the fetus was 26 weeks' size. Targetted sonographic examinations demonstrated multiple abnormal findings. The width of the lateral ventricle at atrium measured was 13 mm. The frontal horn was not visualized. The cavum septum pellicidum was absent. Absence of corpus callosum was clearly demonstrated by visualization of the falx cerebri that came in close contact with the upwardly displaced the third ventricle. Axial view of the head demonstrated a striking enlargement of the atria and wide separation of the bodies of lateral ventricles (tear drop sign) (Figure 1). There were dilatations of right and left renal pelvises, 13, 4 mm and 17, 9 mm respectively. No other structural abnormality could have been visualized sonographically. The placenta was located anteriorly, and amniotic fluid volume was normal.

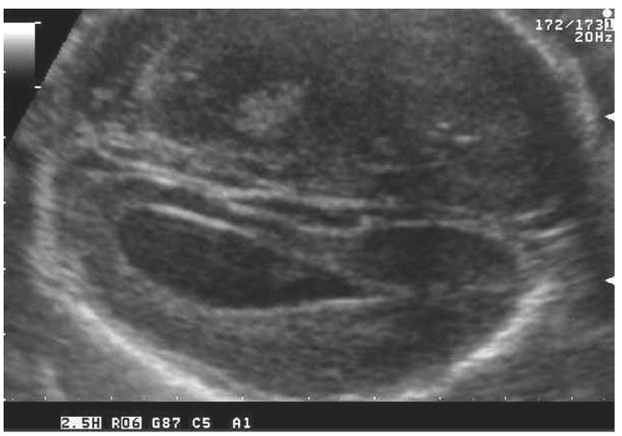

Figure 1: Axial view of the head demonstrating a striking enlargement of the atria and wide separation of the bodies of lateral ventricles (Tear Drop Sign). This is agenesis of the corpus callosum

The patient was informed that these findings were abnormal and were associated with an increased risk for chromosomal abnormalities. Amniocentesis and cordocentesis were performed simultaneously under ultrasound guidance according to standard techniques. The result of cytogenetic analysis of

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cultured amniotic cells revealed trisomy 8 mosaicism (47, XY+ 8/ 46, XY) (Figure 2). Genetic counseling was recommended to the parents. After counseling, they decided to terminate the pregnancy owing to uncertain neurodevelopmental prognosis.

Therapeutic termination of pregnancy was performed. In postmortem examination, there were flexion contractures of the fingers, clinodactyly, camptodactyly, broad bulbous nose, microphtalmia, pectus excavatum, short neck (Figure 3) Autopsy was refused by the parents. So specimen for karyotyping from the fetal and the placental tissues could not have been obtained.

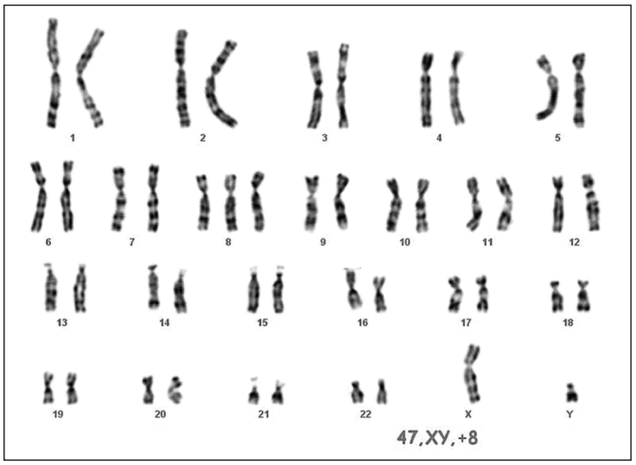

Figure 2: Karyotype showing partial trisomy 8

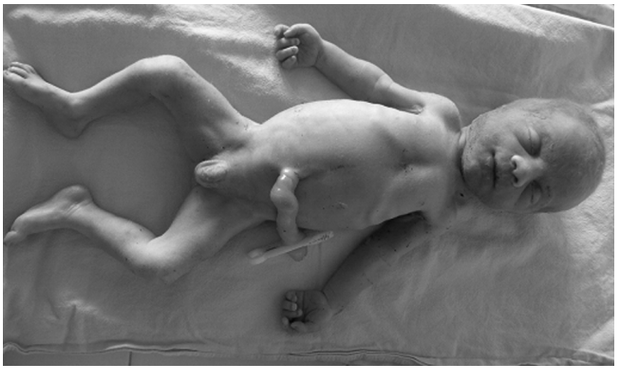

Figure 3: Gross appearance of the stillborn neonate. Note that broad bulbous nose, pectus excavatum, limbs anomalies (flexion contractures of the fingers, clinodactyly, camptodactyly)

Discussion

Chromosomal nondisjunction is one of the remaining unanswered questions of human genetics. As about 50 % of spontaneous abortions are chromosomally abnormal, chromosomal aneuploidy has large individual and socioeconomic consequences.[1,5] Our main knowledge about chromosomal nondisjunction in human comes from the studies in trisomy 21. In trisomy 8, very little is known about the origin of additional chromosome as very few cases have been studied so far. In most of the spontaneous abortion of trisomy 8, errors in maternal meiosis are the main reason.[2] However, post-zygotic (mitotic) nondisjuction error in a diploid conceptus followed by non-random distribution of aneuploid cells between the different compartments is the most likely mechanism of trisomy 8 in the live-born population. When mosaicism is confined to chorionic villi, extra-embryonic tissues have been chromosomally abnormal while the fetal tissues may have a normal karyotype. Within placenta, the proportion of aneuploid cells can be homogenous, however, may vary in studied fetal tissues (bone, skin or muscle).[7] The majority of trisomy 8 mosaicisms have been detected by amniocentesis or chorion villus sampling.[8,9] Although, in general, amniocentesis results are considered to reflect the chromosomal constitution of the fetus accurately, amniotic fluid cell culture is not the best way to reveal trisomy 8 mosaicism so follow up investigations in fetal blood cells are recommended.[10]

The phenotypic variability of trisomy 8 is very high, ranging from minimal effects to severe malformations.[11] Common distinguishing features of trisomy 8 mosaicism include mild to moderate mental retardation, a long face with myopathic appearance, large and lowest ears, high prominent forehead, urogenital anomalies like criptorchidism, hydronephrosis, corpus callosum agenesis, various types of congenital cardiovascular anomalies, skeletal system anomalies like clinodactyly, camptodactyly, absent patella, vertebral defects,ocular and gastrointestinal anomalies.[11] Our case was prenatally diagnosed. Thus, some of these abnormalities would not have been found at 26 weeks' of gestation. However, in our case, callosum agenenesis, bilateral hydronephrosis were reported with ultrasonography. There were clinodactyly, camptodactyly, micropthalmia, flexion contractures of the fingers, broad bulbous nose, pectus excavatum, short neck.

In lıterature, Campbell et al. reported a case of mosaic trisomy 8 diagnosed prenatally at 12 weeks' of gestation in a fetus with normal nuchal translucency thickness and reversed end-diastolic ductus venosus flow.[12] The second case of trisomy 8 mosaicism was also diagnosed prenatally by Jay et al. In this case, the fetus was 22 weeks' of gestation.[7] Postnatal diagnosis of this syndrome may be difficult because of the age-related disappearance of the trisomic cell line in lymphocytes. Pfeiffer et al reported a case of a 16-year-old girl referred for cytogenetic studies due to a short neck, lateralized mammillae, suggesting spastic hemiparesis and mental retardation. She had trisomy 8 mosaicism.[13] Other phenotyping features were broad nose, large ears, dysmorphic face, and skeletal abnormalities like broad clavicles, limited joint mobility, broad metacarpals and phalanges.[13]

In conclusion, trisomy 8 mosaicism is associated with clin-

ically defined syndrome of variable phenotype. Recognition of this chromosomal mosaicism may be difficult unless there are marked structural anomalies or ultrasonographic markers.

Prenatal Tespit Edilen Mozaik Trizomi 8: Olgu Sunumu

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Bu vaka sunumunda, ultrason ile tespit edilen lateral ventrikül genişliği nedeniyle kliniğimize sevk edilen parsiyel trizomi 8 vakası sunulmuştur. 26'ıncı gebelik haftasında yapılan ayrıntılı ultrasonografi, fetusda korpus kallosum agenezisi ve bilateral hidronefroz göstermiştir. Ardından amniosentez ve fetal kan örneklemesi yapılmıştır. Amniotik sıvı kültüründen elde edilen hücrelerde trizomi 8 mozaizmi tespit edilmiştir. Bu karyotipik anormallik amniotik sıvı kültürünün ardından fetal kan örneğinde teyid edilmiştir.

Anahtar Kelimeler: Trizomi 8 mozaizmi, Prenatal tanı, Ultrason bulguları

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