Case Report

Title: Sonographic Findings in Partial type of Trisomy 18: A case report

Running Title: Delay ossification of calvarium bone in trisomy 18

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Abstract:

Trisomy 18 (Edwards Syndrome) is the second highest trisomy among live born fetuses, with poor prognosis. Its incidence is estimated between 1 in 4000-16000 live birth. Most of the chromosomal abnormalities in fetuses are detected by prenatal ultrasound findings in the first
and second trimesters. In this case report we present a partial type of trisomy 18 which has occurred through de novo unbalanced translocation of chromosomes 18 and 21. The ultrasound features enabling the early detection of trisomy 18 include a delayed ossification of calvarium combined with early onset of fetal growth restriction (FGR) and the absence of nasal bone through performing triple test followed by amniocentesis. Finally the parents decided to terminate the pregnancy.

Keywords: Trisomy 18, Ultrasound Findings

INTRODUCTION

After Down Syndrome, Edward syndrome (trisomy 18) is the second most common trisomy among live born fetuses (1,2). Clinicians strive to detect any prenatal chromosomal abnormalities early on in the pregnancy. This is especially true for conditions involving lethal trisomies, such as trisomy 18, in which prenatal care may totally change after diagnosis. It is a fatal disease with very poor prognosis. Ninety percent of affected new born die during the
first year of life and the remaining 10% suffer from severe mental retardation. Edwards syndrome is associated with profound neurological damages and mental deficiency in neonates, who have an average life expectancy of one week (3,4). The only definitive method to make a diagnosis of trisomy 18 is through ultrasound imaging particularly during the first and second trimesters, triple tests and invasive testing with amniocentesis or chorionic villous sampling (1,5,6). Amniocentesis has been associated with an increased risk of miscarriage, therefore it is usually offered for high risk patients.

For the detection of trisomy 18 ultrasound findings in the first and second trimester for trisomy 18 seems to be more effective than biochemical screening (1, 3, 5). In order to achieve a more accurate diagnosis of trisomy 18 we must combine sonography, triple test and amniocentesis (1,3,5). Sensitivity of ultrasound screening for trisomy 18 was reported 70% (7), while a multiple marker test (Alpha fetoprotein, HCG, Unconjugated estriol) was abnormal only in 43% of cases with trisomy 18 (8).

Case Report

A 26 year old woman, gravid 1; para 0; abortion 1 with 2 years primary infertility was admitted to our infertility clinic at the Royan institute. She had an 8 weeks missed abortion followed by dilatation and curettage (D&C) in 2006. Physical history included severe polycystic ovarian syndrome (PCO), hypothyroidism, diabetes mellitus and obesity. The couple’s karyotypes were normal. Semen analysis obtained from the husband showed low Volume (0.2cc), low motility (8%) and abnormal morphology (92%), he also suffered from severe oligospermia. After ICSI, a normal live fetus was revealed by initial transvaginal
sonography at 7.5 weeks. In the 12.5<sup>th</sup> week of gestation, ultrasonography determined normal NT measurement with early onset of FGR which was compatible to 11<sup>th</sup> weeks according to CRL; in addition the nasal bone and some part of calvarium were absent (figure1 and figure2). At 14 weeks, the parietal part of calvarium was formed and nasal bone was seen partially. At this time FGR became more severe and differences between biometric measurements (BPD (biparietal diameter), FL (femor length)) and real gestational age had increased (figure3). Therefore the parents were carried out a triple test which was followed by amniocentesis. The result of the triple test indicated a high risk of trisomy 18 (1/99), which was confirmed by amniocentesis. The karyotype 46xy der(21) t(18:21) (q10:q10) was found in cultured amniotic cells which was compatible to a male fetus with trisomy of Long arm of chromosome 18. At that time the parents decided to terminate the pregnancy at 18 weeks of gestation.

**Discussion**

There are two type of trisomy18 including partial and complete, in 80% of cases, there is complete trisomy and a partial trisomy can only be detected in 20% of cases; a consequence of various abnormalities of chromosome 18 such as duplication, additional isochromosomes of short or long arm and translocations involving other autosomal chromosomes (9,10). Since in this case the parents’ karyotype was normal, we assume this partial trisomy 18q to be due to a de novo unbalanced translocation of chromosomes 18 and 21, of which only a few cases have been reported.

Approximately three-quarters of pregnancies when the fetus is diagnosed with trisomy 18 result in a miscarriage or stillbirth between the 12th week of gestation and term (11). Postnatally, the median survival time is 3-6 days. Less than 50% of infants will survive for a
week, and only about 5-10% will survive for a year (12,13). Long term survival in trisomy 18 has been reported, but this occurs primarily in the context of mosaicism (14, 15).

Recently, Koide et al have published the in utero gene expression profile of second trimester fetuses affected with trisomy 18. According to the results, 251 genes showed significant differential expression in cases with trisomy 18 compared to the controls, but only 7 genes out of 251 were located on chromosome 18 (16).

Fetal sonographic findings which have been relevant to trisomy 18 include congenital heart disease, mainly ventricular septal defect (VSD) (17), choroid plexus cysts, gastrointestinal disease such as diaphragmatic hernia and imperforated anus, microcephaly, microphthalmia, omphalocele, kidney abnormalities, early-onset of fetal growth restriction (FGR) and pyelectasis > 4mm (17,18). Skeletal dysmorphologic signs which have so far been reported include limb abnormalities, polydactyl, absent fibula, radial aplasia, clenched hands, rocker bottom feet which mostly are seen in partial types. The findings of prospective studies demonstrate that there is an absence of the nasal bone in almost 50% of the fetuses with trisomy18 at 11-13 weeks (18-20). In this case we observed a delayed ossification of calvarium and the absence of nasal bone together with partial trisomy 18q. Such a case has not been reported before and we present it for the first time within partial trisomy 18q. Despite all of the skeletal sonographic findings in this case only the two mentioned features were detected.

Most fetuses with Trisomy 18 have an abnormal ultrasound results. This doesn’t mean that all anomalies can be identified through an ultrasound but at least one anomaly can be seen in the majority of cases (1).
With the improvement in availability of first trimester ultrasound, enhanced image resolution and better sonographic techniques, many of the anomalies related to trisomy 18 can be systematically looked for and detected in the early stages of pregnancy.

More studies need to be done in order to know whether calvarium bone screening in early sonography can be an important characteristic in the diagnosis of trisomy 18.

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Fig 1. First trimester transvaginal ultrasonography in a 26 year old pregnant lady, in 12.5\textsuperscript{th} weeks which is compatible with 11-11.5 weeks based on CRL measurement. Most part of calvarium bone is not seen. Nasal bone can’t be detected too.
Fig2. First trimester sonography in a 26 year old pregnant lady, in 12.5th weeks. It can better seen undetectable calvarial bone, which confirms previous diagnosis.
Fig3. Fetal growth restriction and partial calvarium bone can be detected in 14th weeks transabdominal sonography in a 26 year old pregnant lady. Biometric measurement is compatible with 13-13.5 weeks.

**Abbreviation:**

FGR: Fetal growth restriction

HSG: Hysterosalpingography
Reference


