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CASE REPORT

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A Case-Report of Trisomy 12 Mosaicism in Amniotic Fluid

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INTRODUCTION

Trisomy 12 mosaicism has been reported in several live born individuals. It is an additional chromosome 12 that occurs in at least 2 or more cells/colonies in at least 2 independent cell cultures. Trisomy 12 mosaicism in amniotic fluid cultures is extremely rare. In a U.S. survey of chromosomal mosaicism and pseudomosaicism in prenatal diagnosis, no cases of true Trisomy 12 mosaicism were found among 62,279 amniocentesis. However, it has been a rather frequent chromosomal aneuploidy in chorionic villi samples specifically confined to the placenta. There have been 9 cases of Trisomy 12 mosaicism detected in amniotic fluid (1).

From cases described in the literature, four infants with Trisomy 12 mosaicism were carried to term, two infants died with severe anomalies shortly after birth. Of the infants that died after birth, neither infant showed evidence of Trisomy 12 mosaicism in cord blood. In one case, the Trisomy 12 mosaicism was detected in the placenta and shin fibroblasts. In the other case, 62% of the cell colonies from amniotic fluid had Trisomy 12 mosaicism. The infant had multiple anomalies such as heart defects, cataracts, horseshoe kidney and vertebral anomalies. Of the two infants with Trisomy 12 mosaicism who survived, both were phenotypically normal, but one later showed developmental delay after 15 months. The other five cases were therapeutically aborted and had no apparent anatomic anomalies. The failure to find Trisomy 12 mosaicism in peripheral blood of prenatal cases is particularly noteworthy (1).

Two cases of Trisomy 12 mosaicism have been reported in adults. One involved an infertile 31 year old male, the other a 36 year old female with mental retardation and multiple anomalies. (1)

Trisomy 12 mosaicism occurs more in females, with a male to female ratio of 3:20. (2). Some of the congenital anomalies that have been found in individuals with Trisomy 12 mosaicism include heart defects, facial dysmorphism, and digit anomalies (2). One case resulted in fetal demise with intrauterine growth restriction (IUGR) and multiple anomalies including short colon, liver anomalies, congestive heart failure, and large ovaries (3).

CASE PRESENTATION

The patient is a 28 year old gravida 2, para 1 who was referred to our clinic for an abnormal MSAFP, showing an increased risk of Down's syndrome 1:160. She was seen in the Prenatal Diagnosis Clinic where a genetic ultrasound and amniocentesis were performed. She had no significant past medical, surgical or family history. Her past obstetrical history included a normal vaginal delivery, uncomplicated, 7.2 lbs. The ultrasound findings were a 23 weeks fetus, breech presentation, three vessel cord, 635 grams, normal amniotic fluid and normal anatomy. The amniocentesis revealed a low level mosaicism with Trisomy 12. Three of forty-two cells (7.5%) of the metaphase spreads showed Trisomy 12, while 39 of 42 cells evaluated showed a normal 46, XX karyotype. From the second trypsinized culture, flourescent in-situ hybridization (FISH) studies were performed using CEP12 DNA probe. Nine of 500 (1.8%) of the interphase cells revealed three signal patterns for chromosome 12. The patient underwent genetic counseling. She understood that due to the rarity of this particular trisomy, outcomes have varied from normal phenotype without developmental delays to multiple congenital anomalies and severe mental retardation. The patient decided to continue with the pregnancy.

The patient had an unremarkable prenatal course. At 35 weeks, a repeat ultrasound was performed showing an estimated fetal weight of 2966 grams (90 percentile growth) and normal amniotic fluid. At 37 weeks, she presented to the clinic with spontaneous rupture of membranes. She was having regular uterine contractions with a cervical dilation of 3 cm. The patient was admitted to labor and deliveries were she had a vaginal delivery of a live born female infant. The neonatal weight was 2890 grams; Apgars 8 and 9. The infant had a 3 vessel cord.

The neonate underwent an echocardiogram which revealed an extremely small patent ductus arteriosus with left to right flow, and patent foramen ovale. The newborn screening tests and hearing tests were all normal. No other neonatal anomalies were detected.

Chromosomal studies performed on the neonatal peripheral blood revealed five cells with normal 46, XX karyotype. There was normal signal pattern for chromosomes 12 and 21; however the chromosome morphology and banding were poor with low resolution. A low level mosaicism could not be implied or ruled out by this study. Chromosomal analysis will be repeated in the future using tissue samples.

DISCUSSION

Prenatal diagnosis of Trisomy 12 mosaicism by amniotic fluid is rare (2). Trisomy 12 mosaicism is also rarely detected in cord blood or peripheral blood of the affected individuals. (3) The majority of these cases are identified through chorionic villi sam-

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pling, or tissue samples. Trisomy 12 mosaicism is often identified and limited to placental tissue. Trisomy 12 mosaicism can result in outcomes ranging from normal to fetal demise, congenital anomalies, neonatal death or mental retardation. Many of the fetuses with Trisomy 12 mosaicism have normal outcomes. There is very little known about the long term prognosis which poses great difficulty for genetic counseling (3). There is little known about the natural history and life expectancy of individuals with Trisomy 12 mosaicism (4).

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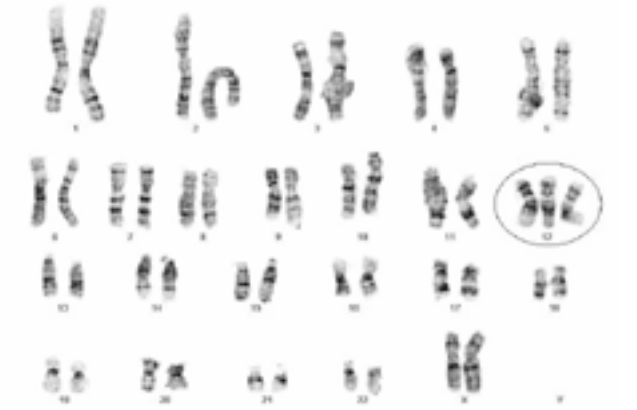
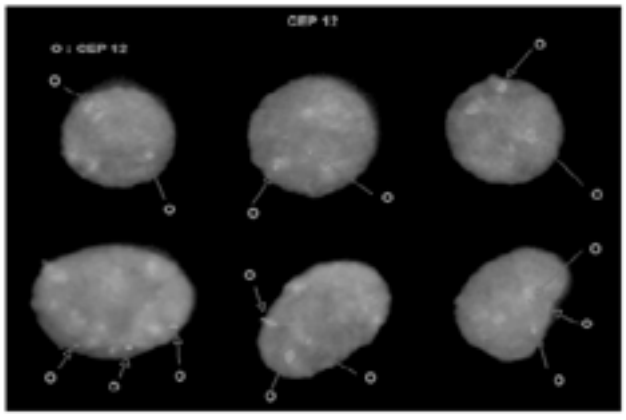


Figure 1. Abnormal karyotype from the amniotic fluid, circle indicates Trisomy 12, 47, XX, +12.



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