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Clinical manifestations and the prenatal diagnosis of trisomy 7 mosaicism: Two case reports

Prenatal diagnosis of trisomy 7 mosaicism

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Abstract

BACKGROUND

The clinical manifestations of trisomy 7 mosaicism are diverse and nonspecific, so prenatal diagnosis is very difficult.

CASE SUMMARY

Two pregnant women with abnormal prenatal screening results were included. One was a 22-year-old woman (G1P0). At 31st week of gestation, ultrasound revealed that the posterior horn of the left lateral ventricle was 10 mm and the right renal pelvis had a separation of 7 mm. The other pregnant woman was 33 years old (G2P1L1A0), and her fetus was found to have a cardiac malformation at the 24th week of gestation. Copy number variation sequencing (CNV-seq), whole-exome sequencing (WES) and karyotype analysis were carried out after amniocentesis, and both fetuses were diagnosed with trisomy 7 mosaicism. After parental counseling, one woman continued the pregnancy, and the other woman terminated the pregnancy.

CONCLUSION

In trisomy 7 mosaicism, the low proportion of trisomy does not lead to abortion, but can result in abnormal fetal development, which can be detected *via* ultrasound. Therefore, clinicians need to pay more attention to various aspects of fetal growth and development, combining with imaging, cellular, molecular genetics and other methods to perform comprehensive evaluations of fetuses to provide more reliable genetic counseling for pregnant women.

Key Words: Trisomy 7 mosaicism; Copy number variation sequencing; Whole-exome sequencing; Karyotype analysis; Prenatal diagnosis; Case report

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Core Tip: Herein, two fetuses were prenatally diagnosed according to abnormal ultrasound findings, including a widened posterior horn of the left lateral ventricle, renal dysplasia and a cardiac malformation. Copy number variation sequencing (CNV-seq), whole-exome sequencing (WES) and karyotype analysis were carried out, and both fetuses were confirmed to have trisomy 7 mosaicism.

INTRODUCTION

Non-mosaic trisomy 7 usually leads to spontaneous abortion in early pregnancy. As a result, the mosaic form of trisomy 7, which is detected by noninvasive prenatal screening (NIPS) or chorionic villus sampling, is more likely to be present, either confined placental mosaicism or fetal mosaicism[1]. Trisomy 7 is the most frequently observed type of rare autosomal trisomy in NIPS[1]. Because it involves imprinting genes, trisomy 7 may lead to uniparental diploidy (UPD) through trisomic rescue. Therefore, it is crucial to provide correct and appropriate prenatal diagnosis and genetic counseling to pregnant women. However, the prenatal diagnosis of trisomy 7 mosaicism is difficult because of its variable and nonspecific clinical features[2]. Here,

we report the ultrasound manifestations and prenatal diagnosis of two cases with trisomy 7 mosaicism.

CASE PRESENTATION

Chief complaints

Two pregnant women with abnormal ultrasound results presented to our hospital for prenatal diagnosis.

History of present illness

The prenatal screening results of both pregnant women revealed low risk. However, their ultrasound examination results suggested abnormal fetal development.

History of past illness

Both pregnant women had no history of past illness.

Personal and family history

Neither the pregnant women nor their husbands had a significant personal or family history.

Physical examination

The physical examinations of the two pregnant women did not reveal any abnormalities.

Laboratory examinations

Copy number variation sequencing (CNV-seq), whole-exome sequencing (WES) and karyotype analysis were carried out after amniocentesis. No pathogenic mutations associated with the clinical presentation were detected by WES. The CNV-seq results revealed that the first fetus had trisomy 7 mosaicism with approximately 40% mosaicism, while the karyotype analysis revealed 47,XN,+7[45]/46,XN[34] (Figure 1).

The results for the second fetus were similar to those for the first fetus. CNV-seq revealed 65% trisomy 7, and karyotype analysis revealed 47,XN,+7[65]/46,XN[36](Figure 2).

Imaging examinations

In the first pregnant woman, at the 16th week of gestation, ultrasound showed that the fetus had a single umbilical artery and a choroid plexus cyst; at the 21st week of gestation, ultrasound showed an echogenic bowel and mild separation of bilateral renal pelvis; and at the 31st week of gestation, ultrasound showed that the posterior horn of left lateral ventricle was 10 mm and the right renal pelvis had a separation of 7 mm. In the second pregnant woman, at the 24th week of gestation, ultrasound revealed a fetal cardiac malformation, including severe aortic stenosis, mild mitral stenosis with severe regurgitation, left ventricular cord sclerosis and a small foramen ovale.

FINAL DIAGNOSIS

According to these findings, both fetuses were diagnosed with trisomy 7 mosaicism.

TREATMENT

We did not provide treatment.

OUTCOME AND FOLLOW-UP

After parental counseling, the second pregnant woman terminated the pregnancy, and the other pregnant woman delivered a baby at the 39th week of gestation. The baby was followed up for 1 year after birth, at which point no obvious abnormalities were found.

DISCUSSION

Trisomy 7 usually leads to spontaneous abortion in early pregnancy, and trisomy 7 mosaicism is most commonly reported. Previous studies have shown that 15%-80% of trisomy 7 in the placenta will not lead to stillbirth or miscarriage, and the prognosis is

good if UPD or fetal chimerism is not involved[3,4]. Trisomy 7 mosaicism may be associated with Potter syndrome or renal dysplasia, cardiac abnormalities, prenatal and postnatal growth retardation, cleft lip and palate, recurrent ear infections, and epilepsy[5]. Consistent with the findings of previous reports, the two fetuses reported in this study exhibited a certain degree of renal dysplasia or a cardiac malformation due to trisomy 7 mosaicism.

A high proportion of trisomy 7 in the placenta or fetus may lead to intrauterine death[6,7]. The lower the proportion of trisomy is, the lower the effect on the fetus. Hsu LY *et al* summarized the outcomes of 8 fetuses prenatally diagnosed with trisomy 7 mosaicism. Among these fetuses, 7 had normal live births, 4 of whom were followed up for 4-54 months and were reported to be developmentally normal. In addition, trisomy 7 mosaicism was confirmed in the foreskin fibroblasts of 2 patients[7]. We found that the proportion of trisomy in the above 4 patients ranged from 5% to 48%. In this study, the first pregnant woman gave birth to a baby with trisomy 7 mosaicism (approximately 40%-45% mosaicism). Like in a previous study, we followed the baby for 1 year after birth and found no significant developmental abnormalities.

Human chromosome 7 is an imprinting chromosomes which contains several imprinted genes related to diseases. It has been confirmed that chromosome 7 is closely related to Silver-Russell syndrome (SRS). SRS is characterized by intrauterine growth restriction and postnatal developmental delay and is mostly caused by maternal UPD[2]. The clinical phenotypes of trisomy 7 mosaicism, which have been reported thus far, are quite different. Therefore, for prenatally diagnosed cases, it is difficult to judge risk. The two trisomy 7 mosaicism cases reported in this paper had different prenatal ultrasound findings due to differences in trisomy proportions, resulting in differences in pregnancy outcomes. When conducting genetic counseling, clinicians should comprehensively evaluate fetuses and provide guidance according to specific conditions.

CONCLUSION

In trisomy 7 mosaicism, the low proportion of trisomy does not lead to abortion, but can result in abnormal fetal development, which can be detected *via* ultrasound. Therefore, clinicians need to pay more attention to various aspects of fetal growth and development, combining with imaging, cellular, molecular genetics and other methods to perform comprehensive evaluations of fetuses to provide more reliable genetic counseling for pregnant women.

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