HJOG An Obstetrics and Gynecology International Journal

Case Report

Trisomy 16 and Tracheo-oesophageal fistula

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Abstract

We report a case of a 40-year-old woman, diagnosed in the first trimester screening with confined placental mosaicism. The result of chorionic villus sampling was trisomy 16 and sequent amniocentesis revealed a normal male karyotype (46XY). Further examinations during pregnancy showed intrauterine growth restriction in the absence of apparent anatomic anomalies. Caesarean section was performed due to fetal distress at the 32nd gestational week. The newborn presented with respiratory distress. Finally, the newborn was diagnosed with a trachea-oesophageal fistula (TOF).

Keywords: τracheo-oesophageal fistula (TOF); intrauterine growth restriction (IUGR); trisomy 16

Tracheo-oesophageal fistula (TOF) is a severe congenital anomaly of unknown etiology. Several chromosomal anomalies have been associated with TOF, but until today none of these has been identified as a single etiological factor.

Trisomy 16 is the most common cause of first-trimester miscarriage, occurring in 1-2% of all pregnancies[1]. Different types of numerical trisomy 16 exist. Full trisomy 16 is not compatible with life. Mosaic trisomy 16 (MT16) is extremely rare and is characterized by the presence of an extra chromosome 16 in some, but not all, of the cells of the affected individual. The clinical presentation of MT16 varies quite a lot, but the most common characteristics include intrauterine growth restriction (IUGR) and congenital heart defects. When MT16 is confined to the Placenta (CPM), constitute a distinct condition and the extra chromosome 16 is present only in the placental tissues and not in the fetus. In the uniparental disomy of chromosome 16 (UPD) the placental trisomy is complicated by fetal chromosomes that appear to be normal but both copies originate from one of the two parents. This is mostly associated with mosaic trisomy 16 and has been shown to be of importance because of genomic imprinting[2,3].

Case report

A 40-year-old Caucasian female, gravida 2, with uncomplicated medical history, received regular antenatal care in our Department. No history of drug abuse was documented. Due to her advanced reproductive age and increased risk for chromosomal abnormalities she was recommended to undergo cho-

rionic villus sampling (CVS) in the 11^{+4th} gestational week. The karyotype was TM16 in chorionic villi (47 XY, +16). She was advised to proceed to amniocentesis at 17^{+5} gestational week, in order to document if the trisomy 16 was confined to the placenta only. The amniocentesis result was a normal male karyotype - (46XY). The diagnosis was confined placental mosaicism (CPM). The obstetric ultrasound at the 21^{st} gestational week showed a divergence of about eight days of the intrauterine growth in relation to the gestational age and an echogenic bowel. The next ultrasound examination showed an intrauterine growth restriction (IUGR) under the 1^{st} percentile. No major malformations were detected. Doppler assessment of the uterine, umbilical and middle cerebral arteries was normal. Also, the mother and the fetus were tested for uniparental disomy in order to investigate if the resulting TM16 had a maternal origin. The result was negative. Caesarean section was performed due to fetal distress at the 32^{nd} gestational week, which was documented by a pathological cardiotocograph and a lack of end diastolic flow on the Doppler ultrasound. A male 1100gr with normal phenotype was born. The newborn presented respiratory distress after birth and was hospitalized at the neonatal intensive care unit (NICU). The cause of the respiratory distress was tracheoesophageal fistula.

Discussion

Trisomy 16 is the most common cause of miscarriage during the first trimester of pregnancy.

It can be diagnosed by performing chromosomal testing after miscarriage. The trisomy can be diagnosed during pregnancy through CVS or amniocentesis[1]. When trisomy 16 is found in chorionic villus sampling (CVS) or amniocentesis in a pregnancy with a normal fetal development, it is almost always mosaic.

However, serial ultrasounds are recommended[3] to determine if the fetus has congenital abnormalities. Trisomy in the chorionic villous stroma, and amniotic mesenchyme is associated with intrauterine growth restriction in contrast with trisomy in the cytotrophoblasts and amniotic fluid that appears to have a significant risk for fetal malformations. Fetal malformations associated with trisomy 16 mosaicism in live-births include: Heart defects, hypospadias, two vessel umbilical cord, clinodactyly, pulmonary hypoplasia and oligohydramnios. It has been also associated with maternal hypertension, increased levels of βHCG and aFP, fetal or neonatal death and increased risk for pre-term delivery (<37 weeks)[3,4,7,8,9].

In CPM (confined placental mosaicism) there is a discrepancy between the fetal karyotype and the placenta. The mosaicism is strictly limited within the placenta[5]. It seems that maternal uniparental disomy (UPD) 16 has a strong influence on fetal development and fetal anomalies[6]. CPM has been associated also with preeclampsia and pregnant women under this diagnosis should be checked for hypertension[10].

Although there are reports of two cases of trisomy in the E group of chromosomes (chromosomes 16-18) complicated with tracheoesophageal fistula, these were cases of trisomy 18[11,12,13]. No cases of trisomy 16 and T-E fistula have been documented until now.

Our case report implies an association since trisomy 16 is a chromosomal abnormality in the group E of chromosomes. In order to identify a case with CPM, chorionic villus sampling (CVS) with simultaneous amniocentesis is necessary. The amniocentesis contributes in comparison of the normal ploidy of the fetus with the placental mosaic cells. Serial ultrasounds are necessary to determine the proper fetal growth and early detection of congenital malformations, defects and pathological conditions which affect fetal phenotype. A close pregnancy monitoring will bear us to intervene in case of any fetal distress.

Conclusion

The appearance of the tracheoesophageal fistula is possibly associated with trisomy 16 but more reports are necessary. Since CPM 16 is very rare, assessing the fetal development with serial ultrasounds, close monitoring of the pregnancy and reporting of these cases are necessary, so as to have

more definitive data that could help us with the management of these cases.

Conflict of interest

We declare that we have no conflict of interest.

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