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Short communication

Detection of confined placental trisomy 16 using non-invasive prenatal testing in a pregnancy associated with intrauterine growth restriction and normal karyotype

Dear Editors

Intrauterine growth restriction (IUGR) represents a major cause of perinatal morbidity and mortality. Various environmental and genetic etiologies have been associated with IUGR, including maternal and placental risk factors. Confined placental mosaicism (CPM) is a risk placental factor for IUGR and/or intrauterine fetal death [1]. In this study, we present the application of non-invasive prenatal testing (NIPT) in detecting CPM in a pregnancy associated with severe early-onset IUGR and normal karyotype.

A 34-year-old G2P1 patient was referred at 19 weeks for further evaluation because of early abnormal fetal growth. An initial dating scan at 8 weeks gave a gestational age consistent with that calculated by her last menstrual period. A second scan three weeks later gave a CRL of 46 mm with a NT of 1.3 mm. The combined first-trimester screening testing was negative. On this referral, a detailed ultrasound at 19 weeks showed fetal biometries (BPD 41 mm, HC 149 mm, AC 121 mm, FL 25 mm) around the 5th percentile, an enlarged placenta (45 mm), and mildly low amniotic fluid levels with single deepest pocket (SDP) of 2.8 cm. An early IUGR was suspected, and invasive genetic testing was suggested. Both routine karyotyping and chromosomal microarray (CMA) by amniocentesis showed no numerical or structural chromosomal abnormalities. A repeat scan at 21 weeks showed fetal biometry measurements at the third percentile (BPD 45 mm, HC 163 mm, AC 136 mm, FL 29 mm), with placentamegaly and decreased amniotic fluid volume (SDP of 2.4 cm). Further Doppler investigation showed bilateral early diastolic notching in both uterine arteries (Fig. 1A).

Considering a large placenta associated with IUGR and mild oligohydramnios but a normal fetal karyotype, CPM for placental aneuploidy was considered. Maternal plasma NIPT at 21 weeks (BGI Corp.) was offered, and showed a Z-score of 24.6 for chromosome 16 (Fig. 1B), indicating trisomy 16 CPM. The patient was counselled regarding the potentially poor prognosis of the affected pregnancy. Serial ultrasound examination every two weeks was recommended. At 24 weeks severe IUGR with anhydramnios was demonstrated. After another counselling, the parents requested termination of pregnancy. Post-mortem examination revealed a female fetus weighing 265 g without obvious physical malformations. The cord blood revealed a karyotype of 46,XX in 100/100 cultured lymphocytes. The placental tissues from different sampling sites all revealed a complete karyotype of 47,XX,+16 (Fig. 1C). Family study using the SNP-based CMA excluded the uniparental disomy (UPD) (16) in the fetus.

Trisomy 16 is the most common autosomal aneuploidy seen in early miscarriages [2]. A proportion of such conceptions regenerate a diploid embryo, either with or without UPD, thus leading to CPM with normal fetal karyotype [3]. In the majority of cases of CPM for trisomy 16, the fetus is structurally normal, although a variety of abnormalities have been reported both with and without evidence of UPD(16). Recent studies found that common complications of CPM pregnancies include gestational hypertension or preeclampsia, IUGR, congenital anomalies, preterm delivery, cesarean delivery, intrauterine fetal death or perinatal death, and neonatal intensive care unit (NICU) admission [4,5]. Therefore, a prenatally identified CPM pregnancy needs careful surveillance for both the mother and fetus. As evidenced by our case, CPM should be considered in a pregnancy with a karyotypically normal fetus but IUGR and an abnormal placenta. NIPT can be used to provide genetic information about the placenta. The CPM for trisomy 16 indicated by NIPT in our case had promoted us to reconsider the prognosis of the fetus and to arrange carefully monitoring the affected pregnancy. Our case gives evidence that NIPT can potentially be used as a predictor of placental health and disease, which may be helpful in clinical counselling and treatment.

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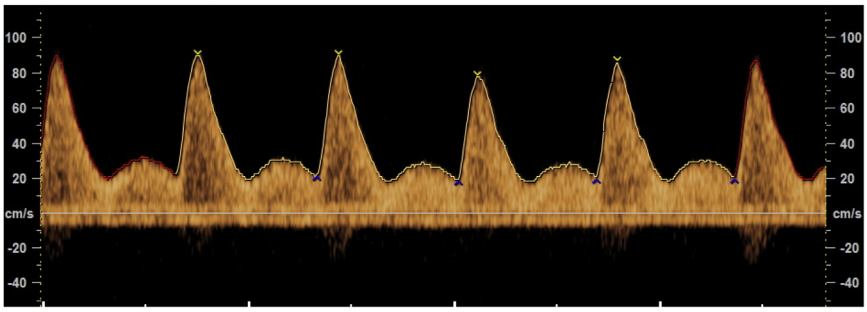
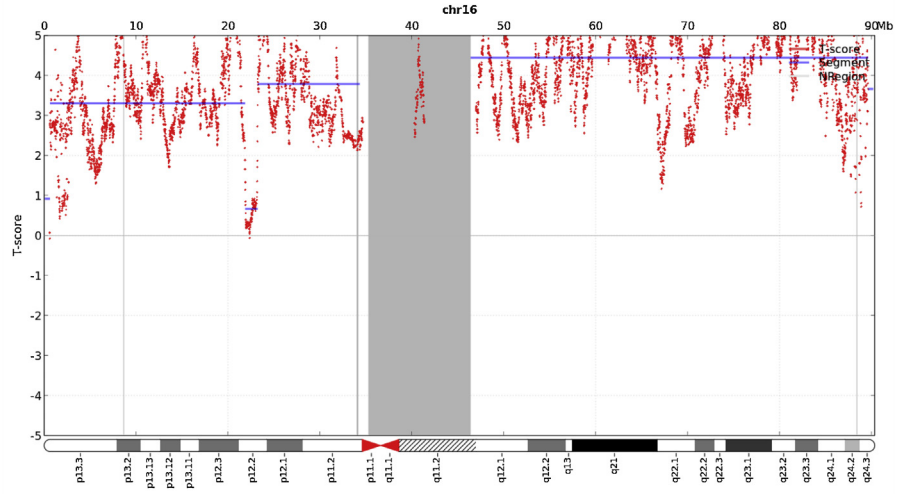


(A)



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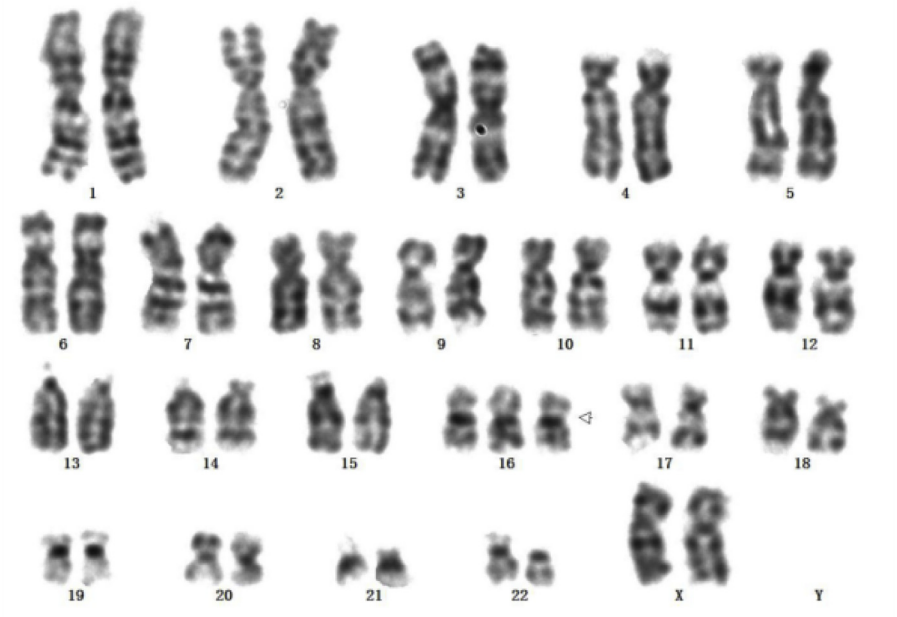

(C)

Fig. 1. Results of ultrasound, NTPT and placenta karyotyping of the pregnancy with CPM for trisomy 16. (A) Uterine artery waveform demonstrating raised PI with an early diastolic notch; (B) NIPT result showing duplication of chromosome 16; (C) The karyotype of the placental tissue.

Acknowledgements

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