Confined placental trisomy detection through cell-free DNA in the maternal circulation: Benefit for pregnancy management

TO THE EDITORS: We read with interest the recent article by di Renzo et al about expanding the indications for cell-free DNA (cfDNA) in the maternal circulation.[1] The authors concluded that because the clinical utility of expanding cell-free DNA testing to include microdeletions or rare autosomal trisomies has yet to be demonstrated, the current implementation of this testing beyond trisomy 21/18/13 is premature. We agree that counseling becomes more challenging when a positive result for rare autosomal trisomies with cfDNA testing is found in high risk-women who have no fetal anomalies other than a positive serum screening. We also agree that the positive predictive value for rare conditions will be low in routine clinical practice. However, in some specific situations, screening for rare autosomal trisomies using cfDNA might benefit pregnancy management.

In the last 3 years, we have had 20 cases of early-onset intrauterine growth restriction (IUGR) before 28 weeks of gestation. All pregnancies were excluded from being affected by fetal chromosomal abnormalities using routine cell culture for karyotyping and chromosomal microarray through amniocentesis. Because confined placental mosaicism (CPM) has been reported as a placental risk factor for IUGR, maternal cfDNA was used to assess the placental karyotype. Five positive results were obtained, including 2 for trisomy 16, 1 result for trisomy 7, 1 for trisomy 8, and 1 for double trisomy 7/8 (Table 1). The patients were counseled regarding the potentially poor prognosis of the affected pregnancy. Serial ultrasound examination every 2 weeks until term was recommended. After delivery, the placental tissues of the 5 affected pregnancies were examined; all confirmed the prenatal cfDNA findings.

Common complications of CPM pregnancies have been reported to include preeclampsia, IUGR, congenital anomalies, preterm delivery, cesarean delivery, intrauterine fetal death or perinatal death, and neonatal intensive care unit admission.[2,3] CPM should be investigated in pregnancies with a karyotypically normal fetus but IUGR. Maternal cfDNA testing can be used to provide karyotypic information about the placenta, as fetal DNA in maternal plasma originates from cyto- and syncytiotrophoblastic cells.[4] This is beneficial for clinical counseling and treatment, because a prenatally identified CPM pregnancy needs careful surveillance for both the mother and fetus. ■

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TABLE 1
Summary of 5 IUGR cases with CPM trisomies

Case	MA (y)	GA at IUGR (wk)	cfDNA	*Z* score	GA at delivery (wk)	BW(g)	Pregnancy outcome	Placental karyotype
1	34	16	Tri 16	24.6	24	265	TOP	47,XX,+16
2	26	24	Tri 16	10.7	30	1150	Alive	47,XX,+16
3	36	26	Tri 7	13.6	34	1820	Alive	47,XY,+7[60]/ 46,XY,[40]
4	29	24	Tri 8	17.2	32	1470	Alive	47,XX,+8[80]/ 47,XX[20]
5	30	26	Tri 7/8	18.0/14.1	32	1450	Alive	48,XY,+7,+8[64]/ 46,XY[37]

BW, birthweight; *CPM,* confined placental mosaicism; *GA,* gestational age; *IUGR,* intrauterine growth restriction; *MA,* maternal age; *TOP,* termination of pregnancy.

Li. Confined placental trisomy detection through maternal cell-free DNA testing. Am J Obstet Gynecol 2019.