Available online at www.sciencedirect.com

ScienceDirect

Taiwanese Journal of Obstetrics & Gynecology 52 (2013) 613–615

www.tjog-online.com

Research Letter

First-trimester sonographic demonstration of digynic triploidy

Chih-Ping Chen [a,b,c,d,e,f,*], Yi-Yung Chen [a], Schu-Rern Chern [b], Yu-Ling Kuo [g], Chen-Chi Lee [a], Wayseen Wang [b,h]

[a] *Department of Obstetrics and Gynecology, Mackay Memorial Hospital, Taipei, Taiwan*
[b] *Department of Medical Research, Mackay Memorial Hospital, Taipei, Taiwan*
[c] *Department of Biotechnology, Asia University, Taichung, Taiwan*
[d] *School of Chinese Medicine, College of Chinese Medicine, China Medical University, Taichung, Taiwan*
[e] *Institute of Clinical and Community Health Nursing, National Yang-Ming University, Taipei, Taiwan*
[f] *Department of Obstetrics and Gynecology, School of Medicine, National Yang-Ming University, Taipei, Taiwan*
[g] *Department of Obstetrics and Gynecology, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan*
[h] *Department of Bioengineering, Tatung University, Taipei, Taiwan*

Accepted 30 September 2013

A 38-year-old, gravida 3, para 0, woman was referred to the hospital at 13 weeks of gestation because of oligohydramnios and ventriculomegaly. Level II ultrasound examination showed a fetus with intrauterine growth restriction (IUGR), oligohydramnios with the largest pocket of 2.6 cm, a small noncystic placenta, a crown-rump length of 5.2 cm (11 weeks' equivalent), holoprosencephaly, and relative macrocephaly with an anteroposterior diameter about half of the crown-rump length (Fig. 1). The urinary tracts were normal. The pregnancy was terminated subsequently, and a male fetus was delivered, which had relative macrocephaly, a small placenta, premaxillary agenesis, and median facial cleft (Fig. 2). Postnatal cytogenetic analysis of umbilical cord revealed a karyotype of 69,XXY (Fig. 3). Postnatal DNA marker analysis using quantitative fluorescent polymerase chain reaction (QF-PCR) assays and polymorphic short tandem repeat markers for chromosomes 18 and 21 showed a diallelic pattern with a dosage ratio of 1:2 (paternal allele to maternal allele ratio) for the chromosome 21-specific and the chromosome 18-specific pericentromeric markers, indicating a maternal origin of triploidy (Fig. 4 and Table 1).

With the advent of prenatal ultrasonography and magnetic resonance imaging, fetuses with digynic triploidy can be identified in the second trimester [1–6]. Dilated fourth ventricle and posterior brain abnormalities have also been observed in triploid fetuses at 11–13 weeks of gestation [7,8]. The present case shows that ultrasonography is very useful for the identification of abnormalities associated with digynic triploid fetuses in the first trimester. Digynic triploidy is characterized by marked asymmetric IUGR, a small placenta without partial mole, oligohydramnios, relative macrocephaly, facial dysmorphism, and abnormalities of limbs, heart, urogenital organs, central nervous system, and endocrine and respiratory system, and diandric triploidy is characterized by normal fetal growth, normal or partial molar placenta, and a range of congenital malformations similar to digynic triploidy [9–11]. Fetuses with triploidy may be associated with abnormal fetal biometry and maternal serum screening such as severe asymmetric IUGR, low levels of pregnancy-associated plasma protein A, free β-human chorionic gonadotrophin, and normal nuchal translucency in digynic triploidy, whereas an extremely high level of free β-human chorionic gonadotrophin and elevated nuchal translucency in diandric triploidy [5,12–15].

The present case highlights the usefulness of QF-PCR in the rapid differential diagnosis of digynic triploidy and diandric triploidy [6,16]. The differential diagnosis between digynic triploidy and diandric triploidy is very important because diandric triploid pregnancies are associated with potential risks of maternal complications such as preeclampsia, postpartum hemorrhage, and gestational trophoblastic disease [17–19]. Molecular genotyping of triploidy using polymorphic DNA markers such as QF-PCR can distinguish between diandric triploidy and digynic triploidy, but has the disadvantage of requiring at least one parental DNA sample [6,20]. Recently, methylation-specific multiplex ligation-dependent probe amplification has been used for prenatal diagnosis of parental origin in human triploidy

* Corresponding author. Department of Obstetrics and Gynecology, Mackay Memorial Hospital, 92, Section 2, Chung-Shan North Road, Taipei, Taiwan.
E-mail address: cpc_mmh@yahoo.com (C.-P. Chen).

http://dx.doi.org/10.1016/j.tjog.2013.10.033

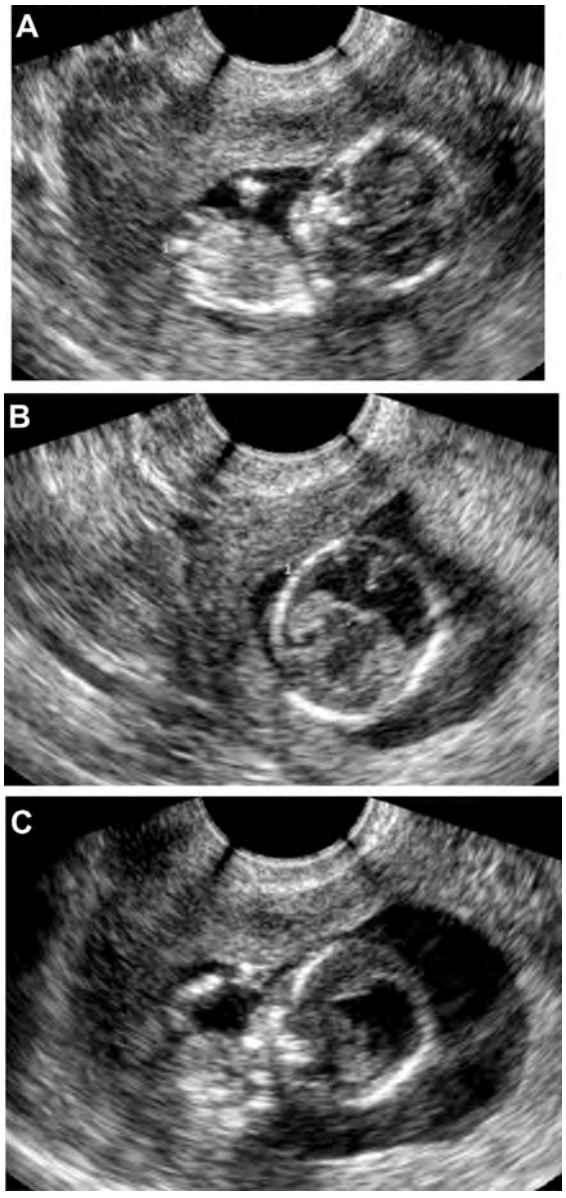

Fig. 1. Prenatal ultrasound of the fetus at 13 weeks of gestation shows: (A) relative macrocephaly and oligohydramnios, and (B and C) holoprosencephaly.

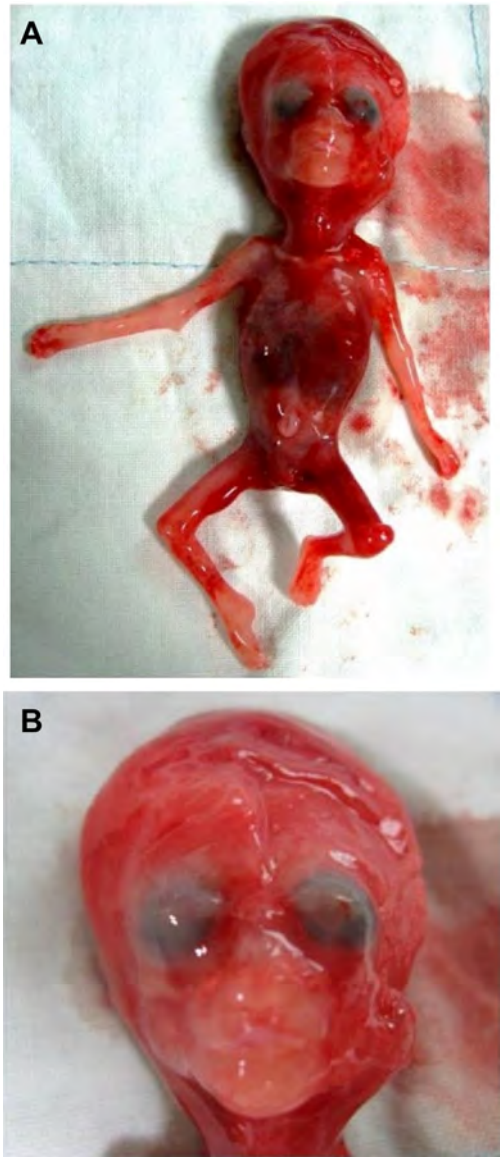

Fig. 2. Fetus at birth with (A) relative macrocephaly and (B) premaxillary agenesis.

without the need of parental samples [21]. The methylation-specific multiplex ligation-dependent probe amplification analysis uses one maternally imprinted region and one paternally imprinted region simultaneously, and compares the results of two oppositely imprinted regions to determine the parental origin of triploidy in the absence of parental samples.

In summary, we present first-trimester sonographic demonstration of digynic triploidy. First-trimester sonographic diagnosis of IUGR, oligohydramnios, and central nervous system anomalies should include a differential diagnosis of digynic triploidy and prompt molecular analysis to determine the parental origin of the triploidy under such a circumstance.

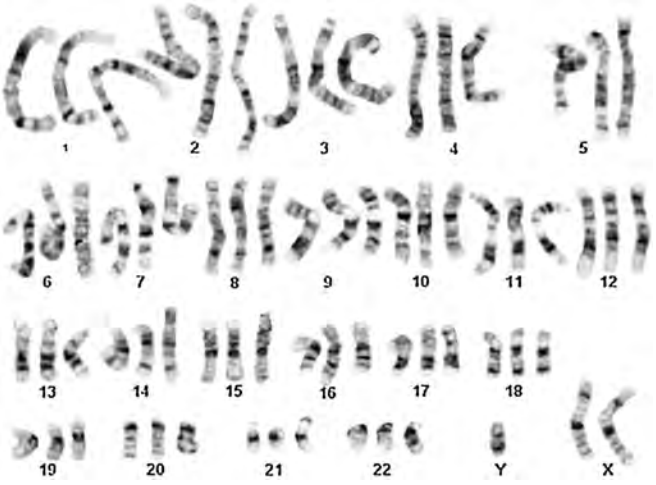

Fig. 3. Karyotype of 69,XXY.

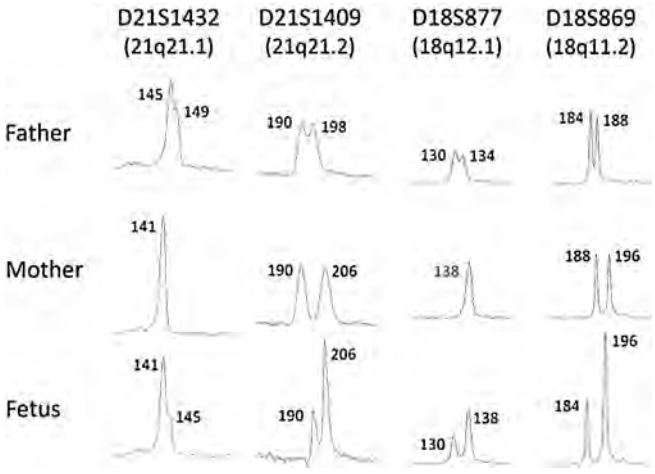

Fig. 4. Polymorphic DNA marker analysis shows digynic triploidy with a maternal origin of triploidy.

Table 1
Genotypic information of the fetus and the parents at STR markers specific for chromosomes 18 and 21 by QF-PCR assays.[a]

STRs	Location	Father	Mother	Fetus
D21S1432	21q21.1	145, 149	141, 141	141, 141, 145
D21S1409	21q21.2	190, 198	190, 206	190, 206, 206
D18S877	18q12.1	130, 134	138, 138	130, 138, 138
D18S869	18q11.2	184, 188	188, 196	184, 196, 196

QF-PCR = quantitative fluorescent polymerase chain reaction; STR = short tandem repeat.

[a] Alleles (base pair sizes) are listed below each individual.

Acknowledgments

This work was supported by research grants NSC-99-2628-B-195-001-MY3 and NSC-101-2314-B-195-011-MY3 from the National Science Council, Taipei, Taiwan and MMH-E-102-04 from Mackay Memorial Hospital, Taipei, Taiwan.

References

[1] Chen C-P. A digynic triploid fetus presenting intrauterine growth restriction, severe oligohydramnios and relative macrocephaly on prenatal ultrasound. Ultrasound Obstet Gynecol 2000;16:291–2.

[2] Chen C-P, Hsu H-C, Chern S-R, Tzen C-Y, Wang W, Lin C-J. Second-trimester diagnosis of digynic triploidy in a case of anhydramnios and fetal cyclopia by ultrasound-guided transabdominal chorionic villus sampling. Ultrasound Obstet Gynecol 2002;20:415–6.

[3] Chen C-P, Chang T-Y, Liu Y-P, Chern S-R, Wang W. Prenatal magnetic resonance imaging evaluation of a digynic triploid fetus. Taiwan J Obstet Gynecol 2007;46:284–5.

[4] Chen C-P, Chien S-C, Lin H-H. Prenatal sonographic features of triploidy. J Med Ultrasound 2007;15:175–82.

[5] Chen C-P, Hsieh E, Chern S-R, Wang W. Triploidy and fetal holoprosencephaly. Genet Couns 2008;19:105–8.

[6] Chen C-P, Chern S-R, Tsai F-J, Hsu C-Y, Ko K, Wang W. Prenatal diagnosis and molecular analysis of triploidy in a fetus with intrauterine growth restriction, relative macrocephaly and holoprosencephaly. Taiwan J Obstet Gynecol 2009;48:323–6.

[7] Ferreira AFA, Syngelaki A, Smolin A, Vayna A-M, Nicolaides KH. Posterior brain in fetuses with trisomy 18, trisomy 13 and triploidy at 11 to 13 weeks' gestation. Prenat Diagn 2012;32:854–8.

[8] Loureiro T, Ferreira AFA, Ushakov F, Montenegro N, Nicolaides KH. Dilated fourth ventricle in fetuses with trisomy 18, trisomy 13 and triploidy at 11–13 weeks' gestation. Fetal Diagn Ther 2012;32:186–9.

[9] McFadden DE, Kalousek DK. Two different phenotypes of fetuses with chromosomal triploidy: correlation with parental origin of the haploid set. Am J Med Genet 1991;38:535–8.

[10] McFadden DE, Kwong LC, Yam IYL, Langlois S. Parental origin of triploidy in human fetuses: evidence for genomic imprinting. Hum Genet 1993;92:465–9.

[11] Mittal TK, Vujanić GM, Morrissey BM, Jones A. Triploidy: antenatal sonographic features with post-mortem correlation. Prenat Diagn 1998;18:1253–62.

[12] McFadden DE, Lockitch G, Langlois S. Triple screen in triploidy. Am J Hum Genet 1998;63(Suppl.):A168.

[13] McFadden DE, Hulait G, Lockitch G, Langlois S. Maternal serum screening in triploidy. Prenat Diagn 2002;22:1113–4.

[14] Yaron Y, Ochshorn Y, Tsabari S, Shira AB. First-trimester nuchal translucency and maternal serum free β-hCG and PAPP-A can detect triploidy and determine the parental origin. Prenat Diagn 2004;24:445–50.

[15] Salomon LJ, Bernard JP, Nizard J, Ville Y. First-trimester screening for fetal triploidy at 11 to 14 weeks: a role for fetal biometry. Prenat Diagn 2005;25:479–83.

[16] Mann K, Ogilvie CM. QF-PCR: application, overview and review of the literature. Prenat Diagn 2012;32:309–14.

[17] Graham Jr JM, Rawnsley EF, Simmons GM, Wurster-Hill DH, Park JP, Marin-Padilla M, et al. Triploidy: pregnancy complications and clinical findings in seven cases. Prenat Diagn 1989;9:409–19.

[18] Zaragoza MV, Surti U, Redline RW, Millie E, Chakravarti A, Hassold TJ. Parental origin and phenotype of triploidy in spontaneous abortions: predominance of diandry and association with the partial hydatidiform mole. Am J Hum Genet 2000;66:1807–20.

[19] Horowitz NS, Goldstein DP, Berkowitz RS. Management of gestational trophoblastic neoplasia. Semin Oncol 2009;36:181–9.

[20] Murphy KM, McConnell TG, Hafez MJ, Vang R, Ronnett BM. Molecular genotyping of hydatidiform moles: analytic validation of a multiplex short tandem repeat assay. J Mol Diagn 2009;11:598–605.

[21] Joergensen MW, Rasmussen AA, Niemann I, Hindkjaer J, Agerholm I, Bolund L, et al. Methylation-specific multiplex ligation-dependent probe amplification: utility for prenatal diagnosis of parental origin in human triploidy. Prenat Diagn 2013;33:1–6.