Reproductive BioMedicine Online (2014) **29**, 136–139

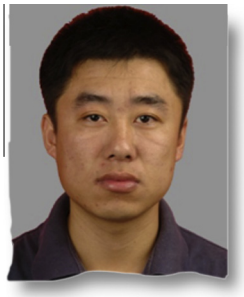
www.sciencedirect.com
www.rbmonline.com

SHORT COMMUNICATION

A pregnancy with discordant fetal and placental chromosome 18 aneuploidies revealed by invasive and noninvasive prenatal diagnosis

Chong Chen [a], David S Cram [b,1], Fanni Xie [a], Ping Wang [a,c], Xueqin Xu [a], Huanzheng Li [a], Zhuo Song [b], Di Chen [b], Jianguang Zhang [b], Shaohua Tang [a,c,*]

[a] *Department of Genetics of Dingli Clinical Medical School of Wenzhou Medical College, Zhejiang, China;* [b] *Berry Genomics C., Limited, China;* [c] *Zhejiang Key Laboratory of Medical Genetics, Zhejiang, China*
[*] Corresponding author. *E-mail addresses:* david.cram@berrygenomics.com (DS Cram), tsh006@126.com (S Tang). [1] Co-corresponding author.



Chong Chen obtained his MSc in medical genetics and bioinformatics in 2012 from the Wenzhou Medical University, Wenzhou, China. He is now a research assistant in the Zhejiang Key Laboratory of Medical Genetics and Department of Genetics of Dingli Clinical Medical School of Wenzhou Medical University. His main research interest is diagnosis of genetic disease using next generation sequencing technologies.

Abstract This study investigated a pregnancy where the fetus was diagnosed with monosomy 18p by invasive amniocentesis and karyotyping. Additional noninvasive prenatal diagnosis, which detects fetal chromosome abnormalities in the circulating cell-free plasma DNA originating from the placenta revealed a related 18p monosomy/18q trisomy, suggesting confined placental mosaicism. Based on recent observations of chromosomal instability in the early preimplantation embryo, this study speculates on the possible embryonic origin(s) of these related but discordant chromosome 18 aneuploidies in the placental and fetal tissues. The findings highlight the potential for both false-positive and -negative noninvasive prenatal diagnosis results in pregnancies where there is either confined placental mosaicism or placental mosaicism.

© 2014, Reproductive Healthcare Ltd. Published by Elsevier Ltd. All rights reserved.

KEYWORDS: circulating cell-free fetal DNA, confined placental mosaicism, noninvasive prenatal diagnosis

http://dx.doi.org/10.1016/j.rbmo.2014.03.017
1472-6483/© 2014, Reproductive Healthcare Ltd. Published by Elsevier Ltd. All rights reserved.

Introduction

Meiotic and mitotic errors are well recognized as a significant cause of aneuploidy in the preimplantation embryos. More recently, detailed molecular studies of blastomeres from cleavage-stage embryos has demonstrated a low but significant degree of chromosome instability resulting in partial chromosome breakages, structural rearrangements as well as deletions and duplication events (Vanneste et al., 2009). Further, at the blastocyst stage during specification of the trophectoderm and inner cell mass, some embryos are susceptible to additional chromosomal events such as trisomic rescue and other mitotic errors, leading to formation of other abnormalities such as uniparental disomy and aneuploidy in the fetus and/or the placental tissue (Wolstenholme, 1996). Prenatal diagnosis of chromosomal abnormalities in the late first trimester and early second trimester is usually performed by a combination of maternal serum screening, ultrasound and invasive amniocentesis or chorionic villus sampling. More recently, the noninvasive prenatal test (NIPT) using either shot-gun or SNP-based sequencing of the circulating cell-free placental DNA is now being increasingly requested by women as a primary pregnancy test (Song et al., 2013). Current NIPT methods target the common trisomies 21, 18 and 13 as well as sex chromosomal aneuploidies that can remain viable throughout prenatal development. Data from prospective studies indicate that NIPT is highly sensitive and specific for these fetal chromosome abnormalities (Song et al., 2013). However, occasional discordant results have been reported and studies to date indicate that confined placental mosaicism (CPM) and placental mosaicism are key contributing factors (Benn et al., 2013).

Materials and methods

Maternal serological screening of alpha-fetoprotein, human chorionic gonadotrophin (β-HCG) was performed using a commercially available enzyme immunoassay (AutoDELFIA hAFP/Free hCGβ Dual; PerkinElmer). Cytogenetic analysis of the parental and fetal cells was conducted on G-banded metaphase chromosomes at a resolution of approximately 450 bands. For NIPT, methods for maternal plasma DNA isolation, library construction, massive parallel sequencing and data analysis have been described previously (Song et al., 2013).

The study was approved by the Office of Research Ethics, Wenzhou Medical University (approval reference number KYK(2013), approved 20 February 2013).

Results

A 34-year-old pregnant women with no family history of genetic disease underwent routine maternal serum screening at 16 weeks of gestational age and returned an abnormal result with a free-HCG value of 36.00 ng/ml (multiple of the median, MoM, 2.26 ng/ml) and alpha-fetoprotein value of 30.60 U/ml (MoM 0.96 U/ml) (**Figure 1**A). An ultrasound scan revealed no neural tube defect or any physical abnormalities. The calculated risks of fetal trisomy 21 and trisomy 18 were one in 217 and one in 27,000, respectively. After counselling, the couple decided to have confirmatory prenatal testing by amniocentesis at 20 weeks. Fetal karyotyping and array comparative genomic hybridization analysis revealed a 14.3 Mb subtelomeric deletion in one copy of chromosome 18 at 18p11.32 (18p−) whereas the parental karyotypes were normal (data not shown). The couple were advised that if the fetus developed to term, their child may be afflicted with short stature, developmental delay, holoprosencaphaly and multiorgan abnormalities (Turleau, 1998). The couple also requested confirmatory NIPT at 25 weeks which identified an increased dosage of chromosome 18, indicative of placental trisomy 18 (**Figure 1**A). However, further data analysis revealed a decreased dosage of 18p and an increased dosage of 18q (**Figure 1**B), indicative of a 18p monosomy/18q trisomy in the placental tissue. The fetus succumbed *in utero* at 30 weeks of gestation, requiring an induced delivery of a premature stillborn child. No gross physical morphological abnormalities were observed in either the fetus or the placental tissue. Unfortunately, the tissues were accidentally discarded and thus the NIPT findings could not be corroborated by cytogenetic analysis of the placental tissue.

Discussion

Confined placental mosaicism in the human is a relatively rare biological phenomenon that occurs in approximately 1% of pregnancies where the chromosomal constitution of the fetal tissue is different from that of the placental tissue (Wolstenholme, 1996). CPM is believed to arise during transition from the morula to blastocyst during early preimplantation development, when the compacted blastomeric cells of the morula undergo polarization into two lineages (Wolstenholme, 1996), namely the trophectoderm and the inner cell mass. Investigation of the pregnancy reported here revealed 18p− in the fetus by karyotyping and 18p−18q+ in the placenta, suggesting CPM. It is intriguing to speculate on the origin of this unusual pregnancy since both parents had normal karyotypes. First, since the 18p− chromosome was present in both the fetal and placental tissues, it must have had a common origin, occurring either before or after fertilization and before cleavage divisions. Perturbations in chromatin remodelling and DNA repair has been proposed as a possible mechanism of chromosomal DNA breaks in spermatozoa (Leduc et al., 2008). However, from molecular studies of chromosomal instability in the early embryo (Vanneste et al., 2009), breakage fusion bridge cycles appear to be a more plausible mechanism to explain the origin of chromosome breaks and is also consistent with the observation of no obvious paternal or maternal bias for these types of deletions (Voet et al., 2011). On this basis, this study speculates that the 1 8p− chromosome was most likely formed at the 1- or 2-cell embryo stage and, together with its normal homologue, was perpetuated through normal mitotic events into all the pluripotent cells at the morula stage. Following tissue specification into trophoblast and inner cell mass cell progenitors, it is further speculated that the 18p− chromosome was duplicated in an early trophoblast progenitor, leading to the formation of placental tissue with monosomy 18p/trisomy18q and fetal tissue with monosomy 18p (**Figure 1**A).

Download English Version:

https://daneshyari.com/en/article/3970151

Download Persian Version:

https://daneshyari.com/article/3970151

Daneshyari.com