Confined Placental Mosaicism: A Case Report of Monosomy Chromosome 21

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ABSTRACT

We report a case of confined placental mosaicism of a 34 year old Chinese woman who was found to be at high risk during first trimester screening. Subsequent chorionic villus sampling showed mosaic monosomy chromosome 21, but amniocentesis revealed normal karyotype. The rest of her antenatal, intrapartum and postpartum progress were uneventful. Her child has normal phenotype, growth and developmental milestones thus far.

Keywords: monosomy mosaicism, chorionic villus sampling

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INTRODUCTION

Chorionic villus sampling (CVS) and amniocentesis are the most common invasive prenatal diagnostic procedures performed worldwide in modern obstetrics and gynecological practice today. In majority of pregnancies, chromosomal abnormalities detected in the fetus are also present in the placenta. However, approximately 1 to 2% of viable pregnancies subjected to CVS testing have been shown to exhibit the cytogenetic abnormality in the placenta only[1] – giving rise to the term confined placental mosaicism (CPM). In this case report, we present a patient diagnosed antenatally with CPM of monosomy chromosome 21 who went on to deliver a normal child.

CASE DESCRIPTION

A 34-year old Chinese female, gravida 3 para 1 with 1 previous miscarriage and 1 full term normal vaginal delivery, was seen early in her current pregnancy in our outpatient specialist clinic. She had no significant past medical or surgical history, and her previous pregnancy was uneventful with no history of intrauterine growth restriction.

Ultrasound dating was done at 9.8 weeks and this was followed by a first trimester screening at 12.3 weeks, which revealed that she was at high risk for trisomy 13

(1:22), trisomy 18 (1:355) and trisomy 21 (1:103). She was hence counseled for and agreed to a chorionic villus sampling (CVS), which was performed at 13.1 weeks of gestation. Cell cultures were unsuccessful and interphase fluorescence in situ hybridization (FISH) was performed using DNA probes for chromosomes 13, 18, 21, X and Y. The result showed one signal for chromosome 21 in 20% of the 50 nuclei examined, suggestive of mosaic monosomy chromosome 21. In view of this, an amniocentesis was done at 17.1 weeks of gestation, which studied an additional 43 metaphases (total of 59 metaphases) to check for monosomy 21. None were found. This excluded a mosaic of 5% or more with 95% confidence; thus the final report was that of a male karyotype with no apparent chromosomal abnormalities. There was no fetal abnormality seen during ultrasound screening at 19.1 weeks. The rest of her antenatal follow up was uneventful with normal ultrasound growth parameters throughout.

The patient went into spontaneous labour at 38 weeks of gestation and progressed to a vaginal delivery of a normal baby boy with birth weight 3045 grams, who was reviewed by the neonatologist and noted to have no abnormal phenotypic features. He was discharged well with the patient the following day. The placenta weighed 625 grams. Subsequent follow up of the neonate has revealed normal postnatal growth and developmental milestones at 6 weeks of life.

DISCUSSION

First described in term placentas of infants born with unexplained intrauterine growth restriction (IUGR) by Kalousek and Dill[2] in 1983, CPM is defined by the presence of two or more different cells lines affecting the placenta only. Clinically, the diagnosis is typically made after a second prenatal test (e.g. amniocentesis) is done following an abnormal first test (e.g. CVS), and confirms a normal diploid karyotype. The prenatal identification of CPM can also be verified at birth by investigation of the term placenta. It is known that the fetus is involved in about 10% of CPM cases.[3]

There are 3 types of CPM, whereby placental mosaicism is confined to cytotrophoblast (type I), chorionic stroma (type II) or both cell lineages (type III).[4] It can also be described as mitotic or meiotic – in which the former arises from a diploid conception and the latter from a viable dividing chromosomally abnormal zygote. It is important to note the association between meiotic CMP involving trisomy and the increased risk of fetal uniparental disomy (UPD) for that specific chromosome pair[5], which may also adversely impact intrauterine growth of the fetus. In rare cases of UPD 21, there is usually an absence of defining phenotypic features.[6] Examples of CPM described in the existing literature include trisomies 2, 3, 7, 13, 18, 20, 21, with 16 being the most common.[1,7] Sex chromosomes, when affected, usually carry no adverse effects on fetal development.[8] Monosomy CPM such as our case has been infrequently reported.

CPM has been associated with a spectrum of outcomes, ranging from normal pregnancies to IUGR and even intrauterine death (IUD). It has been shown that the outcomes depend upon the type of CPM and particular chromosomal involvement. [9-10] Type I has been reported to be associated with spontaneous abortion, IUGR, IUD, or perinatal morbidity in 22% of affected pregnancies. Type II is usually found in pregnancies with normal fetal outcomes. Type III is typically associated with high rates of IUGR or IUD, with the latter mostly linked to CPM 16. One of the hypotheses is that CPM results in abnormal growth of the placenta, which in turn compromises placental function and leads to IUGR.[11-13] Our patient had a placenta weighing 625 grams that is at the 50th centile based on Thompson JMD.[14] This justifies the normal fetal growth in our case report as the placenta growth and function were likely to be normal. However, the true mechanism behind how abnormal cells in the placenta influence fetal growth parameters or even cause IUD has yet to be elucidated. This is especially so as not all prenatally diagnosed CPM result in live births. Thus, to further the understanding and efficiency of CPM detection, it has been suggested that only placentas from idiopathic IUGR pregnancies with no obvious maternal, fetal and placental causes should be thoroughly analyzed. This is to facilitate the correlation between extent of aneuploid involvement in the term placenta and pregnancy course and outcome.[4]

Fortunately, the prenatal diagnosis of CPM has been shown to have no links with increased risk of birth defects or developmental problems, with a study by Miura et al[15] noting no significant difference in developmental quotient at 12 months of age between CPM infants and the control group. However, reduced postnatal growth and short stature were seen more frequently in the CPM group.[15]

More large prospective trials with long term follow ups are needed to determine the true role of CPM in intrauterine, perinatal and postpartum periods. At

present, we recommend that all prenatally diagnosed CPM pregnancies be followed up closely with serial ultrasound monitoring of growth parameters. Given the trend of increasing maternal age, more widespread first trimester screening and improved laboratory techniques of invasive prenatal testing, it is imperative that obstetricians incorporate multidisciplinary care involving the geneticist and pediatrician – and all involved will face unique challenges in the counseling of patients diagnosed with CPM.

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