Taiwanese Journal of Obstetrics & Gynecology 56 (2017) 238–242

Contents lists available at ScienceDirect

Taiwanese Journal of Obstetrics & Gynecology

journal homepage: www.tjog-online.com

Case Report

Prenatal diagnosis and molecular cytogenetic characterization of low-level mosaic trisomy 12 at amniocentesis associated with a favorable pregnancy outcome

Chih-Ping Chen [a, b, c, d, e, f, *], Chen-Ju Lin [a, g], Schu-Rern Chern [b], Peih-Shan Wu [h], Yen-Ni Chen [a], Shin-Wen Chen [a], Chen-Wen Pan [a], Chien-Wen Yang [b], Wayseen Wang [b, i]

[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 Medicine, MacKay Medical College, New Taipei City, Taiwan
[h] Gene Biodesign Co. Ltd., Taipei, Taiwan
[i] Department of Bioengineering, Tatung University, Taipei, Taiwan

ARTICLE INFO

Article history:
Accepted 12 January 2017

Keywords:
amniocentesis
mosaic trisomy 12
prenatal diagnosis
trisomy 12 mosaicism

ABSTRACT

Objective: We present prenatal diagnosis of low-level mosaic trisomy 12.
Case Report: A 40-year-old woman underwent amniocentesis at 18 weeks of gestation because of advanced maternal age, which revealed a karyotype of 47,XX,+12[5]/46,XX[24] consistent with 17.2% (5/29) mosaicism for trisomy 12. Repeat amniocentesis performed at 21 weeks of gestation revealed a karyotype of 47,XX,+12[4]/46,XX[6] consistent with 40% (4/10) mosaicism for trisomy 12. Interphase fluorescence *in situ* hybridization (FISH) on 112 uncultured amniocytes detected 23 cells with trisomy 12 consistent with 20.5% (23/112) mosaicism for trisomy 12. Polymorphic DNA marker analysis excluded uniparental disomy 12. Array comparative genomic hybridization (aCGH) on uncultured amniocytes revealed a result of arr 12p13.33q24.33 (230,451–133,773,499) × 2.2, 17p12 (14,191,925–15,442,037) × 1.0 consistent with 10–20% mosaic trisomy 12. The father carried the 17p12 microdeletion. The fetal ultrasound findings were unremarkable. A 3958-g female fetus was delivered at 37 weeks of gestation with no phenotypic abnormality. The cord blood had a karyotype of 46,XX. Postnatal interphase FISH on urinary cells revealed 7.14% (7/98) mosaicism for trisomy 12.
Conclusion: Low-level mosaic trisomy 12 at amniocentesis can be associated with a favorable pregnancy outcome. Interphase FISH and aCGH on uncultured amniocytes are useful for confirmation of low-level mosaic trisomy 12 at amniocentesis.

Introduction

Clinical reports of mosaic trisomy 12 detected by amniocentesis are very rare. We previously reported prenatal diagnosis and molecular cytogenetic characterization of low-level mosaic trisomy 12 with a favorable pregnancy outcome [1–3]. Here, we present an additional case with a similar result. Our experience may provide useful information for the clinicians, genetic counselors, and parents during genetic counseling of mosaic trisomy 12 at amniocentesis.

Case Report

A 40-year-old, gravida 2, para 0, woman underwent amniocentesis at 18 weeks of gestation because of advanced maternal age. Her husband was 48 years old. The woman and her husband were healthy, and there was no family history of congenital malformations. Amniocentesis revealed a karyotype of 47,XX,+12[5]/46,XX[24] consistent with 17.2% (5/29 colonies) mosaicism for trisomy 12. Among 29 colonies of cultured amniocytes, five colonies had a

* Corresponding author. Department of Obstetrics and Gynecology, MacKay Memorial Hospital, 92, Section 2, Chung-Shan North Road, Taipei 10449, Taiwan.
E-mail address: cpc_mmh@yahoo.com (C.-P. Chen).

http://dx.doi.org/10.1016/j.tjog.2017.01.005

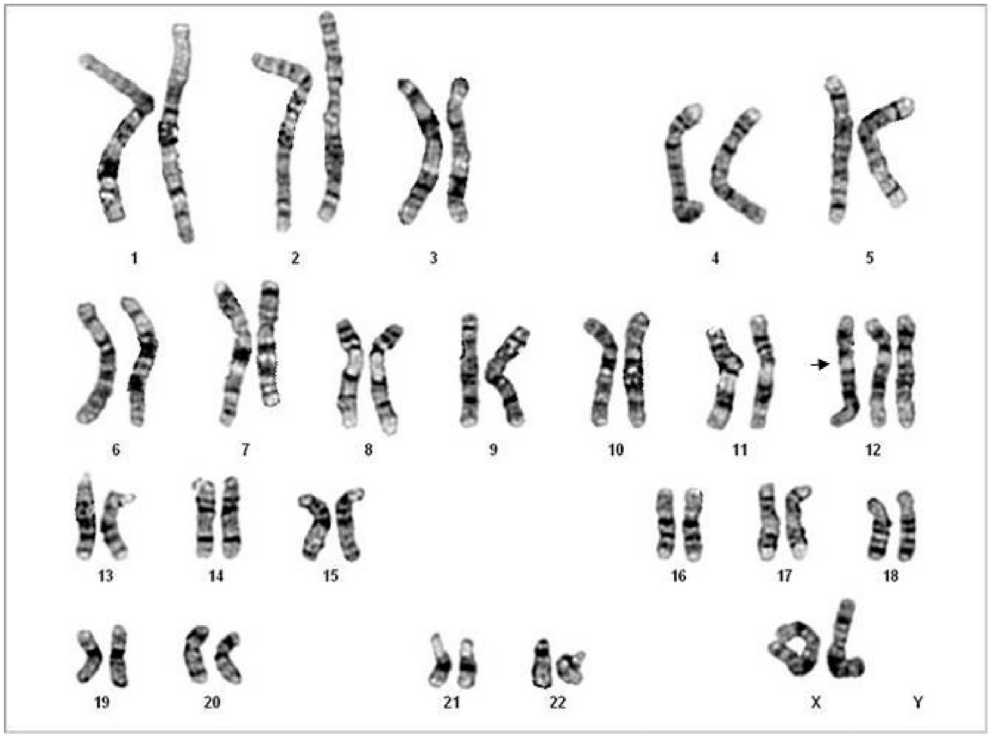

Figure 1. A karyotype of 47,XX,+12.

karyotype of 47,XX,+12 (Figure 1), whereas the rest, 24 colonies, had a karyotype of 46,XX. Prenatal ultrasound findings were unremarkable. The parental karyotypes were normal. Repeat amniocentesis was performed at 21 weeks of gestation. Simultaneous molecular cytogenetic analyses were performed on uncultured amniocytes using array comparative genomic hybridization (aCGH), interphase fluorescence *in situ* hybridization (FISH), and quantitative fluorescent polymerase chain reaction (QF-PCR) assays. Cytogenetic analysis of cultured amniocytes at repeat amniocentesis revealed a karyotype of 47,XX,+12[4]/46,XX[6] consistent with 40% (4/10 colonies) mosaicism for trisomy 12. QF-PCR analysis using the informative markers of D12S823 (12p12.1) and D12S302 (12q23.1) on the DNA extracted from the uncultured amniocytes and the parental peripheral bloods excluded uniparental disomy (UPD) 12 (Table 1). Interphase FISH analysis on 112 uncultured amniocytes using the bacterial artificial chromosome (BAC) probe of RP11-244D12 [12p11.22, fluorescein isothiocyanate (FITC), spectrum green] and RP11-627E5 (12q24.33, Texas Red, spectrum red) detected 23 cells with trisomy 12 consistent with a mosaicism level of 20.5% (23/112 cells) (Figure 2). The normal control amniocytes had a false positive rate of 1.9% (2/104 cells) for RP11-244D12 and a false positive rate of 3.9% (4/104 cells) for RP11-627E5. aCGH analysis of the DNA extracted from uncultured amniocytes using CytoChip ISCA Array (Illumina, San Diego, CA, USA) revealed a result of arr 12p13.33q24.33 (230,451–133,773,499) × 2.2, 17p12 (14,191,925–15,442,037) × 1.0 (Figure 3). The log2 ratio for 12p13.33q24.33 duplication was 0.12 consistent with 10–20% mosaicism. The 1.25-Mb 17p12 microdeletion contained 15 genes including three Online Mendelian Inheritance in Man (OMIM) genes of *HS3ST3B1*, *PMP22*, and *TEKT3*. aCGH analysis of the DNAs extracted from parental bloods revealed no genomic imbalance in the maternal blood and a result of arr 17p12 (14,111,802–15,442,037) × 1.0 in the paternal blood (Figure 4). The father had a 1.33-Mb 17p12 microdeletion encompassing 17 genes including four OMIM genes of *COX10*, *HS3ST3B1*, *PMP22*, and *TEKT3*. The father manifested no peripheral neuropathy. The parents elected to continue the pregnancy. At 37 weeks of gestation, a 3958-g (>97th centile) female baby was delivered smoothly with a body length of 51.5 cm (>97th centile) with neonatal brachial plexus palsy. The cord blood had a karyotype of 46,XX in 40/40 lymphocytes. At age 4 days, interphase FISH analysis on 98 uncultured urinary cells detected seven cells with trisomy 12 consistent with 7.14% mosaicism for trisomy 12. The normal control urinary cells had a false positive rate of 1.96% (2/102 cells) for the FISH probes. The neonate was phenotypically normal during follow-ups at age 1 month. Her body weight was 4.2 Kg (25–50th centile).

Table 1
Molecular results using polymorphic DNA markers specific for chromosome 12.

Markers	Locus	Father	Mother	Fetus (uncultured amniocytes)
D12S823	12p12.1	144, 152	124, 140	124, 144
D12S302	12q23.1	156, 156	152, 152	152, 156

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

Discussion

The present case provides evidence that interphase FISH on uncultured amniocytes at repeat amniocentesis is very practical for determining the real mosaicism level of trisomy 12 at amniocentesis. In the present case, the first amniocentesis revealed 17.2% (5/29 colonies) mosaicism for trisomy 12 in cultured amniocytes, and the second amniocentesis revealed 40% (4/10 colonies) mosaicism for trisomy 12 in cultured amniocytes by conventional cytogenetic analysis. However, the second amniocentesis revealed 20.5% (23/112 cells) mosaicism for trisomy 12 by interphase FISH in uncultured amniocytes. The result obtained from interphase FISH on uncultured amniocytes is very useful for genetic counseling of inconsistent trisomy 12 mosaicism levels in different cultured amniocytes. Inconsistent trisomy mosaicism levels have been