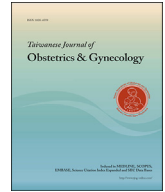




Contents lists available at ScienceDirect

Taiwanese Journal of Obstetrics & Gynecology

journal homepage: www.tjog-online.com

Case Report

Low-level mosaic trisomy 13 at amniocentesis associated with a favorable outcome in a pregnancy

Chih-Ping Chen^{a, b, c, d, e, *}, Schu-Rern Chern^b, Fang-Tzu Wu^a, Yun-Yi Chen^b, Meng-Shan Lee^a, Wayseen Wang^b^a Department of Obstetrics and Gynecology, MacKay Memorial Hospital, Taipei, Taiwan^b Department of Medical Research, MacKay Memorial Hospital, Taipei, Taiwan^c School of Chinese Medicine, College of Chinese Medicine, China Medical University, Taichung, Taiwan^d Institute of Clinical and Community Health Nursing, National Yang-Ming University, Taipei, Taiwan^e Department of Obstetrics and Gynecology, School of Medicine, National Yang-Ming University, Taipei, Taiwan

ARTICLE INFO

Article history:

Accepted 28 August 2020

Keywords:

Amniocentesis

Mosaicism

Trisomy 13

ABSTRACT

Objective: We present low-level mosaic trisomy 13 at amniocentesis associated with a favorable outcome in a pregnancy.**Case report:** A 39-year-old woman underwent amniocentesis at 17 weeks of gestation because of advanced maternal age. Amniocentesis revealed a karyotype of 47,XY,+13[8]/46,XY[20]. The woman underwent cord blood sampling at 22 weeks of gestation. Cytogenetic analysis of cord blood revealed a karyotype of 47,XY,+13[2]/46,XY[98]. Array comparative genomic hybridization (aCGH) analysis on the DNA extracted from cord blood revealed 10% gene dosage increase in chromosome 13. Prenatal ultrasound findings were unremarkable. After genetic counseling, the parents decided to continue the pregnancy, and a 2,280-g healthy male baby was delivered at 38 weeks of gestation. The parental karyotypes were normal. The cord blood at birth had a karyotype of 47,XY,+13[1]/46,XY[49]. At age one month, interphase fluorescence *in situ* hybridization (FISH) analysis revealed no trisomy 13 signals in 100/100 buccal mucosal cells, and trisomy 13 signals in 2/54 (3.7%) urinary cells compared with 0/60 cells in the normal control. The neonate was doing well and presented neither phenotypic abnormalities nor psychomotor disorders at age two months.**Conclusion:** Low-level true mosaic trisomy 13 at amniocentesis without ultrasound abnormalities can be associated with a favorable outcome.© 2020 Taiwan Association of Obstetrics & Gynecology. Publishing services by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

Mosaic trisomy 13 at amniocentesis remains a challenge to obstetricians and genetic counselors because individuals with mosaic trisomy 13 have been reported to present phenotypic variability ranging from grossly normal to the abnormal phenotype of trisomy 13 [1–5]. We previously reported prenatal diagnosis of low-level mosaicism for trisomy 13 at amniocentesis associated with a favorable outcome in a pregnancy [6]. Here, we present an additional case of mosaic trisomy 13 at amniocentesis with a favorable outcome.

* Corresponding author. Department of Obstetrics and Gynecology, MacKay Memorial Hospital, 92, Section 2, Chung-Shan North Road, Taipei, 10449, Taiwan. Fax: +886 2 25433642, +886 2 25232448.

E-mail address: cpc_mmh@yahoo.com (C.-P. Chen).

<https://doi.org/10.1016/j.tjog.2020.09.022>

1028–4559/© 2020 Taiwan Association of Obstetrics & Gynecology. Publishing services by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Case report

A 39-year-old, gravida 2, para 0, woman underwent amniocentesis at 17 weeks of gestation because of advanced maternal age. Amniocentesis revealed a karyotype of 47,XY,+13 [8]/46,XY[20] following *in situ* culture of amniocytes. The woman underwent cord blood sampling at 22 weeks of gestation. Cytogenetic analysis of cord blood revealed a karyotype of 47,XY,+13 [2]/46,XY[98]. Array comparative genomic hybridization (aCGH) analysis on the DNA extracted from cord blood revealed 10% gene dosage increase in chromosome 13. Prenatal ultrasound findings were unremarkable. After genetic counseling, the parents decided to continue the pregnancy, and a 2,280-g healthy male baby was delivered at 38 weeks of gestation. The parental karyotypes were normal. The cord blood at birth had a karyotype of 47,XY,+13 [1]/46,XY[49] (Fig. 1). At age one month, interphase fluorescence *in situ* hybridization (FISH)

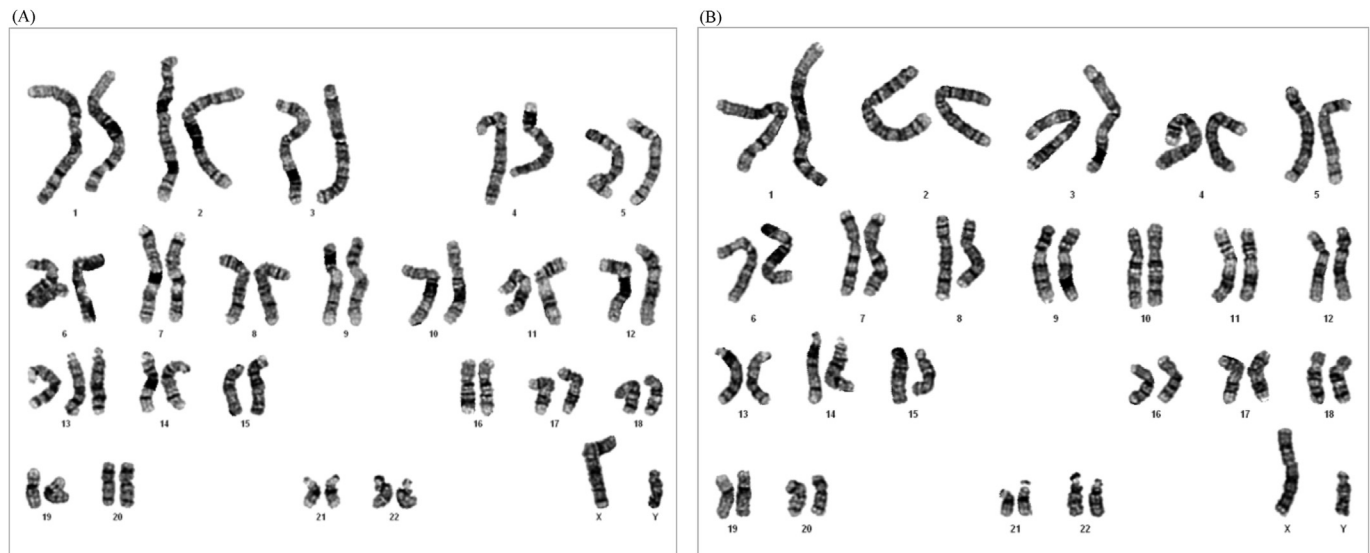


Fig. 1. (A) A karyotype of 47,XY,+13 and (B) A karyotype of 46,XY.

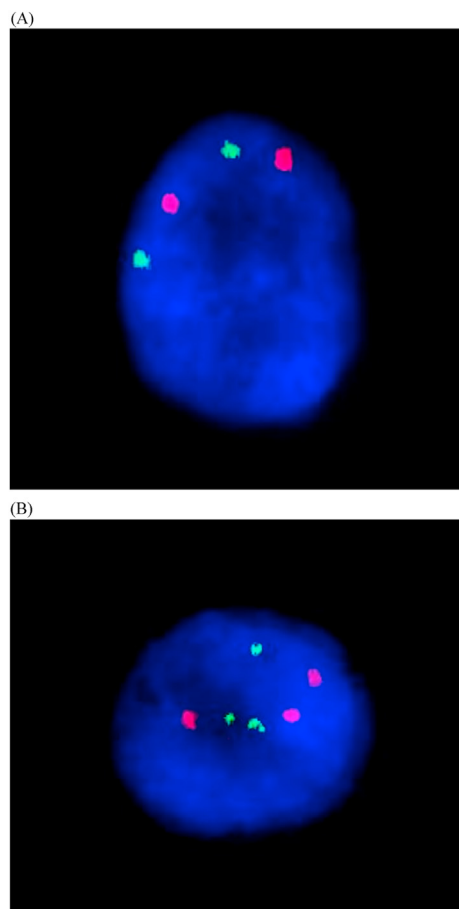


Fig. 2. Interphase fluorescence *in situ* hybridization analysis on urinary cells using bacterial artificial chromosome (BAC) probes of RP11-973F2 [13q33.1, fluorescein isothiocyanate (FITC), spectrum green] and RP11-944F14 (13q12.12, Texas Red, spectrum red) shows (A) a normal cell with two green signals and two red signals and (B) a trisomy 13 cell with three green signals and three red signals.

analysis revealed no trisomy 13 signals in 100/100 buccal mucosal cells, and trisomy 13 signals in 2/54 (3.7%) urinary cells compared with 0/60 cells in the normal control (Fig. 2). The neonate was doing well and presented neither phenotypic abnormalities nor psychomotor disorders at age two months.

Discussion

The present case had 28.6% (8/28 colonies) true chromosome mosaicism for trisomy 13 at amniocentesis and 2% (2/100 cells) of mosaic trisomy 13 in the cord blood lymphocytes at cord blood sampling. aCGH analysis showed about 10% mosaicism for trisomy 13 in the cord blood. Postnatal interphase FISH analysis on buccal mucosal cells revealed no trisomy 13 signals and 3.7% (2/54 cells) mosaicism for trisomy 13 in the urinary cells. The neonate presented no phenotypic abnormalities at age two months. Our case provides evidence that low-level true mosaicism for trisomy 13 at amniocentesis can be associated with a favorable outcome. This information is very useful in genetic counseling of precious babies in the couples who wish to have a baby, especially in pregnancy following difficult assisted reproductive technology or in women with very advanced age.

To date, mosaic trisomy 13 at amniocentesis has been reported to be associated with normal or near-normal liveborns in at least six cases [1–3,6–8]. Delatycki and Gardner [1] first reported two cases of level II mosaic trisomy 13 at amniocentesis with a favorable outcome. One case was followed up to be normal at age three years and six months, and the other case was followed up to be normal at age 17 months. Chen et al. [3] reported a case of high-level mosaic trisomy 13 at amniocentesis with a relatively mild phenotype of low-set ears, absence of the 12th rib and a ventricular septal defect, but normal development in the neonate at the age eight months. In that case, conventional cytogenetic analysis in two amniocenteses revealed 77.4% (24/31 colonies) and 78.3% (36/46 colonies) mosaic trisomy 13, respectively. Cord blood sampling revealed 14% (14/100 cells) mosaic trisomy 13, and neonatal cytogenetic analysis on skin, cardiac tissue and blood at age six months revealed normal results. Di Giacomo et al. [7] reported a case of high-level mosaic trisomy 13 at amniocentesis with normal and no dysmorphic features in the child at age two years. In that case, conventional

cytogenetic analysis revealed 70.6% (24/34 colonies) mosaic trisomy 13 at amniocentesis, 10% (10/100 cells) mosaic trisomy 13 at cord blood sampling, 10.3% (11/107 cells) mosaic trisomy 13 in neonatal blood, and 15.8% (18/114 cells) mosaic trisomy 13 in peripheral blood at age two years. Interphase FISH analysis showed 0% (0/103 cells) mosaicism for trisomy 13 in buccal mucosal cells, 5% (29/575 cells) mosaicism for trisomy 13 in skin fibroblasts and 23% (13/56 cells) mosaicism for trisomy 13 in urinary tract cells. Etoubleau et al. [8] reported a case of low-level mosaic trisomy 13 at amniocentesis with a normal phenotype in the child at age six years. In that case, two amniocenteses revealed mosaic trisomy levels of 14.3% (3/21 cells) and 0% (0/14 cells), respectively. Interphase FISH analysis revealed 6% (14/235 cells) mosaic trisomy 13 at repeat amniocentesis, cord blood sampling revealed a normal karyotype, and interphase FISH analysis on the buccal mucosal cells revealed 0.98% (2/203 cells) mosaic trisomy 13. Chen et al. [6] reported prenatal diagnosis of low-level mosaicism for trisomy 13 at amniocentesis associated with a favorable outcome. In that case, the first amniocentesis revealed 20% (5/25 colonies) mosaic trisomy 13, and the second amniocentesis revealed 46, XY in 23/23 colonies. aCGH analysis on the DNA extracted from uncultured amniocytes showed about 10% mosaic level of trisomy 13 in two consecutive amniocenteses, and interphase FISH analysis on uncultured amniocytes showed 10% (10/100 cells) mosaic trisomy 13. The neonate had a karyotype of 46, XY in peripheral blood and 4.4% (2/45 cells) mosaic trisomy 13 in the urinary cells. The neonate was followed up to be normal at age eight months.

In summary, we present low-level mosaic trisomy 13 at amniocentesis associated with a favorable outcome in a pregnancy. Our presentation provides evidence that low-level true mosaic trisomy 13 at amniocentesis without ultrasound abnormalities can be associated with a favorable outcome.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

Acknowledgements

This work was supported by research grants MOST-107-2314-B-195-005 from the Ministry of Science and Technology, Taiwan, and MMH-E-109-04 from Mackay Memorial Hospital, Taipei, Taiwan.

References

- [1] Delatycki M, Gardner RJM. Three cases of trisomy 13 mosaicism and a review of the literature. *Clin Genet* 1997;51:403–7.
- [2] Rasmussen SA, Wong L-YC, Yang Q, May KM, Friedman JM. Population-based analyses of mortality in trisomy 13 and trisomy 18. *Pediatrics* 2003;111:777–84.
- [3] Chen M, Yeh G-P, Shih J-C, Wang B-T. Trisomy 13 mosaicism: study of serial cytogenetic changes in a case from early pregnancy to infancy. *Prenat Diagn* 2004;24:137–43.
- [4] Griffith CB, Vance GH, Weaver DD. Phenotypic variability in trisomy 13 mosaicism: two new patients and literature review. *Am J Med Genet* 2009;149A:1346–58.
- [5] Chen C-P. Prenatal diagnosis and genetic counseling for mosaic trisomy 13. *Taiwan J Obstet Gynecol* 2010;49:13–22.
- [6] Chen C-P, Chern S-R, Wu P-S, Chen S-W, Lai S-T, Chuang T-Y, et al. Prenatal diagnosis of low-level mosaicism for trisomy 13 at amniocentesis associated with a favorable outcome. *Taiwan J Obstet Gynecol* 2017;56:840–2.
- [7] Di Giacomo MC, Susca FC, Resta N, Bukvic N, Vimercati A, Guanti G. Trisomy 13 mosaicism in a phenotypically normal child: description of cytogenetic and clinical findings from early pregnancy beyond 2 years of age. *Am J Med Genet* 2007;143A:518–20.
- [8] Etoubleau C, Bourthoumieu S, Fiorenza M, Aubard V, Yardin C. Are all cases of low-grade mosaic trisomy 13 in amniotic fluid with no fetal malformation in fact confined placental mosaicism? A case report. *Morphologie* 2011;95:142–5.