



Case Report

Mosaic isochromosome 20q at amniocentesis: Prenatal diagnosis, genetic counseling and literature review



Chih-Ping Chen^{a, b, c, d, e, f, *}, Schu-Rern Chern^b, Peih-Shan Wu^g, Shin-Wen Chen^a, Fang-Tzu Wu^a, Dai-Dyi Town^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 Gene Biodesign Co. Ltd, Taipei, Taiwan

^h Department of Bioengineering, Tatung University, Taipei, Taiwan

ARTICLE INFO

Article history:

Accepted 22 August 2019

Keywords:

Amniocentesis

Amniocytes

Isochromosome 20q

Mosaicism

Prenatal diagnosis

ABSTRACT

Objective: We present prenatal diagnosis of mosaic isochromosome 20q [i(20q)] at amniocentesis, and we review the literature.

Case report: A 36-year-old woman underwent amniocentesis at 17 weeks of gestation because of advanced maternal age. Amniocentesis revealed a karyotype of 46,XY,i(20)(q10)[27]/46,XY[29]. Prenatal ultrasound findings were unremarkable. The parental karyotypes were normal. Repeat amniocentesis was performed at 20 weeks of gestation. During repeat amniocentesis, array comparative genomic hybridization (aCGH), interphase fluorescence *in situ* hybridization (FISH) and quantitative fluorescent polymerase chain reaction (QF-PCR) assay were performed on uncultured amniocytes, and conventional cytogenetic analysis, interphase FISH and aCGH were performed on cultured amniocytes. In the repeat amniocentesis, the cultured amniocytes revealed a karyotype of 46,XY. Interphase FISH analysis showed the i(20q) signal in 5.2% (5/96) of the uncultured amniocytes compared with 2% in the control, and in 0.98% (1/102) of the cultured amniocytes compared with 2% in the control. aCGH detected no genomic imbalance in both uncultured and cultured amniocytes. QF-PCR analysis excluded uniparental disomy 20. At 38 weeks of gestation, a healthy 2870-g male baby was delivered with no phenotypic abnormality. The postnatal blood karyotype was 46,XY. FISH analysis on urinary cells showed 2.1% (2/95 cells) mosaicism compared with 1.9% (2/105 cells) in the control.

Conclusion: Mosaic i(20q) at amniocentesis is a benign condition associated with a favorable outcome in most cases and can be a cell culture artifact confined to cultured amniocytes. Molecular cytogenetic analysis using uncultured amniocytes is useful for rapid confirmation. Prenatal diagnosis of very high percentage of mosaicism for i(20q) at amniocentesis should alert the presence of fetal structural abnormalities. Prenatal diagnosis of mosaic i(20q) at amniocentesis should include a detail examination of fetal brain and spine.

© 2019 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 isochromosome 20q [i(20q)] detected at amniocentesis has been known to be a benign condition in most reported cases. We previously reported prenatal diagnosis of mosaic i(20q) in six cases [1–6] and found cytogenetic discrepancy between uncultured amniocytes and cultured amniocytes [3–6]. Here, we present an additional case with a favorable outcome.

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

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

Table 1
Reported cases of mosaic 46,i(20q) at amniocentesis.

Cases and karyotype of amniocytes		Proportion of abnormal cells or colonies	Confirmatory studies	Phenotype
Chodirker and Jenkins [7]	46,XY/46,XY,i(20q)	20%	46,XY: fetal blood, postnatal blood, foreskin	Normal
Begleiter et al. [8]	46,XX/46,XX,i(20q)	57%	46,XX[126]/46,XX,i(20q)[1]: fetal blood 46,XX: postnatal blood	Normal
Priest et al. [9]	46,XX/46,XX,i(20q)	23%	46,XX: fetal blood, postnatal blood	Normal
Richkind et al. [10]				
Case DC	46,XX/46,XX,i(20q)	28%	46,XX: fetal blood	Normal
Case SF	46,XY/46,XY,i(20q)	14%	46,XY: fetal blood	Normal
Case KK	46,XY/46,XY,i(20q)	15%	46,XY: fetal blood	Normal
Case KR	46,XX/46,XX,i(20q)	61%	46,XX: fetal blood	Normal
Case SW	46,XX/46,XX,i(20q)	25%	46,XX: fetal blood	Normal
Chernos et al. [11]	46,XX/46,XX,i(20q)	62%	No	Diaphragmatic hernia, ventricular dilation, a large calvarium, anophthalmia, craniofacial dysmorphism, a single umbilical artery
Djalali et al. [12]	46,XX/46,XX,i(20q)	81%	46,XX: fetal blood	Normal
Cooper et al. [13]	46,XY/46,XY,i(20q)	16%	46,XY: postnatal blood	Normal
Kershner and Donnenfeld [14]				
Donnenfeld and Kershner [15]				
Case 1	46,XX/46,XX,i(20q)	42%	46,XX: postnatal blood, skin	Nasofrontal protrusion identified as benign dermoid cyst; normal development after surgery
Case 2	46,XX/46,XX,i(20q)	75%	46,XX: postnatal blood, skin, placenta	Normal
Hsu et al. [16]				
Crandall, case Vlb-4	46,XX/46,XX,i(20q)	56%	46,XX: placenta	Normal
Howard-Peebles, case Vlb-8	46,XX/46,XX,i(20q)	17%	46,XX: fetal blood	Normal
Miller, case Vlb-9	46,XY/46,XY,i(20q)	26%	No	Normal
Miller, case Vlb-10	46,XY/46,XY,i(20q)	28%	No	Normal
Richkind, case Vlb-18	46,XY/46,XY,i(20q)	16%	No	Normal
Richkind, case Vlb-19	46,XY/46,XY,i(20q)	31%	No	Normal
Dupont et al. [17]	46,XX/46,XX,i(20q)	42%	46,XX: fetal blood	Normal
Pfeiffer et al. [18]	46,XY/46,XY,i(20q)	90%	46,XY: fetal blood, postnatal blood, placenta, skin 46,XY [18]/46,XY,i(20q) [13]: umbilical cord FISH: 6% mosaicism in buccal smear, 13.7% mosaicism in urinary sediment	Scars on the scalp, orbital cysts with coloboma of the papilla, dyssegmentation of the thoracic spine
Storto and Diehn [19]	46,XY/46,XY,i(20q)	12%	No	Normal
Chen [1]	46,XX/46,XX,i(20q)	50%	46,XX: fetal blood, postnatal blood, skin, liver, placenta	Arthrogryposis multiplex congenita, amyoplasia, a single umbilical artery
Chen [2]	46,XY/46,XY,i(20q)	27%	46,XY: cord blood, amniotic membrane, placenta, umbilical cord, skin, liver, lung	Normal
Goumy et al. [20]	46,XY/46,XY,i(20q)	93%	FISH: normal on uncultured amniocytes; FISH: 24% mosaicism on cultured amniocytes; aCGH: normal on cultured amniocytes	Abnormal fetus: facial dysmorphism, cystic hygroma, club feet, hydrocephalus, cerebellar hypoplasia, ocular anomaly, dyssegmentation of the thoracic spine
Robinson et al. [21]	46,XY/46,XY,i(20q)	53%	FISH: 13% mosaicism on cultured amniocytes; 46,XY: cord blood, placenta, chorion, amnion	Normal
Chen et al. [3]	46,XY/46,XY,i(20q) 46,XY/46,XY,i(20q)	24% (1st) 33% (Repeat)	FISH and aCGH: normal on uncultured amniocytes; FISH: 28% mosaicism and aCGH: abnormal on cultured amniocytes 46,XY: blood	Normal
Chen et al. [4]	46,XY/46,XY,i(20q) 46,XY	19% (1st) 0% (Repeat)	FISH: normal on uncultured amniocytes; 46,XY: cord blood FISH: normal on urinary cells	Normal
Chen et al. [5]	46,XX/46,XX,i(20q) 46,XX/46,XX,i(20q)	16% (1st) 3.7% (Repeat)	FISH and aCGH: normal on uncultured amniocytes; FISH: 22% mosaicism on cultured amniocytes 46,XX: blood FISH: normal on urinary cells	Normal
Chen et al. [6]	46,XY/46,XY,i(20q) 46,XY/46,XY,i(20q)	63% (1st) 20% (Repeat)	FISH and aCGH: normal on uncultured amniocytes; FISH: 15% mosaicism on cultured amniocytes No UPD 20	Normal
Receveur et al. [22]	46,XX,i(20q) 46,XX/46,XX,i(20q)	100% (1st) 86% (Repeat)	46,XX: cord blood, tendon, muscle, skin FISH: normal on uncultured amniocytes and postmortem samples; aCGH: completely abnormal on 1st cultured amniocytes and 86% mosaicism on repeat cultured amniocytes	Abnormal fetus: vertebral anomaly, rocker-bottom feet, facial dysmorphism, hypoplastic vertebral bodies T6-T7, bilateral renal moderate hypoplasia
Present case: Chen et al. [23]	46,XY/46,XY,i(20q) 46,XY	48% (1st) 0% (Repeat)	FISH and aCGH: normal on both uncultured and cultured amniocytes No UPD 20 46,XY: postnatal blood FISH: 2.1% mosaicism on urinary cells (normal contro1: 1.9%)	Normal

i(20q): isochromosome 20q, FISH: fluorescence *in situ* hybridization, aCGH: array comparative genomic hybridization, UPD: uniparental disomy.

Case report

A 36-year-old, gravida 2, para 1, woman underwent amniocentesis at 17 weeks of gestation because of advanced maternal age. Her husband was 44 years old. The couple had a 7-year-old daughter, and there were no congenital malformations in the family. Amniocentesis revealed a karyotype of 46,XY,i(20)(q10)[27]/46,XY[29]. In a total of 56 cultured amniocytes, 29 cells had a karyotype of 46,XY, whereas the other 27 cells had a karyotype of 46,XY,i(20)(q10). Prenatal ultrasound findings were unremarkable. The parental karyotypes were normal. Repeat amniocentesis was performed at 20 weeks of gestation. During repeat amniocentesis, array comparative genomic hybridization (aCGH), interphase fluorescence *in situ* hybridization (FISH) and quantitative fluorescent polymerase chain reaction (QF-PCR) assay were performed on uncultured amniocytes, and conventional cytogenetic analysis, interphase FISH and aCGH were performed on cultured amniocytes. In the repeat amniocentesis, the cultured amniocytes revealed a karyotype of 46,XY in all 20 colonies. Interphase FISH analysis showed the i(20q) signal in 5.2% (5/96) of the uncultured amniocytes compared with 2% in the control, and in 0.98% (1/102) of the cultured amniocytes compared with 2% in the control. aCGH detected no genomic imbalance in both uncultured and cultured amniocytes. QF-PCR analysis excluded uniparental disomy (UPD) 20. At 38 weeks of gestation, a healthy 2870-g male baby was delivered with no phenotypic abnormality. The postnatal blood karyotype was 46,XY. FISH analysis on urinary cells showed 2.1% (2/95 cells) mosaicism compared with 1.9% (2/105 cells) in the control.

Discussion

To date, at least 32 cases of mosaic i(20q) at amniocentesis have been reported (Table 1). The male to female ratio is 17:15. The outcomes are generally normal and favorable. Only five out of 32 cases (5/32 = 15.6%) presented structural abnormalities including a female with diaphragmatic hernia, ventricular dilation, a large calvarium, anophthalmia and craniofacial dysmorphism [11], a male with orbital cysts with coloboma of the papilla, scalp scars and dyssegmentation of the thoracic spine [18], a female with arthrogryposis multiplex congenita and amyoplasia [1], a male with facial dysmorphism, cystic hygroma, club feet, hydrocephalus, cerebellar hypoplasia, ocular anomaly and dyssegmentation of the thoracic spine [20], and a female with facial dysmorphism, rocker-bottom feet, hypoplastic vertebral bodies T6-T7 and bilateral renal moderate hypoplasia [22]. The main structural abnormalities associated with mosaic i(20q) at amniocentesis were spine (3/5), brain (2/5) and eye (2/5) abnormalities. Therefore, prenatal diagnosis of mosaic i(20q) at amniocentesis should include a detail examination of fetal skull, brain and spine. The median percentage of the abnormal cultured amniocytes at amniocentesis in the five phenotypically abnormal cases was 90%, and the median percentage of the abnormal cultured amniocytes at the first amniocentesis in the other 27 phenotypically normal cases was 27%. Therefore, prenatal diagnosis of very high percentage of mosaicism for i(20q) at amniocentesis should alert the presence of fetal structural abnormalities.

In 23 cases with blood cytogenetic analysis, 22 cases revealed normal karyotype in the blood, and only one case [7] showed 1/127 mosaic i(20q) in the blood. In seven cases with skin cytogenetic analysis [1,2,8,15,18,22], all revealed normal karyotype in the skin. In six cases with other organ cytogenetic analysis including liver, lung, muscle, tendon and urinary cells [1,2,4,5,18,22], only one case [18] showed 13.7% mosaicism in the urinary sediment, while the others were normal. In seven cases with molecular cytogenetic

analysis of uncultured amniocytes [3–6,20,22,23], all revealed no mosaic i(20q) in the uncultured amniocytes. In six cases with repeat amniocentesis [3–6,22,23], two cases [4,23] revealed normal karyotype in the cultured amniocytes at repeat amniocentesis, while the others four cases showed mosaic i(20q) in the cultured amniocytes at repeat amniocentesis. In five cases with placental cytogenetic analysis [1,2,15,16,18], all cases revealed normal karyotype in the placenta. In a case of umbilical cord cytogenetic analysis, Pfeiffer et al. [18] detected mosaic i(20q) in the umbilical cord.

There is cytogenetic discrepancy between uncultured and cultured amniocytes in mosaic i(20q) detected at amniocentesis [3–6,20,22,23]. Robinson et al. [21] suggested that the i(20q) at amniocentesis arises due to a postzygotic error, and its growth persists *in vitro* in a few specific cell types of amniocytes. Mosaic i(20q) at amniocentesis is a benign condition associated with a favorable outcome in most cases and can be a cell culture artifact confined to cultured amniocytes. Molecular cytogenetic analysis using uncultured amniocytes is useful for rapid confirmation under such a circumstance. Prenatal diagnosis of very high percentage of mosaicism for i(20q) at amniocentesis should alert the presence of fetal structural abnormalities. Prenatal diagnosis of mosaic i(20q) at amniocentesis should include a detail examination of fetal brain and spine.

Conflicts of interest

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

Acknowledgements

This work was supported by research grant MOST-107-2314-B-195-005 from the Ministry of Science and Technology and MMH-E-108-04 from MacKay Memorial Hospital, Taipei, Taiwan.

References

- [1] Chen C-P. Detection of mosaic isochromosome 20q in amniotic fluid in a pregnancy with fetal arthrogryposis multiplex congenita and normal karyotype in fetal blood and postnatal samples of placenta, skin, and liver. *Prenat Diagn* 2003;23:85–7.
- [2] Chen C-P. Second-trimester diagnosis of mosaic idic(20)(p11) confined to amniocytes without an abnormal phenotype. *Genet Couns* 2003;14:439–41.
- [3] Chen C-P, Liou J-D, Chiang C-H, Su Y-N, Chern S-R, Tsai F-J, et al. Cytogenetic discrepancy between uncultured amniocytes and cultured amniocytes in mosaic isochromosome 20q detected at amniocentesis. *Taiwan J Obstet Gynecol* 2011;50:245–8.
- [4] Chen C-P, Chang S-D, Chen Y-T, Su J-W, Town D-D, Wang W. Mosaic isochromosome 20q detected at amniocentesis: a likely cell culture artifact. *Taiwan J Obstet Gynecol* 2012;51:663–5.
- [5] Chen C-P, Chern S-R, Wu P-S, Su J-W, Chen Y-T, Chen L-F, et al. Application of interphase fluorescence *in situ* hybridization to uncultured amniocytes for differential diagnosis of pseudomosaicism from true mosaicism in mosaic isochromosome 20q detected at amniocentesis. *Taiwan J Obstet Gynecol* 2013;52:450–3.
- [6] Chen C-P, Su J-W, Chern S-R, Kuo Y-L, Wu P-S, Lee M-S, et al. Detection of no isochromosome 20q by interphase fluorescent *in situ* hybridization on uncultured amniocytes in a pregnancy with mosaic isochromosome 20q in cultured amniocytes at amniocentesis. *Taiwan J Obstet Gynecol* 2015;54:58–61.
- [7] Chodirker BN, Jenkins R. Mosaic isochromosome 20q found on amniocentesis with normal outcome. *Prenat Diagn* 1990;10:469–72.
- [8] Begleiter ML, Lim C, Thorp JA. Mosaic isochromosome 20q. *Prenat Diagn* 1991;11:278.
- [9] Priest JH, Sanders TL, Brown AL, May KM. Prenatal diagnosis of mosaic isochromosome 20q. *Prenat Diagn* 1991;11:137.
- [10] Richkind KE, Mahoney MJ, Evans MI, Willner J, Douglass R. Prenatal diagnosis and outcomes of five cases of mosaicism for an isochromosome of 20q. *Prenat Diagn* 1991;11:371–6.
- [11] Chernos JE, McLeod DR, Cox DM. Prenatal diagnosis of mosaic isochromosome 20q associated with an abnormal phenotype. *Am J Hum Genet* 1992;51:A288.

- [12] Djalali M, Barbi G, Grab D. A further case of mosaic isochromosome 20q detected in amniotic fluid cells. *Prenat Diagn* 1992;12:71–2.
- [13] Cooper C, Fifer A, Ocrafft K. A further case of prenatally detected mosaic isochromosome 20q. *Prenat Diagn* 1993;13:226.
- [14] Kershner MA, Donnenfeld AE. A second report of normal outcome with mosaic isochromosome 20q found on amniocentesis. *Prenat Diagn* 1991;11:487.
- [15] Donnenfeld AE, Kershner MA. Significance of mosaic isochromosome 20q on amniocentesis. *Am J Med Genet* 1993;47:1196–7.
- [16] Hsu LYF, Yu M-T, Richkind KE, Van Dyke DL, Crandall BF, Saxe DF, et al. Incidence and significance of chromosome mosaicism involving an autosomal structural abnormality diagnosed prenatally through amniocentesis: a collaborative study. *Prenat Diagn* 1996;16:1–28.
- [17] Dupont J-M, Le Tessier D, Baverel F, Rouffet A, Rabineau D. Mosaic isochromosome 20q and normal outcome: a new case ascertained by fluorescence in situ hybridization and a review of the literature. *Fetal Diagn Ther* 1997;12:283–5.
- [18] Pfeiffer RA, Ulmer R, Rauch A, Trautmann U, Beinder E, Rupprecht T, et al. True fetal mosaicism of an isochromosome of the long arm of a chromosome 20: the dilemma persists. *Prenat Diagn* 1997;17:1171–5.
- [19] Storto P, Diehn T. An additional report of prenatal detection of mosaic isochromosome 20q at amniocentesis. *Prenat Diagn* 1997;17:89–90.
- [20] Goumy C, Beaufrère AM, Francannet C, Tchirkov A, Laurichesse Delmas H, Geissler F, et al. Prenatal detection of mosaic isochromosome 20q: a fourth report with abnormal phenotype. *Prenat Diagn* 2005;25:653–5.
- [21] Robinson WP, McGillivray B, Friedman JM. Pregnancy and postnatal outcome of mosaic isochromosome 20q. *Prenat Diagn* 2007;27:143–5.
- [22] Receveur A, Brisset S, Martinovic J, Bazin A, Lhomann L, Colmant C, et al. Prenatal diagnosis of isochromosome 20q in a fetus with vertebral anomaly and rocker-bottom feet. *Taiwan J Obstet Gynecol* 2017;56:677–80.
- [23] Chen C-P, Chern S-R, Wu P-S, Chen S-W, Wu F-T, Town D-D, et al. Mosaic isochromosome 20q at amniocentesis: prenatal diagnosis, genetic counseling and literature review. *Taiwan J Obstet Gynecol* 2019;58:855–8.