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Case Report

Rapid diagnosis of pseudomosaicism in a case of Level II mosaicism for trisomy 5 in a single colony from an *in situ* culture of amniocytes and a review of mosaic trisomy 5 at amniocentesis

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ABSTRACT

Objective: We present prenatal diagnosis of pseudomosaicism for trisomy 5 and a review of the literature of mosaic trisomy 5 at amniocentesis.

Case Report: A 39-year-old woman underwent amniocentesis at 17 weeks of gestation, which revealed a karyotype of 47,XY,+5[1]/46,XY[20]. The single colony with trisomy 5 had five metaphase cells, and all five cells had the karyotype of 47,XY,+5. Repeat amniocentesis performed at 20 weeks of gestation revealed a karyotype of 46,XY in 27/27 colonies. Simultaneously, interphase fluorescence *in situ* hybridization (FISH), array comparative genomic hybridization (aCGH), and quantitative fluorescent polymerase chain reaction (QF-PCR) were performed on uncultured amniocytes. Interphase FISH revealed no trisomy 5 in 100 uncultured amniocytes. aCGH revealed no genomic imbalance. QF-PCR excluded uniparental disomy 5. A healthy 3662-g male baby was delivered with a normal karyotype in cord blood and 3.75% (3/80 cells) of trisomy 5 cells in uncultured urinary cells compared with 0.95% (1/105 cells) of trisomy 5 cells in normal control examined by FISH at 1.5 months of age. A review of seven cases with mosaic trisomy 5 at amniocentesis shows that 4/7 had clinically normal outcome, 3/7 had structural defects, mainly the heart, 6/6 had normal karyotype in blood, and 2/3 had mosaic trisomy 5 in the fetal tissues.

Conclusion: Prenatal diagnosis of mosaic trisomy 5 should alert the possibility of fetal structural abnormalities, especially the heart, and culture artifacts. We suggest that the application of molecular cytogenetic techniques such as aCGH, interphase FISH, and QF-PCR on uncultured amniocytes is useful in our understanding of the mosaic status at repeat amniocentesis.

Introduction

We previously reported the application of interphase fluorescence *in situ* hybridization (FISH) on uncultured amniocytes at repeat amniocentesis for rapid diagnosis of true mosaicism in a case of Level II mosaicism involving trisomy 21 in a single colony from an *in situ* culture of amniocytes [1]. In this case report, we additionally demonstrate the usefulness of performing interphase FISH and array comparative genomic hybridization (aCGH) on uncultured amniocytes at repeat amniocentesis for rapid diagnosis of pseudomosaicism in a case of Level II mosaicism for trisomy 5 in a single colony from an *in situ* culture of amniocytes at prenatal diagnosis.

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Case Report

A 39-year-old, Gravid 3, Para 2, woman underwent amniocentesis at 17 weeks of gestation because of advanced maternal age. Cytogenetic analysis of cultured amniocytes revealed Level II mosaicism for trisomy 5 and a karyotype of 47,XY,+5[1]/46,XY[20]. Of the 21 colonies of cultured amniocytes, only one colony had the karyotype of 47,XY,+5, whereas the other 20 colonies had the karyotype of 46,XY. The single colony with trisomy 5 had five metaphase cells, and all these five cells had the karyotype of 47,XY,+5. The father had a karyotype of 46,XY and the mother had a karyotype of 46,XX. Prenatal ultrasound findings were unremarkable. At 20 weeks of gestation, the woman underwent repeat amniocentesis. Interphase FISH and aCGH were performed on uncultured amniocytes, and conventional cytogenetic analysis was performed on cultured amniocytes. Polymorphic DNA marker analysis by quantitative fluorescent polymerase chain reaction (QF-PCR) was performed on the DNAs extracted from uncultured amniocytes and parental blood samples. aCGH on uncultured amniocytes using CytoScan 750K array (Affymetrix, Santa Clara, CA, USA) showed no genomic imbalance. Interphase FISH on uncultured amniocytes using a 5p15.33-specific probe (RP11-325I22, dye: fluorescein isothiocyanate, green, 1,318,107–1,509,826) [hg 19] and a 5p11-specific probe (RP11-489A19, dye: Texas Red, red, 46,155,848–46,356,409) [hg 19] showed two green signals and two red signals in all 100 interphase cells examined. For the probe RP11-325I22, the normal control case had a positive result of three signals in 1/105 cells, and for the probe RP11-489A19, the normal control case had a positive result of three signals in 1/105 cells. Cytogenetic analysis of cultured amniocytes at repeated amniocentesis revealed a karyotype of 46,XY in all of the 27 colonies. QF-PCR using the informative marker of D5S592 (5q23.1) excluded uniparental disomy 5. A healthy 3662-g male baby was delivered at 38 weeks of gestation. The cord blood had a karyotype of 46,XY in 40/40 of cultured lymphocytes. The neonate was normal at the age of 1.5 months at postnatal follow-ups. Interphase FISH analysis of uncultured urinary cells at 1.5 months of age revealed 3.75% (3/80 cells) of trisomy 5 cells in uncultured urinary cells compared with 0.95% (1/105 cells) of trisomy 5 cells in normal control using this FISH probe.

Discussion

Mosaic trisomy 5 at amniocentesis is very rare. To date, at least seven cases with mosaic trisomy 5 at amniocentesis had been reported [2–8]. Richkind et al [2] first reported prenatal detection of mosaic trisomy 5 (78.9% in 38 colonies and 81.3% in 16 colonies, respectively, in two samplings) by amniocentesis in a fetus with normal outcome. The neonate was normal at 6 months of age. No trisomy 5 was found in cord blood and foreskin. Penchaszadeh et al [3] reported prenatal diagnosis of mosaic trisomy 5 (18/45 cells = 40%) by amniocentesis in a fetus. The blood karyotype was normal. The neonate postnatally manifested low birth weight, systolic murmur, and preauricular pit. Casamassima et al [4] reported prenatal diagnosis of mosaic trisomy 5 (14/60 cells = 23%) by amniocentesis in a fetus with no mosaicism in the cord blood sample and a clinically normal outcome. Sciorra et al [5] reported prenatal diagnosis of mosaic trisomy 5 (6/24 cells = 25%) by amniocentesis in a fetus with no mosaicism in the cord blood at cord blood sampling. The neonate postnatally manifested multiple dysmorphic features and congenital anomalies including eventration of the diaphragm and ventricular septal defect. Mosaic trisomy 5 (8/40 cells = 20%) was found in the skin fibroblasts of the neonate. The cord blood karyotype was 46,XY (106/106 cells). Hsu et al [6] reported prenatal diagnosis of mosaic trisomy 5 (6.7% in 30 cells) by amniocentesis in a fetus. The neonate was normal after birth. Villa et al [7] reported prenatal diagnosis of mosaic trisomy 5 (5/46 colonies = 10.9%) by amniocentesis in a fetus with a normal karyotype in the blood. The neonate had normal psychomotor development but growth parameters less than the 3rd centile. Brown et al [8] reported prenatal diagnosis of mosaic trisomy 5 (50% mosaicism) by amniocentesis in a fetus with congenital heart defect, agenesis of the corpus callosum, and a cloverleaf skull. Mosaic trisomy 5 was found in fetal tissues, except the blood tissue which had a normal karyotype. A review of the literature shows that among the seven reported cases of mosaic trisomy 5 detected by amniocentesis, 4/7 had clinically normal outcome, and 3/7 had structural defects, mainly ventricular septal defect; and 6/6 had normal karyotype in the blood when blood cytogenetic analysis was performed, and 2/3 had mosaic trisomy 5 in the fetal tissues other than blood when tissue sampling was performed.

In summary, we presented a review of mosaic trisomy 5 at amniocentesis. Prenatal diagnosis of mosaic trisomy 5 should alert the possibility of fetal structural abnormalities, especially the heart, and culture artifacts. We suggest that the application of molecular cytogenetic techniques such as aCGH, interphase FISH, and QF-PCR on uncultured amniocytes is useful in our understanding of the mosaic status at repeat amniocentesis.

Conflict of interest

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

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References

[1] Chen CP, Wang PT, Lin SP, Chern SR, Chen YT, Wu PS, et al. Interphase FISH on uncultured amniocytes at repeat amniocentesis for rapid diagnosis of true mosaicism in a case of level II mosaicism involving trisomy 21 in a single colony from an *in situ* culture of amniocytes. Taiwan J Obstet Gynecol 2014;53:120–2.
[2] Richkind KE, Apostol RA, Puck SM. Prenatal detection of trisomy 5 mosaicism with normal outcome. Prenat Diagn 1987;7:143.
[3] Penchaszadeh VB, Morejon DP, Gervis J, Schwartz M, Mahoney MJ, Babu A. Prenatally detected trisomy 5 mosaicism in amniotic fluid confirmed in the newborn. Am J Hum Genet 1988;43:A64 [Abstract].
[4] Casamassima AC, Wilmot PL, Mahoney MJ, Scott RV, Shapiro LR. Trisomy 5 mosaicism in amniotic fluid with normal outcome. Clin Genet 1989;35:282–4.
[5] Sciorra LJ, Hux C, Day-Salvadore D, Lee ML, Mandelbaum DE, Brady-Yasbin S, et al. Trisomy 5 mosaicism detected prenatally with an affected liveborn. Prenat Diagn 1992;12:477–82.
[6] Hsu LY, Yu MT, Neu RL, Van Dyke DL, Benn PA, Bradshaw CL, et al. Rare trisomy mosaicism diagnosed in amniocytes, involving an autosome other than chromosomes 13, 18, 20, and 21: karyotype/phenotype correlations. Prenat Diagn 1997;17:201–42.
[7] Villa N, Redaelli S, Borroni C, Colombo C, Roncaglia N, Sala E, et al. Fetal trisomy 5 mosaicism: case report and literature review. Am J Med Genet A 2007;143A:2343–6.
[8] Brown S, Higgins S, Hutchinson R, Bain S, Moore L, Haan E. A case of mosaicism for trisomy of chromosome 5 detected at amniocentesis. Twin Res Hum Genet 2009;12:210.