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Research Letter

Discrepancy in the trisomy mosaicism level between cultured amniocytes and uncultured amniocytes in prenatally detected mosaic trisomy 20

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A gravida 2, para 1 woman 35 years of age underwent amniocentesis at 16 weeks of gestation because of advanced maternal age. Cytogenetic analysis of cultured amniocytes revealed a karyotype of 47,XY,+20[26]/46,XY[9]. Among 35 colonies of cultured amniocytes investigated by *in situ* cultured method, 26 colonies had a karyotype of 47,XY,+20, while nine colonies had a karyotype of 46,XY. The level of trisomy in the cultured amniocytes was 74.3% (26/35). She was referred to the hospital for rapid positive confirmation of mosaic trisomy 20 at 23 weeks of gestation, and repeated amniocentesis was performed. Interphase fluorescence *in situ* hybridization (FISH) analysis using the bacterial artificial chromosome (BAC) clone probe RP11-2E8 (20p12.2) showed three 20p-specific signals in 10% (5/50) of the uncultured amniocytes and two 20p-specific signals in 90% (45/50) of the uncultured amniocytes, indicating 10% mosaicism for trisomy 20 in the uncultured amniocytes (Fig. 1). Quantitative fluorescent polymerase chain reaction (QF-PCR) analysis on the uncultured amniocytes showed equal fluorescent activity from two different parental alleles. Array comparative genomic hybridization (aCGH) analysis on the uncultured amniocytes revealed no gene dosage change on chromosome 20. The cultured amniocytes in the repeated amniocentesis had a karyotype of 47,XY,+20[16]/46,XY[19]. Among the 35 colonies of cultured amniocytes investigated by *in situ* cultured method, 16 colonies had a karyotype of 47,XY,+20, while 19 colonies had a karyotype of 46,XY. The level of trisomy in the cultured amniocytes of the repeated amniocentesis was 45.7% (16/35). Prenatal ultrasonographic findings were unremarkable. After genetic counseling, the parents elected to continue the pregnancy. A 3290-g healthy male baby was delivered at 38 weeks of gestation. Postnatal cytogenetic analysis revealed a karyotype of 46,XY in 60/60 of cord blood lymphocytes, 40/40 of umbilical cord fibroblasts, 40/40 of chorionic villi cells, and 40/40 of amniotic membrane fibroblasts. Interphase FISH analysis of the uncultured urinary cells using the BAC clone probe showed two 20p-specific signals in 100% (27/27) of urinary cells, indicating 0% of trisomy 20 in the urine. The baby was doing well, and there was no phenotypic abnormality at the age of 10 months.

Application of molecular cytogenetic techniques on uncultured amniocytes in prenatal diagnosis of trisomy mosaicism has been well described [1–6]. In addition, the present case demonstrates the usefulness of interphase FISH, QF-PCR, and aCGH on uncultured amniocytes in rapid positive confirmation of trisomy 20 mosaicism. The present case provides evidence for the discrepancy in the trisomy mosaicism level between cultured amniocytes and uncultured amniocytes in prenatally detected mosaic trisomy 20.

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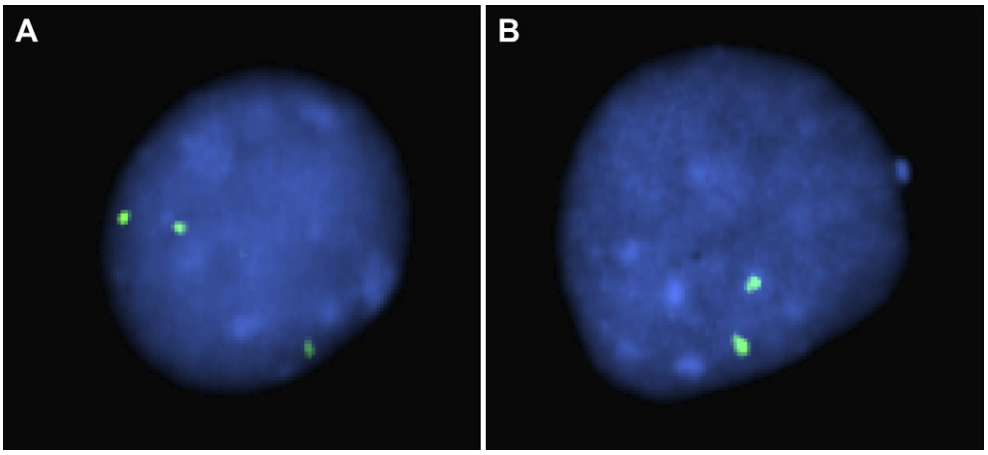

Fig. 1. Interphase fluorescence *in situ* hybridization analysis on uncultured amniocytes using a bacterial artificial chromosome clone probe RP11-2E8 (20p12.2) (green spectrum) shows (A) three green signals in an abnormal cell with trisomy 20; and (B) two green signals in a normal cell with disomy 20.

Mosaic trisomy 20 is one of the most commonly observed mosaic trisomies at amniocentesis, and it has been reported to be associated with grossly normal phenotype in approximately 90% of cases [7]. Genetic counseling of mosaic trisomy 20 at amniocentesis remains a challenge despite various suggested considerations, because all the reported suggestions have been based on observations of the trisomy mosaicism levels in cultured amniocytes [8–11]. In a study of 152 cases with mosaic trisomy 20 at amniocentesis, Wallerstein et al [8] found abnormal outcome in 20% (4/20) of the pregnancies with greater than 50% trisomy 20 cells and in 4.5% (6/132) of the pregnancies with less than 50% trisomy 20 cells. In a meta-analysis of published cases, Robinson et al [9] concluded that there is a clear association with the trisomy mosaicism level at amniocentesis and fetal outcome. Robinson et al [9] found abnormal outcome in 50% (5/10) of the pregnancies with greater than 80% trisomy 20 cells, 28% (17/61) of the pregnancies with greater than 40% trisomy 20 cells, and 4% (8/201) of the pregnancies with less than 40% trisomy 20 cells. However, Bianca et al [10,11] suggested a contradictory proposal insomuch that they suggested trisomy mosaicism levels do not influence the outcome in prenatally detected mosaic trisomy 20, thereby a second amniocentesis would add little value to genetic counseling.

The present case shows that the mosaic level may change after long-term tissue cultures in amniotic fluid with trisomy 20 amniocytes. The present case also suggests that uncultured amniocytes can be considered as a useful tool for confirmation of the presence of a true fetal mosaicism, and a correlation of low-level trisomy 20 mosaicism of uncultured amniocytes may exist with favorable fetal outcomes in pregnancies with prenatally detected mosaic trisomy 20.

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