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Research Letter

Prenatal diagnosis of low-level mosaicism for trisomy 18 associated with a favorable fetal outcome

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Dear Editor,

A 33-year-old, gravida 5, para 1, woman underwent amniocentesis at 22 weeks of gestation because of an abnormal maternal serum screening result indicating Down syndrome risk of 1/212. Amniocentesis revealed a karyotype of 47,XY,+18[2]/46,XY[28]. Among 30 colonies of cultured amniocytes, two had a karyotype of 47,XY,+18, whereas the remaining 28 colonies had a karyotype of 46,XY. The mosaic trisomy 18 level in the cultured amniocytes was 6.7%. Prenatal ultrasound findings were unremarkable. The parental karyotypes were normal. Repeat amniocentesis was performed at 24 weeks of gestation. Simultaneous molecular cytogenetic analyses were performed on uncultured amniocytes using array comparative genomic hybridization, interphase fluorescence *in situ* hybridization, and quantitative fluorescent polymerase chain reaction. Cytogenetic analysis of cultured amniocytes at repeat amniocentesis revealed a karyotype of 46,XY in 32/32 colonies. Array comparative genomic hybridization analysis of the DNA extracted from uncultured amniocytes using CytoChip ISCA Array (Illumina, San Diego, CA, USA) revealed no genomic imbalance in chromosome 18. Quantitative fluorescent polymerase chain reaction analysis using the DNAs extracted from the uncultured amniocytes and the parental peripheral bloods excluded uniparental disomy 18. Interphase fluorescence *in situ* hybridization analysis on 80 uncultured amniocytes using the bacterial artificial chromosome probe of RP11-467D2 (18q12.1, fluorescein isothiocyanate) and RP11-184J20 (18q22.2, Texas Red) detected two cells with trisomy 18 consistent with a mosaic trisomy 18 level of 2.5% (2/80 cells), compared with 1.8% (2/109 cells) in the normal control for RP11-467D2 and 5.2% (5/97 cells) in the normal control for RP11-184J20. At 36 weeks of gestation, a 2478-g male baby was delivered uneventfully. The cord blood had a karyotype of 46,XY in 40/40 cells. The neonate was phenotypically normal during follow-ups at the age of 8 months.

Mosaic trisomy 18 accounts for approximately 5% of trisomy 18 cases [1], and the phenotypic findings of individuals with mosaic trisomy 18 vary from complete trisomy 18 to no dysmorphism and normal intelligence [2–5]. In a review of 33 cases of mosaic trisomy 18, Tucker et al [3] concluded that there is no correlation between the trisomy percentage in either fibroblasts or leukocytes and the patient's phenotype or intellectual function. Asymptomatic adults with mosaic trisomy 18 may be detected to carry trisomy 18 mosaicism because of infertility [2,6], recurrent abortions [7,8], delivery of a child with trisomy 18 [9–11], bone marrow donation [12], and premature ovarian failure [3,13]. Prenatal diagnosis of recurrent trisomy 18 in a family should alert the physician to the possibility of mosaic trisomy 18 in the parents [2,3,10,11,14]. In cases with mosaic trisomy 18, there may be a significant discrepancy between the levels of mosaicism for trisomy 18 in different tissues, i.e., high-level mosaic trisomy 18 in blood lymphocytes but low-level mosaic trisomy 18 in skin fibroblasts [3–5].

The present case provides the evidence that low-level mosaic trisomy 18 at amniocentesis with normal prenatal ultrasound can be associated with a favorable fetal outcome. The present case also shows that interphase fluorescence *in situ* hybridization and array comparative genomic hybridization on uncultured amniocytes are useful for rapid confirmation of low-level mosaic trisomy 18 at

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repeat amniocentesis, and quantitative fluorescent polymerase chain reaction is useful for rapid exclusion of uniparental disomy 18.

Conflicts of interest

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

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