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Research Letter

Prenatal diagnosis of low-level mosaicism for trisomy 12 associated with a favorable pregnancy outcome

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Dear Editor,

A 34-year-old, gravida 4, para 1, woman underwent amniocentesis at 18 weeks of gestation because of advanced maternal age. Amniocentesis revealed a karyotype of 47,XY,+12[2]/46,XY[20]. Among 22 colonies of cultured amniocytes, two colonies had a karyotype of 47,XY,+12, whereas the remaining 20 colonies had a karyotype of 46,XY. The mosaic trisomy 12 level in the cultured amniocytes was 9%. Prenatal ultrasound findings were unremarkable. The parental karyotypes were normal. Repeat amniocentesis was performed at 20 weeks of gestation. Simultaneous molecular cytogenetic analyses were performed on uncultured amniocytes using array comparative genomic hybridization, interphase fluorescence *in situ* hybridization (FISH), and quantitative fluorescent polymerase chain reaction. Cytogenetic analysis of cultured amniocytes at repeat amniocentesis revealed a karyotype of 46,XY in 38/38 colonies. Array comparative genomic hybridization analysis of the DNA extracted from uncultured amniocytes using CytoScan 750K Array (Affymetrix, California, CA, USA) revealed no genomic imbalance. Quantitative fluorescent polymerase chain reaction analysis using the DNAs extracted from the uncultured amniocytes and the parental peripheral bloods excluded uniparental disomy 12. Interphase FISH analysis on 107 uncultured amniocytes using the bacterial artificial chromosome probe of RP11-244D12 (12p11.22, fluorescein isothiocyanate, spectrum green) and RP11-627E5 (12q24.33, Texas Red, spectrum red) detected seven cells with trisomy 12, consistent with a mosaic trisomy 12 level of 6.5% (7/107 cells) compared with 1.9% (2/104 cells) in the normal control. The parents elected to continue the pregnancy. At 38 weeks of gestation, a 4100-g (97th centile) male baby, with a body length of 52 cm (97th centile), was delivered uneventfully by cesarean section. Peripheral blood analysis at the age of 6 months revealed a karyotype of 46,XY in 40/40 lymphocytes. Interphase FISH analysis of urinary cells revealed a mosaic trisomy 12 level of 2.7% (1/37 urinary cells) compared with 0% (0/40 urinary cells) in the normal control. The neonate was phenotypically normal during follow-ups at the age of 8 months, with a body weight of 8400 g (25–50th centile) and a body length of 67 cm (5th centile).

The present case provides the evidence that low-level mosaic trisomy 12 at amniocentesis with normal prenatal ultrasound can be associated with a favorable pregnancy outcome. The present case also shows that interphase FISH and array comparative genomic hybridization on uncultured amniocytes are useful for rapid confirmation of low-level mosaic trisomy 12 at repeat amniocentesis, and quantitative fluorescent polymerase chain reaction is useful for rapid exclusion of uniparental disomy 12. In a review of 32 cases of mosaic trisomy 12 detected by amniocentesis, Chen et al [1] reported that at least 28.1% (9/32) cases were associated with prominent phenotypic abnormalities, and there is a correlation between a higher mosaic trisomy 12 level and an abnormal fetal outcome. The observed abnormal ultrasound findings included polyhydramnios, intrauterine growth restriction, single umbilical artery, congenital heart defects, hydronephrosis, and absence of stomach image [1].

Chen et al [2] previously reported congenital overgrowth associated with prenatally detected mosaic trisomy 12. Congenital overgrowth has been well described in cases with Pallister–Killian

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syndrome or mosaic tetrasomy 12p [3–5] and in cases with 12q duplication syndrome [6,7]. Our case manifested prenatal fetal overgrowth but no postnatal overgrowth syndrome.

Complete trisomy 12 has been reported to be associated with craniofacial abnormalities on prenatal ultrasound and the postmortem findings of absent hypophysis gland, absent olfactory pathways, absent bilateral adrenal glands, and central nervous system anomalies, and may manifest Pallister–Killian syndrome (mosaic tetrasomy 12p), trisomy 12p syndrome, trisomy 12q syndrome, and mosaic trisomy 12 syndrome [8,9]. Therefore, a prenatal diagnosis of mosaic trisomy 12 should alert a clinically significant aneuploidy.

In summary, we present prenatal diagnosis and molecular cytogenetic analysis of mosaic trisomy 12 using uncultured and cultured amniocytes in a pregnancy with a favorable fetal outcome.

Conflicts of interest

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

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