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Research Letter

# Prenatal diagnosis of low-level trisomy 3 mosaicism

Wenjuan Tang [a, 1], Yijun Wu [b, 1], Jie Liu [c, 1], Wei Ren [d, *]

[a] Department of Maternal Health Care, Shiyan Maternal and Child Health Hospital, Shiyan, Hubei, China
[b] Department of Obstetrics, Huanggang Central Hospital, Huanggang, Hubei, China
[c] Center of Reproductive Medicine, Hubei Maternal and Child Health Hospital, Wuhan, Hubei, China
[d] Department of Obstetrics, Hubei Maternal and Child Health Hospital, Wuhan, Hubei, China

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*To the Editor,*

Low-level chromosome mosaicism found at amniocentesis is problematic for clinicians and patients. We report the prenatal diagnosis of a fetus with low-level trisomy 3 mosaicism.

A 34-year-old primigravid woman underwent amniocentesis at 19 weeks of gestation owing to a Down's syndrome risk of 1/150, which was calculated from a maternal serum alpha-fetoprotein level of 0.84 multiples of the median (MOM), a total human chorionic gonadotrophin level of 1.47 MOM, and a serum unconjugated estriol (uE3) level of 0.65 MOM. Conventional karyotyping revealed a rare karyotype of 47,XX,+3 in 3/35 cultured amniocytes. However, both parental karyotypes were normal. Array comparative genomic hybridization (aCGH) analysis on uncultured amniocytes revealed 10% mosaicism for trisomy 3 (Figure 1) [1]. Interphase fluorescence *in situ* hybridization (FISH) analysis on uncultured amniocytes revealed 8% mosaicism for trisomy 3 [2]. Periumbilical blood sampling (PUBS) and a repeat amniocentesis were performed at 30 weeks of gestation. PUBS showed 46,XX in 50/50 cultured lymphocytes. Simultaneous aCGH analysis using uncultured cord blood lymphocytes revealed no pathogenic microdeletion or microduplication. Interphase FISH analysis on uncultured cord blood lymphocytes revealed mosaic trisomy 3 in 3/200 cells. Ultrasound examination showed no facial dysmorphisms and intrauterine growth restrictions (IUGRs) in the fetus. The parents decided to continue the pregnancy. At 40 weeks of gestation, a 3250-g female baby was delivered naturally. The baby had normal physical findings at birth. At delivery, chromosome analysis from 50 peripheral blood lymphocytes revealed 46,XX in all cells. At 1 year of age, the baby was progressing normally.

Trisomy 3 mosaic is a rare autosomal trisomy with only four cases previously detected by amniocentesis [3–5]. The term "mosaic" indicates that some cells contain the extra chromosome 3, where others have the normal chromosomal pair. The present case shows that the mosaic level may change after long-term tissue cultures in amniotic fluid with trisomy 3 amniocytes. Conventional cytogenetic analysis on the cultured amniocytes revealed 3% (3/35 cells) mosaicism for trisomy 3. In contrast, aCGH and FISH on uncultured amniocytes showed 10% and 8% mosaicism for trisomy 3, respectively. This suggests that uncultured amniocytes can be considered a useful tool for rapid confirmation of the presence of low-level mosaic trisomy 3. The level of trisomy mosaicism detected on amniocentesis might be associated with fetal outcome. Hsu et al [3] reviewed two reported cases of trisomy 3 mosaicism detected on amniocentesis. One case with 5% trisomy 3 cells resulted in a normal outcome [3]. The other case with 36% trisomy 3 cells resulted in a child with multiple congenital anomalies who died at 18 months because of a congenital heart disease [3]. Zaslav et al [4] reported a case with 22% of trisomy 3 cells. Sheath et al [5] reported a case with 16% of trisomy 3 cells detected on amniocentesis. In both cases, babies were delivered at 34 weeks of gestation because of severe IUGR on ultrasound scan, but both resulted in a normal outcome. The present case with 10% trisomy 3 cells also resulted in a normal outcome. In contrast to previous cases, prenatal ultrasound showed no fetal abnormalities on ultrasound scan in the present case. Therefore, combination of prenatal ultrasound and amniocentesis will prove a more accurate risk assessment for trisomy 3 mosaicism.

* Corresponding author. Department of Obstetrics, Hubei Maternal and Child Health Hospital, 745 WuLuo Road, HongShan District, Wuhan, Hubei, 430070, China.
*E-mail address:* wangbo1005@163.com (W. Ren).
[1] These authors contributed equally to this work.

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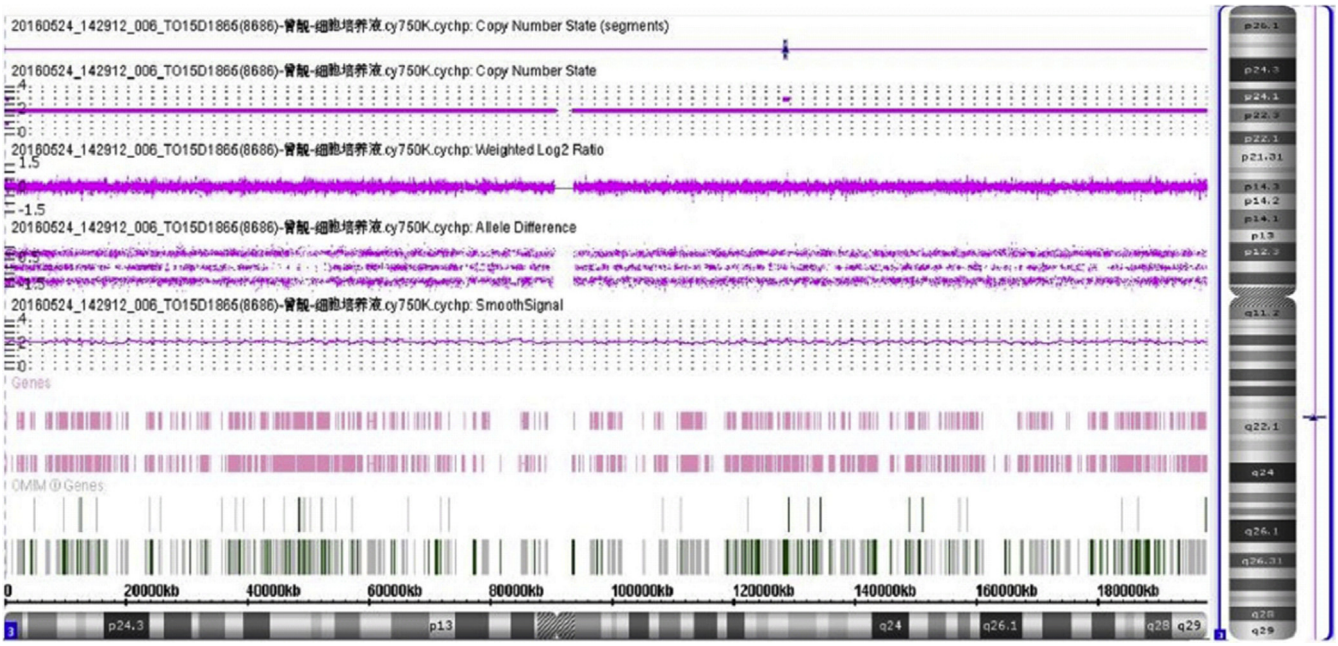


**Figure 1.** aCGH analysis revealed a 197.8-Mb duplication on chromosome 3p26.1-q29 [arr (3) × 2.20]. aCGH = array comparative genomic hybridization.

## Conflicts of interest

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

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