Short Communication

Mosaic tetrasomy 9p at amniocentesis: Prenatal diagnosis, molecular cytogenetic characterization, and literature review

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A R T I C L E    I N F O

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A B S T R A C T

Objective: This study was aimed at prenatal diagnosis of mosaic tetrasomy 9p and reviewing the literature.

Materials and methods: A 37-year-old woman underwent amniocentesis at 20 weeks' gestation because of advanced maternal age and fetal ascites. Cytogenetic analysis of cultured amniocytes revealed 21.4% (6/28 colonies) mosaicism for a supernumerary i(9p). Repeat amniocentesis was performed at 23 weeks' gestation. Array comparative genomic hybridization, interphase fluorescence in situ hybridization, and quantitative fluorescent polymerase chain reaction were applied to uncultured amniocytes, and conventional cytogenetic analysis was applied to cultured amniocytes.

Results: Array comparative genomic hybridization analysis of uncultured amniocytes detected a genomic gain at 9p24.3 e 9q21.11. Interphase fluorescence in situ hybridization analysis of uncultured amniocytes using a 9p24.3-specific probe RP11-31F19 (spectrum red) showed four red signals in 47.1% (49/104 cells) in uncultured amniocytes. Cytogenetic analysis of cultured amniocytes revealed a karyotype of 47,XX,þ idic(9)(pter→q21.11::q21.11→pter)[4]/46,XX[20] and 16.7% (4/24 colonies) mosaicism for tetrasomy 9p. Quantitative fluorescent polymerase chain reaction confirmed a maternal origin of tetrasomy 9p. The pregnancy was terminated, and a malformed fetus was delivered with hydrops fetalis and facial dysmorphism. The fetal blood cells had 32.5% (13/40 cells) mosaicism for tetrasomy 9p.

Conclusion: Mosaic tetrasomy 9p at amniocentesis can be associated with fetal ascites and hydrops fetalis. The mosaic level of tetrasomy 9p may decrease after long-term tissue culture in amniocytes in case of mosaic tetrasomy 9p.

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Introduction

Tetrasomy 9p, or supernumerary isochromosome 9p [i(9p)], is a rare chromosome abnormality resulting from a supernumerary isochromosome 9p that may involve the entire 9p only; the entire 9p with part of the heterochromatic region of 9q; or the entire 9p with heterochromatic region of 9q and part of the euchromatic region of 9q [1,2].

Tetrasomy 9p has been characterized by clinical features of intrauterine growth restriction (IUGR), developmental delay, ventriculomegaly, Dandy–Walker malformation, facial dysmorphism of a bulbous/beaked nose, hypertelorism, micrognathia, ear malformations, and cleft lip/palate, congenital heart defects, hyoplasia of the digits and nails, joint dislocations, and urogenital abnormalities; and the severity of phenotype associated with

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tetrasomy 9p is influenced by the size of the isochromosome involved, the degree of mosaicism, and the presence of tissue mosaicism [1,3–12].

Prenatal diagnosis of mosaic or nonmosaic tetrasomy 9p is uncommon [1,7–10,13–21]. The frequency of prenatally detected tetrasomy 9p at amniocentesis is estimated to be 0.002% [22]. In a population–based study of 88,965 amniocenteses, Forabosco et al [22] found eight cases with isochromosomes including three cases with i(20q), two cases with i(18p), two cases with i(9p) and one case with i(12p). Here, we present our experience of prenatal diagnosis and molecular genetic analysis of mosaic tetrasomy 9p in a fetus with fetal ascites.

Materials and methods

Clinical description

A 37-year-old, gravida 3, para 1, woman underwent amniocentesis at 20 weeks' gestation because of advanced maternal age. She was Rh-positive, and maternal blood thalassemia screening excluded thalassemia carrier status. Maternal syphilis examination was negative. She underwent first-trimester maternal serum screening and fetal nuchal translucency screening, and the results were within the normal limits. The pregnancy was uneventful until 19 weeks' gestation when routine ultrasound examination revealed fetal ascites. Amniocentesis and aspiration of fetal ascites were performed at 20 weeks' gestation. Molecular analyses of congenital infection using fetal ascites excluded infection with Toxoplasma, cytomegalovirus and herpes simplex virus. Cytogenetic analysis of cultured amniocytes revealed 21.4% (6/28) mosaicism for a supernumerary i(9p). The karyotype was 47,XX,+i(9p)[6]/46,XX [22] derived from 28 colonies of cultured amniocytes. The woman requested repeated amniocentesis at 23 weeks gestation. The nature of the supernumerary i(9p) was investigated by array comparative genomic hybridization (aCGH) on uncultured amniocytes. The degree of mosaicism for the supernumerary i(9p) in uncultured amniocytes was investigated by interphase fluorescence in situ hybridization (FISH). The parental origin of the supernumerary i(9p) was investigated by quantitative fluorescent polymerase chain reaction (QF-PCR) assays using uncultured amniocytes. Cytogenetic analysis of cultured amniocytes was also performed at repeated amniocentesis. Level II ultrasound at 24 weeks' gestation revealed IUGR with fetal biometry equivalent to 22 weeks' gestation and hydrops fetalis. The pregnancy was subsequently terminated. The fetal blood was collected for cytogenetic analysis.

Conventional cytogenetic analysis

Routine cytogenetic analysis by G-banding techniques at the 550 bands of resolution was performed. About 20 mL amniotic fluid was collected, and the sample was subjected to in situ amniocyte culture according to the standard cytogenetic protocol [23]. Parental and fetal blood was collected, and the samples were subjected to lymphocyte culture according to the standard blood cytogenetic protocol [24].

Array-CGH

Whole-genome aCGH on the DNA extracted from uncultured amniocytes was performed using NimbleGen ISCA Plus Cytogenetic Array (Roche NimbleGen, Madison, WI, USA), according to the manufacturer’s instructions. The NimbleGen ISCA Plus Cytogenetic Array has 630,000 probes and a median resolution of 15–20 kb across the entire genome. The DNA from amniocytes was extracted first. It was done by following the manufacturer’s protocol for the QIAamp DNA Mini kit (Qiagen, Valencia, CA, USA). Then, 0.5 μg of the extracted DNA was labeled with Cy5 dye compared with an equivalent amount of normal female genomic DNA (G1521; Promega) labeled with Cy3 dye to perform aCGH. The experiment was performed according to the procedures recommended in the user guide for the Roche NimbleGen ISCA plus Cytogenetic Array. The data were finally represented using Nexus 6.1 (BioDiscovery, Hawthorne, CA, USA).

QF-PCR

QF-PCR analysis was performed by using genomic DNAs extracted from uncultured amniocytes and parental blood as described previously [25]. Primers specifically flanking polymorphic markers on chromosome 9p region such as D9S2149 (9p21.1) and D9S303 (9q21.3) were applied to undertake polymorphic marker analysis and parental origin determination of the supernumerary (9p).

FISH

Interphase FISH analysis was performed on uncultured amniocytes using a 9p24.3-specific bacterial artificial chromosome probe RP11–31F19 (dye: Texas Red) (547,217–692,143) and a control 9q34.3-specific bacterial artificial chromosome probe RP11–417A4 (dye: FITC, green) (140,403,320–140,596,187) [hg 19] according to the standard FISH protocol [26].

Results

Whole-genome aCGH analysis on the DNA extracted from uncultured amniocytes detected a 71.03-Mb duplication at 9p24.3–9q21.11, or arr [hg19] 9p24.3p13.1 (0–40,450,202) × 3, 4, 9p13.1q21.11 (40,576,977–71,026,063) × 3 (Fig. 1). The log2 ratio of 9p24.3p13.1 duplication was 0.799, and the log2 ratio of 9p13.1q21.11 duplication was 0.585. The duplicated region of 9p24.3–9q21.11 contained 632 genes including 151 OMIM genes. The supernumerary i(9p) involved the entire 9p, the heterochromatic region of 9q, and part of 9q21.11 (Fig. 1). Interphase FISH analysis of 104 uncultured amniocytes using the 9p24.3-specific probe (RP11–31F19) (spectrum red) and the 9q34.3-specific probe (RP11–417A4) (spectrum green) showed four red signals and two green signals in 49 uncultured amniocytes, and two red signals and two green signals in 55 uncultured amniocytes, indicating 47.1% (49/104 cells) mosaicism for supernumerary i(9p) in uncultured amniocytes (Fig. 2). Cytogenetic analysis of 24 colonies of cultured amniocytes revealed four colonies with a supernumerary i(9p) and 20 colonies with a normal female karyotype. The karyotype of cultured amniocytes was 47,XX,+i(9)p[4]/46,XX [20] (Fig. 3). Cytogenetic analysis of 40 cultured lymphocytes of fetal blood showed a karyotype of 47,XX,+i(9)p[4]/46,XX [27]. The maternal blood had a karyotype of 46,XY. The maternal blood had a karyotype of 46,XX. QF-PCR analysis on the DNAs extracted from uncultured amniocytes and parental blood confirmed a maternal origin of the supernumerary i(9p) (Fig. 4). The parents decided to terminate the pregnancy. A 722-g female fetus was delivered with hydrops fetalis, hypertelorism, a bulbous nose, micrognathia, and low-set ears.

Discussion

Application of molecular cytogenetic techniques on uncultured amniocytes to detect discrepancy in chromosome mosaicism between uncultured and cultured amniocytes has been well reported.
Tetrasomy 9p caused by supernumerary i(9p) has been shown to be associated with tissue-limited mosaicism with the supernumerary i(9p) cell line presenting predominantly in the peripheral blood, but with a low-level mosaicism for the abnormal cell line or even a normal cell line in the cultures of chorionic villus sampling, amniotic fluid, or skin [1,11,14,16,30–36]. The present case provides evidence for the discrepancy in the supernumerary i(9p) mosaicism level between uncultured and cultured amniocytes in prenatally detected mosaic tetrasomy 9p. In the present case, the levels of mosaicism for tetrasomy 9p in cultured amniocytes (first amniocentesis), cultured amniocytes (second amniocentesis), fetal blood, and uncultured amniocytes (second amniocentesis) were 21.4%, 16.7%, 32.5%, and 47.1%, respectively. The present case shows that the mosaic level may decrease after long-term tissue culture in amniotic fluid with mosaic tetrasomy 9p. The present case also suggests that uncultured amniocytes can be a useful tool for confirmation of the presence of a true fetal mosaicism, and a correlation of high-level tetrasomy 9p mosaicism of uncultured...
amniocytes may exist with adverse fetal outcome in the pregnancy with prenatally detected mosaic tetrasomy 9p.

To date, at least 14 cases of prenatally detected mosaic (three cases) and nonmosaic (11 cases) tetrasomy 9p have been reported (Table 1). All of the 11 reported cases with nonmosaic tetrasomy 9p were associated with severe phenotypic abnormalities. Our case adds to the list of prenatal diagnosis of mosaic tetrasomy 9p with fetal abnormalities. Prenatal diagnosis of mosaic tetrasomy 9p is rare [1,7,8], and all of the three reported cases with mosaic tetrasomy 9p were associated with dysmorphism and abnormalities. Table 1 shows that the male: female sex ratio for tetrasomy 9p is rare [1,7,8], and all of the three reported cases with mosaic tetrasomy 9p were associated with dysmorphism and abnormalities. Prenatal diagnosis of mosaic tetrasomy 9p is rare [1,7,8], and all of the three reported cases with mosaic tetrasomy 9p were associated with dysmorphism and abnormalities.

Table 1 shows that the male: female sex ratio for tetrasomy 9p is 1 (7 male/7 female), indicating no sex preponderance in tetrasomy 9p. Table 1 also shows that fetuses with tetrasomy 9p may present increased nuchal translucency in the first trimester [19,20] and cystic hygroma in the second trimester [19]. Our case additionally shows that fetal ascites and hydrops fetalis can be a prenatal feature associated with mosaic tetrasomy 9p. Table 1 shows that prenatal ultrasound abnormalities associated with mosaic or nonmosaic tetrasomy 9p include polyhydramnios, oligohydramnios, IUGR, Dandy–Walker variant or malformation, ventriculomegaly, skeletal abnormalities, cleft lip and palate, hydronephrosis, and congenital heart defects. In a review of 19 fetuses with tetrasomy 9p, Nakamura-Pereira et al [20] summarized that the major prenatal ultrasound findings are as follows: IUGR (58%), ventriculomegaly (58%), genitourinary anomaly (47%), hypoplastic/absent vermis (42%), cleft lip and palate (42%), limb malformations (42%), cardiac anomaly (26%), and polyhydramnios (21%). Our case presented no major structural abnormalities but only fetal ascites and hydrops fetalis.

The present case shows the advantages of application of aCGH and QF-PCR on uncultured amniocytes for rapid detection of the presence of high-level mosaicism for tetrasomy 9p. In the present case, the catastrophic findings were limited to ascites and hydrops fetalis.
In our case, the use of aCGH established the euchromatic content of 9q in the supernumerary i(9p), and the use of QF-PCR established the maternal origin of the supernumerary i(9p). Dutly et al. [5] suggested that the supernumerary i(9p) is predominantly caused by maternal meiosis II non-disjunction followed by rearrangements leading to duplication of 9p and loss of 9q. The QF-PCR result in our case is consistent with the previous reports that the supernumerary i(9p) originates from the maternal chromosome 9 [1,8].

Prenatal diagnosis by chorionic villus sampling using cultured chorionic villous cells or by amniocentesis using cultured amniocytes may obtain a false negative result in pregnancies with fetal mosaic tetrasomy 9p, because of tissue-limited mosaicism, and a selective disadvantage for the abnormal cell line with the supernumerary i(9p) during cell culture [11,34–36]. For example, Grass et al. [34] reported 75% mosaicism for tetrasomy 9p in blood cells in a boy with mild manifestations but a normal karyotype of 46,XY at chorionic villus sampling. Eggermann et al. [35] reported 32% mosaicism for tetrasomy 9p in blood cells in a girl with multiple abnormalities but a normal karyotype of 46,XX at amniocentesis. In this regard, application of molecular cytogenetic techniques such as aCGH, QF-PCR, and interphase FISH on uncultured amniocytes is practical for confirmation and diagnosis of mosaic tetrasomy 9p at repeated amniocentesis. Chen et al. [1] have suggested that fetal blood sampling is valuable for prenatal confirmation of low-level mosaic tetrasomy 9p detected prenatally by amniocentesis. Shehab et al. [36] have suggested that tetrasomy 9p is well tolerated in lymphocytes, and the supernumerary i(9p) is often found in all or a high frequency of blood cells. Our finding of 32.5% mosaicism for tetrasomy 9p in cultured fetal blood lymphocytes is in accordance with the previous observations. Our study provides evidence for the nature of decrease in mosaic level of mosaic tetrasomy 9p in

![Fig. 4. Representative electrophoretogram of quantitative fluorescent polymerase chain reaction analysis at short tandem repeat markers specific for chromosome 9. The marker D9S2149 (9p21.1) shows two different parental alleles with a 3:1 (maternal:paternal) gene dosage increase in the maternal allele, indicating a maternal origin of the supernumerary isochromosome 9p.](image)

### Table 1

Reported cases of mosaic or nonmosaic tetrasomy 9p detected by amniocentesis, cordocentesis, or chorionic villus sampling.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Cases</th>
<th>Indication</th>
<th>Prenatal diagnosis</th>
<th>Confirmatory studies</th>
<th>Outcome and phenotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>McDowall et al. [13]</td>
<td>47,XY,+i(9p)</td>
<td>Abnormal ultrasound</td>
<td>Anmiocentesis: +i(9p) = 100%</td>
<td>No</td>
<td>Ultrasound: ventriculomegaly, agenesis of the corpus callosum, an enlarged cisterna magna. TOP; abnormal fetus: facial dysmorphism, neck edema, cleft lip and palate.</td>
</tr>
<tr>
<td>Schaefer et al. [14]</td>
<td>47,XY,+i(9p)</td>
<td>Abnormal ultrasound</td>
<td>Cordocentesis: +i(9p) = 100% (25 cells)</td>
<td>Skin: +i(9p) = 100% (25 cells)</td>
<td>Ultrasound: IUGR, severe oligohydramnios, absent kidneys and bladder, hydrocephalus. Delivery at 34 wk, 1510 g, neonatal death, facial dysmorphism, bilateral cleft lip and palate, multiple joint deformities, microplegia, cryptorchidism, lissencephaly, agenesis of the corpus callosum.</td>
</tr>
<tr>
<td>Van Hove et al. [15]</td>
<td>47,XY,+i(9p)</td>
<td>Abnormal ultrasound</td>
<td>Anmiocentesis: +i(9p) = 100% (22 cells)</td>
<td>No</td>
<td>Ultrasound: hydrocephalus, bilateral cleft lip and palate, complex cardiac defect, bilateral hydrenephrosis, complex limb malformation. TOP; abnormal fetus: facial dysmorphism, hypoplastic penis and scrotum, single umbilical artery, DORV, VSD, hypoplastic bilateral ventricle.</td>
</tr>
<tr>
<td>Dhandha et al. [7]</td>
<td>Case 1 47,XX,+i(9p)</td>
<td>Abnormal ultrasound</td>
<td>Anmiocentesis: +i(9p) = 100%</td>
<td>Cord blood: +i(9p) = 100% Lung: +i(9p) = 100% Placenta: +i(9p) = 100%</td>
<td>Ultrasound: IUGF, cleft lip, ventriculomegaly, Dandy−Walker variant, neonatal death, facial dysmorphism, bilateral cleft lip and palate, elbow flexion contractures, knee hyperextension, abnormal digits, congenital heart defects.</td>
</tr>
<tr>
<td></td>
<td>Case 2 47,XX,+i(9p)/46,XX</td>
<td>Abnormal ultrasound</td>
<td>Anmiocentesis: +i(9p) = 96.3% (27 colonies)</td>
<td>No</td>
<td>Ultrasound: bilateral cleft lip, hypoplastic left ventricle, VSD, ehorogenic kidneys, short hands and fingers. Delivery at 37 w, 1805 g, facial dysmorphism, short digits, clinodactyly, congenital heart defects.</td>
</tr>
</tbody>
</table>

(continued on next page)
PCR = isochromosome 9p; aCGH = array comparative genomic hybridization; AMA = advanced maternal age; AVSD = atrioventricular septal defect; CVS = chorionic villus sampling; DORV = double outlet of the right ventricle; FISH = fluorescence in situ hybridization; IUGR = intrauterine growth restriction; NT = nuchal translucency; QF-PCR = quantitative fluorescent polymerase chain reaction; TOP = termination of pregnancy; VSD = ventricular septal defect.

Table 1 (continued)

<table>
<thead>
<tr>
<th>Authors</th>
<th>Cases</th>
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<th>Outcome and phenotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cazorla Calleja et al [8]</td>
<td>47,XX, +i(9p)/46,XX</td>
<td>Abnormal ultrasound</td>
<td>Amniocentesis: +i(9p) = 50% (50 cells) Cordocentesis: +i(9p) = 25%</td>
<td>Peripheral blood: +i(9p) = 75.3% (89 cells) Polymorphic DNA markers: maternal origin of +i(9p)</td>
<td>Ultrasound: IUGR, ventriculomegaly. Delivery at 39 w, trigoconeophy, left eye enophtalinos, facial dysmorphism, bilateral hydronephrosis, mega cisterna magna, hydrocephalus, psychomotor development delay at age 4 y.</td>
</tr>
<tr>
<td>Deurloo et al [9]</td>
<td>47,XX, +i(9p)</td>
<td>AMA, Abnormal ultrasound</td>
<td>CVS: +i(9p) = 100% Amniocentesis: +i(9p) = 100%</td>
<td>No</td>
<td>Ultrasound: Dandy–Walker malformation, ventriculomegaly, dilation of renal pelvis. TOP; abnormal fetus: facial dysmorphism.</td>
</tr>
<tr>
<td>Hengstschläger et al [10]</td>
<td>47,XY, +i(9p)</td>
<td>Abnormal ultrasound</td>
<td>CVS: +i(9p) = 100% Amniocentesis: +i(9p) = 100%</td>
<td>No</td>
<td>Ultrasound: abnormal head, Dandy–Walker malformation, clubfeet, polyhydramnios, facial dysmorphism, left rotated heart, VSD, an overriding aorta. TOP; abnormal fetus.</td>
</tr>
<tr>
<td>Tang et al [17]</td>
<td>47,XX, +i(9p)</td>
<td>Abnormal ultrasound</td>
<td>Amniocentesis: +i(9p) = 100% (20 cells)</td>
<td>Blood: +i(9p) = 95% (20 cells) Cord: +i(9p) = 85% (20 cells)</td>
<td>Ultrasound: abnormal skull, ventriculomegaly, clubfeet, cleft lip and palate. Delivery at 35 w, 1730 g. Dandy–Walker variant, agenesis of the corpus callosum, horsehoe kidney.</td>
</tr>
<tr>
<td>Chen et al [11]</td>
<td>47,XX, +i(9p)/46,XX</td>
<td>AMA</td>
<td>Amniocentesis: +i(9p) = 20% (20 colonies) Retap: +i(9p) = 16.7% (24 colonies)</td>
<td>Skin: +i(9p) = 0% (40 cells) Lung: +i(9p) = 0% (40 cells) Cord blood: +i(9p) = 48% (40 cells) Polymorphic DNA markers: maternal origin of +i(9p)</td>
<td>TOP; abnormal fetus: facial dysmorphism.</td>
</tr>
<tr>
<td>Tan et al [18]</td>
<td>47,XY, +i(9p)</td>
<td>Abnormal ultrasound</td>
<td>Amniocentesis: +i(9p) = 100% (30 cells)</td>
<td>No</td>
<td>Ultrasound: IUGR, polyhydramnios, cleft lip and palate, facial dysmorphism. TOP; abnormal fetus: hypoplastic nails, clinodactyly, clubfeet.</td>
</tr>
<tr>
<td>di Vera et al [19]</td>
<td>47,XY, +i(9p)</td>
<td>AMA, Abnormal ultrasound</td>
<td>Amniocentesis: +i(9p) = 100%</td>
<td>No</td>
<td>Ultrasound: increased NT in the first trimester, oligohydramnios, Dandy–Walker malformation, IUGR, micromelia, brachydactyly, rocker-bottom feet, horsehoe kidney, AVSD, bilateral cleft lip and palate, cystic hygroma, ventriculomegaly. TOP; abnormal fetus: ronimencephalosynapsis.</td>
</tr>
<tr>
<td>Nakamura-Pereira et al [20]</td>
<td>47,XY, +i(9p)</td>
<td>Abnormal ultrasound, increased NT</td>
<td>Amniocentesis: +i(9p) = 100% (50 cells)</td>
<td>No</td>
<td>Ultrasound: increased NT (2.9 mm) in the first trimester, subcutaneous edema, clubfeet, hyperechoic kidneys, bilateral pelvic dilation, Dandy–Walker malformation, retrognostism, cleft lip and palate, arthrogryposis. Delivery at 30 w, 1120 g, facial dysmorphism, cryptorchidism, microopenis, neonatal death.</td>
</tr>
<tr>
<td>Podolsky et al [21]</td>
<td>47, +i(9p)</td>
<td>AMA, Abnormal ultrasound</td>
<td>CVS: +i(9p) = 100%</td>
<td>No</td>
<td>Ultrasound: absent nasal bone.</td>
</tr>
<tr>
<td>Present case</td>
<td>47,XX, +i(9p)/46,XX</td>
<td>AMA, Abnormal ultrasound</td>
<td>Amniocentesis: +i(9p) = 21.4% (28 colonies) Retap: +i(9p) = 16.7% (24 colonies) Interphase FISH on uncultured amniocytes: +i(9p) = 47.1% (104 cells) aCGH on uncultured amniocytes: duplication of 9p24.3-q21.11 QF-PCR on uncultured amniocytes: maternal origin of +i(9p)</td>
<td>Fetal blood: +i(9p) = 32.5% (40 cells)</td>
<td>Ultrasound: fetal ascites, hydrops fetalis. IUGR. TOP; abnormal fetus: facial dysmorphism.</td>
</tr>
</tbody>
</table>

In summary, we report prenatal diagnosis and molecular genetic analysis of mosaic tetrasomy 9p at amniocentesis associated with fetal ascites and hydrops fetalis. We have observed discrepancy of the mosaic levels between uncultured and cultured amniocytes, and suggest that the mosaic level of tetrasomy 9p may decrease after long-term tissue culture in amniocytes in case of mosaic tetrasomy 9p.

cultured amniocytes after long-term culture, and may explain the previous observations of possible false-negative diagnosis of mosaic tetrasomy 9p by amniocentesis or chorionic villus sampling. Recently, aCGH application on uncultured amniocytes for rapid diagnosis of aneuploidy has been possible, and it may have the advantage of detection of mosaic tetrasomy 9p without the influence of long-term culture effect on amniocytes.
Acknowledgments

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