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Short Communication

Mosaic trisomy 2 at amniocentesis: Prenatal diagnosis and molecular genetic analysis

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Abstract

Objective: This study aims at presenting prenatal diagnosis of mosaic trisomy 2 and reviewing the literature.
Materials, Methods, and Results: A 32-year-old woman underwent amniocentesis at 21 weeks of gestation because of abnormal maternal serum biochemistry. Amniocentesis revealed a karyotype of 47,XY,+2[1]/46,XY[21] in *in situ* cultures. The single colony with trisomy 2 had two metaphase cells, and both had the karyotype of 47,XY,+2. Repeated amniocentesis was performed at 23 weeks of gestation. Interphase fluorescence *in situ* hybridization (FISH) analysis on uncultured amniocytes using a 2q11.1-specific probe RP11-468G5 (spectrum green) showed three green signals in 11 of 47 uncultured amniocytes, indicating 23.4% mosaicism for trisomy 2. The cultured amniocytes had a karyotype of 46,XY[20 colonies]. Polymorphic DNA marker analysis excluded uniparental disomy 2. The woman underwent the third amniocentesis at 25 weeks of gestation. Interphase FISH analysis on uncultured amniocytes revealed 9.4% (5/53 cells) mosaicism for trisomy 2. The cultured amniocytes had a karyotype of 46,XY[30 colonies]. Prenatal ultrasound was normal. The parents decided to continue the pregnancy to term, and a 3316-g baby was delivered with no phenotypic abnormalities. Cord blood had a karyotype of 46,XY[40 cells]. Interphase FISH analysis on uncultured urinary cells revealed 8.2% (4/49 cells) mosaicism for trisomy 2. The neonate was normal in growth and psychomotor development at 6 months of age.
Conclusion: Prenatal diagnosis of a single colony with two or more cells with trisomy 2 at amniocentesis should alert a clinically significant aneuploidy, and interphase FISH on uncultured amniocytes is useful for rapid confirmation of low-level trisomy 2 mosaicism at amniocentesis. The abnormal cell line of trisomy 2 may disappear after long-term amniocyte cultures.

Keywords: amniocentesis; mosaicism; mosaic trisomy 2; prenatal diagnosis; trisomy 2

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Introduction

Complete trisomy 2 or nonmosaic trisomy 2 is lethal and has been found in 1% to 5–6% of first-trimester spontaneous abortions [1,2]. The prevalence of mosaic trisomy 2 in chorionic villus sampling has been estimated to be one in 2000 samplings [3–6]. Prenatal diagnosis of mosaic trisomy 2 by amniocentesis is uncommon. Sago et al [7] found one case of true cytogenetic trisomy 2 mosaicism among 58,000 amniocenteses. Mosaic trisomy 2 has phenotypic and cytogenetic variability (Table 1). Characteristic phenotypic features in abnormal livebirths with mosaic trisomy 2 include intrauterine growth restriction (IUGR), microcephaly, midface hypoplasia, hypertelorism, cleft lip, cleft palate, widely spaced nipples, radioulnar hypoplasia, scoliosis, growth and motor delay, inguinal hernia, congenital diaphragmatic hernia, rocker-bottom feet, cardiac defects, neural tube defects, intestinal malrotation, portal fibrosis, bronchopulmonary dysplasia, hypomelanosis of Ito, caudal dysgenesis, Hirschsprung disease, and micro-anophthalmia [7,9–12,15,19–22]. Herein, we present our experience of prenatal diagnosis of mosaic trisomy 2 by amniocentesis and a review of the literature.

Materials, methods, and results

A 32-year-old, primigravid woman underwent amniocentesis at 21 weeks of gestation because of an abnormal result of second-trimester maternal serum screening. The maternal serum biochemistry at 15 weeks of gestation revealed a Down syndrome risk of 1/149 calculated from the levels of 0.56, 0.94, 1.09, and 1.76 multiples of the median (MoM) for α-fetoprotein (AFP), unconjugated estriol (uE3), total β-human chorionic gonadotrophin (β-hCG), and inhibin-A, respectively. Cytogenetic analysis of cultured amniocytes revealed a karyotype of 47,XY,+2[1]/46,XY[21]. Of 22 colonies of cultured amniocytes, one colony had the karyotype of 47,XY,+2, whereas the other 21 colonies had the karyotype of 46,XY (Fig. 1). The single colony with trisomy 2 had two metaphase cells, and each cell had a karyotype of 47,XY,+2. The parental karyotypes were normal, and prenatal ultrasound findings were unremarkable. Repeated amniocentesis was performed at 23 weeks of gestation. Array comparative genomic hybridization (aCGH), interphase fluorescence *in situ* hybridization (FISH), and quantitative fluorescent polymerase chain reaction (QF-PCR) were applied on uncultured amniocytes, and conventional cytogenetic analysis was applied on cultured amniocytes. The aCGH analysis on uncultured amniocytes revealed no genomic imbalance in chromosome 2. Interphase FISH analysis on uncultured amniocytes using a 2q11.1-specific probe of RP11-468G5 (spectrum green) showed three green signals in 23.4% (11/47 cells) and two green signals in 76.6% (36/47 cells) of uncultured amniocytes (Fig. 2). QF-PCR analysis on uncultured amniocytes using chromosome 2-specific microsatellite markers revealed a 1:1 biparental diallelic pattern for chromosome 2 and thus excluded uniparental disomy (UPD) 2 (Fig. 3). Cytogenetic analysis of cultured amniocytes revealed a karyotype of 46,XY in 20 cultured colonies. The woman underwent the third amniocentesis at 25 weeks of gestation. Interphase FISH analysis on uncultured amniocytes using the RP11-468G5 (2q11.1; spectrum green) probe showed three green signals in 9.4% (5/53 cells) and two green signals in 91.6% (48/53 cells) of uncultured amniocytes (Fig. 4). Cytogenetic analysis of cultured amniocytes revealed a karyotype of 46,XY in 30 cultured colonies. The parents decided to continue the pregnancy. A healthy 3316-g male baby was delivered at 40 weeks of gestation with no phenotypic abnormalities. Cytogenetic analysis of cord blood revealed a karyotype of 46,XY in 40 cultured lymphocytes. Interphase FISH analysis on uncultured urinary cells using the RP11-468G5 (2q11.1; spectrum green) probe showed three green signals in 8.2% (4/49 cells) and two green signals in 91.8% (45/49 cells) of urinary cells (Fig. 5). The neonate was normal in growth and psychomotor development at 6 months of age.

Discussion

The present case provides evidence for the usefulness of application of interphase FISH on uncultured amniocytes for rapid confirmation of low-level trisomy 2 mosaicism at amniocentesis. The present case also provides evidence that the abnormal cell line of trisomy 2 in cases with mosaic trisomy 2 may disappear after long-term cell cultures. Trisomy 2 mosaicism at amniocentesis has been associated with pseudomosaicism [23] and also with a discrepancy between molecular cytogenetic analyses of uncultured amniocytes and karyotyping of cultured amniocytes [18]. The present case had trisomy 2 in both the metaphase cells of a single colony. According to modified guidelines for the management of cases with suspected amniocyte mosaicism, autosomal trisomy involving a chromosome 2, 5, 8, 9, 12, 13, 14, 15, 16, 18, 20, 21, or 22 in a single colony (single dish) or in multiple colonies (single dish) in an *in situ* culture method is an indication for extensive workup requiring the examination of 24 colonies from two further separate cultures [24]. The Association for Clinical Cytogenetics [25] has suggested that particular care should be taken in interpreting level II mosaicism (2 or more cells with the same abnormality in a suspicion culture from a single flask, or in a single abnormal colony from an *in situ* culture) for a clinically significant aneuploidy, and interphase FISH may be used for the investigation of mosaicism in a prenatal setting. The present case shows that interphase FISH on uncultured amniocytes in repeated amniocentesis is very practical for differential diagnosis of true mosaicism from pseudomosaicism under such a circumstance. We suggest that interphase FISH is the molecular cytogenetic method of choice for rapid confirmation of low-level mosaicism at amniocentesis. In the present case, the first amniocentesis revealed 4.5% (1/22 colonies) mosaicism for trisomy 2 in cultured amniocytes, the second amniocentesis revealed a normal 46,XY karyotype in all 20 colonies of cultured amniocytes, and the third amniocentesis revealed a normal 46,XY karyotype in all 30 colonies of cultured amniocytes. However, at the second amniocentesis, the

Table 1
Reported cases of mosaic trisomy 2 detected by amniocentesis.

Authors	Cases	Indication	Amniocentesis studies	Confirmatory studies	Outcome and phenotype
Bui et al [8]	47,XY,+2/46,XY	NA	NA	NA	TOP, transverse hemimelia
	47,XY,+2/46,XY	NA	NA	NA	TOP, ambiguous external genitalia
Casey et al [9]	47,XY,+2/46,XY	Abnormal ultrasound: ventriculomegaly, discordance of limbs with body size	Amniocentesis: T2 = 11.8% (17 colonies)	Cord blood: T2 = 0% Peripheral blood: T2 = 0% Cord: T2 = 0% Placenta: T2 = 0% Foreskin: T2 = one cell	Delivery at 39 wk, 2445 g, small for gestational age, high arched palate, low-set ears, simian creases, overlapping fingers, widely spaced nipples
Golabi et al [10] Sago et al [7]	47,XY,+2/46,XY	Elevated MSAFP	Amniocentesis: T2 = 22.6% (31 colonies)	Blood: T2 = 0% (100 cells) Skin: T2 = 0% (100 cells) Ascites: T2 = 0% (100 cells) Intestine: T2 = 0% (39 cells) Liver: T2 = 4% (100 cells) Skin: UPD2 excluded	Ultrasound at 26 wk: IUGR, DORV, ASD, VSD, hydronephrosis. Delivery at 30 wk, 1135 g, small for gestational age, prominent occiput, beaked and prominent nose, flat malar area, thin lip, pointed chin, pectus excavatum, inguinal hernias, V-shaped palate, rocker-bottom feet, congenital heart defects, hydronephrosis, vesicoureteral reflux, delay myelination, a thin corpus callosum, hippocampal dysplasia, portal fibrosis. At age 16 mo: hypotonia, microcephaly, growth retardation, developmental delay
Harrison et al [11]	47,XY,+2/46,XY	Abnormal maternal serum screen: elevated MShCG, Down risk = 1/145	Amniocentesis: T2 = 32.5% (40 cells)	Cord blood: T2 = 0% (100 cells) Amnion: T2 = 32% Chorion: T2 = 20% Villi: T2 = 12% Maternal UPD2	Ultrasound at 28−34 wk: IUGR, oligohydramnios. Delivery at 36 wk, 1710 g, bronchopulmonary dysplasia. At age 31 mo: growth delay, normal development, no neuromuscular delay
Pappas et al [12]	Case 2				
	47,XY,+2/46,XY	AMA Abnormal ultrasound: lumbosacral spina bifida, ventriculomegaly Elevated AFAFP	Amniocentesis: T2 = 23.4% (64 cells)	Skin: T2 = 0% Muscle: T2 = 0% Placenta: T2 = 30% (20 cells) Amnion: T2 = 15% (20 cells)	TOP, lumbosacral spina bifida
Webb et al [13]	47,XX,+2/46,XX	AMA Trisomy 2 at CVS	Amniocentesis: culture A: T2 = 23.3% (30 cells) culture B: T2 = 0% (30 cells)	Cordocentesis: T2 = 0% (100 cells) Blood: T2 = 0% (100 cells) Placenta: T2 = 100% (120 cells) Skin: T2 = 0% (100 cells) Maternal UPD2	Oligohydramnios on prenatal ultrasound. Delivery at 31 wk, 765 g, patent ductus arteriosus, congenital pyloric stenosis, sliding hiatus hernia, vesicoureteral reflux. At age 8 mo: normal development, no obvious dysmorphic features
Hsu et al [14]	Case II-1				
	47,XY,+2/46,XY	AMA	Amniocentesis: T2 = 4% (52 cells)	Blood: T2 = 0% (79 cells) Placenta: T2 = 0% (52 cells)	Normal liveborn

(*continued on next page*)

Table 1 (*continued*)

Authors	Cases	Indication	Amniocentesis studies	Confirmatory studies	Outcome and phenotype
	Case II-5 47,XX,+2/46,XX	Elevated MSAFP	Amniocentesis: T2 = 6.3% (32 colonies)	Placenta: T2 = 25% (20 cells)	Stillbirth at 21 wk of gestation, no visible birth defects
	Case II-6 47,XX,+2/46,XX	NA	Amniocentesis: T2 = 6.7% (30 colonies)	Placenta: T2 = 25% (20 cells)	IUFD
	Case II-10 47,XX,+2/46,XX	Elevated MSAFP	Amniocentesis: T2 = 33.3% (30 cells)	Lung: T2 = 13.3% (30 cells) Placenta: T2 = 20% (30 cells) Skin: T2 = 0% (50 cells) Skin: T2 = 0% (50 cells)	TOP, abnormal abortus, dolichocephaly, oligohydramnios
	Case II-11 47,XX,+2/46,XX	NA	Amniocentesis: T2 = 20% (40 cells)	NA	Stillbirth
Robinson et al [15]	47,XY,+2/46,XY	Abnormal maternal serum screen for AFP and hCG, Down risk = 1/90	Amniocentesis: culture A: T2 = 36.7% (30 cells) culture B: T2 = 50% (30 cells) culture C: T2 = 83.3% (30 cells)	Skin (right): T2 = 4% (100 cells) Kidney (right): T2 = 3.9% (77 cells) Adrenal (right): T2 = 7% (100 cells) Brain: T2 = 0% (35 cells) Heart: T2 = 3.9% (77 cells) Testis: T2 = 4% (100 cells) Cord blood: T2 = 0% (100 cells) Cord: T2 = 1% (100 cells) Placenta (site 1): T2 = 73.3% (30 cells)	TOP, mild dysmorphic features, absent gall bladder, cystic left kidney, a 13th left rib, mild unilateral talipes
Roberts et al [16]	47,XY,+2/46,XY	Elevated MSAFP and MShCG Abnormal prenatal ultrasound: IUGR, increased bowel echogenicity Trisomy 2 at CVS	Amniocentesis: T2 = 9% (89 cells) UPD2 excluded	Blood: T2 = 0% (60 cells) Placenta: T2 = 100% (115 cells) Cord: T2 = 23% (13 cells)	Severe IUGR, oligohydramnios on prenatal ultrasound. Delivery at 26 wk, 440 g, phenotypically normal liveborn, neonatal death due to prematurity
Sifakis et al [17]	47,XY,+2/46,XY	AMA	Amniocentesis: T2 = 16% (25 cells)	NA	TOP, a male fetus without external or internal organ malformation at autopsy
Sifakis et al [6]	Mosaic T2	Trisomy 2 at CVS	Amniocentesis: T2 = 1.9% (53 cells)	NA	At 12 wk of gestation: fetal crown-rump length: 50th centile, NT = 1.0 mm, MS free β-hCG = 0.55 MoM, MS PAPP-A = 0.04 MoM. At 18 wk of gestation: IUGR, oligohydramnios, absent end-diastolic flow, coarctation of the aorta, TOP
Chen et al [18]	47,XX,+2/46,XX	AMA, abnormal prenatal ultrasound: IUGR	Amniocentesis (1st): Cultured amniocytes: T2 = 0% (25 colonies) Amniocentesis (2nd): Uncultured amniocytes: aCGH: mosaic T2 Interphase FISH: T2 = 12% (50 cells) Cultured amniocytes: T2 = 0% (19 colonies)	Amnion: T2 = 7.5% (50 cells) Cord: T2 = 0% (60 cells) Blood: T2 = 0% (100 cells) Placenta: complete T2 (aCGH) Skin: disomy 2 (aCGH, QF-PCR), UPD2 excluded	Severe IUGR, oligohydramnios on prenatal ultrasound. Delivery at 26 wk, 488 g, small for age, low-set ears, macroglossia, clenched hands, neonatal death

Present case	47,XY,+2/46,XY	Abnormal maternal serum screen for AFP, uE3, total β-hCG, and inhibin-A; Down risk = 1/149	Amniocentesis (1st): Cultured amniocytes: T2 = 4.5% (22 colonies) Amniocentesis (2nd): Cultured amniocytes: T2 = 0% (20 colonies) Uncultured amniocytes: aCGH: no genomic imbalance of chromosome 2 Interphase FISH: T2 = 23.4% (47 cells) QF-PCR: UPD2 excluded Amniocentesis (3rd): Cultured amniocytes: T2 = 0% (30 colonies) Uncultured amniocytes: Interphase FISH: T2 = 9.4% (53 cells)	Cord blood: T2 = 0% (40 cells) Urinary cells: Interphase FISH: T2 = 8.2% (49 cells)	Normal liveborn. Delivery at term, 3.316 g, normal development at age 6 mo, no phenotypic abnormalities

aCGH = array comparative genomic hybridization; AFAFP = amniotic fluid α-fetoprotein; AMA = advanced maternal age; ASD = atrial septal defect; CVS = chorionic villus sampling; DORV = double-outlet right ventricle; FISH = fluorescence *in situ* hybridization; IUFD = intrauterine fetal death; MoM = multiples of the median; mo = month; MSAFP = maternal serum α-fetoprotein; MShCG = maternal serum human chorionic gonadotrophin; NA = not available; NT = nuchal translucency; QF-PCR = quantitative fluorescent polymerase chain reaction; T2 = trisomy 2; TOP = termination of pregnancy; uE3 = unconjugated estriol; UPD 2 = uniparental disomy 2; VSD = ventricular septal defect; wk = week.

interphase FISH on uncultured amniocytes revealed 23.4% (11/47 cells) mosaicism for trisomy 2, but QF-PCR and aCGH failed to detect trisomy 2 mosaicism on uncultured amniocytes. This is because QF-PCR and aCGH have limitations in detecting low-level mosaicism trisomy [26,27]. At the third amniocentesis, the interphase FISH on uncultured amniocytes revealed 9.4% (5/53 cells) mosaicism for trisomy 2. The cord blood revealed a normal 46,XY karyotype in all 40 cultured lymphocytes. By use of interphase FISH analysis, the urinary cells was found to have 8.2% (4/49 cells) mosaicism for trisomy 2.

To date, at least 18 cases of mosaic trisomy 2 detected by amniocentesis have been reported (Table 1). Of these, at least nine cases (50%) [6–8,10,12–15,18] were associated with prominent phenotypic abnormalities, suggesting that the malformation risk should be concerned in prenatal diagnosis of mosaic trisomy 2 by amniocentesis. Table 1 shows that the male:female sex ratio for fetal mosaic trisomy 2 is 1.8 (11 males/6 females), indicating a male preponderance in fetal mosaic trisomy 2 and a natural selection against female mosaic trisomy 2 conceptuses. Table 1 also shows that mosaic trisomy 2 can prenatally be associated with elevated maternal serum AFP (MSAFP), abnormal maternal serum screening, and abnormal ultrasound findings. Golabi et al [10] and Sago et al [7] reported an elevated MSAFP level of 2.93 MoM in a pregnancy with mosaic trisomy 2, congenital heart defects, IUGR, and hydronephrosis. Pappas et al [12] reported an elevated amniotic fluid AFP level of 13 standard deviations above the mean with positive acetylcholinesterase in a pregnancy with mosaic trisomy 2, lumbosacral spina bifida, and ventriculomegaly. Hsu et al [14] reported a pregnancy with an elevated MSAFP level of 4 MoM, fetal mosaic trisomy 2, dolichocephaly, and oligohydramnios, and another case with elevated MSAFP, fetal mosaic trisomy 2, and stillbirth. Harrison et al [11] reported an elevated maternal serum human chorionic gonadotrophin (MShCG) level of 3.67 MoM, indicating a 1:145 risk of Down syndrome in a pregnancy with mosaic trisomy 2 and maternal UPD 2. Robinson et al [15] reported a raised Down syndrome risk of 1:90 on maternal serum screening for AFP and hCG in a pregnancy with mosaic trisomy 2 and multiple anomalies. Roberts et al [16] reported an elevated MSAFP level of 3.67 MoM and an elevated MShCG level of 3.9 MoM in a pregnancy with mosaic trisomy 2, IUGR, and oligohydramnios. The present case was associated with abnormal maternal serum screening for AFP, uE3, total β-hCG, and inhibin-A, and a 1:145 risk of Down syndrome. Table 1 additionally shows that the reported abnormal ultrasound findings associated with mosaic trisomy 2 at amniocentesis include IUGR, oligohydramnios, congenital heart defects, ventriculomegaly, spina bifida, and hydronephrosis.

Mosaic trisomy 2 detected postnatally has been described in four cases [19–22], and there exists phenotypic and cytogenetic variability. Cramer et al [19] first reported a 6-month-old girl with 40% trisomy 2 mosaicism in skin fibroblasts and a normal 46,XX karyotype in 100 lymphocytes. The girl manifested IUGR, gross motor and growth delay, scoliosis,

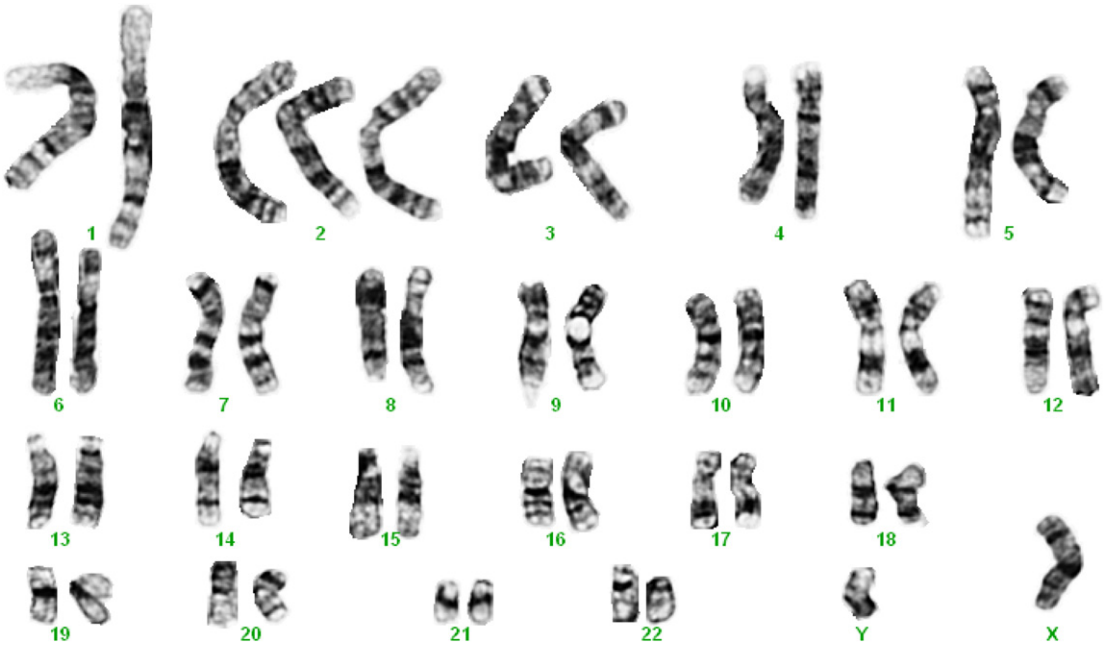

Fig. 1. A karyotype of 47,XY,+2.

unilateral radioulnar hypoplasia, craniosynostosis, broad halluces, radial deviation of the wrist, frontal bossing, unilateral proptosis, and contralateral ptosis. Gupta et al [20] reported a 3-month-old girl with mosaic trisomy 2, normal perinatal findings, normal development, and normal growth. The girl manifested hypomelanosis of Ito. Her blood karyotype was normal, but the skin biopsy and cell culture in skin fibroblasts over the area of pigmentation showed a karyotype of 47,XX,+2[9]/46,XX[11]. Mihci et al [21] reported a girl aged 2.5 years with multiple congenital anomalies, 3% (3/100 cells) trisomy 2 mosaicism in skin fibroblasts, and a normal 46,XX karyotype in peripheral blood. The girl was found to have large kidneys and diaphragmatic hernia on prenatal ultrasound. She had a history of diaphragmatic hernia, duodenal atresia, intestinal malrotation, microcephaly, atrial and ventricular septal defects, developmental delay, hypotonia, and seizures. She manifested microbrachycephaly, a receded frontal hair line, a dysmorphic face with small and wide-set eyes, epicanthic folds, midface hypoplasia, thin upper lip, small mouth, down-turned corners of the mouth, a prominent

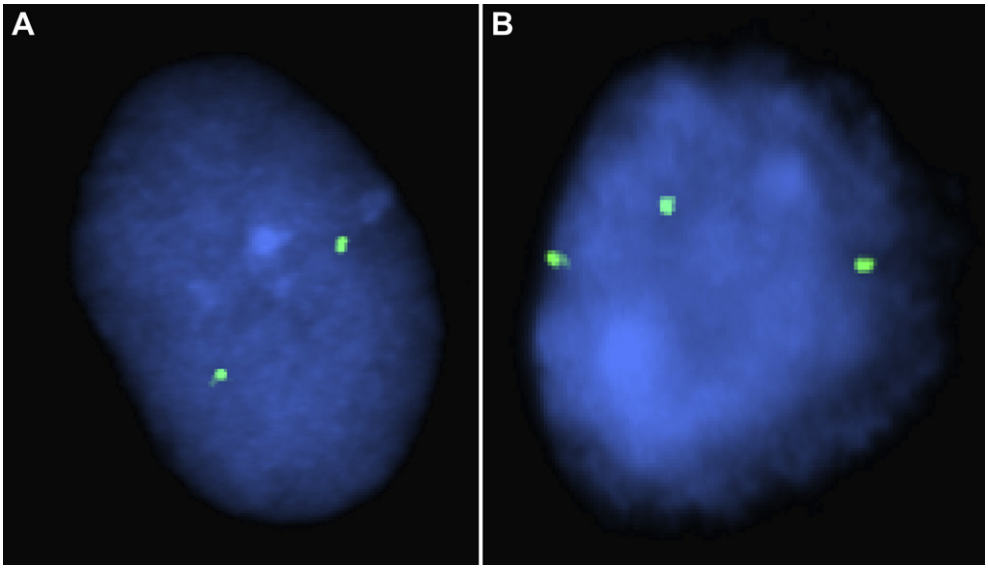

Fig. 2. Interphase FISH analysis of uncultured amniocytes using the BAC probe RP11-468G5 (2q11.1) (spectrum green) at the second amniocentesis shows (A) two green signals in an amniocyte with disomy 2 and (B) three green signals in an amniocyte with trisomy 2. BAC = bacterial artificial chromosome; FISH = fluorescence *in situ* hybridization.

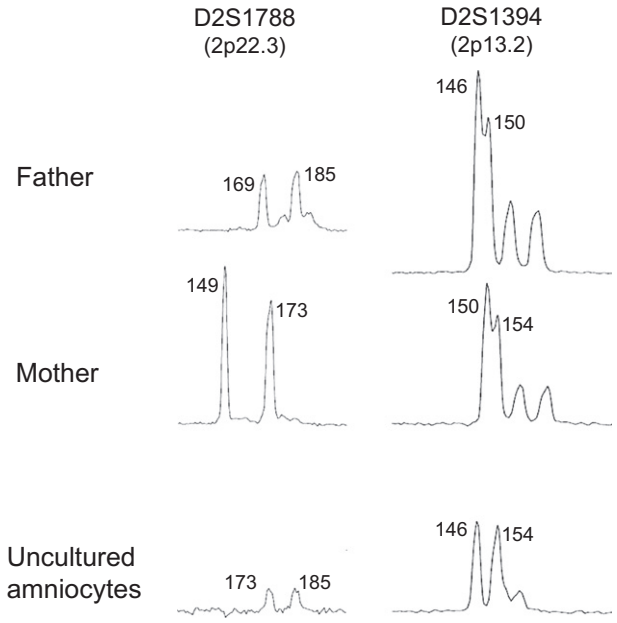

Fig. 3. Representative electrophoretograms of quantitative fluorescent polymerase chain reaction assays. The markers D2S1788 and D2S1394 show two peaks of equal fluorescent activity from two different parental alleles in uncultured amniocytes with a dosage ratio of 1:1 (paternal allele:maternal allele).

mandible, and hypopigmented spots on the skin of the anterior abdominal wall. Prontera et al [22] reported a 7-year-old boy with multiple malformations, intellectual disabilities, 25% trisomy 2 mosaicism in skin fibroblasts, and a normal 46,XY karyotype in peripheral blood. Severe oligohydramnios was noted prenatally. The boy postnatally manifested smallness for age, bilateral deafness, psychomotor retardation, microcephaly, microanophthalmia, cleft palate, high forehead, full cheeks, microstomia, abnormal ears, smooth philtrum, grooved chin, short neck, torticollis, valgus club foot, camptodactyly, clinodactyly, hallux valgus, overriding toes, bilateral cryptorchidism, small penis, face and body asymmetry, caudal dysgenesis, lack of sacrum and part of coccyx, and Hirschsprung disease.

Complete trisomy 2 detected postnatally has always been associated with congenital anomalies [21,28–30]. Chaliha et al [28] reported a 34-gestational-week acardiac twin with a karyotype of 47,XY,+2 in the skin. Blaicher et al [29] reported a term acardiac twin with a karyotype of 47,XX,+2 in the skin. Seller et al [30] reported a 13-gestational-week fetus with microcephaly, iniencephaly, encephalocele, thoracic spina bifida, a karyotype of 47,XY,+2 in the umbilical cord, and trisomy 2 in the skin by interphase FISH. Mihci et al [21] reported a term acardiac twin with a karyotype of 47,XX,+2 in the skin.

Mosaic trisomy 2 at amniocentesis can be associated with mosaic trisomy 2 or complete trisomy 2 in the placenta (Table 1). High-level trisomy 2 mosaicism and complete trisomy 2 in the placenta with or without fetal UPD 2 have been well known to be associated with IUGR, oligohydramnios, and adverse fetal outcome [6,13,15,18,31–36]. The presence of trisomy 2 in amnion has additionally been found to correlate with poor pregnancy outcome even when the fetus has a normal karyotype [36]. Mosaic trisomy 2 at amniocentesis has always been associated with a normal karyotype in the blood. Therefore, cord blood sampling for rapid confirmation of mosaic trisomy 2 at amniocentesis is not practical.

In summary, we present prenatal diagnosis and molecular cytogenetic analysis of mosaic trisomy 2 using uncultured and cultured amniocytes in a pregnancy with favorable fetal outcome. We demonstrate the usefulness of interphase FISH on uncultured amniocytes for rapid confirmation of low-level trisomy 2 mosaicism at amniocentesis and provide evidence that the abnormal cell line of trisomy 2 may disappear after long-term amniocyte cultures.

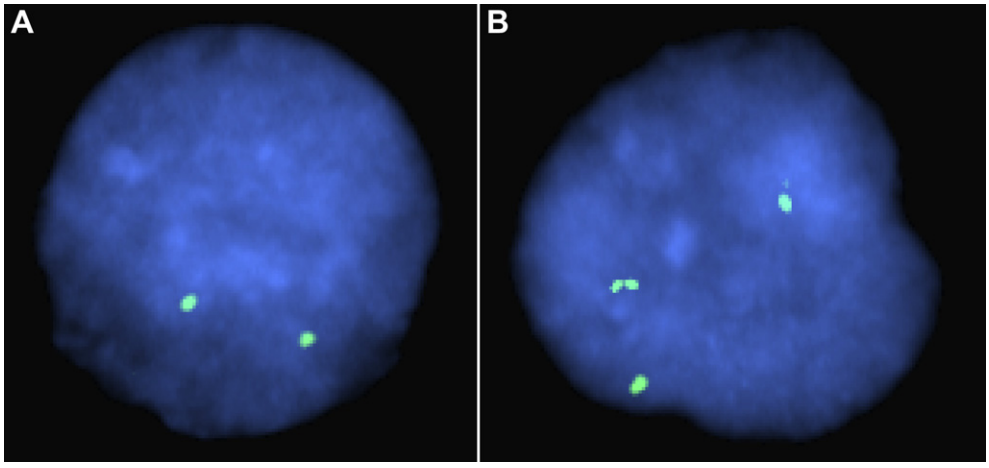

Fig. 4. Interphase FISH analysis of uncultured amniocytes using the BAC probe RP11-468G5 (2q11.1) (spectrum green) at the third amniocentesis shows (A) two green signals in an amniocyte with disomy 2 and (B) three green signals in an amniocyte with trisomy 2. BAC = bacterial artificial chromosome; FISH = fluorescence *in situ* hybridization.

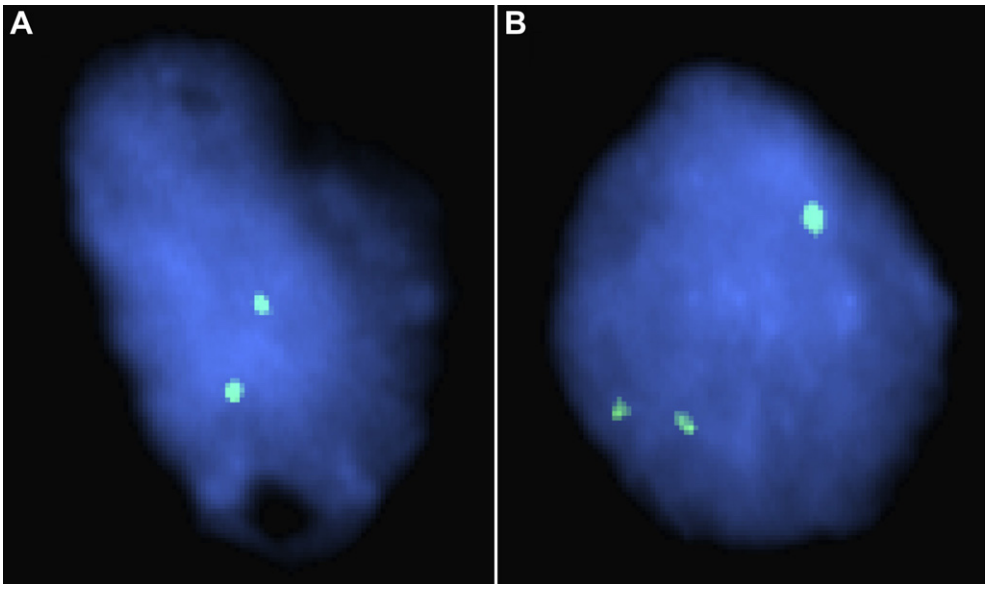

Fig. 5. Interphase FISH analysis of uncultured urinary cells using the BAC probe RP11-468G5 (2q11.1) (spectrum green) after birth shows (A) two green signals in a urinary cell with disomy 2 and (B) three green signals in a urinary cell with trisomy 2. BAC = bacterial artificial chromosome; FISH = fluorescence *in situ* hybridization.

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