Prenatal Diagnosis and Molecular Analysis of Trisomy 13 Mosaicism

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A 26-year-old gravida 1, para 0, woman was referred to the hospital at 18 weeks of gestation for evaluation of trisomy 13 mosaicism. She had undergone amniocentesis at 16 weeks of gestation because of an abnormal result in maternal serum screening for Down syndrome. Among 16 colonies of amniocytes, five had a karyotype of 47,XY, + 13 and 11 had a karyotype of 46,XY, and the karyotype was 47,XY, + 13[5]/46,XY[11]. Level II ultrasound showed no structural abnormalities. Repeated amniocentesis at 19 weeks of gestation revealed a karyotype of 47,XY, + 13[3]/46,XY[17]. Among 20 colonies of amniocytes, three had a karyotype of 47,XY, +13 and 17 had a karyotype of 46,XY. The woman subsequently elected to terminate the pregnancy. A male fetus was delivered with no demonstrable gross abnormalities.

DNA was isolated from the uncultured tissues of cord blood, umbilical cord and placenta. Quantitative fluorescent polymerase chain reaction (QF-PCR) assays and polymorphic short tandem repeat markers for chromosome 13 were used for determination of aneuploidy and the parental origin of the extra chromosome (Table, Figure). Complete trisomy 13 was evident in the tissue of placenta. The specimen of placenta showed a diallelic pattern with a dosage ratio of 1:2 (paternal allele: maternal allele) for the chromosome 13-specific markers. The specimen of placenta showed one copy of a paternal allele and two copies of a single maternal allele in chromosome 13. The specimens of cord blood and umbilical cord showed a diallelic pattern with a dosage ratio of 1:1.3 (paternal allele to maternal allele ratio) and 1:1.2 (paternal allele to maternal allele ratio), respectively, for the chromosome 13-specific markers.

We have presented the clinical and molecular findings of prenatally diagnosed mosaic trisomy 13. Our presentation shows the usefulness of QF-PCR in the rapid tissue confirmation of mosaic trisomy 13 in the fetal tissues and trisomy 13 in placental tissue. Trisomy 13 mosaicism in the fetal tissues in this case was most likely the result of partial trisomic zygote rescue of a meiosis II nondisjunction error of maternal origin or possibly a postzygotic mitotic error.

Trisomy 13 or Patau syndrome occurs in 0.5–1 per 10,000 births [1]. Magenis et al [2] proposed that

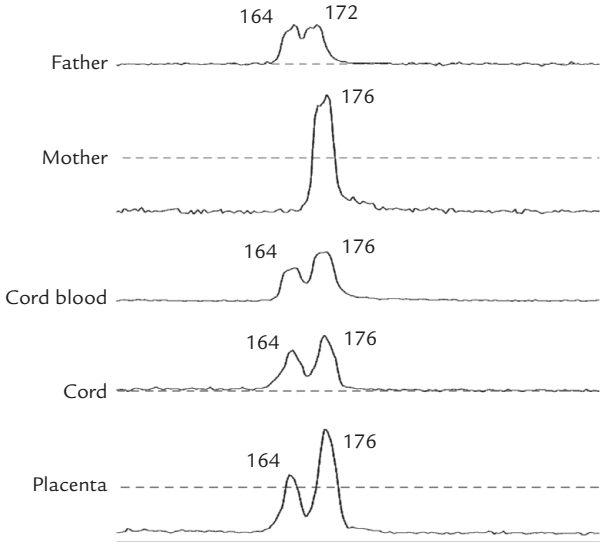

Figure. Representative electrophoretogram of quantitative fluorescent polymerase chain reaction assays at short tandem repeat markers for chromosome 13 using parental blood, cord blood, umbilical cord, and placenta. With the microsatellite marker D13S789, one paternally originated 164-base pair (bp) allele and one maternally originated 176-bp allele are seen in cord blood, umbilical cord and placenta. The two peaks (164:176 bp) of unequal fluorescent activity with a ratio of 1:2 in the placenta, 1:1.3 in the cord blood and 1:1.2 in the umbilical cord indicate a maternal origin of mosaic trisomy 13.

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Table. Genotypic information of the fetus, extraembryonic tissues and the parents at short tandem repeat (STR) markers specific for chromosome 13 by quantitative fluorescent polymerase chain reaction assays*

STRs	Locus	Father	Mother	Proband	Position (base pair)
D13S789	13q22.3	164,172	175,176	164,176†	77646678–77646835
D13S1809	13q33.2	178,200	200,200	178,200†	104930755–104930944
D13S797	13q33.2	187,207	207,207	187,207†	104930779–104930974
D13S766	13q33.2	135,143	127,135	127,135†	105701369–105701493
D13S248	13q33.3	209,209	235,235	209,235†	106418051–106418252
D13S796	13q33.3	165,165	169,169	165,169†	106686966–106687128
D13S1354	13q34	192,192	192,192	192,192	109230600–109230780

**Alleles (base pair sizes) are listed below each individual; †partial dosage increase approximately 100%, 30% and 20% in placenta, cord blood and umbilical cord, respectively.*

trisomy 13 mosaicism occurs in only 5% of all trisomy 13 cases. Trisomy 13 mosaicism is very unusual and has rarely been recognized at amniocentesis. In a study of chromosomal mosaicism in 22,000 amniocenteses, Hsu et al [3] found true chromosomal mosaicism in 0.23% (50/22,000) of the cases, including only two cases of trisomy 13 mosaicism among the 50 cases of true chromosomal mosaicism. Patients with complete trisomy 13 usually manifest early death, severe mental retardation, and characteristic structural abnormalities such as holoprosencephaly, Dandy-Walker complex, congenital heart defects, facial cleft, nuchal edema, cystic hygroma, scalp defects, omphalocele, urinary tract abnormalities, and polydactyly. However, patients with mosaic trisomy 13 most often have longer survival and a less severe phenotype, with a wide variation from essentially normal to grossly abnormal, according to the tissue distribution of trisomy 13 cells [4–6].

Counseling parents of a child with trisomy 13 mosaicism remains difficult because of phenotypic variability seen in trisomy 13 mosaicism, with some patients having a typical phenotype of complete trisomy 13 with neonatal death, and others having few dysmorphic features with prolonged survival [7]. In a literature review of 49 published cases with trisomy 13 mosaicism, Griffith et al [7] found that six reported cases had normal development and intellect, and the common associated anomalies in other cases with phenotypic abnormalities were ear anomalies, cleft lip and palate, and congenital heart defects. The present case had about 30% of abnormal trisomy 13 cells in the cord blood but manifested no phenotypic abnormalities. Although the present case was not associated with characteristic structural abnormalities, the intellectual condition of this case could not be determined. Griffith et al [7] suggested that there is no clear correlation between the percentage of trisomy 13 cells and the level of intellectual function in patients with trisomy 13 mosaicism. This information should be included in parental counseling during prenatal diagnosis of a low level of mosaicism for trisomy 13 with no sonographically demonstrable structural abnormalities.

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