International Congress Series 1261 (2004) 446–448

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A triplet pregnancy case with a complete hydatidiform mole and two fetuses diagnosed by polymorphic STR markers

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Abstract. We encountered a triplet pregnancy case with a mole and two normal fetuses, analyzed their karyotypes, and genotyped 15 STR markers and amelogenin after their termination in early pregnancy. The results of genotypes indicated that the triplets were trizygotic. The molar tissue lacked any of the maternal alleles at seven loci and, at one (D2S1338) of the seven loci, transmissions of the heterozygous paternal alleles to the mole were observed. These findings indicated that the mole resulted from dispermic androgenesis. The diagnosis with STR markers should prove very useful to better understand the zygosity of gestation and the genetic origin of hydatidiform moles.

Keywords: STR polymorphism; Diagnosis

1. Introduction

It is well known that the presence or absence of fetal tissue has been used to classify hydatidiform moles into complete (CHM) and partial moles [1]. Both moles are essentially different as to cytogenicity and the risk of trophoblastic neoplasma. The incidence of molar pregnancy is known to be associated with increased maternal age. Recent reports have indicated that CHM occurs in approximately 1 in 1200 pregnancies in the United States, 1 in 500 in Japan and 1 in 100 in Indonesia [2,3]. However, the incidence of CHM in twin pregnancies is not as frequent, about 1 in 22,000–100,000 pregnancies and that in triplet is even rarer. We report here a triplet pregnancy involving a CHM mole and two

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0531-5131/
doi:10.1016/j.ics.2003.12.078

normal fetuses with a diagnosis in early pregnancy with an analysis of the polymorphic marker-based genotyping.

2. Materials and methods

2.1. Case

A 34-year-old Japanese woman was treated for infertility for 3 years. She became pregnant after artificial insemination from her husband. An ultrasonographic examination at 7 weeks revealed the two living fetuses in separate gestational sacs but also a small gestational sac without a fetus. At 9 weeks, the patient felt a pain with slight genital bleeding. Further ultrasonographic examination revealed two living fetuses and uniformly thickened cystic areas without doppler signal. After hospitalization owing to her extremely high serum β-HCG level, termination of the pregnancy was decided. Both fetuses (fetuses 1 and 2) and the bulk of the mole were removed by aspiration (Fig. 1). Pathological examination of the molar tissue confirmed the presence of a CHM.

2.2. Karyotyping and genotyping

A piece of skin tissue from each fetus and the molar villi were cultured and karyotyped with the standard methods. DNA was extracted from the placenta of each fetus, the molar tissue and from blood of the parents. The DNA (2 ng) was amplified using a AmpFlSTR

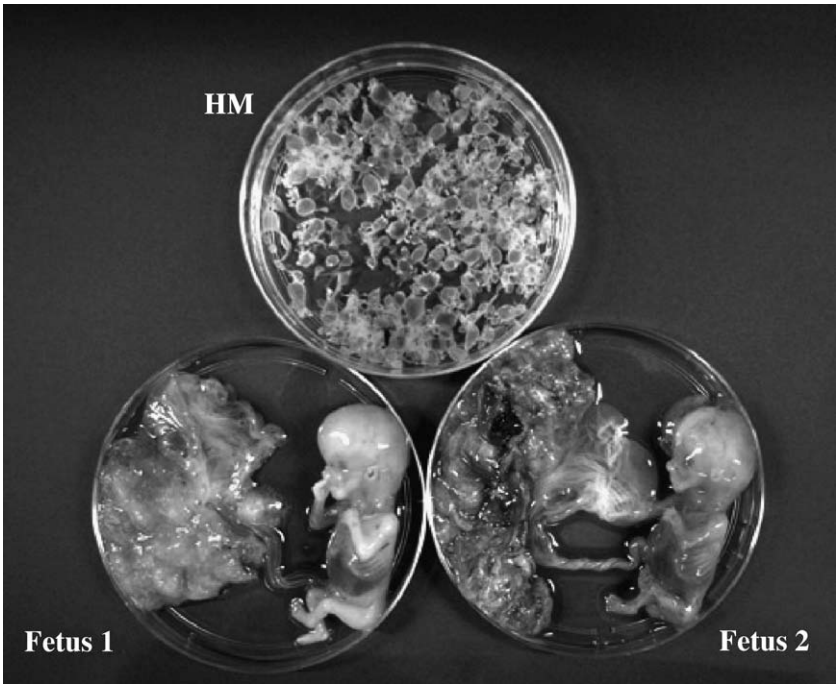

Fig. 1. Photograph of the hydatidiform mole (HM) and two normal fetuses (fetus 1 and fetus 2).

Table 1
Genotypes of the two fetuses, the mole tissues and the parents at 15 STR loci and amelogenin

Locus (karyotype)	Father (46,XY)	Mother (46,XX)	Fetus 1 (46,XX)	Fetus 2 (46,XX)	Mole (46,XY)
D8S1179	13,15	10,13	13,15	10,15	13,13
D21S11	30,32.2	29,30	29,30	30,32.2	32.2,32.2[a]
D7S820	8,12	11,12	8,12	8,12	8,12
CSF1PO	11,12	12,12	12,12	11,12	12,12
D3S1358	15,18	16,17	16,18	15,17	18,18[a]
TH01	6,8	6,7	7,8	6,7	6,6
D13S317	8,8	10,11	8,10	8,11	8,8[a]
D16S539	9,12	11,12	9,12	9,12	9,12
D2S1338	17,18	24,24	17,24	17,24	17,18[a,b]
D19S433	13,14	13,14	13,13	13,13	13,14
vWA	15,17	19,19	17,19	17,19	17,17[a]
TPOX	8,11	11,11	8,11	11,11	8,11
D18S51	13,14	13,17	13,13	13,14	14,14[a]
Amelogenin	X,Y	X,X	X,X	X,X	X,Y
D5S818	12,12	10,12	12,12	10,12	12,12
FGA	22,23	21,22	21,22	21,22	23,23[a]

[a] Evidence of androgenesis.
[b] Evidence of dispermic origin.

Identifiler™ PCR amplification kit with 15 STR markers and a gender determination marker (amelogenin) according to the user's manual, and analyzed with a Genetic Analyzer 310 and genotyped with Genotyper.

3. Results and discussion

To determine the zygosity of gestation and the genetic origin of the mole, karyotyping and genotyping of the fetal and molar tissues were performed (Table 1). Karyotypes of fetus 1, fetus 2 and the molar tissue were 46,XX, 46,XX and 46,XY, respectively, the same as the genotyping results of amelogenin. Thirteen loci were helpful in differentiating genotypes among the triplets (Table 1). Genotypes of the two fetuses were distinct at nine loci and those between the male fetus 1 and the XY mole were different at nine loci. The results confirmed that the triplets were trizygotic. The molar tissue lacked any of the maternal alleles at seven loci. Furthermore, transmissions of the heterozygous paternal alleles to the mole were observed at one of the seven loci (D2S1338), and homozygous paternal alleles at six loci. These findings indicated that the mole resulted from dispermic androgenesis. A diagnosis with STR markers should prove very useful to know the zygosity of gestation and the genetic origin of hydatidiform moles.

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