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LETTER

Three consecutive triploidy pregnancies in a woman: genetic predisposition?

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We read with interest 'Recurrent triploidy of maternal origin' by Brancati *et al*[1] published earlier in this journal. We report in detail of a similar family.

A 35-year-old woman was referred for genetic counseling due to recurrent pregnancy loss. The patient's paternal grandmother had eight miscarriages and two liveborns. This grandmother's sister was unable to have children, although no reason was ever determined. The remaining family history was unremarkable. The patient had a total of three detectable pregnancies. She had her first pregnancy at age 31. Ultrasound examination detected multiple abnormalities; including bilateral club feet, agenesis of the cerebrum, heart and spinal anomalies. This pregnancy was terminated at 16 weeks of gestation and chromosome analysis revealed a 69,XXX karyotype. The two subsequent pregnancies occurred when she was 34 and 35 years of age, respectively. The second pregnancy was miscarried at 8 weeks gestation and the last pregnancy was lost at 8–9 weeks gestation. No histological examination was performed. Chromosome analysis revealed that both embryos were triploid with 69,XXY karyotype. Chromosome analysis on the patient and her spouse showed that they both had normal karyotypes.

Microsatellite analysis was performed on parental blood specimen and on the cells from the last embryo. A total of 15 markers on 13 different chromosomes from a commercially available kit (AmpFLSTR® Identifiler® PCR Amplification Kit, Applied Biosystems, Foster City, CA, USA) were used for genotyping (Table 1). Six markers revealed that the embryo inherited two maternal alleles and one paternal allele, indicating that the triploidy is maternal in origin (digyny). The time and mode of the triploidy formation cannot be accurately determined. Although most of the fully informative markers revealed a maternal meiosis I error, maternal meiosis II error was inferred from the other markers (see Table 1). This was due to the occurrence of recombination in these chromosomes. The most proximal marker, D7S820, was not informative.

Triploidy is one of the most common chromosome abnormalities in humans, occurring in approximately 1–2% of all conceptuses and accounts for about 10% of all spontaneous abortions.[2] The primary mechanisms leading to triploidy include dispermy and maternal (digynic triploidy) or paternal (diandric triploidy) meiotic errors.[3–5] Despite the high frequency and numerous studies, the etiology of triploidy remains unknown.

Table 1 Micrasatellite analysis of the 3rd triploid pregnancy

Markers	*Chromosome locations*	*Genotypes*			*Interpretation*
		Mother	*Father*	*Fetus*	
TPOX	2p23-pter	13	23	123	If Mat, MI
D2S1338	2q35-37.1	14	23	124	Mat MI
D3S1358	3p21	12	33	123	Mat MI
FGA	4q28	12	11	112	If Mat, MI
D5S818	5q21-31	11	23	113	Mat
CSF1PO	5q33.3-34	12	11	111	If Mat, MII
D7S820	7q11.21-22	22	12	122	Not informative
D8S1179	8q24.1-24.2	13	23	233	If Mat, MII
TH01	11p15.5	33	12	233	Mat
vWA	12p12-pter	12	11	122	If Mat, MII
D13S317	13q22-31	13	23	133	If Mat, MI
D16S539	16q24-qter	12	12	222	If Mat, MII
D18S51	18q21.33	24	13	234	Mat,MI
D19S433	19q12-13.1	23	14	234	Mat, MI
D21S11	21q21	12	23	223	If Mat,MII

Mat: Maternal, MI: Meiosis I error, MII: Meiosis II error.

Therefore, investigation of families with recurrent triploidy may provide helpful information regarding the intrinsic genetic predisposition to the triploidy. Two other studies have reported on the parental origin of recurrent triploidy. Brancati *et al*[1] reported maternal origin in two of the three triploid pregnancies in one family. Pergament *et al*[6] reported another family in which maternal origin was determined in the last of three triploid pregnancies. In the family presented here, the last triploid pregnancy was also determined to be maternal (digynic) in origin. In addition, the mother had a family history of multiple miscarriages and infertility. These studies suggest a possible maternal genetic factor contributing to the recurrent triploid pregnancies. Interestingly, genetic factors affecting female meiosis have previously been reported. Based on the findings from a consanguineous family with six molar pregnancies, Judson *et al*[7] suggest that a recessive gene may cause imprinting failure of female germ line, resulting in the formation of hydatidiform moles. By using a combination of linkage search through the genome and homozygosity analysis, Moglabey *et al*[8] mapped a maternal locus responsible for recurrent hydatidiform moles to chromosome 19q13.3–13.4. In summary, the maternal origin of all reported recurrent triploid pregnancies, combined with maternal family history of multiple reproduction difficulties in this family, strongly support the previous studies and suggest an underlying genetic predisposition to errors in oogenesis, which may lead to digynic triploidy pregnancies and/or other reproduction difficulties.

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