CASE REPORT

# Parental karyotype may reveal the source of a pregnancy loss even in the presence of a reportedly euploid fetal karyotype

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**Objective:** To present a case of a fetal loss in which a normal fetal karyotype was obtained by banding studies. Identification of an abnormal maternal karyotype prompted subsequent reanalysis using fluorescence in situ hybridization (FISH).
**Design:** Case report.
**Setting:** University-affiliated IVF center.
**Patient(s):** A 32-year-old woman, G1 P0, underwent a fetal loss at 8 weeks, and a suction curettage was performed. The patient had a previous first-trimester loss.
**Intervention(s):** The fetal tissue was evaluated by banding studies and found to be normal. Parental karyotyping was performed, and the fetal tissue was reanalyzed by FISH.
**Main Outcome Measure(s):** Analysis of fetal karyotype by targeted FISH.
**Result(s):** Maternal karyotype demonstrated a translocation [46,XX, t(8;10)(q24.3:q25.2)]. The fetal tissue was reanalyzed by FISH, and a segment of chromosome 10 was found on chromosome 8.
**Conclusion(s):** A normal fetal karyotype, as measured by banding, does not exclude a genetic etiology for pregnancy loss. In this case, maternal translocation prompted the genetics laboratory to search for a small segment of translocated extra chromosomal material. This demonstrated that despite the finding of a normal fetal karyotype, in some cases parental karyotyping may have value. (Fertil Steril® 2011;95:1120.e9–e10. ©2011 by American Society for Reproductive Medicine.)

**Key Words:** Recurrent pregnancy loss, aneuploidy, karyotype, FISH

Pregnancy loss accounts for 15%–70% of pregnancies, depending on the age of the patient (1). Approximately 1% of women will experience three or more losses in the first trimester (2). The most important test to determine the etiology of the loss is a karyotype of the placental tissue. Fifty percent to 80% of losses are due to chromosomal abnormalities (3). Despite the known incidence of fetal aneuploidy in pregnancy loss, the cost-effectiveness of karyotyping is still debated (4). An aneuploid karyotype definitively proves that the loss is due to a fetal abnormality. A normal karyotype often triggers a search for alternative etiologies for the loss, including, for example, uterine abnormalities, endocrinopathies, or possible thrombophilias. A cytogenetic finding of female karyotype in the products of conception may be secondary to endometrial contamination that masks an aneuploidy loss. Maternal contamination with a 46,XX karyotype would, however, exclude a maternal translocation as the culprit for the recurrent loss.

We present a case in which a normal fetal karyotype (46,XX) was present in the examination of the products of conception. Despite this, parental karyotyping was performed, and a translocation was discovered in the maternal karyotype.

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## CASE REPORT

The patient was a 32-year-old woman, G1 P0, with a previous loss at 8 weeks due to a blighted ovum. Her hysterosalpingogram demonstrated a normal endometrial cavity with bilateral tubal patency. She underwent ovulation induction because of prolonged menstrual intervals. Her FSH level on day 3 was 8.5 mIU/mL, and her $E_2$ level was 26 pg/mL. Her basal antral follicle count totaled two preantral follicles per ovary.

Ovulation induction consisted of 225–300 IU of menotropin for 7 days, with the development of one mature follicle and a peak $E_2$ of 152 pg/mL. Intrauterine insemination was performed 36 hours after the administration of recombinant hCG.

The patient conceived, but 40 days after hCG administration no fetal heart was documented, and a dilation and curettage was performed.

Fetal karyotyping was performed with a banding resolution of 450 bands per haploid set of chromosomes and returned a 46,XX karyotype (Fig. 1A).

Paternal karyotyping was 46,XY, but the maternal karyotype revealed a translocation [46,XX, t(8;10)(q24.3:q25.2)] (Fig. 1B).

In light of the maternal karyotyping, fluorescence in situ hybridization (FISH) was performed on the fetal tissue, probing for the known translocation segments. A fragment of chromosome 10 was



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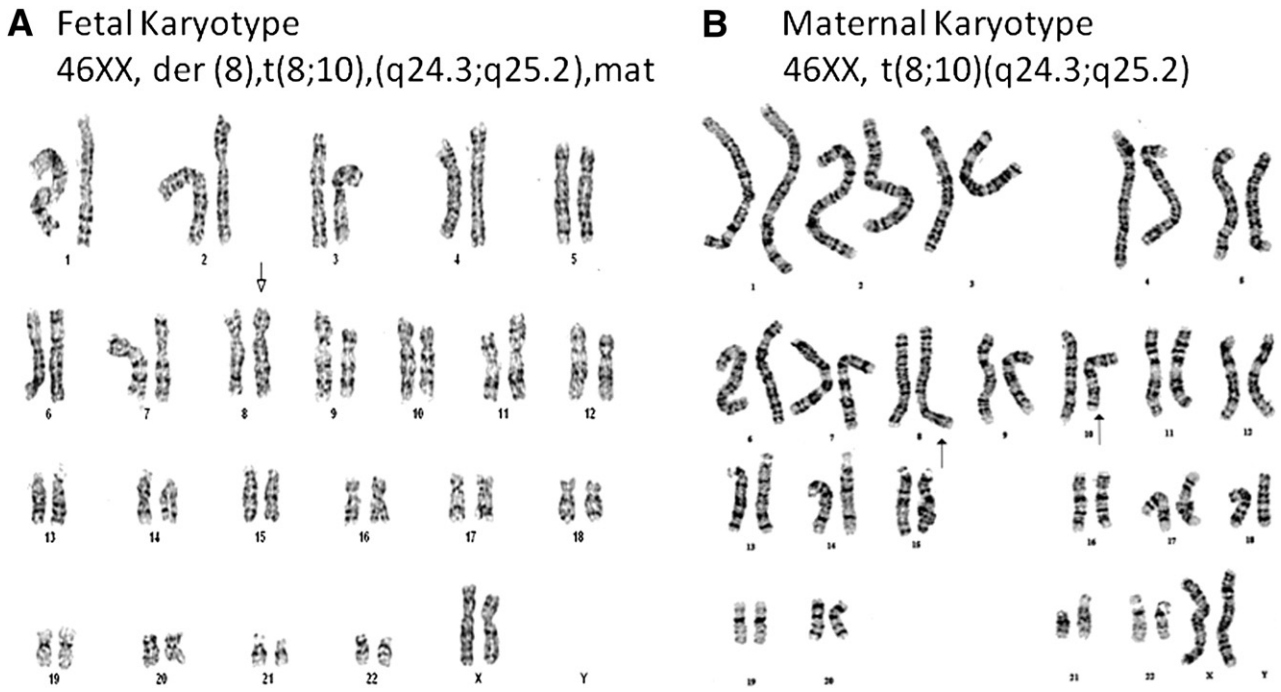
## FIGURE 1

**(A)** Fetal banding study that was thought to be normal. Fluorescence in situ hybridization on chromosome 8 ultimately detected segments derived from chromosome 10. **(B)** Maternal karyotype.




*Grunfeld. Translocation despite normal karyotype. Fertil Steril 2011.*

found on chromosome 8. The fetal karyotype was revised to 46,XX, der (8),t(8;10),(q24.3;q25.2), mat.

## DISCUSSION

The presence of a normal fetal karyotype fails to identify the etiology of pregnancy loss and can lead to the potentially erroneous conclusion that there may be a maternal factor contributing to embryo rejection. An aneuploid karyotype implies a fetal origin to the pregnancy loss. We present a case in which the initial fetal karyotype was reported to be normal but a more detailed analysis revealed that the loss was indeed fetal in origin. The FISH probe for chromosome 10 was performed only because the maternal karyotype demonstrated a reciprocal translocation of chromosome 8 and 10. Despite the normal fetal karyotype, parental karyotypes were performed. The parental data were helpful in elucidating the etiology of the loss by identifying an appropriate target for FISH analysis of the fetal tissue.

This case demonstrates to the clinician that despite a normal fetal karyotype performed through banding analysis, a genetic etiology to the fetal loss should be considered. Parental karyotyping to look for a translocation may be indicated even in the presence of a reportedly normal fetal karyotype.

## REFERENCES


1. Centers for Disease Control and Prevention. 2007 ART report section 2—ART cycles using fresh, nondonor eggs or embryos (part B). Available at: http://www.cdc.gov/art/ART2007/section2b.htm. Accessed November 1, 2010.
2. Roberts CP, Murphy AA. Endocrinopathies associated with recurrent pregnancy loss. Semin Reprod Med 2000;18:357–62.
3. Hogge WA, Byrnes AL, Lanasa MC, Surti U. The clinical use of karyotyping spontaneous abortions. Am J Obstet Gynecol 2003;189:397–400; discussion 400–2.
4. Goddijn M, Joosten JH, Knegt AC, van der Veen F, Franssen MT, Bonsel GJ, et al. Clinical relevance of diagnosing structural chromosome abnormalities in couples with repeated miscarriage. Hum Reprod 2004;19:1013–7.