


Cell-Free DNA as an Addition to Ultrasound for Screening of a Complete Hydatidiform Mole and Coexisting Normal Fetus Pregnancy: A Case Report

Martina G. Gabra, MD¹  Maritza G. Gonzalez, MD¹ Holly N. Bullock, MD, MPH¹ Meghan G. Hill, MBBS¹

¹Department of Obstetrics and Gynecology, Banner-University Medical Center, University of Arizona, Tucson, Arizona

Am J Perinatol Rep 2020;10:e176–e178.

Address for correspondence Martina Gabra, MD, Department of Obstetrics and Gynecology, Banner-University Medical Center, University of Arizona, 1501 North Campbell Avenue, Box 245078, Tucson, AZ 85724 (e-mail: mgabra@obgyn.arizona.edu).

Abstract

Keywords

- ▶ complete hydatidiform mole and coexisting normal fetus
- ▶ cell-free DNA
- ▶ twin-molar pregnancy
- ▶ hyperemesis gravidarum

Background Complete hydatidiform mole and coexisting normal fetus pregnancies (CHMCF) are rare and can be life-threatening to the mother. Definitive diagnosis can be made with chorionic villus sampling or amniocentesis. However invasive procedures carry a risk of bleeding. We present the case of a twin molar pregnancy where a cell-free DNA screening test was utilized to evaluate for CHMCF pregnancy.

Case A patient presented at 15-week gestational age with suspected CHMCF pregnancy. Ultrasound revealed a normal-appearing pregnancy abutting a multicystic lesion concerning for a complete mole. Cell-free DNA was obtained and was suggestive of complete paternal uniparental disomy. Pathological evaluation of the products of conception confirmed the diagnosis of CHMCF.

Conclusion In atypical cases, cell-free DNA may be useful in evaluation of molar pregnancy.

Complete hydatidiform mole and coexisting normal fetus (CHMCF) pregnancies are rare, occurring in 1:22,000 to 1:100,000 pregnancies.¹ The diagnosis can be suspected based on ultrasound findings. It is important to make a diagnosis to guide counseling and management. Definitive diagnosis can be made with chorionic villus testing or amniocentesis; however, these procedures risk bleeding necessitating surgery. The use of cell-free DNA has not been previously evaluated as an adjunct to other laboratory and ultrasound-based diagnosis of CHMCF.

Case

The patient is a 21-year-old G1P0 at 15-week gestational age who was referred with a possible twin-molar pregnancy based on ultrasound. Of note, the patient had prenatal care at a community facility, with ultrasound imaging at 5 and 12 weeks of gestation on which the abnormality had not been previously suspected. The patient reported spotting throughout her pregnancy and hyperemesis gravidarum with an 8 pound weight

loss during the pregnancy. Laboratory evaluation revealed a serum β -human chorionic gonadotropin (β -HCG) level of 375,954 mIU/mL and a thyroid stimulating hormone level of <0.01 mIU/L with normal free thyroxine level of 1.41 ng/dL. Complete blood count, comprehensive metabolic panel, and chest X-ray were unremarkable.

Ultrasound at our facility revealed a single fetus with a normal placenta and a coexisting complete molar pregnancy (**▶ Fig. 1**). The singleton fetus appeared anatomically normal, with normal limb and body movements and with an anterior fundal placenta. An 8.37 cm \times 4.05 cm \times 8.73 cm multicystic mass was visualized adjacent to the normal placenta, and an amniotic membrane appeared to separate the normal placenta from the multicystic mass. Finally, there was a 3.4 cm \times 0.65 cm posterior fundal subchorionic hematoma (**▶ Fig. 2**). These findings were consistent with a viable single fetus with normal placenta and coexisting complete molar pregnancy. After counseling regarding risks and benefits of both noninvasive and invasive testing, the patient elected to have cell-free DNA screening to guide management. This screening was significant

received
February 5, 2020
accepted after revision
February 20, 2020

DOI <https://doi.org/10.1055/s-0040-1709981>.
ISSN 2157-6998.

Copyright © 2020 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York, NY 10001, USA.
Tel: +1(212) 760-0888.

License terms



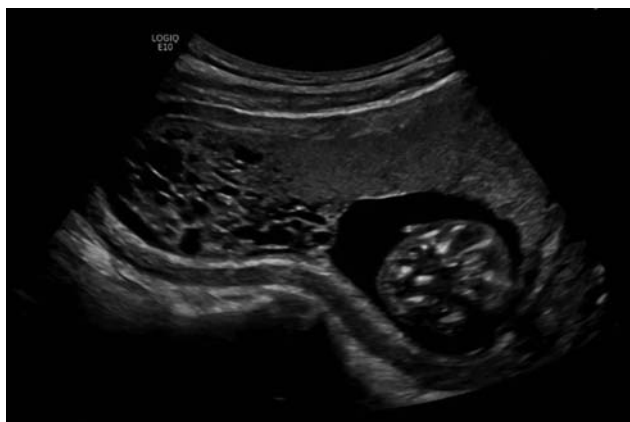


Fig. 1 Transabdominal ultrasound at 15 weeks of gestation, revealing a viable fetus with normal placenta and coexisting complete molar pregnancy. Appearance of membrane between normal pregnancy and molar pregnancy. Placental location is anterior and molar pregnancy is fundal in location.



Fig. 2 Posterior fundal subchorionic hematoma measuring 3.4 cm × 0.65 cm.

for complete paternal uniparental disomy, most consistent with a complete molar pregnancy.

Findings of the cell-free DNA in combination with the typical ultrasound findings and high β -HCG were communicated to the patient as highly suspicious for a complete molar pregnancy with coexisting normal pregnancy. An approximate 30% chance of a live birth with the possibility of major morbidity and mortality were discussed as concerns with continuing the pregnancy. The patient chose to terminate the pregnancy at 17 weeks of gestation with dilation and evacuation (D&E). She underwent cervical preparation which included a paracervical block of 20-cc 1% lidocaine prior to laminaria placement. She was admitted for overnight observation to monitor vaginal bleeding. A D&E was performed in standard fashion under ultrasound guidance. She received a paracervical block with 20-cc 1% lidocaine with 8 units of vasopressin prior to the procedure and prophylactic oxytocin following the procedure. Estimated blood loss was 75 cc. Histologic evaluation revealed hydropic chorionic villi with trophoblastic hyperplasia consistent with complete molar pregnancy and fragments of well-developed fetal tissue, consistent with CHMCF.

Discussion

CHMCF pregnancies occur in 1:22,000 to 1:100,000 pregnancies.¹ The diagnosis of CHMCF is suspected by identifying two separate concepts: (1) a fetus with normal placentation and (2) an adjacent molar gestation separated by a membrane. The molar component has a characteristic vesicular sonographic pattern. Complete moles are diploid and the chromosomes are derived only from paternal genome. Differential diagnosis of CHMCF includes partial hydatidiform mole, twin pregnancy with a partial hydatidiform mole and coexisting normal fetus, and placental mesenchymal dysplasia.^{2,3} Placental mesenchymal dysplasia is a benign placental vascular anomaly that is difficult to distinguish from CHMCF and is not an indication for termination of pregnancy.⁴ Differentiating these entities using ultrasound alone can be difficult. In addition, molar change is a progressive phenomenon and hydatidiform changes are often less prominent in the first trimester.⁵

We employed cell-free DNA in this case of CHMCF to assist in patient counseling and management. Cell-free DNA screening was performed with single-nucleotide polymorphism (SNP) sequencing of maternal blood. The test is widely utilized for screening for single chromosomal aneuploidy.⁶ A case report demonstrated the use of cell-free DNA to determine the origin of the genome in a choriocarcinoma in a woman with a choriocarcinoma with coexisting normal fetus.⁷ And now, we suggest that cell-free DNA may be useful for screening in cases where CHMCF is suspected. The potential for cell-free DNA screening to differentiate a complete hydatidiform mole from a partial hydatidiform mole or placental mesenchymal dysplasia deserves investigation in a larger patient cohort to assess accuracy of the test for this purpose. Its use may complement findings noted on ultrasound.

Complications of CHMCF are similar to molar pregnancy alone, and include but are not limited to thyrotoxicosis, hyperemesis gravidarum, preeclampsia, intrauterine fetal demise, previable premature rupture of membranes, preterm delivery, obstetric hemorrhage, coagulopathy, gestational trophoblastic neoplasia (GTN), and trophoblastic embolization.⁸ GTN occurs in a significant number of women.⁹ The high risk of maternal complications without accurate predictors of which patients will progress to a live birth makes the decision regarding termination or continuation of pregnancy a difficult one for patients. Termination of pregnancy should be offered and it minimizes maternal risk.⁹ Careful continuation of pregnancy with close follow-up is possible in some patients.⁵

In this case, the patient presented with an abnormal ultrasound. Though there is a high sensitivity and specificity of ultrasound for the diagnosis of molar pregnancy, laboratory adjuncts are potentially of value in differentiating molar pregnancies from placental mesenchymal dysplasia.¹⁰ In this case, the pregnancy's appearance on ultrasound suggested CHMCF and the results of Cell-free DNA screening were used as part of the risk assessment. The overwhelming amount of paternal DNA detected in the maternal circulation was identified by a Cell-free DNA screening test and suggested the

presence of a complete molar pregnancy. The patient experienced hyperemesis gravidarum and bleeding complications and ultimately decided not to continue the pregnancy because of the associated risks. The patient had an uneventful dilation and evacuation and continues surveillance for persistent trophoblastic disease. We found the use of cell-free DNA was helpful in her care and believe that test validation in more pregnancies would be beneficial in the management of CHMCF. Additionally, the use of cell-free DNA for follow-up surveillance would be of interest.

Key Points

1. Complete hydatidiform mole and coexisting normal fetus (CHMCF) is a rare and life-threatening condition.
2. Cell-free DNA testing may be of use to increase the certainty of molar pregnancy diagnoses.

Note

Patient consent was obtained for publication of this article.

Funding

None.

Conflict of Interest

None declared.

References

- 1 Jones WB, Lauersen NH. Hydatidiform mole with coexistent fetus. *Am J Obstet Gynecol* 1975;122(03):267–272
- 2 Sauerbrei EE, Salem S, Fayle B. Coexistent hydatidiform mole and live fetus in the second trimester: an ultrasound study. *Radiology* 1980;135(02):415–417
- 3 Chu W, Chapman J, Persons DL, Fan F. Twin pregnancy with partial hydatidiform mole and coexistent fetus. *Arch Pathol Lab Med* 2004;128(11):1305–1306
- 4 Mittal D, Anand R, Sisodia N, Singh S, Biswas R. Placental mesenchymal dysplasia: what every radiologist needs to know. *Indian J Radiol Imaging* 2017;27(01):62–64
- 5 Wee L, Jauniaux E. Prenatal diagnosis and management of twin pregnancies complicated by a co-existing molar pregnancy. *Prenat Diagn* 2005;25(09):772–776
- 6 Dar P, Curnow KJ, Gross SJ, et al. Clinical experience and follow-up with large scale single-nucleotide polymorphism-based noninvasive prenatal aneuploidy testing. *Am J Obstet Gynecol* 2014;211(05):527.e1–527.e17
- 7 Kristiansen MK, Niemann I, Lindegaard JC, et al. Cell-free DNA in pregnancy with choriocarcinoma and coexistent live fetus: a case report. *Medicine (Baltimore)* 2016;95(37):e4721
- 8 Lee SW, Kim MY, Chung JH, Yang JH, Lee YH, Chun YK. Clinical findings of multiple pregnancy with a complete hydatidiform mole and coexisting fetus. *J Ultrasound Med* 2010;29(02):271–280
- 9 Fishman DA, Padilla LA, Keh P, Cohen L, Frederiksen M, Lurain JR. Management of twin pregnancies consisting of a complete hydatidiform mole and normal fetus. *Obstet Gynecol* 1998;91(04):546–550
- 10 Ross JA, Unipan A, Clarke J, Magee C, Johns J. Ultrasound diagnosis of molar pregnancy. *Ultrasound* 2018;26(03):153–159