Twin gestation with complete hydatidiform mole and a coexisting live fetus: case report and brief review of literature

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Summary: Complete hydatidiform (also referred to as hydatiform) mole with coexisting live fetus is an exceedingly rare event. The fetus usually has a normal karyotype, and approximately 25–40% chance of survival, if pregnancy is allowed to continue until reasonable fetal lung maturity is achieved. However, risk of maternal complications including preeclampsia and subsequent trophoblastic disease are significant. We report a case of a 19-year-old primigravida, at 25 weeks gestation with a complete hydatidiform mole and a coexisting live fetus. She developed severe preeclampsia with uncontrolled hypertension, and pregnancy was terminated by caesarean section, after a short course of dexamethasone to accelerate fetal lung maturity. A morphologically normal live female fetus and placenta were delivered without complications, along with a separate mass of complete mole. The postpartum course was complicated by uterine choriocarcinoma with metastases to lung and left kidney, which responded to chemotherapy. Our case is a rare example of a twin gestation composed of a complete hydatidiform mole with a coexisting live fetus, and illustrates the associated spectrum of maternal complications that mandate close pre- and post-natal surveillance.

Keywords: twin gestation, complete hydatidiform mole, live fetus, choriocarcinoma

INTRODUCTION

Hydatidiform mole with a coexisting fetus may be the result of a dizygotic twin gestation consisting of a complete mole and a coexisting normal fetus and placenta, or a singleton gestation with a partial mole associated with a triploid fetus.¹ Complete hydatidiform mole with a coexisting fetus (CHMCF) is an exceedingly rare event complicating approximately 1 in 10,000 to 1 in 100,000 pregnancies.² CHMCF is mostly associated with a normal diploid and potentially viable fetus; in contrast, partial mole is lethal to the associated fetus due to triploidy.³

Our case report of a 19-year-old patient with CHMCF addresses the importance of clinically distinguishing between partial mole and CHMCF for planning treatment: termination of pregnancy versus continuation of pregnancy. It also sheds light on the management of high-risk maternal complications encountered while continuing pregnancy in CHMCF to achieve fetal maturity and viability.

CASE REPORT

A 19-year-old African-American primigravida with intrauterine pregnancy of estimated 25 weeks was referred to our institution

with complaints of headache and blurred vision for four weeks. She had sought regular prenatal care starting at 10 weeks of gestation when anaemia with beta-thalassemia trait was diagnosed. Trans-abdominal ultrasound, one month prior to her referral, demonstrated an intrauterine pregnancy of approximately 20 weeks with an anteriorly located placenta and a single fetus. However, ultrasound at that time failed to reveal coexistence of a molar pregnancy. On admission, her blood pressure (BP) was 180/110 mmHg. She reported fetal movements and denied vaginal bleeding or contractions. A 24-hour urine collection showed 1190 mg of protein confirming the diagnosis of preeclampsia. Serum β -HCG was 228,000 mIU/mL. Ultrasound at this time revealed a live fetus in frank breech presentation consistent with 25 weeks of gestation, with no evidence of fetal growth retardation or anomalies. A normal-appearing placenta was present along the anterior uterine wall (Figure 1A, long arrows), and a separate large cystic mass was seen in the posterior wall, most consistent with complete mole (Figure 1A, short arrows). Chest X-ray was normal.

Following hospitalization, the patient was administered 10 mg intravenous hydralazine, and 200 mg of labetalol twice orally for three days. During this time, the BP was reduced from 186/113 to 128/87 mmHg. However, on the fourth day of hospitalization, her BP spiked to 190/125 mmHg. This was treated with further doses of intravenous hydralazine (10 mg) followed by intravenous labetalol, titrated to the level of hypertension. The latter was adjusted according to systolic blood pressure (SBP) levels (80 mg at SBP > 175, 40 mg at SBP 175–165 and 20 mg at SBP 165–160). When the BP reached around

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Figure 1 (A) Ultrasound showing a normal appearing placenta (long arrows) along the anterior uterine wall, and a separate large cystic mass of complete hydatidiform mole (short arrows) along the posterior uterine wall. (B) Grossly normal appearing placenta (serially sectioned top of photograph), and complete hydatidiform mole (bottom of photograph). (C) H&E sections of the normal placenta. (D) Complete hydatidiform mole with trophoblastic hyperplasia (top left) and cistern formation (right and bottom). (E) Cytological atypia in the molar trophoblastic tissue (C $\times 25$; D $\times 40$; E $\times 200$)

136/107, oral labetalol 200 mg twice daily was started. Oral dexamethasone was given to accelerate fetal lung maturation. Intravenous magnesium sulphate was given to prevent seizures. Delivery was performed by caesarean section and a viable normal appearing female fetus (birth weight 730 g, Apgar scores 3, 4 and 5 at 1, 3 and 5 minutes, respectively) and placenta were delivered without complications. The separate mass of cystic vesicles was removed by suction curettage to ensure complete removal of the molar tissue.

The placenta weighed 197 g and was grossly normal in appearance with a centrally inserted umbilical cord containing three blood vessels (Figure 1B, top). The separate mass of molar tissue measured $9 \times 8 \times 2$ cm and was composed of grape-sized vesicles (Figure 1B, bottom). Microscopically, the placenta was normal-appearing (Figure 1C); however, the complete mole displayed large hydropic avascular chorionic villi and cistern formation (Figure 1D). Also, prominent cyto/syncytiotrophoblastic proliferation with cytological atypia was seen (Figure 1E). Genetic karyotyping could not be performed, because the specimen was submitted in formalin fixative.

After delivery, the BP was unstable for four days fluctuating between 122/82 and 200/114 mmHg. Intravenous hydralazine (10 mg) and labetalol were resumed initially and titrated according to the BP response. Subsequently, oral metoprolol (200 mg twice daily), clonidine (0.2 mg twice daily), hydrochlorothiazide (25 mg daily) and amlodipine (5 mg daily) were added until the BP stabilized at 128/80 mmHg. All but the hydrochlorothiazide 25 mg daily was withdrawn by the time of discharge. The patient was advised to prevent pregnancy for a year; however, no specific contraceptive measure

was prescribed, and arrangements were made for outpatient follow-up.

The patient did not attend for scheduled follow-up but returned after two months complaining of acute lower back pain, persistent vaginal bleeding and vomiting. She denied any sexual activity since her last delivery. Serum β -HCG was 301,500 mIU/mL, and imaging revealed a large irregular intrauterine mass, a mass enveloping her left kidney, and multiple pulmonary nodules, consistent with metastatic disease. Based on these findings, a clinical diagnosis of choriocarcinoma was made and the patient was started on chemotherapy (etoposide, methotrexate, actinomycin with leucovorin rescue). During chemotherapy she continued to have elevated BP and severe anaemia requiring several blood transfusions. After eight cycles of chemotherapy, the serum β -HCG level dropped to 3.55 mIU/mL. Eleven months after delivery, the patient is asymptomatic and her serum β -HCG level has returned to normal (0.1 mIU/mL). She continues follow-up in the gynaecology-oncology clinic and she and her baby are doing well.

DISCUSSION

When facing a molar pregnancy with a coexisting fetus, the decision whether to continue or to terminate the pregnancy depends upon establishing the correct diagnosis of CHMCF versus partial mole. Upon confirmation of diagnosis of CHMCF, continuation of pregnancy is dependent on successful management of maternal complications. The prenatal

diagnostic tools that help in such decision-making include ultrasound and genotyping.

On ultrasound, complete mole classically appears as a heterogeneous mass with 'cluster of grapes' or 'snow-storm' appearance without embryonic or fetal structures within the heterogeneous mass. Partial mole is distinguishable from complete mole on ultrasound, by the presence of fetal parts. In our case, ultrasound clearly revealed a normal appearing placenta in the anterior uterine wall and a separate sharply defined molar tissue in the posterior wall.

Accurate prenatal diagnosis of CHMCF versus partial mole is possible by molecular genotyping and segregation analysis of both parental (maternal and paternal) and placental alleles in chorionic villi by amniocentesis or transabdominal fetal blood samples.³ Karyotyping is diploid in complete mole, and is purely paternal in origin. In partial mole karyotype is triploid and the DNA is both maternal and paternal in origin.⁴

Partial mole associated with triploid fetus carries a lower risk of maternal complications including subsequent risk of placental trophoblastic disease.³ However, the disease is lethal to the fetus and usually ends in early spontaneous abortion.⁵ Therefore, in partial mole with triploid fetus immediate termination of pregnancy is performed. On the other hand, fetus coexisting with complete mole usually has normal karyotype with 25–40% chance of survival, if the pregnancy is continued beyond 32 weeks or until reasonable lung maturity was achieved.^{6,7} However, pregnant women with CHMCF are at a higher risk for complications due to preeclampsia, ante-partum haemorrhage and placental trophoblastic disease. The incidence of placental trophoblastic disease, especially choriocarcinoma, is higher (50%) with CHMCF than with complete mole (12.5%).^{8,9}

Preeclampsia is a leading cause of maternal and fetal morbidity with the highest rate of complications associated with more severe disease. Maternal complications may include acute renal failure, pulmonary oedema, adult respiratory distress disease, puerperal cerebrovascular events, disseminated intravascular coagulation syndrome, ventilation problems and maternal mortality.¹⁰ Similarly, the fetus and newborn are at increased risk of pre- and post-natal complications due to severe preeclampsia/eclampsia. A study by Bombrys *et al.*, reported low birth weight (below the tenth percentile) in 53% and severe growth retardation (birth weight below the fifth percentile) in 35% of their cases. Fetal demise occurred in 44% of cases with severe growth retardation. Gestational age (GA) significantly affected perinatal survival in severe preeclampsia. No perinatal survival was seen below 23 weeks GA compared with a survival rate of 20%, 71%, 76% and 90% at 23, 24, 25 and 26 weeks GA, respectively. However, the survivors were at increased risk for developing complications associated with prematurity, including respiratory distress syndrome, bronchopulmonary dysplasia, chronic lung disease, intraventricular haemorrhage, periventricular leukomalacia and neonatal death.¹¹

The management of CHMCF remains complex and controversial due to conflicting data from different parts of the world. Immediate termination of pregnancy has been recommended to avoid severe maternal complications and risk of malignant transformation.¹² Others have suggested continued conservative management in the presence of a normal fetal karyotype and relatively stable clinical course, to enhance fetal viability.^{2,9} The increased risk of maternal complications and placental trophoblastic disease should be explained to the

patient, particularly the potential for developing choriocarcinoma. Women may opt for continuation of pregnancy despite the risk of complications, especially those women who achieved conception for the first time in their later life or who have undergone several attempts of assisted conception. Special focus should be given to the early detection and treatment of any possible complications at an appropriate tertiary centre.

The management of complete mole after evacuation or delivery is similar whether there is a coexisting fetus or not. Uterine evacuation is followed by β -HCG monitoring. Chest X-ray is mandatory (if positive, chemotherapy is needed). Additional imaging investigations may be needed as directed by symptoms. β -HCG is performed weekly until normal for two weeks, then monthly up to one year. Highly effective means of contraception are recommended to avoid pregnancy for at least 6–12 months. Chemotherapy is indicated if β -HCG levels are persistent or rising, or metastases to lung or other sites appear. Hysterectomy is indicated for life-threatening uterine haemorrhage, or in a patient with rising β -HCG on follow-up but with no evidence of metastasis, who does not desire fertility or refuses chemotherapy.

In summary, our case exemplifies the high risk of maternal complications associated with CHMCF. Even though CHMCF is a rare event, its diagnosis has a dramatic impact on antenatal and postnatal management of the patient. In our case, the antenatal course was complicated by severe preeclampsia, and postnatal course by choriocarcinoma with metastases to lungs and left kidney, controlled by chemotherapy. This case also illustrates the good fetal outcome, and the importance of accurate diagnosis and careful monitoring by a peri- and postnatal team experienced in high-risk obstetric complications.

REFERENCES

- Sumigama S, Itakura A, Yamamoto T, *et al.* Genetically identified complete hydatidiform mole coexisting with a live twin fetus: comparison with conventional diagnosis. *Gynecol Obstet Invest* 2007;**64**:228–31
- Marcorelles P, Audrezet MP, Le Bris MJ, *et al.* Diagnosis and outcome of complete hydatidiform mole coexisting with a live twin fetus. *Eur J Obstet Gynecol Reprod Biol* 2005;**118**:21–7
- Bovicelli L, Ghi T, Pilu G, *et al.* Prenatal diagnosis of a complete mole coexisting with a dichorionic twin pregnancy: case report. *Hum Reprod* 2004;**19**:1231–4
- Lai CY, Chan KY, Khoo US, *et al.* Analysis of gestational trophoblastic disease by genotyping and chromosome in situ hybridization. *Mod Pathol* 2004;**17**:40–8
- Jauniaux E, Brown R, Snijders RJM, *et al.* Early prenatal diagnosis of triploidy. *Am J Obstet Gynecol* 1997;**176**:550–4
- Wee L, Jauniaux E. Prenatal diagnosis and management of twin pregnancies complicated by a co-existing molar pregnancy. *Prenat Diagn* 2005;**25**:772–6
- Sebire NJ, Fokkett M, Paradinas FJ, *et al.* Outcome of twin pregnancies with complete hydatidiform mole and healthy co-twin. *Lancet* 2002;**359**:2165–6
- Matsui H, Iitsuka Y, Ishii J, *et al.* Androgenetic complete mole coexistent with a live fetus. *Gynecol Oncol* 1999;**74**:217–21
- Matsui H, Sekiya S, Hando T, *et al.* Hydatidiform mole coexistent with a twin live fetus: a national collaborative study in Japan. *Hum Reprod* 2000;**15**:608–11
- Kuklina EV, Ayala C, Callaghan WM. Hypertensive disorders and severe obstetric morbidity in the United States. *Obstet Gynecol* 2009;**113**:1299–306
- Bombrys AE, Barton JR, Nowacki EA, *et al.* Expectant management of severe preeclampsia at less than 27 weeks gestation: Maternal and perinatal outcomes according to gestational age by weeks at onset of expectant management. *Am J Obstet Gynecol* 2008;**199**:247.e1–6
- Jones WB, Lauersen NH. Hydatidiform mole with coexistent fetus. *Am J Obstet Gynecol* 1975;**122**:267–72