Twin Pregnancy with Hydatidiform Mole and Coexisting Fetus: Report of Three Cases and Review of Literature

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Abstract
A twin pregnancy with a coexisting complete hydatidiform mole and a healthy fetus (CMCF) is rare. Here we report three cases of CMCF with different clinical courses but similar outcome without a surviving neonate. Two women required uterine evacuation before 20 weeks of gestational age because of vaginal bleeding and medical complications and the other patient underwent termination of her pregnancy at 24 weeks of gestation due to severe pre-eclampsia. The pathologic diagnosis of complete hydatidiform mole was confirmed in each case and the chromosome complement was 46XX in two molar gestations and 46XY in one gestation. One of the three women required chemotherapy for treatment of low-risk gestational trophoblastic disease. The hCG level was normalized after 4 cycles and the patient was free of disease at 1 year follow-up. Review of the literature discussing the diagnostic tools, clinical features, management and outcome of pregnancies with CMCF are presented.

Keywords: Twin pregnancy, Hydatidiform mole, Coexisting fetus

Introduction
Twin pregnancy consisting of a hydatidiform mole and a normal coexisting fetus is rare; the incidence of such an occurrence ranges from 1 in 22 000 to 100 000 pregnancies and this may be increasing with the greater use of assisted reproductive techniques (1). The management of these pregnancies is difficult because they can be associated with complications such as fetal death, vaginal bleeding, pre-eclampsia, and an increased risk of persistent trophoblastic disease (PTD) (2). Consequently, early termination of pregnancy has traditionally been advised, though not all women will consider this option.

Three cases of a complete hydatidiform mole along with a coexisting live fetus (CMCF) with different clinical courses but similar outcome without a surviving neonate are presented along with a review of the literature.

Case 1
A 30–year–old woman G3P1, was admitted to our clinic at 23 weeks of gestation with elevated blood pressure (180 / 90 mmHg), dyspnea and proteinuria (3+ on urine dipstick). Symphysis–fundal height was 24 cm and uterine size was equivalent to 26 weeks of...
gestational age. Chest X-ray showed pleural effusion. Her obstetrical history included one previous cesarean delivery due to fetal breech presentation. At 18 weeks of gestation, ultrasound scan revealed a single active fetus whose size was consistent with gestational age. Moreover, an area in the placenta containing multiple small cystic structures without blood flow resembling a complete molar pregnancy was identified. Theca lutein cysts were detected in both ovaries. Maternal serum level of β-hCG was 240000 IU/L. Genetic amniocentesis revealed a normal 46XY karyotype. Diagnosis of CMCF was made. The woman was not willing to consider termination of the pregnancy. The laboratory tests were normal. Thyrotropin (TSH) was below 0.1 IU/mL, with elevated thyroxin (T4 = 21.9 μg/dL). Urine analysis and blood cell count demonstrated marked proteinuria (>300 mg/dL) and mild thrombocytopenia (95000 in micro liter). Due to severe pre-eclampsia termination of pregnancy by evacuation was carried out at 24 weeks of gestation. A stillborn male infant weighing 650g was delivered. The fetus had no structural abnormality; the placenta appeared separated from the molar tissue and was grossly normal. The molar tissue consisted of a large number of vesicles characterized by a grape-like appearance (Fig. 1). Pathology examination was consistent with a complete hydatidiform mole. Postoperatively, the clinical situation improved immediately. Serum level of β-hCG had decreased remarkably 2 weeks after surgery. After one year of follow up; no evidence of PTD was obtained.

Case 2
A 29–year–old woman G₁P₂ was referred to our clinic at 14 weeks gestation with ultrasound diagnosis of twin pregnancy showing one hydatidiform mole and a co – existing viable fetus. She had vaginal spotting for the last 4 weeks till the time of admission. On physical examination the height of the fundus of the uterus corresponded to a four–month pregnancy. The vaginal discharge was bright red. The patient was anemic; tachycardia and the blood pressure of 160 / 70 mmHg were detected. Pulmonary wet rale was noted bilaterally and chest X–ray showed pulmonary edema. Ultrasound examination revealed a viable fetus matching 12 weeks of gestation, along with a normal placenta close to an echogenic area resembling a complete molar pregnancy. The ovaries were nearly 10 cm in diameter each consisting of theca lutein cysts. The serum β–hCG level was 197000 IU/L. Her vaginal bleeding increased significantly, amounting to >1000 ml. Because of the seriousness of her condition, the patient and her husband agreed to terminate the pregnancy.

During hysterotomy the uterine contents weighted approximately 1700 g, including 150 g of fetal tissue, 50 g of placenta tissue, and 900 g of molar tissue. The placenta appeared separated from the molar tissue and was macroscopically normal (Fig. 2). Pathologic examination and DNA analysis (46XX) was consistent with a complete hydatidiform mole. Two weeks after hysterotomy, the serum β-hCG level fell to 1870 IU/L.

β–hCG level normalized within 10 weeks without any cytotoxic therapy. During a 1 year follow up period, there was no evidence of persistent or metastatic disease.

Case 3
A 25–year–old woman G₁P₁L₁ was admitted in
our clinic at 14 weeks of gestational age (according to her last menstrual period) due to vaginal bleeding. She gave a history of severe nausea and vomiting for the last week. Her blood pressure was 180/90 mmHg and the chest X-ray was normal. Physical examination revealed a fundus – symphysys length of 20 cm. The β-hCG level was 140000 IU/L. Ultrasound revealed a live fetus coexisted with a well – defined and separate multiple cystic, snowstorm-like mass in the lower segment of uterus, connecting with the normal placenta. There were large theca lutein cysts bilaterally. Coexisting complete hydatidiform mole was strongly suspected. The patient was recommended pregnancy termination, but she refused to accept. One week after admission, hysterotomy was performed because of massive vaginal bleeding. During the operation, the internal os was covered by relatively large vesicles, which were macroscopically judged as a complete mole (Fig. 3). Pathologic examination confirmed complete hydatidiform molar pregnancy with a chromosome complement of 46 XX. Serial β-hCG determinations were obtained and oral contraceptives were prescribed. Four weeks after surgery the β-hCG rose by 25%. A chest X-ray and Doppler ultrasound examination of the uterus did not reveal any abnormality. She was diagnosed as having a low risk gestational trophoblastic neoplasia and treated with four courses of intramuscular methotrexate at dose of 30 mg/m² weekly.

Then the β-hCG level rapidly fell to undetectable levels. One year follow-up was normal.

**Discussion**

A complete hydatidiform mole (CHM) consists of a generalized swelling of the villous tissue, diffuse trophoblastic hyperplasia and no embryonic or fetal tissue. The complete mole is diploid and the chromosomes are totally derived from the paternal genome (3). A partial hydatidiform mole (PHM) refers to the combination of a fetus with localized placental hydatidiform changes. PHMs are triploid in about 90% of cases, having inherited two sets of chromosomes from the father and one from the mother. CHM and PHM can both be found in association with a fetus in a twin pregnancy.

In cases of PHM, growth retardation and multiple anomalies related to triploidy have been described; women should also be offered pregnancy termination soon after the diagnosis (4). In contrast to CMCF, there have been no cases with the fetus having abnormalities and in some cases a live infant has been born (5). Therefore accurate differentiation between a CMCF and a partial mole is crucial because of the chance of survival in the instances that include a CMCF.

As with singleton molar pregnancy, patients with twin molar pregnancy have a risk of developing PTDF. The estimated risk has been reported as high as 50% (based on case reports and small series) in CMCF cases (2). Although, in the largest reported series, only a 19% risk for developing PTDF was found, but the ploidy of the molar component had not been examined in the study (6). The risk for PTDF of twin pregnancy with PHM has been reported to be 1-5% (5). It is uncertain whether the reported increased risk for PTDF following CMCF is due to a delay in termination of the pregnancy or rather to a more aggressive biological behavior of the abnormal trophoblastic tissue in these twin gestations (7). However advanced gestational age does not appear to be an independent risk factor for developing PTDF (2).

Prenatal diagnosis of coexistent mole and fetus can depend upon the clinical symptoms and signs, physical examination, sonographic findings, and abnormal biochemical data. Clinically, the patient may present hyper emesis, hyperthyroidism, vaginal spotting or even heavy bleeding, pregnancy – induced hypertension and larger than gestational age uterus.

CHM in a twin pregnancy will appear on ultrasound scan as a normal fetus and placenta next to a molar mass. A complete mole produces a characteristic vesicular sonographic pattern, so that association with a normal gestational sac can accurately be determined around 12-14 weeks (8).

Maternal serum human chorionic gonadotrophin
(MShCG) and alpha–fetoprotein (AFP) have been used to assist in the early prenatal diagnosis of the different types of molar pregnancies. Free β–hCG concentration is extremely high in CMCF pregnancies, but this is not reliable enough especially in twin pregnancies where hCG levels can be significantly, but normally, elevated and a relationship between free β–hCG and coexisting molar pregnancy has not been reported. By contrast, AFP concentrations which are extremely low in all cases of singleton complete moles can be normal to slightly increased in CMCF pregnancies (9). Bilateral multicystic ovaries due to theca lutein cystic transformation under influence of high maternal serum β–hCG are also found in about a quarter of the cases from the end of the first trimester (10). Morphological distinction between a CMCF and a partial mole is often difficult, particularly in cases aborted at an early stage of gestation. They can be definitively diagnosed only by indentifying two different genetic origins by using analytical techniques involving DNA polymorphisms (11).

These investigations may be important in prenatal management of a viable fetus complicated by a coexisting molar pregnancy. When the fetus is sonographically normal, an amniocentesis or a fetal blood sampling is a possible alternative after 15 weeks. If the fetus is euploid and the mother is clinically well, she should be followed fortnightly with ultrasound assessment of fetal anatomy and growth. However this should be done only after a detailed discussion (and informed consent) with the couple, and when close surveillance to detect potential early signs of maternal complications (pre–eclampsia, hyperthyroidism and pulmonary embolism) and fetal ones such as spontaneous miscarriage, intrauterine death and preterm labour can be guaranteed.

Molar pregnancy with a coexisting fetus progressing to a viable healthy infant is an extreme rarity. A review done by Ling Wei and Eric Jauniaux in 2005 suggests that a woman who decides to continue with the pregnancy including a CHM must be aware that overall she less than a 50% chance of a live term birth and that in around a third of cases she will develop PTD after delivery. In ongoing pregnancies, about 20% of the cases will get early onset of pre-eclampsia (12).

Al in all, the management guidelines for decision making are limited as there are only a few published reports in the literature and most are case reports. The diagnosis of CMCF presents several diagnostic dilemmas and the woman should be counseled regarding complications and risk of a PTD.

References