Postprint of a Case Report: Successful Induction of Labor and Vaginal Delivery at 16 Weeks in a Twin Pregnancy with One Hydatidiform Mole

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Abstract

Hydatidiform mole is a benign gestational trophoblastic disease. Hydatidiform mole with coexisting fetus is extremely rare, and its diagnosis is usually delayed; pregnancy termination is often required due to severe vaginal bleeding or other complications, but there are no clear guidelines regarding the choice of termination method. This article reports a case of hydatidiform mole with coexisting fetus at 16 weeks that underwent induction of labor with vaginal delivery, and analyzes its diagnosis, management principles, and choice of delivery mode.

Full Text

Successful Labor Induction and Vaginal Delivery of Twin Pregnancy with Hydatidiform Mole and a Coexistent Fetus at 16 Weeks: A Case Report

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Abstract

Hydatidiform mole is a benign gestational trophoblastic disease. Twin pregnancy with hydatidiform mole and a coexistent fetus is extremely rare, typically diagnosed late in pregnancy and often necessitating termination due to severe vaginal bleeding or other complications. However, there are few established guidelines regarding the optimal method for pregnancy termination in

such cases. Here we report a case of successful labor induction and vaginal delivery of a twin pregnancy with hydatidiform mole at 16 weeks, discussing the diagnosis, treatment principles, and selection of delivery method.

Keywords: Hydatidiform mole; Twin pregnancy; Induction

Case Report

A 36-year-old woman, gravida 3 para 1, was admitted on December 26, 2016, at 16 weeks of gestation with a twin pregnancy complicated by hydatidiform mole of one twin, diagnosed six weeks earlier. The patient had regular menstrual cycles of 5/28-30 days with moderate flow and no dysmenorrhea. Her last menstrual period was September 5, 2016.

At 5 weeks of gestation, ultrasound revealed an intrauterine twin pregnancy [Figure 1: see original paper]. At 7 weeks, ultrasound showed one viable fetus and a gestational sac-like echo in the other sac without fetal pole or cardiac activity. The patient began experiencing nausea and vomiting at 8 weeks. Ultrasound at 10-12 weeks demonstrated normal development of one twin while a mixed echogenic mass in the other sac progressively enlarged, suspicious for hydatidiform mole. Her hyperemesis worsened to 3-4 episodes of vomiting daily. She denied abdominal pain or vaginal bleeding since the missed period. At 12 weeks, ultrasound showed a gestational sac measuring $6.7\$\times7.4\times3.4cmcontainingaformedfetuswithcrown-rumplengthof6.0cmandvisiblecardiacactivity.Adjacenttothissacwasamixedechogenicmassmeasuring10.0\times9$ cm with regular morphology, clear borders, and honeycomb-like small anechoic areas [Figure 2: see original paper]. Color Doppler flow imaging showed no definite blood flow signals. Both adnexa appeared normal. At 14 weeks, pelvic MRI revealed a gestational sac within the uterine cavity containing a fetal image, with a large abnormal signal inferior and to the left of the fetus [Figure 3: see original paper]. Serum β-hCG was 608,390.0 mIU/ml.

Past and reproductive history included a medical abortion in 2005 and a full-term cesarean delivery in October 2008 due to umbilical cord entanglement. She remarried before the current pregnancy. Both her spouse and child were healthy. Gynecologic examination revealed a uterine fundus two fingerbreadths below the umbilicus, soft, without contractions. Initial diagnosis: (1) 16 weeks intrauterine pregnancy, G3P1; (2) Twin pregnancy with hydatidiform mole; (3) History of cesarean section.

After thorough discussion with the patient and family regarding the poor prognosis indicated by serum β-hCG exceeding 600,000 mIU/ml, they requested termination of pregnancy. On December 28, 2016, treatment began with oral mifepristone 50 mg twice daily for two days. On the third day, oral misoprostol 0.6 mg was administered for induction, followed by vaginal posterior fornix administration of misoprostol 0.2 mg every 2-3 hours for four doses to regulate

uterine contractions.

Regular contractions began 12 hours after medication initiation. One hour later, vesicular tissue of varying sizes was expelled, followed by spontaneous rupture of membranes. After delivery of the fetus, curettage was performed. The placenta, approximately 10$×$8 cm, was removed with forceps. The maternal surface showed numerous vesicular lesions with relatively clear demarcation from normal placental tissue. Approximately 100 g of vesicular tissue was aspirated [Figure 4: see original paper], with intraoperative blood loss of about 200 ml. On postoperative day 4, serum β-hCG was 38,449 mIU/ml at discharge.

Pathology revealed a fetus measuring 20.5 cm in length without obvious malformations. The placenta and vesicular tissue measured 22$×17×$5 cm total, with partially normal placenta and partially vesicular changes. Microscopy showed hydatidiform mole with moderate trophoblastic hyperplasia [Figure 5: see original paper], consistent with a twin pregnancy with hydatidiform mole. Immunohistochemistry of the mole tissue showed p57 positivity.

Postoperatively, the patient had no irregular vaginal bleeding. She was followed regularly with weekly serum β-hCG measurements, which normalized after 4 months. Follow-up continued for 40 weeks post-procedure (detailed values in). At 2 weeks postpartum, pelvic examination showed a uterus the size of a 7-week gestation, soft, with no adnexal masses. Menses resumed at 6 weeks postpartum. At 12 weeks, repeat ultrasound showed a uterus measuring 6.9$×8.1×$6.1 cm with heterogeneous myometrial echoes and visible vascular dilation; both adnexa were normal. Chest X-ray showed no abnormalities. The patient remains under regular follow-up.

Discussion

1. Diagnosis of Twin Pregnancy with Hydatidiform Mole Hydatidiform mole is a benign gestational trophoblastic disease (GTD) classified into complete hydatidiform mole (CHM) and partial hydatidiform mole (PHM) based on histopathology and genetic origin. Twin pregnancy with hydatidiform mole and a coexistent fetus is extremely rare, occurring in approximately 0.5-1 per million pregnancies [1]. The pathogenesis involves two simultaneously ovulated eggs fertilized by sperm: one normal egg forms a diploid zygote with normal development, while the other may be an empty egg fertilized by a single sperm forming a diploid complete mole, or less commonly, a normal egg fertilized by two sperm forming a triploid partial mole.

Clinical manifestations include irregular vaginal bleeding after amenorrhea, excessive uterine enlargement, markedly elevated serum β-hCG levels, and characteristic ultrasound findings. Compared with singleton molar pregnancies, twin pregnancies with hydatidiform mole have larger uteri, higher hCG levels, and increased risks of complications and persistent trophoblastic disease. Diagnosis

is generally delayed, with most pregnancies terminated before 20 weeks due to severe vaginal bleeding or other complications. Some patients may maintain the pregnancy beyond 20 weeks, but with higher risks of late-pregnancy bleeding and preterm delivery [2].

Twin pregnancy with hydatidiform mole must be distinguished from a partial mole with coexistent fetus, as their management and prognosis differ. In twin pregnancy with hydatidiform mole, the fetus is a normally developing diploid with potential viability, and ultrasound typically shows a viable fetus with normal placenta appropriate for gestational age alongside characteristic molar tissue. In contrast, partial mole with coexistent fetus occurs in approximately 10-20 per million pregnancies [1], where both fetal and molar components are usually triploid. The fetus often has multiple anomalies and is nonviable, with ultrasound showing triploid features such as symmetric growth restriction and structural malformations. Second-trimester ultrasound effectively differentiates these conditions.

Visualization of two gestational sacs in early pregnancy supports the diagnosis of twin pregnancy with hydatidiform mole. Fetal structural abnormalities may not be identifiable in early pregnancy, and early embryonic demise can confound diagnosis [3]. Therefore, chromosomal karyotype analysis of the fetus and placenta is crucial for differential diagnosis. CHM is diploid, most commonly resulting from fertilization of an empty egg by a single sperm (homozygous androgenetic CHM), less commonly by double sperm fertilization or biparental CHM. PHM is typically triploid from dispermic fertilization (diandric triploidy: two paternal and one maternal haploid sets). Karyotype analysis can be performed via amniocentesis or chorionic villus sampling from both molar and normal placental sites. However, karyotyping is technically difficult, time-consuming, and molar tissue culture is challenging. Fluorescence in situ hybridization (FISH) offers advantages of accuracy, direct visualization, high sensitivity and specificity, with rapid and simple performance [4]. Triploid karyotype indicates partial mole requiring immediate termination, while diploid karyotype suggests twin pregnancy with hydatidiform mole, where continuation requires individualized decision-making.

Postoperative pathology also provides important diagnostic differentiation. CHM shows complete villous degeneration and swelling without normal villous structures, embryos, or fetal adnexa. PHM shows partial villous degeneration with some normal villous tissue and possible embryonic components. p57 is a paternally imprinted suppressor gene that cannot be expressed or is minimally expressed without maternal genes. Therefore, p57 immunohistochemistry is negative in CHM tissue (except rare cases) but positive in PHM tissue.

Our patient declined genetic testing, but imaging and pathology supported a diagnosis of twin pregnancy with partial hydatidiform mole based on: (1) two gestational sacs visible on early ultrasound suggesting twin pregnancy; (2) MRI showing the gestational sac in the upper uterine segment with placenta at the fundus and molar tissue in the lower segment, suggesting separate fetal-placental

and molar tissues; (3) fetal pathology showing no obvious abnormalities, suggesting normal diploid development; and (4) positive p57 immunohistochemistry in molar tissue indicating partial hydatidiform mole.

2. Management of Twin Pregnancy with Hydatidiform Mole

2.1. Is Pregnancy Termination Necessary? Management of twin pregnancy with hydatidiform mole remains controversial. Conservative management generally recommends early termination, though patients with strong fertility desires may consider continuation with close surveillance. Large case series have reported no significant difference in the incidence of persistent gestational trophoblastic disease between cases terminated in early pregnancy versus those continuing into the second trimester or beyond [5]. Expectant management requires amniocentesis and chorionic villus sampling to exclude fetal chromosomal abnormalities, with detailed ultrasound surveillance for fetal anatomical anomalies and potential complications such as fetal demise, retroplacental hematoma, and other placental abnormalities. Major complications affecting pregnancy outcome include antepartum hemorrhage, endocrine disturbances from tumor paraneoplastic effects such as preeclampsia and HELLP syndrome, and rare gestational trophoblastic tumor metastasis. No evidence-based guidelines exist for managing continued pregnancies. Progressive molar enlargement and stable or rising serum β-hCG levels indicate poor prognosis and warrant timely termination. Immediate termination is required for severe complications. In our case, the patient experienced severe vomiting, rapid molar tissue growth, and progressively rising serum β-hCG to over 600,000 mIU/ml, prompting termination.

2.2. Method of Pregnancy Termination No clear guidelines exist for selecting termination methods in twin pregnancy with hydatidiform mole, requiring individualized decisions based on gestational age, uterine size, and complication severity. Suction curettage is generally chosen in early pregnancy. Most second-trimester cases undergo hysterotomy, with few reports of ethacridine lactate induction [6]. Cesarean section is recommended for near-term viable fetuses because molar placentas often locate in the lower uterine segment, increasing hemorrhage risk, and vaginal delivery is difficult to control with high intrauterine pressure that may increase myometrial invasion and metastasis risk. For patients with placenta previa or accreta and high hemorrhage risk, balloon tamponade or interventional procedures before termination have been suggested [7].

Second-trimester termination presents the greatest challenge. Medical induction causes less uterine damage but increases intrauterine pressure and potential invasion risk. Hysterotomy allows rapid termination but carries long-term complications affecting future pregnancies. Since 2000, only three cases of twin/triplet pregnancies with partial hydatidiform mole undergoing second-trimester medical induction have been reported [8-10]; all three showed rising serum β-hCG and lung metastasis within 2-4 weeks post-procedure requiring chemotherapy.

However, the small number of reports and lack of comparative clinical data are insufficient to contraindicate medical induction.

In our case, considering gestational age, uterine size, formed fetus making fragmentation difficult, and the patient' s desire for future fertility, we selected medical induction to minimize uterine damage. The procedure proceeded smoothly without major hemorrhage or pulmonary embolism. Close postoperative follow-up showed no myometrial invasion or distant metastasis, with serum β-hCG normalizing 4 months after termination. The patient remains under surveillance.

Conclusion

Twin pregnancy with hydatidiform mole is clinically rare, lacking standardized diagnostic and therapeutic guidelines. Management requires careful patient assessment, prenatal diagnosis to evaluate fetal viability, thorough communication with patients, and individualized treatment selection. Clinicians must remain vigilant for potential complications during treatment and conduct close serological and imaging follow-up after pregnancy termination.

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Note: Figure translations are in progress. See original paper for figures.