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Case Report

Partial hydatidiform mole pregnancy ended in full-term delivery of a normal infant: a case presentation

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Abstract: Background: Twin pregnancy with a partial hydatidiform mole (PHM) and a coexistent live fetus is extremely rare. The fetus usually has a normal karyotype. The surviving rate of the fetus till lung maturity is only about 25-40%. PHM pregnancy almost ends in abortion due to the presence of triploid embryo. Here, we report a case of PHM coexistent with a live fetus resulting in a live baby. Case presentation: A PHM pregnancy was diagnosed by ultrasonography in a 28-year-old Chinese woman, with normal fetal morphology and mosaicism as indicated by amniocentesis. After being fully informed of the risks, the woman chose to proceed with the pregnancy and finally gave birth to a baby girl and the infant was delivered at term. A single placenta with vesicular changes and peripheral blood diploid chromosomes were observed. There were no serious maternal complications. In conclusion, the diagnosis, management, and monitoring of this condition, which is very rare in clinical practice, remain challenging. Under proper management, a PHM-combined pregnancy can still end in full-term delivery of a normal living fetus.

Keywords: Partial hydatidiform mole, prenatal diagnosis, normal live fetus, case presentation

Introduction

Co-existence of a molar and a live fetus in pregnancy is extremely rare, occurring in 1 of 20,000-100,000 pregnancies [1]. Hydatidiform moles (HMs) can be classified as complete (CHM) and partial hydatidiform mole (PHM), which are distinct in terms of clinical, histological, and cytogenetic characteristics [2]. Of them, PHM, with a triploid set of chromosomes, is derived from dispermy of normal haploid oocytes; while CHM has 46 diploid paternal chromosomes. Fetuses in PHM pregnancies tend to develop malformations, whereas fetuses in CHM pregnancies do not develop. Most HM-associated twin pregnancies are CHM pregnancies with a normal fetus and placenta [3]. While PHM pregnancy coexisting with a live fetus is exceedingly rare, as triploid fetuses are usually miscarried in early pregnancy [4, 5]. To our knowledge, only few cases of PHM pregnancy have been reported with full access and in English, as shown in **Table 1**.

Herein, we present a case of PHM coexisting with a diploid fetus, which later resulted in a full-term live birth by caesarean section (CS). No maternal complications were found.

Case presentation

The patient was a 28-year-old Han Chinese woman (gravida 0, para 0), who had no family history of obstetrical and gynecological diseases and denied using any sex hormone drugs. Obstetric examinations were performed regularly in the Department of Obstetric Clinic, Chongqing Health Center for Women and Children. On November 7, 2018 (24^{th} week of gestation), ultrasonography (US) revealed an anatomically normal fetus with no obvious abnormality. The placenta was vesicular with a size of 13.3×5.8 cm; the placenta showed vesicular changes of the villi and partial glucose consumption (**Figure 1**). A provisional diagnosis of coexistence of a HM with a live fetus was made after amniocentesis (AC). The examination showed no abnormalities in the chromosomes 21, 18, and 13 or sex chromosomes in the fetus. After being fully informed of the risks of premature birth and gestational trophoblastic diseases, the woman chose to continue the

Table 1. Literatures reported cases of partial hydatidiform mole coexisting with a fetus in English

Published Year	Authors	Maternal age	Gravida/Para	Maximum serum β-hCG	Delivery or termination (weeks)
1975	Jones, W B, and N H Lauersen. [6]	not mentioned	not mentioned	not mentioned	40
1975	Wunderlich. M. [7]	not mentioned	not mentioned	not mentioned	40
1983	Hartfield, V J. [8]	not mentioned	1/0	not mentioned	38
1989	Pool, R et al. [9]	20	1/0	1387 IU/L	38
2004	Dhingra, Kajal Kiran et al. [10]	28	1/0	not mentioned	38
2004	Parveen, Zahida et al. [11]	23	3/1	not mentioned	39
2019	Zeng, Chengying et al. [12]	32	3/2	169200 mIU/mL	29
2020	Gajewska, Malgorzata et al. [13]	28	not mentioned	1601660 IU/L	25
2020	Ray, Alokananda, and Sarita Kumari. [14]	20	2/0	232518 mIU/ml	15
2021	Lin, Minhuan et al. [15]	33	2/0	105851 mIU/mL	40

pregnancy. A PHM was indicated by multicolor Doppler ultrasound. No obvious abnormalities were found in blood, urine routine, or liver and kidney function in the third trimester of pregnancy. At 38^{+1} weeks of gestation, the pregnant woman felt less fetal movement and no abdominal pain, but presented with vaginal bleeding, discharge and other discomfort. The non-stress test (NST) of fetal heart monitoring in the outpatient department was suspicious.

On 11 April 11, 2019 (38^{+2} weeks of gestation), the patient underwent CS with a low transverse incision combined with spinal-epidural anesthesia because of her excessive worrying, and a 3240 g, 50-centimeter live baby girl was born with the 1-, 5-, and 10-minute Apgar scores of all 10 points. There were some vesicular villi on placenta. Histopathological examination of the placenta (19×18×2.0 cm) revealed a partial vesicular placental mass and trophoblastic hyperplasia (grade I) with partial infarction of the placenta as well as amniotic edema and stenosis of the umbilical artery and vein with interstitial edema (**Figure 2**). Immunohistochemistry for p57 and Ki67 determined positive expression of p57 and Ki67 (**Figures 3** and **4**).

The postnatal karyotype was 46, XX. After smooth postoperative recovery, the patient was discharged on the third day after CS. On day 1 after discharge, the level of β-hCG was 45,127 mIU/mL, which decreased to 3,114 mIU/mL at week 2, 418 mIU/mL at week 4, and 0 at week 10. The baby is currently growing well.

Discussion and conclusion

A hydatidiform mole (HM) is a rare complication of pregnancy that can be divided into CHM and PHM, with some differences in pathogenesis, clinical manifestations and treatment. CHM is a twin pregnancy that can be continued, with a fetal survival rate of 24% and almost as high as 69% after 28 weeks of pregnancy [15], while PHM is a single pregnancy in which the fetus is triploid and rarely develops to the second and third trimesters, with a lower risk of obstetric complications during pregnancy and persistent gestational trophoblastic disease (PGTD) (4%) than CHM, and there are rarely lung metastases that seldom need chemotherapy [16]. A search for the literature from 1975 to 2021 in PubMed revealed that only several similar cases with partial mole had been reported (**Table 1**).

HM, with no fetal structure, has 46 chromosomes with all genetic material from paternal line; of note, CHM pregnancies present with a higher risk of trophoblastic sequelae (15-20%) than PHM pregnancies (<5%) [17]. A PHM pregnancy occurs when a normal-looking egg is fertilized by two sperm, producing a triploid karyotype (69, XXY). At present, three types of HM pregnancies with normal live births have been identified, the most common of which is a twin pregnancy in which one normal fetus has a normal placenta and the other is a CHM. The second type is a twin pregnancy with a normal fetus and placenta and the other being a PHM. The third, and rarest, is a singleton normal fetus with a PHM pregnancy [18]. In the study of Bristow et al. [19], data abstracted from 25 well-documented cases of twin pregnancies consisting of a CHM and a coexisting fetus from the literature were analyzed. The results showed that in patients with CHM and coexistent fetus, fetal survival is associated with clinical characteristics suggestive of less exuberant molar growth.

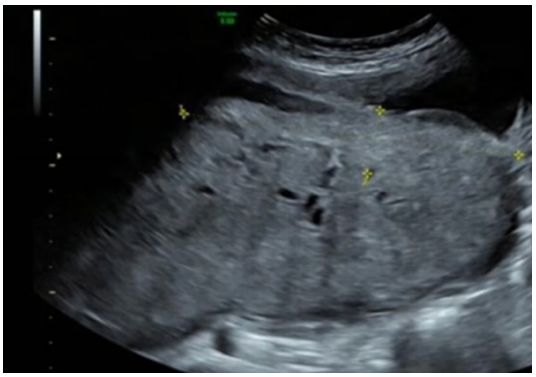

Figure 1. The fetal surface of the placenta is about 13.0 cm×2.6 cm in size with local heterogeneity, and slightly hyperechoic, with a few non-echoic areas of different sizes in it. Partial hydatidiform mole is considered.

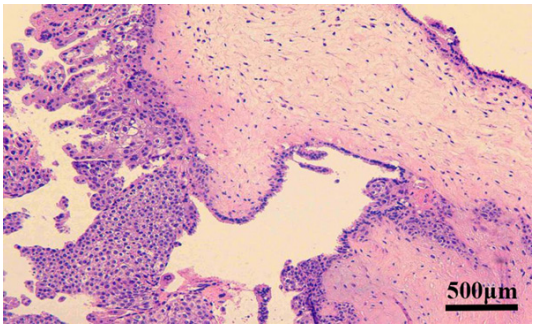

Figure 2. Histopathological examination of the placenta showed a partial vesicular placental mass and grade I trophoblastic hyperplasia with partial infarction of the placenta as well as amniotic edema and stenosis of te umbilical artery and vein with interstitial edema. Original magnification: ×100.

Prenatal diagnosis of pregnancy associated with HM is mainly based on US [20]. PHM on prenatal US is usually manifested as a honeycomb-like echo in the placenta, with ill-defined boundary between normal placental tissue and honeycomb echo, and death of malformed fetuses in most cases [21, 22], while rarely shows normal structure [3]. US revealed normal fetal anatomy in this patient at week 24. Fetal heart ultrasound showed no obvious abnormality. The placenta was vesicular and 13.3 cm×5.8 cm in size; the placenta had vesicular changes of the villi and PHM. AC was performed and a tentative diagnosis of a HM coexisting with a live fetus was proposed. There was no abnormality in chromosomes (21, 18, or 13) or sex chromosomes in the fetus. We considered the possibility of amniotic fluid

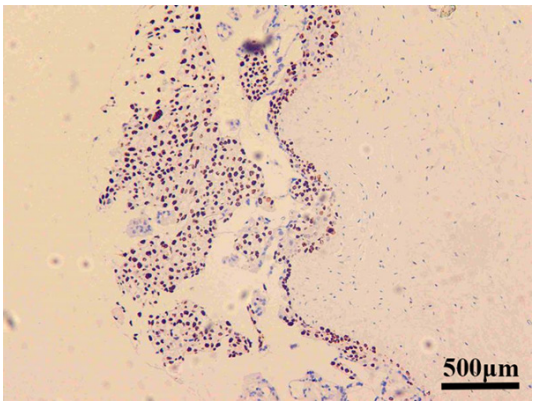

Figure 3. Immunohistochemistry for Ki67 in the placenta was positive. Original magnification: ×100.

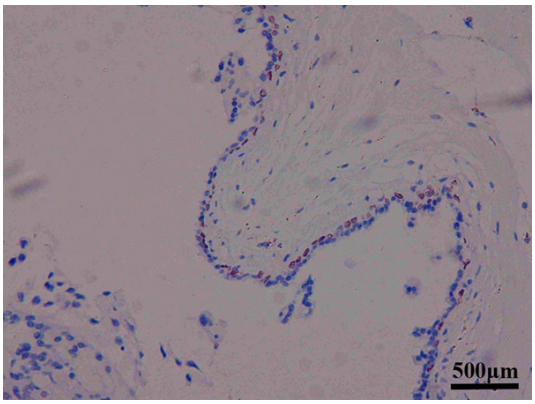

Figure 4. Immunohistochemistry for p57 in the placenta was positive. Original magnification: ×100.

pseudo-chimerism as the US showed a normal fetal structure. Furthermore, the pregnant woman and fetus were monitored according to the patient's wishes, and no significant elevation in serum hCG and normal fetal growth indexes were observed. Finally, the patient gave birth to a normal-looking and normal karyotypic live baby at 38th week of gestation. Postoperative placental pathology and immunohistochemistry confirmed the diagnosis of PHM.

HM pregnancy, once diagnosed, is generally terminated [6]. Most CHM fetuses develop normally, so with appropriate support, a woman can choose to continue her pregnancy [23]. However, it is important to fully inform the pregnant women of potential maternal and infant complications, such as hyperthyroidism, colporrhagia, preeclampsia, and theca-lutein ovarian cysts. There is also a probability of develop-

ing postpartum PGTD. In PHM, only a few villous vesicles are altered, with highly proliferated cells, and 90% of the fetal chromosome karyotype being triploid, resulting in abortion and fetal death in most pregnancies. The probability of developing postpartum PGTD was 4%, much lower than that of CHM, so chemotherapy is rarely required [16, 24]. A number of articles have been published in this field [25], including metastasis during pregnancy [26] or postpartum [27].

The diagnosis of pregnancy with HM still depends on pathological diagnosisexamination. However, PHM is morphologically similar to HM, and CHM is often difficult to identify, so further immunohistochemistry is required. p57 is a maternally expressed gene. PHM contains both parents' chromosomes, while CHM contains only paternal chromosomes, so p57 is positive in PHM and negative in CHM [28, 29].

In this study, the patient's blood hCG decreased to the reference range one month after childbirth. PHM was confirmed by postoperative placental pathology, and immunohistochemistry showed positive expression of p57 and Ki67. Ki67 protein is present in all active phases of the cell cycle (G1, S, G2 and mitosis) but absent in resting cells (G0), which makes it an excellent marker to reflect tissue proliferation [30]. Immunohistochemistry is a relatively simple choice compared with more complex techniques [31]. In a study of twin pregnancy with metastatic CHM and coexisting live fetus, Ki67 was found to increase the mitotic index and stained almost 100% of the cytotrophoblast s [32].

We initially proposed termination of pregnancy after the diagnosis of PHM. But this case demonstrates that, under proper management, PHM-complicated pregnancy can still result in birth of normal infant. Therefore, although extremely rare, this case is important because the identification and diagnosis of PHM are critical to patient care. Prenatal differential diagnosis plays an important role in determining the clinical treatment of HM and fetus. Prenatal interventional diagnosis was performed by US-guided transabdominal chorionic villus biopsy and AC, and fetal karyotype was determined by combining with the interphase FISH technique [33]. If the chromosome karyotype was diploid, expectant therapy, regular prenatal examination, timely detection of complications and early treatment, and postpartum follow-up could be considered, especially for women at advanced pregnant age with induced ovulation and assisted reproduction. It has been reported that about 24% of the patients may give birth to a survival new-born. If it is triploid, the pregnancy should be terminated immediately upon diagnosis, and follow-up should be carried out after delivery. In this patient, maternal and fetal monitoring and follow-up were carried out strictly following HM follow-up principles.

Twin pregnancy with CHM are associated with a higher risk of maternal complications, such as antepartum hemorrhage, severe early-onset pre-eclampsia or eclampsia, placenta previa, preterm premature rupture of the membranes, and preterm labor [34]. Pregnancy termination in women with HM depends largely on gestational duration and disease status. Early in pregnancy, the termination is usually accomplished by complete uterine curettage, while there is still a great controversy regarding the use of intra-amniotic Rivanol injection, intravenous oxytocin and CS in the second trimester [35]. CS is recommended for women with HM pregnancy because the risk of pulmonary embolism is increased due to repeated uterine contractions that increase the likelihood of HM tissue being squeezed into the abdominal cavity.

Conclusion

Although extremely rare, twin pregnancy with HM should be considered by obstetricians during prenatal care. We still need to identify them carefully in clinical practice, especially for older mothers who have difficulty in conceiving or withhave fetuses of diploid karyotype. For such patients, the pregnancy should be continued under strict monitor and in a fully informed manner to increase the probability of a live birth.

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Disclosure of conflict of interest

None.

Abbreviations

HM, hydatidiform mole; PHM, partial hydatidiform mole; CHM, complete hydatidiform mole; US, ultrasonography; NST, non-stress test; CS, cesarean section; hCG, human chorionic gonadotropin; PGTD, persistent gestational trophoblastic disease; AC, amniocentesis.

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