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CASE REPORT

Rare Case Report: Coexistence of Complete Hydatidiform Mole and Normal Fetus in a Twin Pregnancy

Ping Li, XiuPing Liu

Obstetrics and Gynecology Department of the Hebei Medical University Third Hospital, Shijiazhuang, People's Republic of China

Correspondence: Ping Li, Obstetrics and Gynecology Department of the Hebei Medical University Third Hospital, No. 139, Ziqiang Road, Qiaoxi District, Shijiazhuang, Hebei Province, People's Republic of China, Tel +86-13472101436, Email liping111p@163.com

Background: The coexistence of a complete hydatidiform mole with a normal fetus in a twin pregnancy is a rare, high-risk obstetric condition with an extremely low incidence rate, presenting numerous clinical management challenges. The rarity of such cases, coupled with the scarcity of comprehensive literature, makes the successful management of this case a source of valuable experience and novel insights for clinical practice.

Case Presentation: A 32-year-old patient conceived following a clomiphene-induced ovulation regimen. Mid-pregnancy ultrasound indicated a twin pregnancy (one viable fetus, the other consistent with the appearance of a complete hydatidiform mole), and the patient chose to continue the pregnancy. At 36+4 weeks of gestation, the patient was admitted for pregnancy-induced hypertension and underwent a cesarean section, delivering a healthy female infant and simultaneously removing the molar tissue. Postoperative pathological examination confirmed a complete hydatidiform mole with invasive lesions, which progressed to an invasive hydatidiform mole. The patient underwent seven cycles of methotrexate combination chemotherapy, with a follow-up period of three years showing no recurrence, ensuring the health of both mother and child.

Conclusion: Managing twin gestations involving a complete hydatidiform mole and a normal fetus necessitates a multidisciplinary approach, grounded in individualized assessment. The successful treatment of this case demonstrates that standardized diagnosis, close postoperative follow-up, and chemotherapy are crucial factors in improving maternal and fetal outcomes, offering significant clinical reference value.

Keywords: complete hydatidiform mole, twin pregnancy, individualized management, chemotherapy, pregnancy-induced hypertension

Background

The coexistence of a complete hydatidiform mole and a normal fetus in a twin pregnancy is an extremely rare and complex obstetric condition, with an incidence rate of approximately $1–2\times10^{-5}$.[1] The formation of a complete hydatidiform mole typically results from the absence of maternal genetic material in the egg, with fertilization occurring solely with paternal diploid chromosomes, while the presence of a normal fetus may result from fertilization of two independent eggs or abnormal splitting of a single fertilized egg. Complete hydatidiform moles typically present as "snowflake" or "honeycomb" mixed echoes on ultrasound, caused by abnormal proliferation of trophoblastic cells and accumulation of vesicular tissue.[2]

Twin pregnancies with a coexisting hydatidiform mole and normal fetus carry an extremely high risk of maternal complications, including pregnancy-induced hypertension, pre-eclampsia, hyperthyroidism, and trophoblastic embolism. The risk of trophoblastic tumors (such as invasive moles and choriocarcinoma) significantly increases, with some studies indicating an incidence rate of 27%-46%, far higher than the 15%-20% in singleton molar pregnancies.[3] Additionally, the fetal survival rate is only 40%, with a median gestational age at delivery of about 35 weeks, closely related to impaired

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placental function due to abnormal trophoblastic proliferation.[4] Therefore, the diagnosis and treatment of this condition pose significant clinical management challenges.

In recent years, advancements in ultrasound technology and cytogenetic analysis have greatly improved the early diagnosis and differentiation of complete hydatidiform moles. However, reports and systematic studies on cases of coexisting complete hydatidiform moles and normal fetuses are scarce in China, especially regarding pregnancy management and outcome assessment. For example, in decision-making on whether to terminate the pregnancy, most studies suggest terminating pregnancies with partial moles accompanied by severe maternal complications, while cases of complete hydatidiform moles coexisting with normal fetuses require individualized assessment based on maternal and fetal conditions.

This study reports a successful pregnancy and delivery case of twin pregnancy with a complete hydatidiform mole coexisting with a normal fetus, featuring the following novelties and clinical values: ① Rarity of the case: Such cases are extremely rare, especially in China, where systematic management and treatment experience are lacking; ② Innovative diagnosis and treatment process: This case was successfully diagnosed in mid-pregnancy, and an individualized treatment plan was formulated, ultimately achieving a favorable maternal and infant outcome; ③ Practical reference value: By summarizing the diagnosis, treatment process, and long-term follow-up data of this case, this study provides important references for the early diagnosis, pregnancy management, and postoperative follow-up of similar cases in China, filling a research gap in the related field.

The report aims to raise awareness of twin pregnancies with a complete hydatidiform mole coexisting with a normal fetus and provide clinicians with experiential guidance for managing analogous high-risk cases.

Case Introduction

A 32-year-old married woman, with a history of one medical abortion at the age of 30 (8 weeks of gestation, treated with mifepristone combined with misoprostol), and irregular menstruation (cycles ranging from 30 to 180 days), underwent clomiphene-induced ovulation treatment for infertility. The dosage was 50mg/d for 5 consecutive days, and follicular rupture and ovulation as well as successful pregnancy were confirmed on day 12 post-treatment. The early pregnancy was uneventful, with no nausea, vomiting, history of viral infections, or exposure to toxins, and ultrasound indicated an anechoic area beneath the gestational sac, with no vaginal bleeding during pregnancy. At 17 weeks gestation, an external hospital ultrasound suggested a twin pregnancy (one viable fetus and the other likely a complete hydatidiform mole), with blood HCG at 216190mIU/mL. The patient chose to continue the pregnancy without further diagnostic confirmation. The patient first visited our hospital at 33 weeks of gestation. Ultrasound suggested a twin pregnancy (one viable fetus with a gestational age of 33 weeks and 4 days by ultrasound, and the other suspected to be a hydatidiform mole). The serum β-HCG level was 53,563 mIU/mL (Figure 1). At 35 weeks gestation, the patient's blood pressure rose to 162/110mmHg, diagnosed as pregnancy-induced hypertension, initially managed with oral labetalol 100mg/12h, later adjusted to 200mg/12h and 100mg/8h. Subsequent ultrasound examination suggested "a single viable fetus with intrauterine honeycomb-like mixed echoes", consistent with a complete hydatidiform mole.

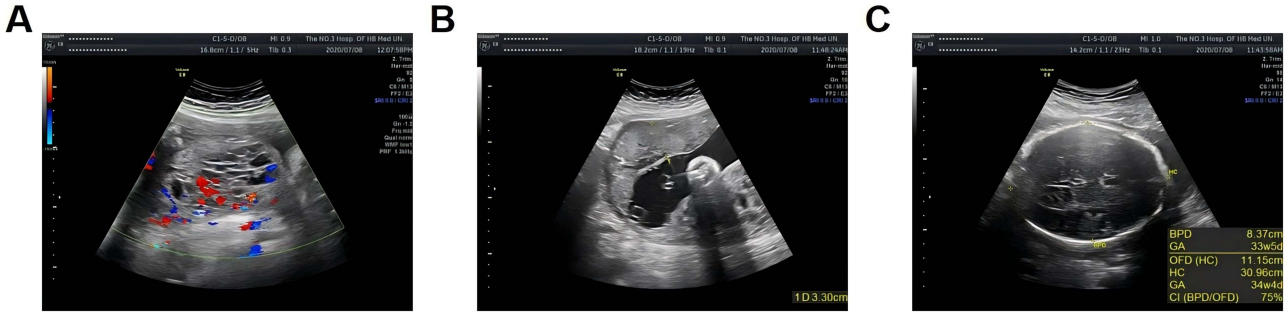

Figure 1 (**A**) Ultrasound appearance of "snowflake-like" hydatidiform mole tissue. (**B**) The ultrasound shows normal placental tissue. (**C**) The viable fetus with an ultrasound gestational age of 33 weeks and 4 days.

At 36+4 weeks gestation, the patient was admitted due to the complexity of her condition. Upon admission, her blood pressure was 152/102mmHg, fetal heart rate was 153 beats/min, fundal height was 33cm, and amniotic fluid index was 103mm. Color Doppler ultrasound showed a single viable fetus in the left occiput anterior position, accompanied by mixed echoes consistent with a complete hydatidiform mole. At 37+6 weeks, a lower segment cesarean section and molar tissue removal were performed.

Intraoperatively, the placenta was attached to the anterior uterine wall, with intact placental lobules and a large amount of vesicular tissue (diameter 0.5–2cm). Postoperative pathology results confirmed a complete hydatidiform mole, with immunohistochemistry showing negative P57, positive HCG, and a Ki-67 proliferation index of 40%. The patient recovered well postoperatively, but was readmitted 42 days postpartum due to heavy vaginal bleeding, with a blood HCG level of 1916mIU/mL, diagnosed as an invasive mole (FIGO III:2).

The chemotherapy regimen consisted of methotrexate 50mg/m^2, once a week, combined with calcium folinate 15mg. The patient's weight was 90kg, with methotrexate dosed at 1mg/Kg and calcium folinate at 0.1mg/Kg. Specific medication included: on days 1, 3, 5, and 7, methotrexate 90mg was administered intramuscularly, and on days 2, 4, 6, and 8, calcium folinate 9mg was administered intramuscularly for detoxification treatment (24h after methotrexate administration). The specific dosages were tailored to the patient's weight and overall clinical condition to ensure effective treatment while minimizing the risk of toxicity. Calcium folinate was administered as a rescue agent to mitigate potential side effects of methotrexate, in line with standard protocols.

After four cycles of chemotherapy, HCG levels returned to normal (1.8mIU/mL), and a total of seven consolidation therapy cycles were completed. The patient remained recurrence-free during a 3-year follow-up, and both mother and child are healthy.

Pathological diagnosis (Figures 2–4): 1. (Placental tissue) Localized placental infarction with minimal calcification.

Immunohistochemistry: P57 (+) HCG (+) P53 (wild-type +) ki-67 (+, 5%)

2. (Hydatidiform mole) Consistent with a complete hydatidiform mole with necrosis.

Immunohistochemistry: P57 (-) HCG (+) P53 (wild-type +) ki-67 (+, 40%)

The patient's serum β-HCG levels were closely monitored during the postpartum period and throughout the chemotherapy regimen, as shown in the Table 1.

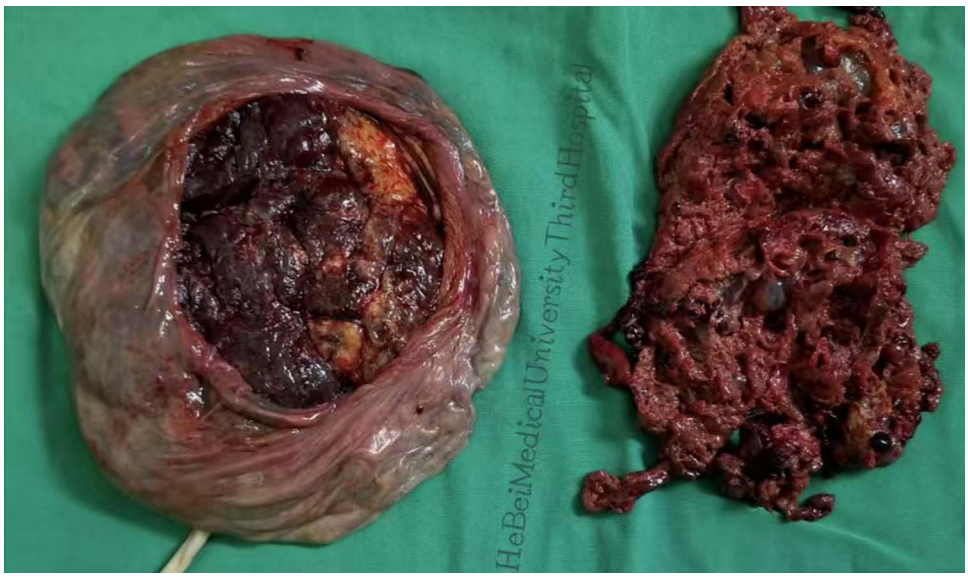

Figure 2 Comparative image of normal placenta (left) and hydatidiform mole tissue (right).

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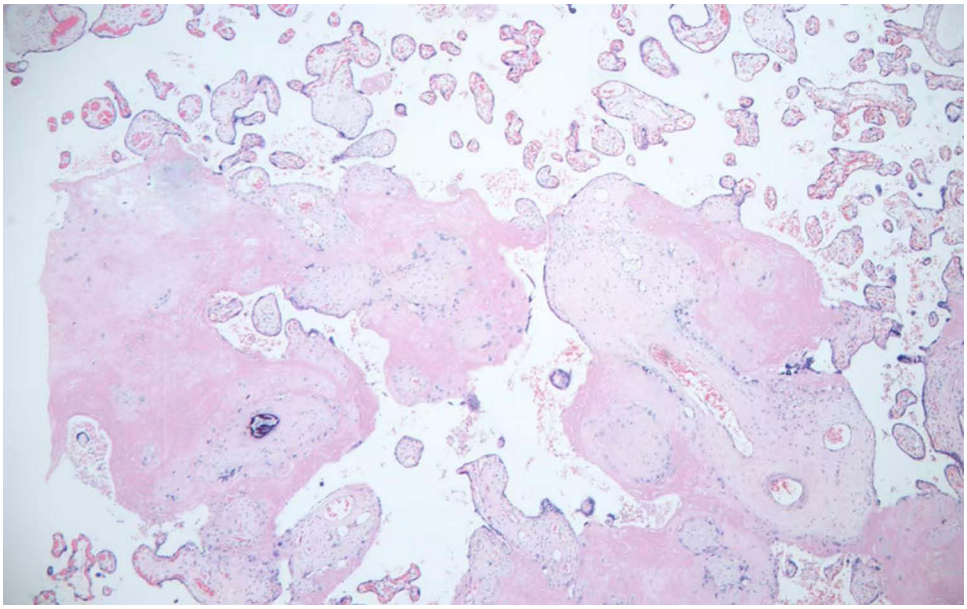

Figure 3 Pathological slice showing localized placental infarction with minimal calcification.

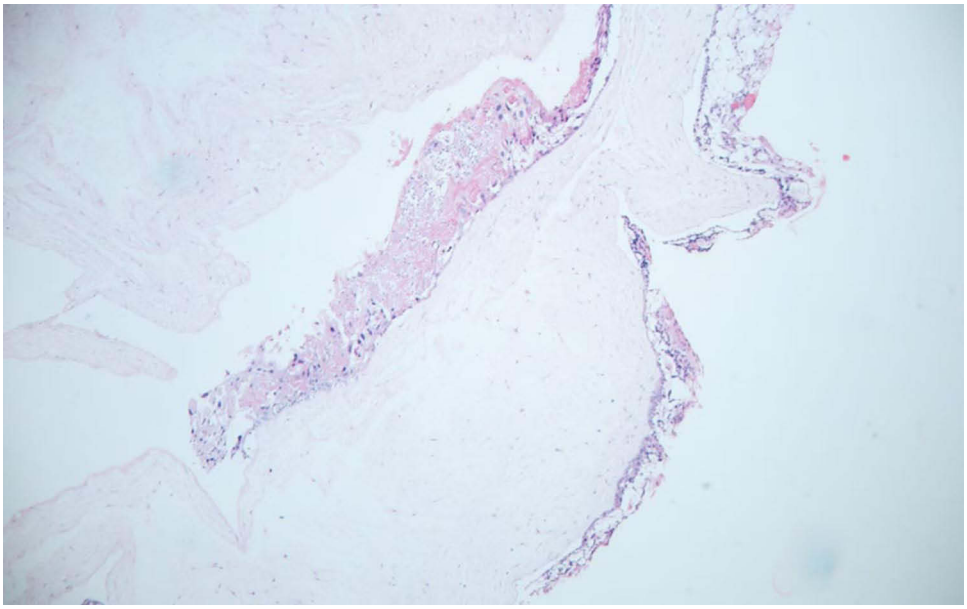

Figure 4 Pathological slice of a complete hydatidiform mole showing abnormal proliferation of trophoblastic cells and necrotic tissue.

Discussion

The coexistence of a complete hydatidiform mole and a normal fetus in a twin pregnancy is an extremely rare and high-risk obstetric condition that poses significant challenges in clinical management. Our case highlights the importance of early diagnosis, close monitoring of maternal complications, and standardized postoperative follow-up in achieving favorable outcomes. The successful management of this case underscores the value of a multidisciplinary approach and individualized treatment plans tailored to the specific needs of the patient.

Existing literature primarily focuses on its pathogenesis, pregnancy outcomes, and maternal-fetal management, providing important references for the diagnosis and treatment of such cases.[5–7] However, due to the rarity of the disease, the systematic nature and comprehensiveness of related research still need improvement. International literature

Table 1 Dynamic Changes in β-HCG Levels

Timepoint	β-HCG Level (mIU/mL)	Event Description
7 days postpartum	100.5	Initial postpartum measurement
45 days postpartum	451.9	
48 days postpartum	1916.0	
50 days postpartum	2391.0	Initiation of chemotherapy
7 days after 1st chemotherapy cycle	830.5	
7 days after 2nd chemotherapy cycle	57.0	
7 days after 3rd chemotherapy cycle	7.3	
7 days after 4th chemotherapy cycle	1.8	
7 days after 5th chemotherapy cycle	1.0	
7 days after 6th chemotherapy cycle	0.9	
7 days after 7th chemotherapy cycle	0.2	

Notes: These data demonstrate the patient's favorable response to chemotherapy, with a significant decline in β-HCG levels to within the normal range and maintained stability during follow-up.

indicates that the main risk of complete hydatidiform mole lies in the high incidence of severe maternal complications and the lower survival rate of the fetus.[8] A study by Suksai et al, which analyzed 63 patients, found that close monitoring of maternal complications (such as blood pressure and thyroid function) plays a key role in improving pregnancy outcomes.[4] Meanwhile, Lin et al, through a retrospective study of cases in North and South America, pointed out that early diagnosis and multidisciplinary collaboration are important factors in increasing fetal survival rates.[3] However, the fetal survival rate remains low, with literature reporting only about 40%, and a median gestational week of 35 weeks. This aligns with the current case, where the patient delivered a healthy infant via cesarean section at 37+6 weeks, but experienced severe maternal complications such as pregnancy-induced hypertension during management, highlighting the need for special attention to maternal condition monitoring and intervention in managing such cases.

In addition to pregnancy management, postoperative follow-up and prognosis assessment are also important topics of literature research. A study by Sebire et al indicated that the risk of trophoblastic tumors significantly increases postoperatively in patients with complete hydatidiform mole, with an incidence rate of 15%-46%.[2] The dynamic monitoring of serum β-HCG levels was crucial in managing this case. As detailed in the Table 1, the patient's β-HCG levels were tracked from the early postpartum period through the entire chemotherapy regimen. The significant decline in β-HCG levels after each chemotherapy cycle demonstrated the effectiveness of the methotrexate combination regimen. The patient completed a total of seven cycles of consolidation therapy and remained recurrence-free during the 3-year follow-up period. This case highlights the importance of close monitoring of β-HCG levels and standardized chemotherapy protocols in achieving favorable outcomes in high-risk cases involving complete hydatidiform moles. Therefore, strict postoperative monitoring (such as regular serum HCG testing) and standardized chemotherapy protocols are key to reducing the risk of recurrence. The patient in this case experienced a recurrence of trophoblastic invasive disease 42 days postoperatively but achieved complete remission through a methotrexate combination chemotherapy regimen, with a 3-year follow-up showing no recurrence. This result demonstrates that even in high-risk cases, standardized follow-up and treatment can effectively improve long-term prognosis.

This case adds significant value to the global understanding of hydatidiform mole management, especially considering the noted scarcity of systematic studies and comprehensive case reports in China. The successful outcome of this case demonstrates that individualized, multidisciplinary management can achieve favorable results even in high-risk pregnancies, aligning with international best practices. For example, studies from North and South America have reported fetal survival rates of approximately 40% in twin pregnancies with complete hydatidiform mole, with a median gestational age at delivery around 35 weeks.[3] Our case achieved a healthy delivery at 37+6 weeks, exceeding the median reported in international literature. This highlights the potential benefits of early diagnosis and close monitoring of maternal complications, which are critical factors in improving pregnancy outcomes.

Genetic and molecular diagnostics played a crucial role in confirming the diagnosis and guiding treatment decisions. Immunohistochemical staining for P57, a maternally imprinted gene, was particularly instrumental in differentiating between complete and partial hydatidiform moles. The absence of P57 expression in the molar tissue, as seen in our case, confirmed the diagnosis of a complete hydatidiform mole.[1] This molecular confirmation is essential, as complete hydatidiform moles carry a higher risk of invasive disease and subsequent gestational trophoblastic neoplasia compared to partial moles. The use of P57 staining not only provided a definitive diagnosis but also informed our decision to closely monitor the patient postpartum for signs of invasive disease. The detection of elevated β-HCG levels 42 days postpartum, combined with the histopathological findings, led to the diagnosis of invasive mole. This early detection allowed for prompt initiation of chemotherapy, which was critical in achieving complete remission and preventing further complications.

Our case highlights the importance of a multidisciplinary approach in managing pregnancies complicated by complete hydatidiform mole, emphasizing the essential collaboration between obstetricians, oncologists, and pathologists to achieve favorable maternal and fetal outcomes. The successful management underscores the benefits of individualized treatment plans that consider the specific risks and needs of the patient. While existing research provides strong support for early diagnosis, individualized treatment, and follow-up management, there remains a lack of systematic studies and case reports, especially in domestic literature. Future research should focus on optimizing diagnostic protocols and refining treatment strategies, including the use of advanced genetic and molecular diagnostics for early detection and risk stratification. Multicenter studies with larger sample sizes are needed to validate the effectiveness of individualized treatment plans and standardized postoperative follow-up protocols. This case offers valuable insights for further optimizing management processes, such as conducting individualized assessments based on maternal and fetal conditions, performing routine ultrasound and genetic testing in high-risk pregnancies to improve early diagnosis rates, and emphasizing long-term postoperative follow-up to enhance outcomes, particularly for patients at higher risk of trophoblastic tumor recurrence.

Conclusion

The coexistence of a complete hydatidiform mole and a normal fetus in a twin pregnancy is a rare high-risk disease, whose successful management relies on early diagnosis, monitoring of maternal complications, and standardized postoperative follow-up. This case, through individualized treatment and rigorous chemotherapy, achieved favorable maternal and infant outcomes, providing significant references for the diagnosis and treatment of such cases. Meanwhile, domestic research in this field should be strengthened through multicenter studies to refine diagnostic and treatment standards and improve management levels.

Ethical Considerations

This case report was conducted in accordance with the ethical standards of the institution and the 1964 helsinki Declaration and its later amendments. Institutional approval was obtained from Hebei Medical University Third Hospital. for the study and publication of this case report. Written informed consent was provided by the patient to have the case details and any accompanying images published. The patient's privacy and confidentiality were maintained throughout the study and publication process.

Consent for Publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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