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Second-Trimester Pregnancy Loss Associated with Suspected Partial Hydatidiform Mole: Two Case Reports from a Moroccan Tertiary Center

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Abstract

Partial hydatidiform mole is an uncommon form of gestational trophoblastic disease and is usually diagnosed during the first trimester. Persistence into the second trimester with fetal development is rare and may present as late miscarriage or fetal demise, creating diagnostic and therapeutic challenges. We report two anonymized cases managed at Hassan II University Hospital Center in Fez, Morocco. The first patient was a 34-year-old gravida 4 para 2 referred at approximately 17 weeks of gestation for suspected trophoblastic disease after recurrent metrorrhagia, exaggerated pregnancy symptoms, severe anemia, markedly elevated beta-hCG and ultrasound findings of a live fetus with a thick heterogeneous multicystic placenta and bilateral theca lutein cysts. During admission, she expelled a living male fetus with the placenta. Post-expulsion follow-up was marked by an initial beta-hCG decrease followed by persistent re-elevation. Control ultrasound showed an empty uterine cavity in a globular enlarged adenomyotic uterus and persistent bilateral theca lutein cysts reaching 15 cm after two months. Hysteroscopy revealed placental debris, prompting aspiration for histopathological proof because the initial placental pathology had not confirmed a molar lesion. The second specimen was also negative for molar changes, but beta-hCG continued to rise. Cerebral, thoracic, abdominal and pelvic computed tomography did not identify another lesion likely to secrete beta-hCG. The patient was therefore managed as postmolar gestational trophoblastic neoplasia and received six cycles of methotrexate. The second patient was a 25-year-old primigravida followed at 21 weeks of gestation after ultrasound suspicion of partial molar pregnancy, with a live fetus, suspected cardiac malformations, a thick vacuolated placenta, large theca lutein cysts and beta-hCG greater than 225,000 IU/L. She subsequently delivered a stillborn female fetus by vaginal delivery, followed by progressive decline of beta-hCG under weekly surveillance. These cases emphasize that partial molar pregnancy should be considered when second-trimester pregnancy loss is associated with cystic placental changes, markedly elevated beta-hCG and theca lutein cysts. They also highlight the importance of histopathological confirmation, serial beta-hCG monitoring and multidisciplinary follow-up to detect retained trophoblastic tissue or postmolar gestational trophoblastic neoplasia.

Keywords: *Partial Hydatidiform Mole; Molar Pregnancy; Gestational Trophoblastic Disease; Gestational Trophoblastic Neoplasia; Late Miscarriage; Second-Trimester Pregnancy Loss; Beta-hCG; Theca Lutein Cysts*

Abbreviations

Beta-hCG: Beta-Human Chorionic Gonadotropin; CT: Computed Tomography; GTD: Gestational Trophoblastic Disease; GTN: Gestational Trophoblastic Neoplasia; MTX: Methotrexate; PHM: Partial Hydatidiform Mole; RAI: Red Blood Cell Antibody Screening

Introduction

Gestational trophoblastic disease comprises a spectrum of disorders arising from abnormal placental trophoblast, ranging from hydatidiform mole to malignant gestational trophoblastic neoplasia [1,2]. Hydatidiform moles are classically divided into complete and partial forms according to their genetic, histopathological and clinical characteristics. Partial hydatidiform mole is most often triploid, commonly diandric, and may be associated with embryonic or fetal tissue, whereas complete mole is typically diploid and androgenetic, without fetal development [1,3].

Prenatal diagnosis becomes more challenging when a cystic or vacuolated placenta coexists with a fetus in the second trimester. Differential diagnoses include singleton partial mole with an abnormal fetus, twin gestation with a coexisting mole and normal fetus, confined placental mosaicism, placental mesenchymal dysplasia and non-molar placental cystic degeneration [4,5]. In this setting, histopathological examination, beta-hCG kinetics and, when available, ancillary techniques such as p57 immunostaining, ploidy analysis or genetic studies may be required to establish the final diagnosis [1,3,5].

We report two cases of ultrasound-suspected partial hydatidiform mole presenting with second-trimester pregnancy loss. The aim is to highlight clinical warning signs, diagnostic limitations, postpartum surveillance and the need for multidisciplinary follow-up in a tertiary referral setting.

Materials and Methods

This is a descriptive report of two anonymized cases managed in the Department of Gynecology and Obstetrics II at Hassan II University Hospital Center in Fez, Morocco. Clinical data were extracted from medical records, including maternal age, obstetric history, gestational age, symptoms, ultrasound findings, biological assessment, therapeutic management, histopathological information when available and post-expulsion beta-hCG follow-up.

Both cases were selected because they combined second-trimester pregnancy loss with prenatal or clinical suspicion of partial molar pregnancy. The manuscript was prepared according to the structure requested by the provided journal template. All direct identifiers were removed from the manuscript.

Ethical approval: The file was validated by the Ethics Committee of Hassan II University Hospital Center, Fez, Morocco.

Patient consent: Written or documented consent for publication was obtained from both patients.

Case Presentations

Case 1

A 34-year-old patient, gravida 4 para 2 with one previous miscarriage, was referred for management of suspected trophoblastic disease during an ongoing pregnancy estimated at 17 weeks of gestation. The pregnancy had been marked by repeated episodes of metrorrhagia and exaggerated sympathetic symptoms from early pregnancy. She developed abdominopelvic pain associated with moderate metrorrhagia, which motivated referral to our center. On admission, she was hemodynamically and respiratory stable but had mucocutaneous pallor. Abdominal examination found no tenderness, guarding or palpable mass. Obstetric examination showed a gravid cervix and uterine height greater than expected for gestational age, without visible vesicles.

Initial biological assessment showed severe anemia with hemoglobin at 6.5 g/dL, platelet count at 379,000/mm^3, blood group B positive and beta-hCG greater than 225,000 IU/L. Pelvic ultrasound showed a live singleton pregnancy with biometry corresponding to 17 weeks and a thick heterogeneous multicystic intrauterine image with a honeycomb appearance suggestive of an embryonated mole. The ovaries were enlarged bilaterally, measuring approximately 15 x 10 cm on the right and 10 x 7 cm on the left, with multiple theca lutein cysts (Figure 1).

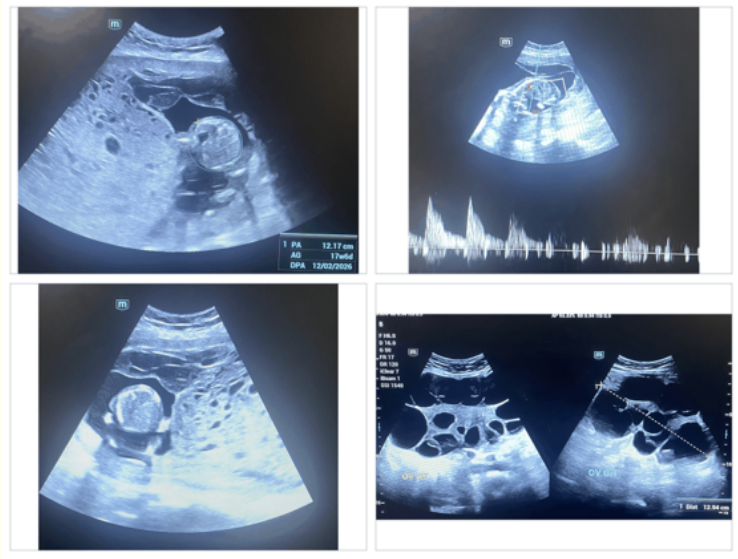

Figure 1: *Ultrasound findings in case 1 showing an ongoing singleton pregnancy with biometric measurements below the 3rd percentile, no obvious structural anomaly, a vacuolated honeycomb-like placenta, and bilateral theca-lutein cysts.*

The patient was hospitalized for clinical and biological surveillance. During admission, she developed close uterine contractions with complete cervical dilatation, followed by en bloc expulsion of a living male fetus weighing 140g with the placenta. A bidigital curettage was negative, and an oxytocin infusion was started. Pelvic ultrasound one week after expulsion showed an empty uterine cavity in an adenomyotic uterus, with persistent enlarged ovaries suggesting ovarian hyperstimulation.

Placental histopathology, reviewed by a senior pathologist, showed placental ischemic lesions with suppuration, without specific inflammatory lesion or viral inclusion and without formal confirmation of a molar lesion. During weekly post-expulsion monitoring, beta-hCG initially decreased to approximately 7,000 IU/L and then rose again. Control pelvic ultrasound showed a well-visualized empty uterine cavity in a globular enlarged adenomyotic uterus with heterogeneous hyperechogenic striae and posterior acoustic shadowing. On the adnexal side, bilateral theca lutein cysts persisted two months after expulsion, reaching approximately 15 cm in greatest diameter on each side (Figure 2). Ambulatory hysteroscopy identified several placental debris consistent with retained products of conception. Aspiration was therefore performed to obtain histopathological proof, given the negative initial placental pathology. Histopathological examination of the second specimen was also negative for molar changes and showed no definitive trophoblastic tumor. Despite these findings, beta-hCG continued to rise on serial monitoring. A cerebral, thoracic, abdominal and pelvic CT scan was requested to search for another lesion potentially secreting beta-hCG and showed no abnormality. In view of the persistent beta-hCG rise in the clinical context of suspected molar pregnancy, the patient was managed as postmolar GTN and received six cycles of methotrexate at 0.4 mg/kg per administration; each cycle consisted of two doses administered 15 days apart.

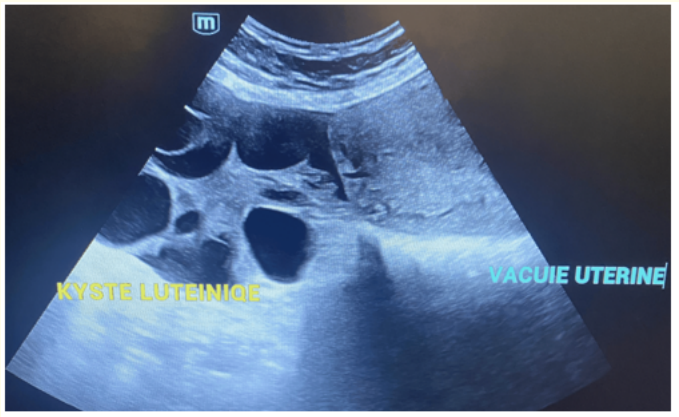

Figure 2: *Post-evacuation ultrasound findings in case 1 showing persistent bilateral theca-lutein cysts one month after pregnancy evacuation.*

Case 2

A 25-year-old primigravida with no notable medical history was followed for a pregnancy dated at 21 weeks according to the last menstrual period. Clinical examination found a normotensive and normocardic patient with negative urine dipstick. Prenatal ultrasound showed a live singleton pregnancy, suspected cardiac malformations, a thick vacuolated placenta and large theca lutein cysts, raising suspicion of partial molar pregnancy (Figure 3).

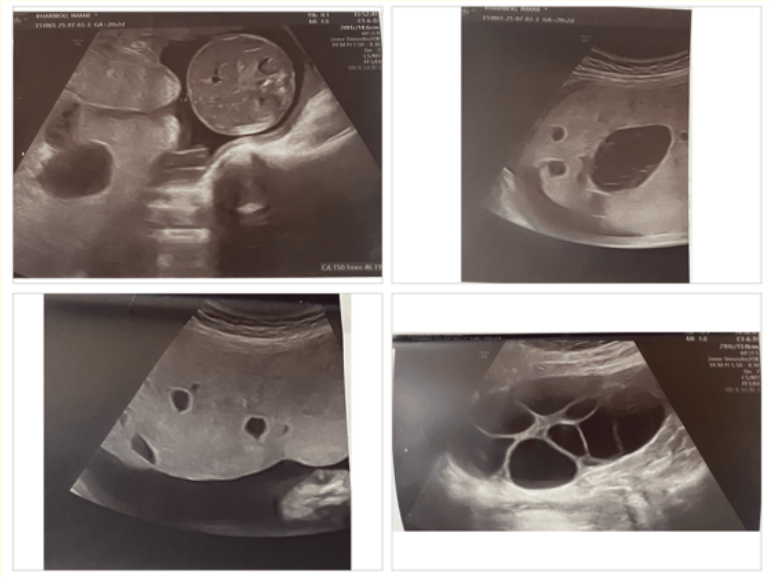

Figure 3: *Ultrasound findings in case 2 showing an ongoing singleton pregnancy with biometric measurements below the 1st percentile, microcephaly, suspected atrioventricular canal defect with a ventricular septal defect and a large atrial septal defect, a normal amniotic fluid volume, a thick vacuolated placenta, and bilateral theca-lutein cysts.*

Laboratory assessment showed hemoglobin at 9.58 g/dL, platelet count at 270,000/mm^3, normal coagulation tests, blood group B positive, negative red blood cell antibody screening and beta-hCG greater than 225,000 IU/L. The patient subsequently delivered vaginally a stillborn female fetus at the gynecological emergency department. Placental histopathology confirmed the diagnosis of partial hydatidiform mole (Figure 4).

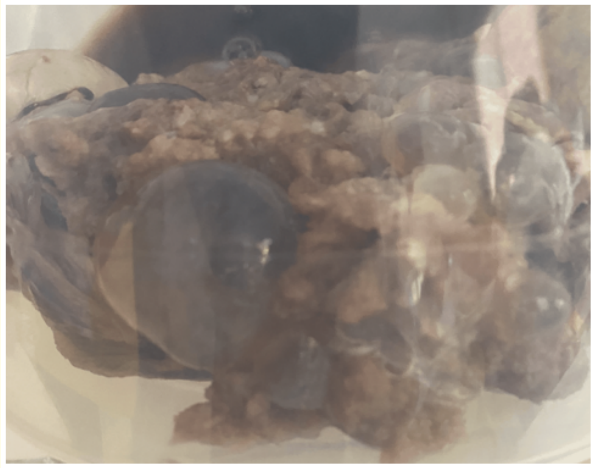

Figure 4: *Macroscopic specimen from case 2 after pregnancy evacuation, submitted for histopathological examination, which confirmed partial hydatidiform mole.*

Postpartum management included oral contraception and serial beta-hCG monitoring. The hormonal course was progressively decreasing, from 2,403 IU/L on 08 August 2025 to 749.3 IU/L on 14 August 2025, 450 IU/L on 28 August 2025 and 243 IU/L on 11 September 2025. Weekly beta-hCG monitoring until negativation was planned, actually the patient has 3 beta-hCG at the interval of one month.

Variable	Case 1	Case 2
Maternal age	34 years	25 years
Obstetric history	G4P2, one previous miscarriage	Primigravida
Gestational age at diagnosis	Approximately 17 weeks	Approximately 21 weeks
Main clinical presentation	Metrorrhagia, pelvic pain, severe anemia, enlarged uterus for gestational age	Ultrasound suspicion during second-trimester follow-up; clinically stable
Key ultrasound findings	Live fetus, thick heterogeneous multicystic honeycomb-like intrauterine image, bilateral enlarged ovaries with multiple theca lutein cysts	Live fetus, suspected cardiac malformations, thick vacuolated placenta, large theca lutein cysts
Initial beta-hCG	Greater than 225,000 IU/L	Greater than 225,000 IU/L
Pregnancy outcome	En bloc expulsion of a living male fetus weighing 140g with placenta	Vaginal delivery of a stillborn female fetus weighing 300g
Histopathology available in records	Placental ischemic lesions with suppuration; aspiration material compatible with gestational remnants	Placental pathology in favor of a partial molar pregnancy

Follow-up	Initial fall of beta-hCG followed by persistent re-elevation; ultrasound showed an empty uterine cavity in an enlarged adenomyotic uterus and persistent bilateral theca lutein cysts reaching 15 cm at two months; hysteroscopy showed placental debris followed by aspiration; CT brain/chest/abdomen/pelvis was normal.	Progressive decrease of beta-hCG under weekly monitoring until negativation
Treatment after persistent beta-hCG rise	Managed as postmolar GTN; six cycles of methotrexate at 0.4 mg/kg per administration, with two doses per cycle administered 15 days apart	No chemotherapy; weekly beta-hCG surveillance

Table 1: *Summary of the two anonymized cases.*

Discussion

The present cases illustrate the clinical difficulty of diagnosing partial molar pregnancy in the second trimester. In both cases, the association of fetal development at diagnosis, a thick cystic or vacuolated placenta, markedly elevated beta-hCG and bilateral theca lutein cysts raised strong suspicion of partial hydatidiform mole. These features are consistent with the typical clinical context of partial mole, although definitive diagnosis requires histopathological confirmation and, when morphology is equivocal, ancillary tests [1,3].

Partial hydatidiform mole is commonly associated with triploidy and abnormal fetal development. Consequently, progression to the second trimester is unusual and often complicated by miscarriage, fetal demise, bleeding, anemia, uterine enlargement, hyperemesis, preeclampsia or ovarian hyperstimulation [1,2]. The two cases presented here are clinically relevant because both were detected at a relatively late gestational age and presented with late pregnancy loss rather than first-trimester evacuation.

The literature also supports the need for cautious postmolar surveillance after partial mole. Vejerslev., *et al*. described a 23-week partial hydatidiform mole confirmed by morphology and genetic markers, followed by persistent serum hCG elevation and curettage findings suspicious for gestational choriocarcinoma before chemotherapy [5]. Although persistent trophoblastic disease is less frequent after partial mole than after complete mole, published cases show that rising or plateauing beta-hCG after evacuation cannot be considered benign without careful assessment [1,2,5].

Case 1 particularly illustrates this issue. The initial decline followed by persistent re-elevation of beta-hCG prompted repeated pelvic imaging, hysteroscopy and aspiration. Although placental debris was identified hysteroscopically, both the initial placental pathology and the aspiration specimen were negative for definite molar changes or trophoblastic tumor. Persistent beta-hCG elevation despite negative histology required broader evaluation, including cerebral, thoracic, abdominal and pelvic CT, which did not identify another beta-hCG-secreting lesion. In this setting, management as postmolar GTN was retained and methotrexate was administered. This evolution underlines that treatment decisions after suspected molar pregnancy may rely on the hormonal course and overall clinical context, even when histology is not confirmatory. Current recommendations emphasize serial quantitative hCG monitoring after molar pregnancy, with further evaluation when hCG levels plateau, rise or remain detectable beyond expected time frames [1-3,6].

An important point is that histopathological confirmation of partial hydatidiform mole was obtained only in the second case, whereas the first case was managed as suspected post-molar gestational trophoblastic neoplasia based on clinical, biological and radiological findings. Both patients presented with second-trimester pregnancy loss associated with ultrasound features suggestive of molar degeneration, markedly elevated beta-hCG levels and large bilateral theca-lutein cysts. In the 34-year-old patient, the initial placental

histopathology and the subsequent aspiration specimen were negative for molar tissue. However, the persistent rise of beta-hCG after evacuation, the absence of another beta-hCG-secreting lesion on cerebral, thoracic, abdominal and pelvic CT scan, and the overall clinical context supported the diagnosis of post-molar gestational trophoblastic neoplasia. This justified multidisciplinary management and chemotherapy with methotrexate. These cases highlight that partial molar pregnancy may exceptionally present as a late miscarriage and that persistent beta-hCG elevation after evacuation requires strict monitoring and appropriate management, even when histopathological confirmation is not obtained in all specimens.

Management of suspected partial mole with fetal development must be individualized according to maternal symptoms, gestational age, fetal status, ultrasound findings, beta-hCG levels and patient preference. Once the pregnancy ends, contraception is recommended during surveillance to avoid confusion between a new pregnancy and persistent disease, and patients should receive counseling regarding the importance of completing beta-hCG follow-up [1,3,6].

Conclusion

Partial hydatidiform mole associated with second-trimester pregnancy loss is rare and may be difficult to distinguish from other causes of cystic placental disease. The combination of late miscarriage or fetal demise, markedly elevated beta-hCG, cystic placental changes and bilateral theca lutein cysts should prompt suspicion of partial molar pregnancy. These two cases emphasize the importance of histopathological confirmation, careful post-expulsion uterine evaluation when beta-hCG rises, and strict serial beta-hCG surveillance until negativation. The first case also shows that persistent beta-hCG elevation may require management as postmolar gestational trophoblastic neoplasia after exclusion of retained tissue and other beta-hCG-secreting lesions, even when histology remains non-confirmatory. Multidisciplinary management in referral centers is essential for early detection and appropriate treatment of postmolar complications.

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Conflict of Interest

The authors declare that they have no financial interest or conflict of interest related to this work.

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