Partial Hydatidiform Mole with Subclinical Hyperthyroidism – A Case Report

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Abstract

Partial hydatidiform mole is a rare gestational trophoblastic disease marked by triploid karyotype, fetal abnormalities, and growth disorders, sometimes accompanied by subclinical hyperthyroidism. Diagnosis relies on β-hCG testing, ultrasound, and immunohistochemistry. Management, especially regarding chemotherapy, remains debated due to fertility concerns. This case report presents a rare instance of partial hydatidiform mole with subclinical hyperthyroidism, emphasizing key diagnostic and therapeutic considerations. A case report 22-year-old primigravida at 16 weeks presented with abortion imminens, placentomegaly, anemia, and massive bleeding. Evaluation confirmed a partial mole with subclinical hyperthyroidism. She was stabilized for hemorrhagic shock and IUFD, then underwent molar evacuation and caesarean hysterectomy. Although chemotherapy was initially planned, β-hCG levels normalized within 4 months without it, and follow-up showed no malignant transformation or recurrence. Low-risk partial hydatidiform mole can regress without chemotherapy, but comorbidities like subclinical hyperthyroidism require attention. At least 6 months of β-hCG monitoring is essential to confirm resolution and detect complications.

Keyword: Chemotherapy, Hyperthyroid Subclinical, Partial Hydatidiform Mole.

INTRODUCTION

Partial hydatidiform mole is a form of gestational trophoblastic disease (GTD) marked by villous edema and trophoblastic proliferation, but less extensive than in complete mole (Guvendag Guven et al., 2007; Hoffman et al., 2020; Koregol, Bellad, & Malapati, 2009; Salima, Wibowo, Dewayani, Nisa, & Alkaff, 2023). In Indonesia, only seven cases of partial hydatidiform mole were recorded over the past ten years (2013–2023) (Salima et al., 2023). Partial hydatidiform mole often mimics missed or incomplete abortion, presenting with vaginal bleeding and an enlarged fundal height (Guvendag Guven et al., 2007; Koregol et al., 2009).

Comorbid conditions such as preeclampsia, theca lutein cysts, and hyperthyroidism may be associated with partial hydatidiform mole, although these are relatively rare (Rathod, Pajai, & Gaddikeri, 2014). β-hCG levels in partial mole are usually <100,000 mIU/L, making early diagnosis difficult and often requiring histopathological confirmation (Berek, 2025; Hoffman et al., 2020; Tolcha, Usman, Senbeta, & Tadesse, 2022). Partial hydatidiform mole is usually triploid (69,XXX or 69,XXY, less often 69,XYY) from one maternal and two

paternal haploid sets (Casanova, Borozdina, Chong, Harris, & Ngu, 2018; Mangla, Kaur, & Khoiwal, 2022; Tolcha et al., 2022).

A coexisting fetus may occur in partial mole but is usually non-viable with malformations and growth restriction (Bruce & Sorosky, 2024; Hoffman et al., 2020; Schoenen et al., 2022). Histopathology of partial mole shows two villi populations, enlarged dysmorphic villi with inclusions, cavitation, and syncytiotrophoblastic atypia (Cue, Farci, Ghassemzadeh, & Kang, 2025; Hemida, Khashaba, & Zalata, 2022; Hoffman et al., 2020; Rathod et al., 2014). After evacuation, 15–20% of moles may progress to GTN; in partial mole, 4–6% transform, with metastatic choriocarcinoma occurring in ~0.1% (Hokman & Wulandari, 2023; Noal, Joly, & Leblanc, 2010). In Indonesia, data on managing partial mole with subclinical hyperthyroidism, especially the role of adjuvant chemotherapy, remain limited.

METHODS

The study design was a retrospective case report. The sample consisted of one patient (n=1), a 22-year-old primigravida, 16–17 weeks' gestation, diagnosed with partial hydatidiform mole and subclinical hyperthyroidism. The study was conducted at the tertiary care service of the Department of Obstetrics and Gynecology at Prof. Dr. Margono Soekarjo Regional Hospital, Purwokerto, Indonesia, with academic collaboration and supporting studies from Dr. Hasan Sadikin General Hospital, Bandung, Indonesia. Clinical data and treatment procedures were collected from August 2023, starting with initial admission, stabilization, surgery, or evacuation, with serial β-hCG monitoring, through December 2023.

Data were curated from medical records and care monitoring sheets, including demographic characteristics, symptoms, physical findings, laboratory parameters (hematology, coagulation, liver/renal, β-hCG, FT3/FT4/TSH), and supporting procedures (obstetric ultrasound, chest X-ray). Thyroid storm risk was assessed using the Burch–Wartofsky Point Scale. The diagnosis of partial mole was clinically and sonographically confirmed (a cystic "Swiss-cheese" pattern of the placenta) and histopathologically confirmed after evacuation; immunohistochemistry (p57 KIP2) was recorded when available. Management was described chronologically: stabilization of hemorrhagic shock (oxygenation, fluids, PRBCs), control of bleeding, hyperthyroidism therapy (β-blockers, PTU), mole evacuation/cesarean hysterotomy with bilateral internal iliac artery ligation, and ICU/HCU care. The primary outcomes were normalization of β-hCG (<5 mIU/mL), attainment of euthyroidism, and absence of GTN progression during observation; β-hCG was monitored periodically until undetectable and maintained for ≥6 months. The planned methotrexate chemotherapy for low-risk patients was documented along with the patient's decision to refuse it, ensuring close monitoring. The report

was prepared following the CARE Guidelines, with data anonymization and written informed consent for publication from the patient or family. Ethical considerations were met according to local ethics committee policy.

A single-case descriptive analysis. β-hCG values were presented as a post-evacuation time series to calculate time to negativity (<5 mIU/mL), weekly percentage decline, and assess GTN practice criteria (plateau ≥2 weeks or recurrent rise). Thyroid parameters (FT3/FT4/TSH) were classified as subclinical when TSH was suppressed with a normal FT4, and euthyroid when returning to the reference range; thyroid storm risk was reported as low, intermediate, and high BWPS scores. Perioperative hemodynamics, blood loss, and transfusion requirements were presented narratively. The analysis used complete-case analysis without imputation and was performed in spreadsheet/basic statistics for trend visualization.

RESULTS

A 22-year-old primigravida at 16 weeks was referred with threatened abortion, suspected partial mole, placentomegaly, and anemia. She reported 2–3 pads/day of vaginal bleeding for two days with grape-like vesicles but no clots, trauma, or urinary symptoms. Initial therapy included tranexamic acid, analgesics, and nifedipine before referral.

On examination, BP was 102/68 mmHg, pulse 126 bpm, with conjunctival pallor. Fundal height was 27 cm, larger than expected for 16 weeks. Speculum showed active bleeding with grape-like vesicles. The patient was diagnosed with grade 2 hemorrhagic shock and stabilized with oxygen, IV fluids, tranexamic acid, analgesics, and nifedipine, pending USG evaluation.

Ultrasound on August 3, 2023, showed a live intrauterine fetus at 16+5 weeks (EFW 171 g, FHR 158 bpm) with normal amniotic fluid. The fundal placenta covered the cervical os and contained a cystic “Swiss cheese” mass, indicating partial mole. (Figure 2). The patient was admitted to the maternal HCU for stabilization and serial labs (Table 1). On August 4, 2024, endocrinology consultation confirmed subclinical hyperthyroidism, and therapy with propranolol 10 mg BID and PTU 100 mg TID was initiated.

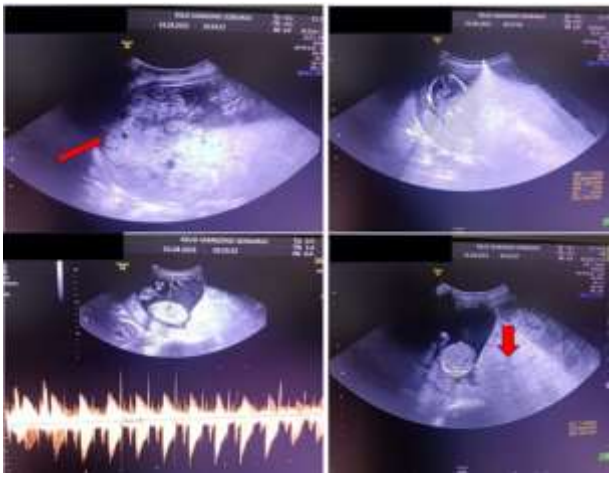

Figure 1. *Ultrasound image of partial hydatidiform mole*

Figure 2. *Patient's chest x-ray showed no cardiomegaly and abnormality of lungs*

Table 1 Patient's serial laboratory examination

Examination	Pre-Evacuation			Post cesarean hysterotomy				Unit	Normal value
	03	05	06	07	08	09	11		
Hb	5.4	7.6	7.2	8.5	8.3-9.3	9.3		g/dl	10,9-14,9
Hct	16.8	23.7	22.1	26	25.4-28.1	28.4		%	34-45
Leu	10840	9930	8820	11450	13670 - 11810	10290		/mm3	4790-11340
Tro	233000	196.000	177000	189000	183000 - 165000	186000		/uL	216.000-451.000
PT	12.5		11.8					Detik	9,9-11,8
APTT	28		28.5					Detik	25-31,3
LDH	148							U/L	<247
SGOT	26							U/L	<31
SGPT	17							U/L	<31
Albumin	3.20				1.95		3.41	g/dl	3,5-5,2
GDS	82.7				79			mg/dl	80-139
Ureum	14.7				26.11			mg/dl	15-40
Creatinin	0.49				0.44			mg/dl	0,5-1
Sodium	134				133		136	mEq/L	134-145

Examination	Pre-Evacuation			Post cesarean hysterotomy				Unit	Normal value
	03	05	06	07	08	09	11		
Potassium	3.7				4.1		4.2	mEq/L	3,4-4,5
Calsium	8.5				7.4		8.6	mEq/L	8,6-10,3
Chlorida	105				106		104	mEq/L	96-108
HbsAg	Non reactive							-	Non reactive
B hCG	580648				74204			mIU/mL	-
Free T3	6.03		3.59					pg/mL	2.21-4.43
Free T4	2.9		2.43					ng/dl	0.82-1.77
TSHS	<0.005		<0.005					uIU/mL	0.27-4.2
D dimer			430					ng/mL	<500
Serum iron						51		µg/dL	37-145
TIBC						280		µg/dL	228-428
Swab antigen	Non reactive			Non reactive				-	Non reactive
Blood Gas Analysis									
Base excess				-2				mmol/L	-2-3
HCO3 standard				23.20				mmol/L	21-28
O2 saturation				100				%	94-98
PCO2				39.3				mmHg	32-43
pH				7.376					7.35-7.45
PO2				415.0				mmHg	71-104
Total CO2				24				mmol/L	-
Lactate				0.83				mmol/L	1-1.8
Urinalisis									
Leukocyte	0-1							/lpb	Negative/lpb
Bacterial	1-10							/lpb	Negative/lpb
Eritrocyte	5+/250							RBC/ul	Negative
Protein	Negative							mg/dl	Negative

The patient received four units of PRC, after which IUFD was confirmed. On August 7, 2024, she underwent laparotomy with cesarean hysterotomy for mole and fetus evacuation, plus bilateral iliac artery ligation for hemorrhage control. Surgery lasted 1 hour 20 minutes with ~2000 mL blood loss. She was monitored in the ICU until POD 1 and in the HCU until POD 3.

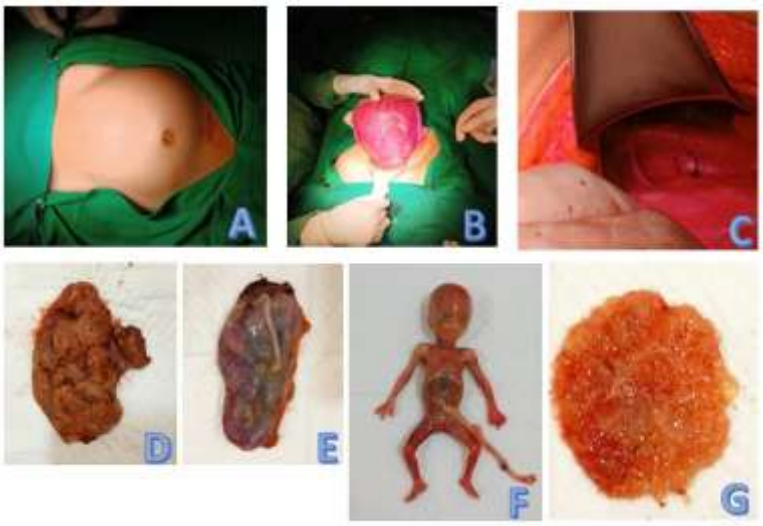

Figure 3. *Molar evacuation, cesarean hysterotomy, and bilateral internal iliac artery ligation*

On August 10, 2023, blood smear showed normocytic, normochromic anemia with neutrophilia, suggesting chronic anemia with infection/inflammation; further iron studies and CRP were advised. The patient was discharged on August 12 and, at follow-up on August 19, had no complications. Ultrasound showed a normal uterus with intact scar. Chemotherapy with methotrexate was planned three weeks post-op with serial β-hCG monitoring. Histopathology (August 11) revealed avascular chorionic villi with trophoblastic lining, hydropic degeneration, and edematous stroma (Figure 4). Although the patient declined and therefore did not undergo the planned adjuvant methotrexate chemotherapy regimen, a significant decline in β-hCG levels was observed. Table 2 showed the results of serial β-hCG evaluations.

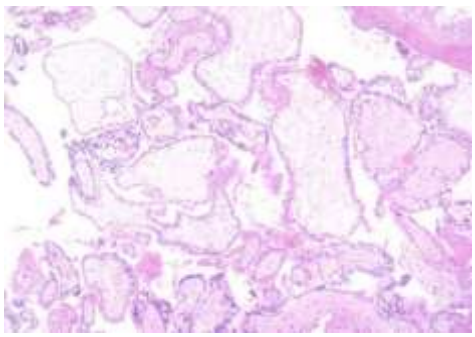

Figure 4. *Wet preparation of anatomical pathology showed svascular villi are observed with features of hydropic degeneration, Irregular villi with edematous stroma are also noted*

Table 2 Serial β-hCG Laboratory Results

Examination Date	β hCG value	Unit	Normal value
September 7, 2023	2535.8	mIU/mL	**< 5 mIU/mL**
October 7, 2023	1609.7		β-hCG levels according to gestational age (in
October 12, 2023	1086		weeks):
October 30, 2023	342.5		1-10: 202->225000
December 12, 2023	<1.2		11-15: 22536->225000
			16-22: 8007-50064
			23-40: 1600-49413

DISCUSSION

Gestational trophoblastic disease (GTD) is classified into two major groups according to the WHO classification: molar pregnancy including complete, partial, and invasive hydatidiform moles and trophoblastic tumors, including choriocarcinoma, placental site trophoblastic tumor (PSTT), and epithelioid trophoblastic tumor (ETT). The first group is characterized by changes in chorionic villi and elevated β-hCG (highest in invasive moles), while the second group is non-villous trophoblastic neoplasms (very high β-hCG in choriocarcinoma, lower in PSTT/ETT) with different therapeutic and prognostic implications.

Partial hydatidiform mole is marked by a triploid karyotype (69 XXX/XXY), presence of an embryo, focal villous edema, minimal trophoblastic proliferation, positive p57^KIP2 staining, and often mimics missed abortion, with a 4–6% risk of malignancy (Casanova et al., 2018; Mangla et al., 2022; Tolcha et al., 2022). Epidemiological studies have identified several risk factors for gestational trophoblastic disease (GTD), including low socioeconomic status, advanced maternal age, a history of molar pregnancy, and prior use of combined oral contraceptives (COCs) (Berek, 2025; Hoffman et al., 2020). Low vitamin A and carotene intake increase the risk of complete mole, while partial mole is associated with education level, smoking, irregular menstruation, and a history of male-only offspring (Hoffman et al., 2020). The incidence of partial hydatidiform mole with a coexisting fetus is approximately 1 in 20,000 pregnancies. Therefore, fetal karyotyping is recommended as a screening tool in post-GTD patients (Hemida et al., 2022; Hoffman et al., 2020; Mangla et al., 2022; Tolcha et al., 2022).

Complications of partial hydatidiform mole include growth restriction, CNS and neural tube defects, holoprosencephaly, cerebellar hypoplasia, corpus callosum agenesis, and facial anomalies. Male fetuses may present with hypospadias, cryptorchidism, or micropenis. Other reported complications include intestinal atresia, hernias, biliary abnormalities, congenital heart disease, and polycystic kidney disease (Hemida et al., 2022; Mangla et al., 2022).

Hyperthyroidism occurs in about 7% of gestational trophoblastic disease cases, primarily due to elevated β-hCG, which mimics thyroid-stimulating hormone (TSH) (Ndong et al., 2021; Pereira & Lim, 2021). Clinical hyperthyroidism occurs in approximately 1 in 100 pregnancies, demonstrating that increased β-hCG levels can bind to TSH receptors and inhibit TSH production (Hokman & Wulandari, 2023; Pereira & Lim, 2021). Studies report that 49% of patients present with subclinical hyperthyroidism, with β-hCG levels showing a significant correlation with TSH ($P<0.05$), as 41.9% have <10,000 mIU/mL and 51.8% >10,000 mIU/mL (Hoffman et al., 2020; Ndong et al., 2021). In normal pregnancy, hCG has low thyrotropic activity, and spillover effects usually prevent TSH elevation and clinical hyperthyroidism

(Hoffman et al., 2020; Ndong et al., 2021). Studies show serum hCG correlates with thyroid hormone levels, making it a potential predictor of hyperthyroidism severity (Berek, 2025; Hoffman et al., 2020; Pereira & Lim, 2021).

Management of hyperthyroidism in GTD is similar to that of non-GTD-related primary thyroid disorders, involving anti-thyroid medications and supportive treatment with beta-blockers.(Berek, 2025; Hoffman et al., 2020). Euthyroid status is generally achieved following evacuation of the molar tissue, which remains the primary treatment modality.(Ndong et al., 2021; Pereira & Lim, 2021). Case reports describe persistent hyperthyroidism despite therapy, and others highlight severe bleeding requiring urgent hormonal control and stabilization to prevent thyroid storm and reduce surgical risk (Hokman & Wulandari, 2023; Ndong et al., 2021; Pereira & Lim, 2021). In this case, a Burch-Wartofsky Point Scale (BWPS) score of 15 was recorded, indicating a low risk of thyroid storm (Berek, 2025; Hoffman et al., 2020). In this patient, intrauterine fetal death (IUFD) occurred, which may have been caused by massive maternal hemorrhage and the direct effects of thyroid hormones on the fetus (Soper, 2021). Management may require HCU/ICU care and plasmapheresis. In this case, thyroid levels improved with PTU and bisoprolol, reaching euthyroid status after mole evacuation (Green-top Guideline No.38, 2021; Noal et al., 2010; Oosterhouse & Knight, 2023; Soper, 2021).

Methotrexate (MTX), a folic acid antagonist that inhibits DNA synthesis, is the first-line therapy for low-risk gestational trophoblastic disease (GTD) and can be administered either intramuscularly or intravenously (Patsner, 1992; Wallin, Niemann, Faaborg, Fokdal, & Joneborg, 2022). The indication for MTX administration includes rising or persistently elevated β-hCG levels, suggesting a potential malignant transformation, and in post-molar GTD patients (Biswas et al., 2022; Hoffman et al., 2020). The International Federation of Gynecology and Obstetrics (FIGO) established a prognostic scoring system based on the duration of disease, β-hCG levels, type of antecedent pregnancy, and the length of prior treatment.(Wallin et al., 2022). Low-risk GTD (FIGO score 0–6) responds well to single-agent MTX with near 100% cure, while high-risk cases (score >7) require combination chemotherapy such as EMA/CO or Cyclophosphamide–Vincristine for better efficacy and tolerance (Berek, 2025; Hoffman et al., 2020). Actinomycin D is an alternative to MTX but has more side effects, making MTX the preferred first-line agent. The standard MTX protocol is 50 mg IM on days 1, 3, 5, and 7 with folinic acid 15 mg on alternate days, repeated every 14 days, plus 200 mg MTX per cycle (Biswas et al., 2022; Hoffman et al., 2020; Wallin et al., 2022).

Low-risk GTD requires serial β-hCG monitoring until undetectable for three consecutive tests or 12 months, while high-risk GTD patients need up to 24 months of follow-

up due to relapse risk (Berek, 2025; Hoffman et al., 2020). In patients who have completed chemotherapy, it is recommended to delay pregnancy for at least 12 months post-chemotherapy, as this is considered the safest option (Green-top Guideline No.38, 2021; Noal et al., 2010). After molar evacuation, 15–20% risk GTN development; in partial moles, 4–6% may transform, with metastatic choriocarcinoma occurring in ~0.1% (Hoffman et al., 2020; Salima et al., 2023).

Serial β-hCG monitoring should begin 1–2 weeks post-evacuation and continue until levels are undetectable (<5 mIU/L) for at least 6 months. Pregnancy should be avoided during this period to prevent misinterpretation of results, though compliance is often poor (Hoffman et al., 2020; Matsui, 2001). In high-risk GTN such as maternal age >40, prior molar pregnancy, or very high pre-evacuation β-hCG, prophylactic chemotherapy may be considered (Berek, 2025; Hoffman et al., 2020). Adjuvant chemotherapy can reduce GTN risk from 50% to 14%. In this case, the patient declined methotrexate and opted for serial β-hCG monitoring, which normalized after 4 months. Nevertheless, continued follow-up for at least 6 months remains recommended. (Hoffman et al., 2020; Oosterhouse & Knight, 2023; Soper, 2021).

CONCLUSIONS

This case highlights that partial hydatidiform mole complicated by subclinical hyperthyroidism can be successfully managed with surgical evacuation and supportive therapy, without the immediate need for chemotherapy. The management of partial hydatidiform mole must be carried out adequately, and treatment of hyperthyroid conditions should be conducted comprehensively to prevent the risk of thyrotoxicosis. Serial β-hCG monitoring played a crucial role in confirming remission, and the absence of malignant transformation underscores the importance of individualized management. Careful evaluation of comorbidities, timely surgical intervention, and close follow-up remain essential to optimize outcomes while minimizing unnecessary exposure to chemotherapy. Additionally, the administration of single-agent adjuvant chemotherapy in patients with low-risk gestational trophoblastic disease (GTD) is recommended to reduce the risk of recurrence or malignant transformation of GTD.

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