Case Report

When stage does not reflect risk: A case of FIGO Stage I high-risk gestational trophoblastic neoplasia successfully treated with etoposide, methotrexate, and actinomycin D-cyclophosphamide and vincristine

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ABSTRACT

Gestational trophoblastic neoplasia (GTN) encompasses a range of trophoblastic disorders characterized by elevated serum beta-human chorionic gonadotropin (β-hCG) levels and notable sensitivity to chemotherapy. Although invasive mole is the most common subtype of GTN, bulky uterine disease with extensive myometrial invasion and serosal involvement poses diagnostic and therapeutic challenges. We report a case of a 45-year-old multiparous woman who presented with lower abdominal pain 1 month following suction evacuation for molar pregnancy. Histopathological examination revealed residual incomplete molar tissue. Pelvic magnetic resonance imaging revealed a bulky uterus with a posterior myometrial lesion showing loss of interface with the uterine serosa and abutment of the left ovary. At the time of diagnosis of GTN, the serum β-hCG level was 159,407 mIU/mLthe time of diagnosis of GTN, the serum β-hCG level was 159,407 mIU/mL. Imaging studies, including computed tomography of the thorax and abdomen as well as magnetic resonance imaging of the brain, revealed no signs of metastatic disease. The patient was diagnosed with non-metastatic GTN and treated with multi-agent etoposide, methotrexate, and actinomycin D-cyclophosphamide and vincristine chemotherapy. Serial β-hCG monitoring demonstrated a rapid decline with eventual normalization. Consolidation chemotherapy was administered after biochemical remission. Despite treatment-related hematological toxicity requiring transfusion support, the patient completed therapy successfully. β-hCG remained within normal limits during follow-up.

Key words: Beta-human chorionic gonadotropin, Chemotherapy, EMA-CO, Gestational trophoblastic neoplasia, Invasive mole, Non-metastatic gestational trophoblastic neoplasia

Gestational trophoblastic neoplasia (GTN) comprises malignant trophoblastic disorders that may follow molar or non-molar pregnancy and is among the most chemosensitive human malignancies. Cure rates approach 100% in low-risk disease, while 80–95% of women with high-risk disease survive when appropriately treated. The World Health Organization (WHO–FIGO) scoring system integrates clinical and biochemical prognostic factors; a score ≥7 denotes high-risk GTN and supports first-line multi-agent chemotherapy [1,2]. EMA-CO, comprising etoposide, methotrexate, and actinomycin D alternating with cyclophosphamide and vincristine, remains the most widely used initial regimen. Landmark reports by Newlands *et al*. and Bower *et al*., followed by studies in diverse populations, demonstrated high remission and durable survival with acceptable and manageable toxicity [3-7]. Outcomes have improved further through specialized care, biochemical surveillance, and effective salvage treatment, with survival now exceeding 90% in many referral centers. Low-dose etoposide-cisplatin induction may reduce early treatment-related mortality in patients with extensive disease, while resistant disease may respond to EMA-EP or other platinum-based regimens. Nevertheless, ultra-high-risk disease, particularly with FIGO scores ≥12 or liver or brain metastases, continues to require individualized multidisciplinary management [8,9].

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CASE PRESENTATION

A 45-year-old multiparous woman (P3L3) presented with complaints of lower abdominal pain of 1-month duration. Before the index pregnancy, her menstrual cycles were

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regular. At presentation, she had no active vaginal bleeding; her body mass index was within the normal range, and bimanual examination revealed a mobile, non-tender, bulky uterus of approximately 12-week size, with no palpable adnexal mass. She underwent suction evacuation for a molar pregnancy in July 2025. Her medical history included Type 2 diabetes mellitus, hypertension, hypothyroidism, and hyponatremia. There was no significant family history of malignancy.

Histopathological examination of the evacuated specimen revealed residual molar tissue with decidual elements and extensive hemorrhage. Further evaluation was performed due to persistent symptoms.

Pelvic magnetic resonance imaging revealed a bulky uterus containing a T1 hypointense and T2/short tau inversion recovery hyperintense lesion involving the posterior myometrium of the uterus. Multiple flow voids were observed within the lesion, and there was a loss of the normal interface with the uterine serosa. The lesion abutted the left ovary, raising concerns about locally invasive trophoblastic disease.

Following suction evacuation, serum β-hCG was >275,200 mIU/mL on September 18, 2025; at the time of subsequent diagnosis and evaluation for GTN, the serum β-hCG level was 159,407 mIU/mL. Contrast-enhanced computed tomography of the thorax and abdomen and magnetic resonance imaging of the brain revealed no evidence of metastatic disease.

The patient was diagnosed with non-metastatic GTN. The patient was staged as FIGO Stage I disease with a WHO prognostic score of 7, categorizing her as a high-risk GTN patient (Table 1). Considering the high-risk status, first-line multi-agent chemotherapy with EMA-CO was initiated.

The patient underwent EMA-CO chemotherapy, which includes etoposide, methotrexate, actinomycin-D, cyclophosphamide, and vincristine, as detailed in Table 2. Serial monitoring of β-hCG levels indicated a rapid decline throughout the treatment period. β-hCG levels decreased from 159,407 mIU/mL at diagnosis to 3232 mIU/mL after the initial cycles and subsequently normalized to <5 mIU/mL (Table 3).

Two consolidation cycles were administered after normalization of β-hCG levels, in accordance with standard GTN management principles. Treatment was complicated by chemotherapy-induced anemia and myelosuppression, necessitating packed red blood cell transfusions and supportive care. Nevertheless, the treatment was successfully completed. At follow-up, serum β-hCG levels remained within normal limits (approximately 2–3 mIU/mL) (Table 3), and the patient remained asymptomatic without evidence of recurrence.

For this retrospective single-patient case report, ethical committee approval was not required according to the institutional policy. Written informed consent was obtained from the patient for the publication of clinical information.

Table 1: WHO Prognostic scoring for GTN

Risk factor		Score
Age	>40 years	1
Antecedent pregnancy	Mole	0
Interval from index pregnancy (months)	<4	0
Pre-treatment serum hCG (IU/L)	>100,000	4
Largest tumor size (including uterus)	>5	2
Site of metastases	0	0
Number of metastases	0	0
Previous failed chemotherapy	0	0
Total Score: 7		

WHO: World Health Organization, GTN: Gestational trophoblastic neoplasia, hCG: Human chorionic gonadotropin

DISCUSSION

This case demonstrates the successful first-line treatment of high-risk GTN confined to the uterus with EMA-CO. Although anatomically classified as FIGO Stage I, a

Table 2: EMA-CO Regimen (14-day cycle)

Drug	Dose and administration	Day/ Schedule
Inj Etoposide	100 mg/m^2 in 250 mL NS over 30 min f/b 100mL NS iv flush	On Day 1 and 2
Inj Actinomycin D	0.5 mg iv push f/b 100 mL NS iv push	On Day 1 and 2
Inj Methotrexate	100 mg/m^2 iv bolus f/b 200 mg/m^2 iv infusion	On Day 1
Inj Folinic acid	15 mg, 4 doses, 12 h	24 h after starting Methotrexate
Inj Vincristine	0.8 mg/m^2 in 500 mL NS over 90 min	On Day 8
Inj Cyclophosphamide	600 mg/m^2 in 500 mL NS over 1 h	On day 8

EMA-CO: Etoposide, methotrexate, and actinomycin D-cyclophosphamide and vincristine

Table 3: Serial Beta -hCG monitoring

Date	Beta hCG (mIU/ mL)	Remarks
September 18, 2025	>275200	Post-suction evacuation for molar pregnancy
October 03, 2025	159407	At diagnosis
November 04, 2025	3232	After 1st cycle
November 24, 2025	143	After 2nd cycle
December 13, 2025	27.2	After 1 week of starting 3rd cycle
December 22, 2025	14	After 3rd cycle
January 12, 2026	<0.2	After 4th cycle
January 27, 2026	4.21	Before starting Consolidative cycle (5th Cycle)
February 07, 2026	2.01	After 1 week of starting 5th cycle
February 23, 2026	2.25	After 5th cycle
March 08, 2026	2.12	After 6th cycle
April 24, 2026	2.06	At 1st follow-up
June 16, 2026	2.3	Latest follow-up

hCG: Human chorionic gonadotropin

WHO prognostic score of 7, driven by markedly elevated β-hCG and other risk factors, established the high-risk category and justified multi-agent chemotherapy.

The discordance between the anatomical stage and prognostic risk was notable. Despite the absence of pulmonary, hepatic, cerebral, or other distant metastases, the WHO-FIGO system designates the disease as high-risk, underscoring that treatment should be guided by risk stratification rather than by anatomical stage alone.

Hasanzadeh *et al*. described Stage I GTN with a 54-mm uterine lesion reaching the serosa without metastasis. Sequential chemotherapy failed, necessitating localized uterine resection followed by EMA-CO. In contrast, our patient had bulky, deeply invasive posterior myometrial disease with magnetic resonance imaging -suspected near-serosal extension and a WHO-FIGO score of 7 but achieved rapid and sustained remission with upfront EMA-CO and consolidation. Our case is distinguished by the avoidance of uterine rupture, hemoperitoneum, and hysterectomy despite extensive invasion [10]. Lee and Kim reported a 3.6 × 2.9 × 2.4-cm non-metastatic invasive mole in the fundal-posterior myometrium. After an inadequate response and hepatotoxicity with methotrexate, laparoscopic resection preserved fertility. Although their report confirmed local invasion without distant metastasis, the lesion was smaller, serosal extension was unclear, and surgery was required. Our patient achieved complete remission with upfront EMA-CO and consolidation alone despite bulkier, near-serosal disease without rupture or surgery [11]. Wu *et al*. provided the closest comparison: FIGO Stage I high-risk GTN, a WHO-FIGO score of 7, β-hCG of 106,189 mIU/mL, and a 12.3 × 8.0-cm lesion invading the uterine serosa without metastasis. Their patient developed uterine rupture and hemorrhagic shock before chemotherapy and required hysterectomy followed by six chemotherapy cycles. Our patient achieved complete remission with upfront EMA-CO and consolidation, avoiding rupture and surgery despite comparable near-serosal disease [12].

The biochemical response was rapid: β-hCG levels declined from 159,407 mIU/mL at diagnosis to 3,232 mIU/mL after the first cycle and 143 mIU/mL after the second cycle, normalizing to <5 mIU/mL after four cycles. This decline demonstrates the chemosensitivity of trophoblastic tumors and the effectiveness of EMA-CO, even with very high initial β-hCG levels.

Two consolidation cycles were administered, followed by β-hCG normalization. At the latest follow-up in June 2026, β-hCG remained at 2.3 mIU/mL without clinical or radiological evidence of recurrence, confirming sustained remission and supporting treatment beyond biochemical normalization to reduce the relapse risk.

Toxicity consisted mainly of chemotherapy-induced anemia and myelosuppression requiring packed red cell transfusions and supportive care. Nevertheless, the treatment was completed without interruption, dose reduction, or discontinuation. These manageable adverse effects did not compromise efficacy, indicating that EMA-CO can be safely administered with careful monitoring and support. Favorable factors included a molar antecedent pregnancy, detection before metastatic spread, and serial β-hCG monitoring, which enabled early diagnosis and treatment. Close biochemical surveillance also documented the response and guided the consolidation therapy. This case confirms that high-risk GTN remains highly curable with the WHO-FIGO-guided management. Even non-metastatic high-risk disease can achieve rapid β-hCG normalization and durable remission with standard EMA/CO. Careful risk assessment, serial β-hCG monitoring, prompt treatment, and adequate consolidation are central to the successful management of GTN.

A notable challenge encountered was treatment-related myelosuppression and anemia requiring transfusion support. However, these toxicities were manageable and did not prevent the completion of therapy, highlighting the importance of close monitoring and multidisciplinary supportive care during treatment.

From a practical standpoint, this case reinforces the fact that patients with high-risk GTN can achieve durable remission with standard EMA-CO chemotherapy when treatment is initiated promptly and followed by appropriate consolidation cycles. It also emphasizes the need for continued post-treatment surveillance, as long-term success depends not only on achieving remission but also on maintaining vigilant follow-up through serial β-hCG assessments.

CONCLUSION

This case highlights several important clinical lessons regarding the management of GTN. First, high-risk GTN can occur even in the absence of metastatic disease, underscoring the importance of the WHO-FIGO risk score in guiding treatment decisions rather than relying solely on anatomical staging. Second, persistent elevation of β-hCG following molar evacuation should prompt early evaluation for GTN, as timely diagnosis and initiation of treatment can significantly influence the outcomes.

This case also demonstrates the remarkable chemosensitivity of GTN, with rapid normalization of β-hCG achieved using first-line EMA-CO chemotherapy despite an initial β-hCG level exceeding 150,000 mIU/mL. Furthermore, serial β-hCG monitoring is invaluable for assessing the treatment response and guiding the duration of therapy.

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