

Choriocarcinoma in a Perimenopausal Woman Mimicking Cervical Carcinoma: A Diagnostic Pitfall with Life-Threatening Hemorrhage

Salah Houda*, Khalfaoui Aymen, Larbi Nizar, Amara Khouloud and Mrezguia Chaouki

Department of Obstetrics and Gynaecology, University Tunis El Manar-University of Medicine, Tunis, Tunisia.

*Correspondence:

Salah Houda, Department of Obstetrics and Gynaecology, University Tunis El Manar-University of Medicine, Tunis, Tunisia

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ABSTRACT

Background: Gestational trophoblastic neoplasia (GTN) is a rare but highly curable malignancy arising from trophoblastic tissue. Although it predominantly affects women of reproductive age, its occurrence in perimenopausal women is exceptional and often leads to diagnostic delay due to atypical clinical presentation.

Case presentation: We report the case of a 52-year-old gravida 3 para 2 woman, still menstruating, who presented with abnormal uterine bleeding. Clinical examination revealed a cervical mass initially suggestive of a prolapsed submucosal fibroid. Pelvic ultrasound demonstrated a 4 × 5 cm heterogeneous, non-vascularized cervical lesion associated with endometrial thickening. Initial histopathological analysis suggested squamous cell carcinoma. However, markedly elevated serum β -human chorionic gonadotropin (β -hCG) levels (120,000 mIU/mL) led to the diagnosis of GTN. The patient subsequently developed life-threatening hemorrhage requiring emergency hemostatic hysterectomy. Staging investigations showed no metastases, and the FIGO/WHO score was 7, indicating high-risk disease. The patient received adjuvant multi-agent chemotherapy with complete biochemical remission.

Conclusion: GTN should be considered in the differential diagnosis of abnormal uterine bleeding and pelvic masses regardless of age. Early measurement of serum β -hCG is essential to avoid misdiagnosis. This case highlights the importance of recognizing atypical presentations and the role of emergency surgery in life-threatening complications.

Keywords

Gestational trophoblastic neoplasia, Choriocarcinoma, Perimenopausal, Uterine bleeding, β -hCG, Hysterectomy.

Abbreviations

β -hCG : Beta-human Chorionic Gonadotropin, cm: Centimeter, EMA-CO: Etoposide, Methotrexate, Actinomycin D, Cyclophosphamide, Vincristine (Oncovin), FIGO: International Federation of Gynecology and Obstetrics, g/dL: Grams per deciliter, GTN: Gestational Trophoblastic Neoplasia, mIU/mL: Milli-International Units per milliliter, WHO: World Health Organization.

Introduction

Gestational trophoblastic neoplasia (GTN) encompasses a

heterogeneous group of malignant disorders derived from placental trophoblastic tissue, including invasive mole, choriocarcinoma, placental site trophoblastic tumor, and epithelioid trophoblastic tumor. These entities are characterized by abnormal proliferation of trophoblastic cells and are notable for their remarkable sensitivity to chemotherapy, resulting in excellent cure rates even in metastatic disease [1,2].

GTN most commonly occurs following a molar pregnancy but may also develop after spontaneous abortion, ectopic pregnancy, or term delivery [3]. The global incidence varies widely, with higher rates reported in low- and middle-income countries. Despite advances in early diagnosis and treatment, GTN remains a clinically significant condition due to its potential for aggressive behavior if not promptly recognized [1].

The disease primarily affects women of reproductive age, with peak incidence between 20 and 40 years. In contrast, GTN occurring in perimenopausal or postmenopausal women is exceedingly rare, representing less than 5% of cases [2,4]. In this age group, clinical suspicion is often low, and symptoms such as abnormal uterine bleeding are frequently attributed to more common gynecologic conditions, including uterine fibroids, endometrial hyperplasia, or malignancy. This diagnostic attribution often results in delayed diagnosis or misdiagnosis, potentially compromising patient outcomes [3,4].

The diagnosis of GTN relies on a combination of clinical presentation, imaging findings, histopathological evaluation, and, critically, quantitative serum β -hCG measurement, which serves as both a diagnostic and follow-up biomarker [2,5]. The FIGO/WHO scoring system remains the cornerstone for risk stratification and guides therapeutic decisions [2,6].

We present a rare case of choriocarcinoma in a perimenopausal woman initially misdiagnosed as cervical carcinoma, complicated by life-threatening hemorrhage requiring emergency hysterectomy. This case illustrates the diagnostic challenges, potential pitfalls, and critical importance of early β -hCG testing in atypical presentations.

Case Presentation

A 52-year-old woman, gravida 3 para 2, with no significant past medical or surgical history and ongoing regular menstrual cycles, presented to our department with abnormal uterine bleeding of recent onset. The bleeding was intermittent but progressively increasing in volume, without associated pelvic pain or systemic symptoms. The patient denied recent pregnancy or any antecedent gestational events. On physical examination, the patient was hemodynamically stable with normal vital signs. Speculum examination revealed a friable, hemorrhagic mass protruding through the cervical os, measuring approximately 4–5 cm in diameter. The mass appeared necrotic and bled easily on contact, features initially suggestive of a prolapsed submucosal fibroid or possible cervical malignancy. Transvaginal ultrasound demonstrated a well-circumscribed heterogeneous cervical mass measuring 4 × 5 cm. Notably, Doppler imaging revealed no detectable vascularization within the lesion. The endometrium measured 12 mm and appeared heterogeneous in echotexture. Both ovaries and adnexa were normal in appearance, and no pelvic free fluid was observed. A biopsy of the cervical mass was performed for histopathological diagnosis. Initial pathological evaluation suggested squamous cell carcinoma of the cervix, based on the presence of marked cellular atypia and necrosis. However, given atypical histological features and clinical discordance, a second pathological review was requested by the treating gynecologist. The reviewing pathologist raised suspicion for a trophoblastic tumor based on the pattern of cellular arrangement and degree of hemorrhage. In light of this diagnostic uncertainty, quantitative serum β -hCG measurement was obtained, revealing a markedly elevated level of 120,000 mIU/mL. This finding confirmed the

diagnosis of gestational trophoblastic neoplasia and explained the atypical presentation.

Three days following the diagnostic biopsy, the patient presented emergently with acute massive vaginal bleeding. On arrival, she was hemodynamically unstable with tachycardia (heart rate 115 beats per minute) and hypotension (blood pressure 90/60 mmHg). Laboratory investigations revealed symptomatic anemia with hemoglobin of 8 g/dL, requiring urgent blood transfusion. Despite aggressive medical management including intravenous tranexamic acid, etamsylate, and uterotonic agents, the hemorrhage persisted. Given the life-threatening nature of the bleeding and failure of conservative measures, an emergency decision was made to proceed with hemostatic total hysterectomy. Intraoperative findings confirmed a large, hemorrhagic, friable uterine mass involving the cervix and lower uterine segment, with active bleeding from the tumor surface. There was no evidence of extrauterine spread or peritoneal metastases. The procedure was completed successfully without complications. Final histopathological examination of the hysterectomy specimen confirmed choriocarcinoma, characterized by biphasic population of cytotrophoblasts and syncytiotrophoblasts with extensive hemorrhage and necrosis. Postoperative staging evaluation, including chest radiography and thoraco-abdominopelvic computed tomography (CT) scan, revealed no evidence of distant metastases. Based on the FIGO/WHO prognostic scoring system, the patient's score was calculated as 7 (age >40 years: 1 point; antecedent pregnancy unknown/term: 1 point; interval from index pregnancy >12 months: 4 points; pretreatment β -hCG >100,000 mIU/mL: 1 point), classifying her as high-risk GTN.

The patient was referred to medical oncology and received multi-agent chemotherapy using the standard EMA-CO regimen (etoposide, methotrexate, actinomycin D alternating with cyclophosphamide and vincristine). Serial β -hCG measurements demonstrated rapid decline following initiation of chemotherapy, with eventual normalization after six cycles, indicating complete biochemical remission. At 18-month follow-up, the patient remains in complete remission with undetectable β -hCG levels and no evidence of disease recurrence.

Discussion

This case exemplifies several important clinical and diagnostic challenges associated with gestational trophoblastic neoplasia in perimenopausal women. The rarity of GTN in this age group, combined with its ability to mimic more common gynecological conditions, creates significant potential for diagnostic delay and inappropriate management.

Epidemiology and Rarity in Perimenopausal Women

Gestational trophoblastic neoplasia predominantly affects women of reproductive age, with the highest incidence observed in the third and fourth decades of life [1,3]. The occurrence of GTN in women over 50 years is exceptional, accounting for less than 5% of reported cases [2,4]. This demographic rarity contributes

significantly to low clinical suspicion and delayed diagnosis. Furthermore, perimenopausal women with GTN tend to present with more advanced disease and poorer prognostic features compared to younger patients [1,7]. The biological basis for this age-related disparity remains incompletely understood but may relate to delayed diagnosis, altered immune surveillance, or intrinsic tumor biology in older women.

In the perimenopausal population, abnormal uterine bleeding is an extremely common presenting symptom that is more frequently attributed to benign conditions such as leiomyomas, endometrial polyps, or anovulatory cycles, or to malignant conditions such as endometrial or cervical carcinoma [8]. Consequently, GTN is rarely included in the initial differential diagnosis, leading to potential diagnostic and therapeutic delays [3,4].

Diagnostic Challenges: GTN as a Great Mimicker

Our case illustrates a fundamental clinical principle: gestational trophoblastic neoplasia can mimic a wide spectrum of gynecological conditions, earning its reputation as a diagnostic chameleon [9,10]. This mimicry occurs at multiple diagnostic levels—clinical, radiological, and histopathological.

Clinical Presentation

In our patient, the presenting features of abnormal uterine bleeding and a cervical mass were consistent with multiple diagnostic possibilities, including cervical carcinoma, prolapsed submucosal fibroid, endometrial carcinoma with cervical extension, or retained products of conception. The absence of a recent known pregnancy further obscured the diagnosis, as clinicians may not consider GTN when there is no obvious antecedent gestational event [3].

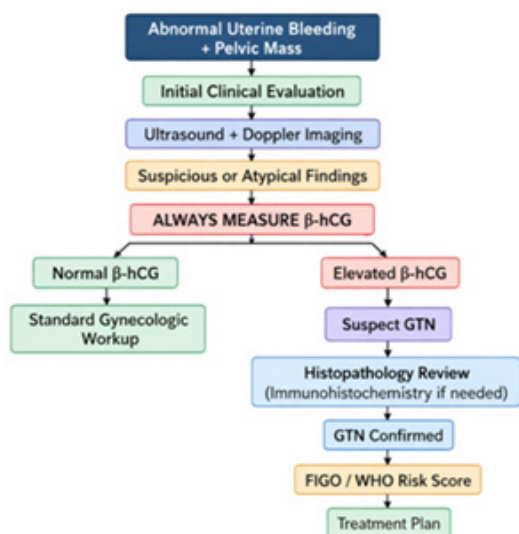


Figure 1: Diagnostic algorithm for suspected GTN.

Radiological Findings

Although GTN, particularly choriocarcinoma, is classically described as a highly vascular tumor with characteristic "Swiss

cheese" appearance on ultrasound or intense enhancement on contrast imaging, this finding is neither universal nor specific [10,11]. In our case, Doppler ultrasound demonstrated no detectable vascularization, a finding that initially steered the diagnosis away from GTN. This absence of vascularity may be explained by extensive tumor necrosis, hemorrhage, or technical limitations of the examination. Clinicians must recognize that lack of hypervascularity does not exclude GTN, particularly in necrotic or hemorrhagic tumors [10].

Histopathological Complexity

Perhaps the most significant diagnostic challenge in this case was the initial histopathological interpretation. Choriocarcinoma is characterized by marked cellular atypia, pleomorphism, hemorrhage, and necrosis—features that overlap considerably with poorly differentiated carcinomas [1]. In limited biopsy samples, particularly those obscured by hemorrhage or necrosis, distinguishing choriocarcinoma from other malignancies can be extremely difficult. The biphasic pattern of cytotrophoblasts and syncytiotrophoblasts, while characteristic, may not be evident in small or poorly preserved specimens [3]. This case underscores the importance of maintaining clinical suspicion and pursuing ancillary diagnostic tests when histopathology is discordant with clinical features.

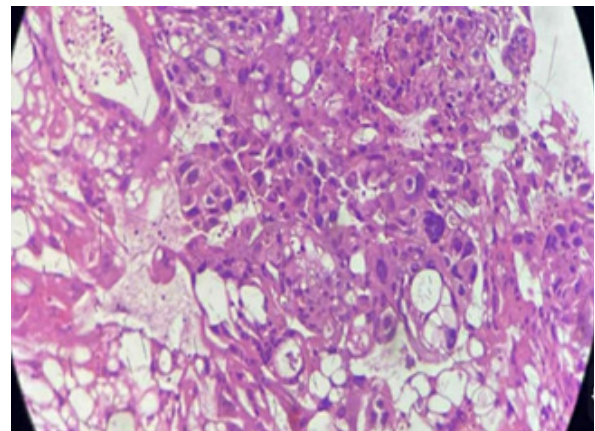


Figure 2: Histologic aspect of choriocarcinoma: Malignant neoplastic proliferation invading the endometrium, consisting of three cell types: cytotrophoblastic cells, atypical and mitotic intermediate trophoblastic cells, and, less frequently, multinucleated syncytiotrophoblastic cells.

The Central Role of β-hCG

Serum β-human chorionic gonadotropin (β-hCG) measurement is the single most important diagnostic and monitoring tool in GTN [1,2,5]. In our case, the markedly elevated β-hCG level (120,000 mIU/mL) was decisive in establishing the correct diagnosis and redirecting management. This highlights a critical clinical principle: β-hCG measurement should be mandatory in any woman presenting with unexplained uterine bleeding and a pelvic mass, regardless of age [4,5].

Early β-hCG testing is particularly crucial in several clinical

scenarios: perimenopausal or postmenopausal women with atypical presentations; cases with discordant imaging findings; situations where histopathological interpretation is uncertain or suggests poorly differentiated malignancy; and any woman with a pelvic mass and unknown pregnancy history [5,10]. The failure to perform early β -hCG testing is a recurring issue in case reports of delayed GTN diagnosis [3,4]. As demonstrated in our case, this simple, inexpensive test can prevent misdiagnosis, inappropriate treatment, and potential complications.

Emergency Hysterectomy: Justification and Controversy

Chemotherapy remains the cornerstone of GTN treatment, even in high-risk and metastatic disease, due to its exceptional efficacy [6,12,13]. Surgery is generally reserved for specific indications and is not considered first-line oncologic therapy for GTN [6]. However, in our case, the decision to perform emergency hemostatic hysterectomy was clearly justified by life-threatening hemorrhage, hemodynamic instability, and failure of conservative medical management.

Current clinical guidelines recognize that surgical intervention is indicated in GTN as a life-saving measure in cases of uncontrolled bleeding or uterine perforation [6,12]. Additionally, in select patients—particularly perimenopausal women with completed fertility—hysterectomy may reduce tumor burden, eliminate the primary source of bleeding, and complement systemic chemotherapy [6,13]. Some studies suggest that surgical debulking in high-risk GTN may improve outcomes by reducing chemotherapy requirements and resistance, although this remains controversial [13,14].

It is essential to emphasize that hysterectomy does not eliminate the need for systemic chemotherapy in high-risk GTN, as the disease often has microscopic metastatic spread [6]. In our patient, despite complete surgical resection, adjuvant multi-agent chemotherapy was necessary due to the high-risk FIGO score and potential for occult metastases.

Risk Stratification and Chemotherapy

The FIGO/WHO prognostic scoring system is fundamental for risk stratification and treatment planning in GTN [2,6]. This validated scoring system incorporates age, antecedent pregnancy, interval from index pregnancy, pretreatment β -hCG level, largest tumor size, sites of metastases, number of metastases, and previous failed chemotherapy [2]. Patients are classified as low-risk (score ≤ 6) or high-risk (score ≥ 7), which determines the intensity of chemotherapy required.

Our patient's FIGO/WHO score of 7 classified her as high-risk GTN, necessitating multi-agent chemotherapy. The EMA-CO regimen (etoposide, methotrexate, actinomycin D alternating with cyclophosphamide and vincristine) remains the gold standard for high-risk GTN and has achieved cure rates exceeding 90%, even in advanced cases with metastases [12,13,15]. This remarkable chemosensitivity distinguishes GTN from most other solid

malignancies and underscores the importance of correct diagnosis.

The rapid normalization of β -hCG levels in our patient confirms the excellent chemosensitivity characteristic of GTN [15,16]. Serial β -hCG monitoring is essential during and after treatment, serving as a highly sensitive marker of treatment response and early indicator of resistance or relapse [5,16]. Current recommendations include weekly β -hCG measurements until three consecutive normal values, followed by monthly measurements for 12 months to confirm sustained remission [2,6].

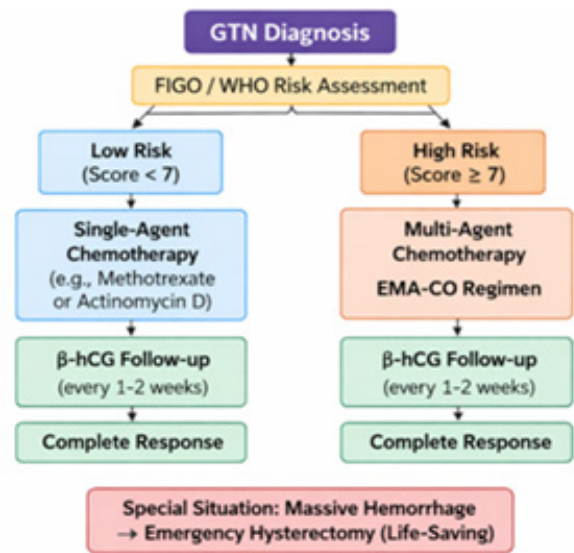


Figure 3: Therapeutic management strategy of GTN.

Comparison with Published Literature

Similar cases of GTN in perimenopausal women mimicking cervical carcinoma, endometrial carcinoma, or uterine fibroids have been reported in the literature, though they remain uncommon [4,10]. These case reports consistently highlight several recurring themes: delayed diagnosis due to atypical presentation and low clinical suspicion; failure to perform early β -hCG testing; initial misdiagnosis as more common gynecological conditions; and ultimate favorable outcomes when appropriate therapy is instituted [3,4,10].

A systematic review of GTN in postmenopausal women found that diagnosis was delayed by an average of 6–12 months compared to younger patients, and that these women more frequently presented with advanced-stage disease [4]. However, when managed with appropriate risk-stratified chemotherapy, cure rates remained excellent, approaching those in younger populations [4,13].

Clinical Implications and Lessons Learned

This case emphasizes several key clinical messages for practicing clinicians:

1. **Maintain diagnostic suspicion:** GTN should be considered in the differential diagnosis of all cases of unexplained uterine

bleeding, particularly when associated with a pelvic mass, regardless of patient age.

2. **Early β -hCG testing:** Quantitative serum β -hCG should be measured early in the diagnostic evaluation of any woman with abnormal uterine bleeding and a pelvic mass, especially when clinical, radiological, or histopathological findings are atypical or discordant.
3. **Recognize diagnostic limitations:** Imaging and histopathology may be misleading in atypical presentations. Absence of hypervascularity on Doppler does not exclude GTN, and choriocarcinoma can be misinterpreted as poorly differentiated carcinoma on limited biopsy samples.
4. **Prepare for complications:** GTN can present as a life-threatening hemorrhagic emergency. Clinicians should be prepared for rapid clinical deterioration and the potential need for emergency surgical intervention.
5. **Multidisciplinary approach:** Optimal management of GTN, particularly high-risk cases, requires collaboration among gynecologists, pathologists, radiologists, and medical oncologists.
6. **Excellent prognosis:** Despite diagnostic challenges and potential complications, GTN remains one of the most curable solid malignancies. Even high-risk and metastatic disease can be cured with appropriate chemotherapy.

Conclusions

Gestational trophoblastic neoplasia in perimenopausal women represents a rare but clinically important diagnostic entity that may mimic common gynecological conditions, leading to delayed diagnosis and potential mismanagement. This case demonstrates that GTN can present with atypical clinical, radiological, and histopathological features that obscure the diagnosis and delay appropriate treatment.

The critical importance of systematic β -hCG measurement in any woman presenting with unexplained uterine bleeding and a pelvic mass, regardless of age, cannot be overstated. This simple laboratory test is essential to avoid diagnostic errors and initiate appropriate therapy. Early recognition allows for prompt risk stratification and institution of curative treatment.

Although chemotherapy remains the cornerstone of GTN treatment, emergency hysterectomy may be life-saving in cases of severe hemorrhage and hemodynamic instability. In perimenopausal women with completed fertility, surgical intervention can serve both as a hemostatic measure and as tumor debulking to complement systemic therapy.

When managed appropriately with risk-stratified chemotherapy, even high-risk GTN carries an excellent prognosis, with cure rates exceeding 90%. This case demonstrates that despite initial diagnostic challenges and life-threatening complications, complete remission can be achieved with a multidisciplinary approach. A high index of suspicion, early biological assessment with β -hCG measurement, and multidisciplinary collaboration among

gynecologists, pathologists, radiologists, and medical oncologists are essential to improve outcomes in these rare but potentially life-threatening presentations. Clinicians should remember that GTN can occur at any age and should maintain vigilance for this highly curable malignancy, even in atypical clinical scenarios.

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