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Case Report

Gestational trophoblastic neoplasia in a perimenopausal woman: A rare case report and literature review

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Abstract

Gestational trophoblastic neoplasia (GTN) comprises a spectrum of malignant trophoblastic disorders that may arise following any gestational event. Although uncommon, these lesions respond well to chemotherapy when detected early; however, they can present significant diagnostic challenges, especially in perimenopausal women.

We report a case of a 49-year-old multiparous woman presenting with prolonged vaginal bleeding and severe anemia. She had a history of a spontaneous abortion that was managed conservatively one year prior. Serum β-hCG was markedly elevated at 325,000 mIU/mL. Transvaginal ultrasound revealed a heterogeneous, vascular intrauterine lesion with cystic spaces suggesting an invasive mole. MRI confirmed myometrial invasion without serosal breach or distant metastasis. Based on clinical, laboratory, and imaging criteria, a diagnosis of low-risk GTN was made. The patient responded well to single-agent chemotherapy with normalization of β-hCG levels. This case underscores the importance of considering GTN in perimenopausal women with abnormal bleeding and elevated β-hCG. Early detection, guided by clinical suspicion and supported by imaging and tumor markers, is crucial for effective treatment. Chemotherapy remains the cornerstone of management with favorable prognosis in low-risk cases.

Keywords: Gestational trophoblastic neoplasia, Invasive mole, Trophoblastic, β-hCG, Dynamic MRI, Gestational trophoblastic disease.

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1. Introduction

Gestational trophoblastic disease (GTD) encompasses a rare spectrum of pregnancy-related disorders characterized by abnormal proliferation of trophoblastic tissue. It includes both premalignant entities such as partial hydatidiform mole (PHM) and complete hydatidiform mole (CHM) as well as malignant forms collectively referred to as gestational trophoblastic neoplasia (GTN), which comprise invasive mole, choriocarcinoma, placental site trophoblastic tumor (PSTT), and epithelioid trophoblastic tumor (ETT). These neoplastic variants can arise following any form of pregnancy, including molar gestation, miscarriage, ectopic pregnancy, or term delivery.[1]

Classification of GTD has recently been expanded to include atypical placental site nodule (APSN), a lesion associated with a 10%–15% risk of coexistence with or progression to PSTT or ETT. While CHM and PHM typically produce markedly elevated levels of human chorionic gonadotropin (hCG), malignant variants such as PSTT, ETT, and APSN often exhibit more variable or modest hCG secretion.[2]

Nonetheless, serum hCG remains a highly sensitive and indispensable biomarker for monitoring disease progression, evaluating therapeutic response, and guiding post-treatment surveillance. A plateau or rise in hCG levels is often the earliest sign of malignant transformation—occurring in approximately 15%–20% of CHM cases and 0.5%–5% of PHM cases. Due to the accuracy of hCG-based monitoring and the availability of effective treatment protocols, nearly all

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women diagnosed with GTN can achieve complete remission when appropriately managed.[3]

In recent years, advanced oncologic imaging techniques have emerged as valuable adjuncts in GTD evaluation. Functional imaging modalities such as diffusion weighted imaging (DWI) and dynamic contrast-enhanced MRI (DCE-MRI) can detect microscopic changes in tumor physiology by assessing tissue perfusion, oxygenation, and metabolic activity, providing insights into the tumor's microenvironment and structural organization.[4-6]

2. Case Presentation

We report the case of a 49-year-old woman, gravida 2, para 2, abortus 0 (G2P2A0) who presented to the gynecology outpatient department of a tertiary care center in India with complaints of abnormal uterine bleeding and associated symptoms of severe anemia. She reported intermittent, heavy, and prolonged vaginal bleeding over the preceding month, accompanied by dizziness and fatigue, which significantly impaired her daily functioning. Her obstetric history included a spontaneous abortion about a year ago, which was managed conservatively without undergoing histopathological evaluation. There was no previous history of molar pregnancy or gestational trophoblastic disease (GTD).

On general examination, the patient appeared pale and was hemodynamically unstable. Per speculum examination revealed moderate active bleeding from the cervix, while bimanual examination identified a mildly enlarged and tender uterus, with no evidence of adnexal masses or cervical motion tenderness. Laboratory investigations showed a hemoglobin concentration of 6.8 g/dL, consistent with severe anemia. A urine pregnancy test was positive, despite the absence of any recent pregnancy. Serum β-human chorionic gonadotropin (β-hCG) levels were markedly elevated at 325,000 mIU/mL, raising clinical suspicion of gestational trophoblastic neoplasia (GTN).

The patient's risk status was evaluated using the International Federation of Gynecology and Obstetrics (FIGO) scoring system and World Health Organization (WHO) prognostic criteria. Her pre-treatment β-hCG level of 325000 mIU/mL and clinical presentation placed her in the low-risk GTN category, with a total FIGO score of 6.

Transvaginal ultrasonography revealed a large, ill-defined, heterogeneous, vascular intrauterine mass with multiple cystic spaces, producing the characteristic "snowstorm appearance" pathognomonic for GTD. The lesion showed evidence of myometrial invasion with extension into the cervical stroma, suggestive of an invasive mole. No fetal parts were visualized, ruling out coexisting gestation.

To further delineate the extent of disease, a dynamic contrast-enhanced MRI (DCE-MRI) of the pelvis was performed. MRI demonstrated a large lesion (3.8 × 10.2 × 13.5 cm) involving the anterior myometrium, extending into the cervix but without serosal breach or adnexal involvement (**Figure 1**-**Figure 3**). The lesion exhibited early intense contrast enhancement followed by rapid washout on DCE-MRI, consistent with a Type 3 time-intensity curve, typically seen in highly vascularized, aggressive neoplastic processes (**Figure 4**). Diffusion-weighted imaging (DWI) showed heterogeneous restriction, reinforcing the diagnosis of an invasive mole (**Figure 5**). There was no parametrial extension or pelvic lymphadenopathy.

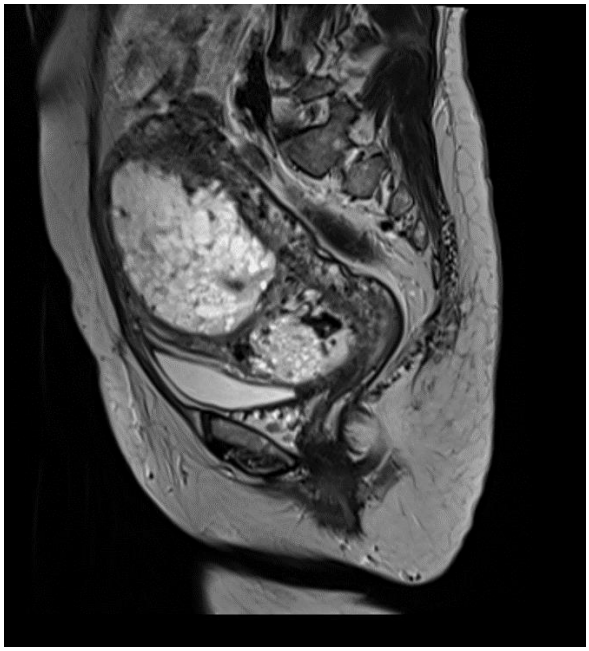

Figure 1: T2 Sagittal image showing a large lesion involving the anterior myometrium with its extent into the cervix

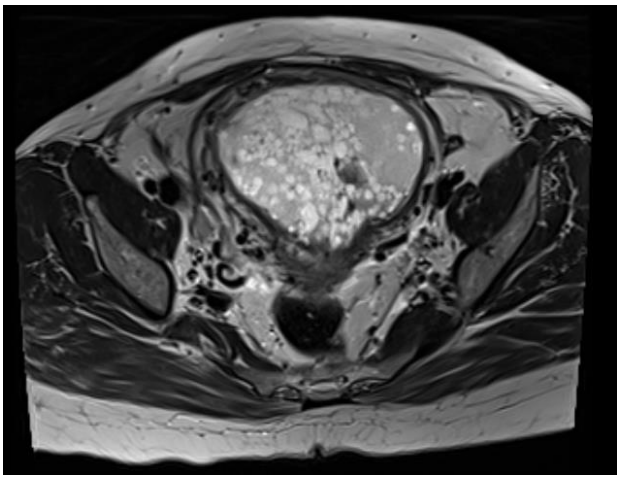

Figure 2: Axial T2- weighted MRI image illustrating the lesion in the myomterium

A chest X-ray was performed to evaluate for metastatic spread, commonly involving the lungs in GTN, but no lesions were observed. Liver and renal function tests were within normal limits, excluding systemic involvement.

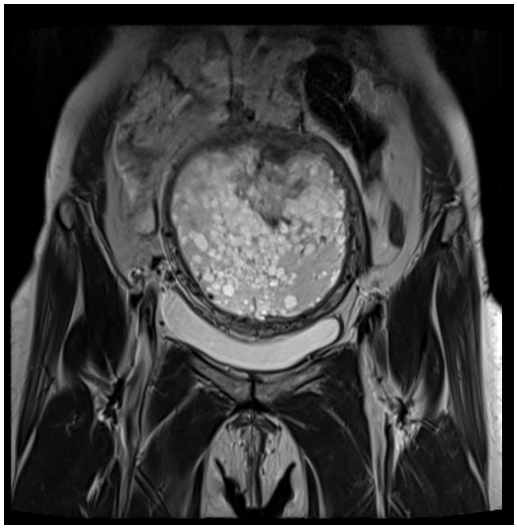

Figure 3: Coronal T2- weighted MRI image showing heterogenous lesion in the uterus

Based on the composite findings—clinical, laboratory, and imaging—the diagnosis of low-risk gestational trophoblastic neoplasia (GTN) was confirmed. The patient was counseled regarding her diagnosis and the available treatment options. She was initiated on single-agent chemotherapy with methotrexate, the standard of care for low-risk GTN, with plans for close monitoring through serial β-hCG measurements to assess treatment response and confirm complete remission.

The patient received methotrexate intramuscularly according to the 8-day regimen (1 mg/kg on days 1, 3, 5, and 7, alternating with leucovorin 0.1 mg/kg on days 2, 4, 6, and 8). Tolerance to chemotherapy was good, with no significant adverse effects noted. Weekly β-hCG levels demonstrated a consistent and progressive decline.

By the end of the second chemotherapy cycle, β-hCG levels had decreased to within the normal reference range. A complete remission was confirmed after three consecutive weekly normal β-hCG values. The patient subsequently received one additional consolidation cycle of methotrexate to minimize the risk of relapse.

She was advised on the importance of follow-up and contraception for at least 12 months post-remission to ensure accurate surveillance of any potential recurrence. Monthly β-hCG monitoring was planned during the first year. At her 6-month follow-up, the patient remained asymptomatic with persistently undetectable β-hCG levels and no evidence of disease recurrence on pelvic ultrasound.

This case underscores the importance of early recognition and management of GTN, even in perimenopausal women, where diagnosis can be delayed due to atypical presentations. Prompt initiation of standard single-agent chemotherapy led to successful remission and favorable clinical outcomes.

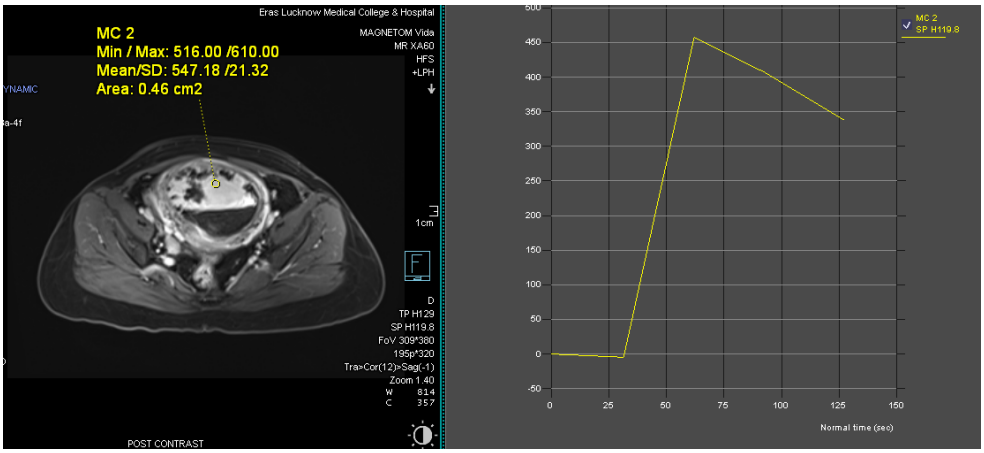

Figure 4: Dynamic contrast enhanced MRI showing Type 3 time intensity curve (Washout Pattern)

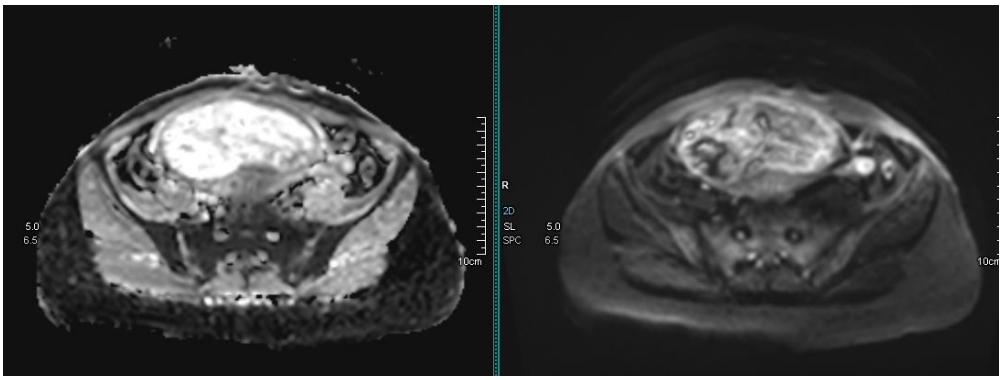

Figure 5: DWI MRI Images showing heterogeneous restriction in the lesion

3. Discussion

Invasive mole, a malignant form within the spectrum of gestational trophoblastic neoplasia (GTN), is an uncommon condition that typically arises following a molar pregnancy, but it may also occur after other gestational events such as spontaneous abortion or term delivery.[3,4] Although rare, invasive moles pose a significant risk of local uterine invasion and, less commonly, distant metastasis, primarily to the lungs, brain, or liver.[12,13] The estimated incidence of GTN in Western populations is approximately 1 in 40,000 pregnancies, with invasive mole accounting for 15%–20% of cases following complete hydatidiform mole, and less than 1% following partial mole.[11]

Recent advancements in medical imaging have significantly enhanced diagnostic precision and treatment monitoring. Techniques such as functional MRI, diffusion-weighted imaging (DWI), and dynamic contrast-enhanced MRI are now increasingly used to assess tumor response, particularly in gynecologic malignancies.[5-7] These modalities can detect early therapeutic effects that precede anatomical changes, which is crucial for monitoring GTN progression or remission.[6,7] Furthermore, whole-body diffusion-weighted MRI offers a non-invasive method to evaluate systemic disease spread, improving patient stratification and guiding individualized treatment plans.[8] Dynamic contrast-enhanced MRI has also shown potential in assessing vascular function in tumors, providing valuable data for early-stage clinical decisions.[9]

Sonographic and Doppler imaging, due to their accessibility and non-invasive nature, remain frontline tools in the diagnosis and follow-up of GTN.[11] Additionally, rare presentations and atypical imaging findings in perimenopausal patients underscore the need for multimodal evaluation supported by established clinical guidelines.[12,13]

The diagnosis is often suspected based on clinical presentation—most commonly abnormal uterine bleeding—and persistently elevated serum β-hCG levels after a recent pregnancy. In the present case, the patient exhibited heavy vaginal bleeding and a markedly elevated β-hCG concentration, supporting a diagnosis of GTN. Importantly, her prior pregnancy event was not molar, highlighting the need for a high index of suspicion even in patients without known antecedent molar gestation.

Imaging plays a crucial role in both diagnosis and staging. Ultrasonography remains the first-line imaging modality and the gold standard for identifying invasive mole. Sonographically, these lesions appear as heterogeneous, hyperechoic intrauterine masses with multiple cystic spaces—a classic "snowstorm" appearance—often accompanied by evidence of myometrial invasion.

Magnetic resonance imaging (MRI) provides superior soft tissue contrast and is particularly valuable for assessing depth of myometrial invasion, cervical involvement, and exclusion of parametrial or adnexal extension. In this case, T2-weighted sagittal and axial MRI images confirmed a large lesion involving the anterior myometrium with extension into the cervix (**Figure 1** and **Figure 2**), while the coronal image further illustrated the lesion's heterogeneous nature (**Figure 3**). These findings were consistent with an invasive mole.

Functional MRI techniques, including diffusion-weighted imaging (DWI) and dynamic contrast-enhanced MRI (DCE-MRI), have further expanded diagnostic capabilities. DWI detected areas of heterogeneous restriction, indicative of high cellularity (**Figure 5**), and DCE-MRI demonstrated a Type 3 time-intensity curve (washout pattern), reflecting abnormal vascular permeability and aggressive neoplastic behavior (**Figure 4**). These imaging characteristics collectively confirmed a localized yet invasive lesion without serosal breach or adnexal involvement.

Although MRI contributes to anatomical and functional characterization, it does not alter the management strategy for low-risk GTN, which remains systemic chemotherapy, most often with single-agent methotrexate or actinomycin D. In this case, the patient's FIGO score of 6 classified her as low risk, allowing for single-agent chemotherapy with close monitoring of serum β-hCG.

Long-term follow-up is essential, as recurrence is possible. Current guidelines recommend monitoring β-hCG levels monthly for 12 months after normalization, beginning two weeks after two consecutive negative results.[12,13] This surveillance is vital to detect early relapse and ensure complete remission.

A review of similar case reports in literature underscores that perimenopausal presentation of GTN is exceedingly rare, and such cases may be misdiagnosed as uterine fibroids or dysfunctional uterine bleeding. Therefore, clinicians must maintain vigilance when evaluating abnormal uterine bleeding in this age group, especially with unexplained elevation in β-hCG levels.

4. Conclusion

This case emphasizes the necessity of including GTN in differential diagnoses for perimenopausal women with abnormal bleeding and elevated β-hCG. Prompt diagnosis using β-hCG levels and ultrasound is critical, with MRI offering additional staging insight when necessary. Single-agent chemotherapy leads to excellent outcomes in low-risk cases. Regular monitoring of β-hCG is essential to confirm remission and detect relapse early.

5. Source of Funding

No funding was required for the case.

6. Conflict of Interest

The authors declare that they have no competing interests.

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