

GESTATIONAL TROPHOBLASTIC NEOPLASIA WITH SEVERE HYPERTHYROIDISM ASSOCIATED WITH MARKEDLY ELEVATED B-HCG AND PERSISTENT DISEASE AFTER TAH-BSO: A CASE REPORT

NEOPLASIA TROFOBLASTIK GESTASIONAL DENGAN HIPERTIROIDISME BERAT YANG DIMEDIASI B-HCG DAN PENYAKIT PERSISTEN SETELAH TAH-BSO: LAPORAN KASUS

Nabila Kinantia Sarjono^{1*}, Heru Priyanto²

¹Fakultas Kedokteran Universitas Pembangunan Nasional Veteran Jakarta

²Rumah Sakit Onkologi Solo

*Korespondensi: fanabkinbalabala@gmail.com

ABSTRACT

Gestational Trophoblastic Neoplasia (GTN) is a malignant gestational disorder characterized by abnormal trophoblastic proliferation and elevated β -hCG levels. At markedly increased concentrations, β -hCG may exert thyrotropic activity through stimulation of the thyroid-stimulating hormone (TSH) receptor and contribute to clinically significant hyperthyroidism. GTN in perimenopausal women presents particular diagnostic and therapeutic challenges because its manifestations may overlap with common gastrointestinal complaints and physiological changes associated with the menopausal transition. This case report describes a 50-year-old P2A0 perimenopausal woman with GTN complicated by severe thyrotoxicosis and persistent disease following surgical management. The patient initially presented with progressive lower abdominal discomfort, nausea, recurrent vomiting, and mild vaginal spotting and was initially diagnosed with dyspepsia. Further evaluation revealed a uterine mass, serum β -hCG $>50,000$ mIU/mL, suppressed TSH, and markedly elevated FT4 >7.77 ng/dL, consistent with severe thyrotoxicosis. Preoperative treatment included propylthiouracil, Lugol's iodine, dexamethasone, and propranolol to reduce the perioperative risk associated with severe thyrotoxicosis. The patient subsequently underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAH-BSO). Histopathological examination demonstrated malignant trophoblastic proliferation with myometrial invasion. Following surgery, β -hCG levels initially declined substantially but subsequently showed a secondary rise and plateau, consistent with persistent GTN according to FIGO criteria. The patient was then treated with methotrexate-etoposide chemotherapy with leucovorin rescue, with subsequent clinical improvement. This case highlights the importance of considering GTN in perimenopausal women presenting with atypical gastrointestinal or gynecological symptoms, particularly in the presence of markedly elevated β -hCG. Evaluation of thyroid function is important in patients with high β -hCG levels because β -hCG-mediated stimulation of the TSH receptor may represent a likely mechanism of severe thyrotoxicosis. Serial postoperative β -hCG monitoring is also essential for early detection of persistent disease and timely initiation of further therapy.

Keywords: Gestational Trophoblastic Neoplasia, β -hCG, Hyperthyroidism, Thyrotoxicosis, Perimenopause

ABSTRAK

Neoplasia Trofoblastik Gestasional (GTN) merupakan keganasan gestasional yang ditandai oleh proliferasi trofoblas abnormal dan peningkatan kadar β -hCG. Pada kadar yang sangat tinggi, β -hCG dapat memberikan aktivitas tirotropik melalui stimulasi reseptor thyroid-stimulating hormone (TSH) dan berkontribusi terhadap terjadinya hipertiroidisme yang bermakna secara klinis. GTN pada perempuan perimenopause menimbulkan tantangan diagnostik dan terapeutik karena manifestasinya dapat tumpang tindih dengan keluhan gastrointestinal maupun perubahan fisiologis pada masa transisi menopause. Laporan kasus ini menggambarkan seorang perempuan perimenopause P2A0 berusia 50 tahun dengan GTN yang disertai tirotoksikosis berat dan penyakit persisten setelah tata laksana operatif. Pasien awalnya datang dengan keluhan nyeri perut bawah yang progresif, mual, muntah berulang, dan spotting vagina ringan, serta sempat didiagnosis sebagai dispepsia. Evaluasi lebih lanjut menunjukkan adanya massa uterus, kadar β -hCG serum



>50.000 mIU/mL, TSH yang tersupresi, dan FT4 yang sangat tinggi >7,77 ng/dL, sesuai dengan tirotoksikosis berat. Tata laksana preoperatif meliputi propylthiouracil, Lugol's iodine, dexamethasone, dan propranolol untuk menurunkan risiko perioperatif yang berkaitan dengan tirotoksikosis berat. Pasien kemudian menjalani *total abdominal hysterectomy with bilateral salpingo-oophorectomy* (TAH-BSO). Pemeriksaan histopatologi menunjukkan proliferasi trofoblastik ganas dengan invasi miometrium. Setelah operasi, kadar β -hCG awalnya menurun secara bermakna, namun kemudian menunjukkan peningkatan sekunder dan pola plateau yang sesuai dengan persistent GTN berdasarkan kriteria FIGO. Pasien selanjutnya mendapat kemoterapi *methotrexate-etoposide* dengan *leucovorin rescue* dan menunjukkan perbaikan klinis. Kasus ini menekankan pentingnya mempertimbangkan GTN pada perempuan perimenopause dengan gejala gastrointestinal atau ginekologis yang tidak khas, terutama bila disertai peningkatan β -hCG yang nyata. Evaluasi fungsi tiroid penting pada pasien dengan kadar β -hCG tinggi karena stimulasi reseptor TSH yang dimediasi β -hCG dapat menjadi mekanisme yang paling mungkin mendasari tirotoksikosis berat. Pemantauan serial β -hCG pascaoperasi juga penting untuk mendeteksi penyakit persisten secara dini dan menentukan kebutuhan terapi lanjutan.

Kata kunci: Neoplasia Trofoblastik Gestasional, β -hCG, Hipertiroidisme, Tirotoksikosis, Perimenopause

Submitted : 21-08-2026

Revision : 12-09-2026

Accepted: 30-09-2026

Introduction

Gestational trophoblastic disease (GTD) comprises a heterogeneous group of pregnancy-related disorders arising from abnormal proliferation of placental trophoblasts. The spectrum includes complete and partial hydatidiform moles and malignant forms collectively referred to as gestational trophoblastic neoplasia (GTN), including invasive mole, gestational choriocarcinoma, placental site trophoblastic tumor (PSTT), and epithelioid trophoblastic tumor (ETT) [1–4]. GTN may be diagnosed histologically or clinically following a molar pregnancy when serial human chorionic gonadotropin (hCG) measurements demonstrate characteristic persistent, plateauing, or rising concentrations [1,2]. Despite its rarity, GTD remains clinically important because of its malignant potential and high curability when appropriately diagnosed and treated. Post-molar GTN develops more frequently after complete hydatidiform mole than after partial hydatidiform mole, occurring in approximately 15–20% and 0.5–5% of cases, respectively [1,3,4].

The epidemiology of GTD varies considerably across geographical regions and populations, and maternal age is one of the most consistently recognized risk factors [5–7]. The incidence of hydatidiform mole increases at the extremes of reproductive age, with a particularly marked increase among women aged 40 years or older [6–8]. In the current FIGO-modified WHO prognostic scoring system, age ≥ 40 years remains one component of risk assessment for GTN [2]. However, the likelihood and prognosis of persistent GTN should not be attributed to maternal age alone, because several additional factors contribute to risk, including the type of antecedent pregnancy, interval from the index pregnancy, pretreatment hCG concentration, tumor size, and the number and sites of metastases [1,2]. In perimenopausal women, recognition of GTD or GTN may be particularly challenging because manifestations such as irregular vaginal bleeding, abdominal discomfort, nausea, and vomiting are nonspecific and may initially be attributed to gastrointestinal disorders or physiological changes associated with the menopausal transition. Therefore, trophoblastic disease should remain within the differential diagnosis in perimenopausal women presenting with compatible clinical findings, particularly when serum hCG is unexpectedly elevated.

An important endocrine manifestation of markedly elevated hCG concentrations is thyroid stimulation. Human chorionic gonadotropin and thyroid-stimulating hormone (TSH) belong to the glycoprotein hormone family and share a common α -subunit, while their β -subunits exhibit sufficient structural homology to permit interaction of hCG with

the TSH receptor [9,10]. Although hCG has substantially weaker thyrotropic activity than TSH, markedly elevated and sustained hCG concentrations can stimulate TSH receptors, resulting in increased thyroid hormone production and suppression of pituitary TSH secretion [9–12]. Consequently, clinically significant hyperthyroidism is uncommon during normal pregnancy but may occur in conditions characterized by excessive hCG production, particularly hydatidiform mole and gestational trophoblastic neoplasia [9,11,12].

The relationship between circulating hCG concentration and the severity of thyrotoxicosis is not uniform. Molecular heterogeneity of hCG, including variations in glycosylation, sialylation, and structural modification of the molecule, may influence its biological and thyrotropic activity [10–13]. Certain molecular variants of hCG identified in trophoblastic disease may demonstrate greater TSH-receptor-stimulating activity than conventional hCG, which may partly explain why only a subset of patients with markedly elevated hCG concentrations develop clinically significant hyperthyroidism [10–13]. Therefore, in patients with GTN and severe thyrotoxicosis, hCG-mediated TSH-receptor stimulation represents an important and biologically plausible mechanism, although alternative causes of hyperthyroidism should also be considered.

Clinically, hCG-mediated thyrotoxicosis may manifest with tachycardia, heat intolerance, tremor, weight loss, nausea, and vomiting, whereas characteristic manifestations of Graves disease, including ophthalmopathy and diffuse goiter, may be absent [11,12,14]. Evaluation of serum TSH and free thyroxine (FT4) is fundamental, while additional assessment such as triiodothyronine (T3), TSH-receptor antibodies, and thyroid imaging may be considered when the underlying etiology remains uncertain [14]. Severe thyrotoxicosis is particularly important in the perioperative setting because surgical and anesthetic stress may precipitate clinical deterioration. In severe cases, thyroid storm may occur as a life-threatening multisystem manifestation of thyrotoxicosis and requires prompt clinical recognition and management [15].

Management of GTN should be individualized according to histological subtype, anatomical stage, tumor burden, and FIGO prognostic risk classification [1–4]. Most GTNs are highly chemosensitive; low-risk disease is generally treated with single-agent chemotherapy, whereas high-risk disease requires multi-agent chemotherapy [1–4]. Hysterectomy has a selective rather than routine role and may be considered in patients who have completed childbearing, have significant uterine disease or hemorrhage, or have selected histological subtypes for which surgical management contributes to disease control [1,3,4]. Serial quantitative hCG surveillance remains essential after treatment because persistent, plateauing, or rising hCG concentrations may indicate persistent trophoblastic disease and guide the need for further therapy [1,2].

This case report describes a 50-year-old perimenopausal woman with GTN accompanied by severe thyrotoxicosis in the setting of markedly elevated β -hCG and persistent disease following total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAH-BSO). This case highlights the diagnostic challenges of GTN in perimenopausal women, the probable contribution of β -hCG-mediated TSH-receptor stimulation to severe thyrotoxicosis, the importance of perioperative endocrine stabilization, and the value of serial β -hCG monitoring for the early recognition of persistent disease.

Case Description

A 50-year-old multiparous woman (P2A0) presented with a 20-day history of progressive lower abdominal pain accompanied by an unusual sensation of heat in the abdomen. The symptoms were associated with persistent nausea, recurrent postprandial

vomiting, and mild intermittent vaginal spotting. Her menstrual cycles had been irregular, which had previously been attributed to the use of three-monthly injectable contraception. Her medical history was notable for longstanding poorly controlled hypertension. She had no known previous history of thyroid disease or molar pregnancy.

The patient was initially evaluated at a local clinic and was diagnosed with dyspepsia. Because her symptoms persisted, she subsequently underwent further assessment at a secondary hospital, where a qualitative urine pregnancy test was unexpectedly positive. Laboratory investigations revealed a serum β -hCG concentration of $>50,000$ mIU/mL and a suppressed thyroid-stimulating hormone (TSH) level of <0.1 mIU/L. Pelvic ultrasonography demonstrated an enlarged uterus with a heterogeneous vesicular or honeycomb-like appearance, raising suspicion of gestational trophoblastic disease.

On physical examination, the patient had a blood pressure of 154/89 mmHg and tachycardia. Thyroid examination revealed no clinically apparent goiter or thyroid bruit. Abdominal examination demonstrated a palpable pelvic-abdominal mass with ballottement. Further ultrasonographic examination showed an enlarged uterus with a snowstorm-like appearance. Chest radiography did not demonstrate pulmonary metastases. Based on the available clinical and imaging findings, the disease appeared to be confined to the uterus.

Because of the markedly elevated β -hCG concentration and severe thyrotoxicosis, the patient was considered to be at increased perioperative risk. Preoperative medical treatment was therefore initiated with propylthiouracil (PTU) 200 mg three times daily, Lugol's iodine 6 drops three times daily, dexamethasone 2 mg twice daily, and propranolol 10 mg three times daily. The patient subsequently underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAH-BSO).

Histopathological examination of the surgical specimen demonstrated malignant trophoblastic proliferation with superficial myometrial invasion and atypical pleomorphic cells. Based on the available histopathological report, the lesion was considered consistent with malignant gestational trophoblastic disease. However, no additional immunohistochemical characterization was available to further define the histological subtype.

Serial biochemical monitoring was performed after surgery. At postoperative week 2, the serum β -hCG concentration had decreased to 3,111.4 mIU/mL, while FT4 had decreased to 1.02 ng/dL. By postoperative week 4, β -hCG had further decreased to 88.80 mIU/mL. However, subsequent monitoring demonstrated a secondary increase to 477.69 mIU/mL, followed by a plateau ranging from 259.70 to 266.24 mIU/mL over the subsequent evaluation period. This abnormal β -hCG kinetic pattern was considered consistent with persistent GTN according to FIGO criteria.

The patient had a reported FIGO prognostic score of 3 and was therefore classified as having low-risk GTN. According to the available case documentation, chemotherapy was subsequently administered using methotrexate and leucovorin rescue. However, the chemotherapy was treated using 20mg dose of methotrexate in the first 5 days and adding 15mg dose of leucovorin rescue started in day 3 and day 5 to minimize mucosal and hematologic toxicity.

The gross uterine specimen following total abdominal hysterectomy with bilateral salpingo-oophorectomy is shown in Figure 1.



Figure 1. Gross specimen of the uterus following total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAH-BSO). Source: Personal documentation.

The ultrasonographic findings are shown in Figure 2.

The ultrasonographic findings are shown in Figure 2.



Figure 2. Pelvic ultrasonographic appearance of the uterine lesion. Source: Personal documentation.

Discussion

This case illustrates the complex interaction between gestational trophoblastic neoplasia, markedly elevated β -hCG concentrations, and severe thyroid dysfunction in a perimenopausal woman. Several clinically relevant issues arise from this presentation, including the diagnostic challenges of GTN in women approaching menopause, the probable contribution of β -hCG-mediated TSH-receptor stimulation to thyrotoxicosis,

perioperative management of severe hyperthyroidism, interpretation of postoperative β -hCG kinetics, histopathological classification, and subsequent management of persistent disease.

The association between gestational trophoblastic disease and hyperthyroidism is biologically plausible because human chorionic gonadotropin and TSH belong to the glycoprotein hormone family and share a common α -subunit, while their β -subunits demonstrate sufficient structural homology to permit hCG interaction with the TSH receptor [9–12]. Although hCG is a substantially weaker thyrotropic agonist than TSH, markedly elevated and sustained hCG concentrations may stimulate thyroid hormone synthesis and suppress pituitary TSH secretion [9–13]. Furthermore, the degree of thyroid stimulation does not depend exclusively on the absolute serum hCG concentration. Molecular variants of hCG produced in trophoblastic disease may differ in glycosylation, sialylation, and other structural characteristics that influence their biological and thyrotropic activity [10,13,20]. These differences may partly explain why some patients with markedly elevated hCG concentrations develop clinically significant thyrotoxicosis whereas others with comparable concentrations remain relatively euthyroid.

In the present patient, the combination of β -hCG >50,000 mIU/mL, suppressed TSH <0.1 mIU/L, and markedly elevated FT4 >7.77 ng/dL strongly supports an association between trophoblastic disease and severe thyrotoxicosis. However, a direct causal relationship should be interpreted cautiously. The available case documentation did not include serum T3, TSH-receptor antibody (TRAb), anti-thyroid peroxidase antibody, anti-thyroglobulin antibody, or thyroid ultrasonography. Consequently, alternative causes of thyrotoxicosis, particularly Graves disease, autonomous thyroid disease, or thyroiditis, were not completely excluded [21]. Nevertheless, the absence of clinically apparent goiter or thyroid bruit, the markedly elevated β -hCG concentration, and improvement of thyroid function following treatment of the trophoblastic disease make β -hCG-mediated TSH-receptor stimulation the most plausible mechanism in this clinical context [9,11,12,20]. This interpretation is preferable to stating definitively that β -hCG was the sole cause of the patient's hyperthyroidism.

An additional concern in this patient was the potential development of thyroid storm during the perioperative period. Thyroid storm is primarily a clinical diagnosis characterized by severe thyrotoxicosis accompanied by systemic decompensation involving the cardiovascular, thermoregulatory, gastrointestinal-hepatic, and central nervous systems [15,22,23]. The Burch-Wartofsky Point Scale (BWPS) and the Japanese Thyroid Association criteria are commonly used as adjunctive diagnostic tools [15,22,23]. In this case, tachycardia, nausea, vomiting, and markedly elevated FT4 were documented; however, the available information did not include the exact heart rate, body temperature, neurological status, evidence of heart failure, or sufficient additional parameters to retrospectively calculate a reliable BWPS or determine whether Japanese Thyroid Association criteria were fulfilled. Therefore, the patient is more appropriately described as having severe thyrotoxicosis with an increased perioperative risk of thyroid storm, rather than confirmed thyroid storm.

Preoperative treatment consisted of propylthiouracil (PTU), Lugol's iodine, dexamethasone, and propranolol. This multimodal approach is consistent with the pharmacological principles used to rapidly control severe thyrotoxicosis and prevent clinical deterioration [21,23]. PTU inhibits thyroid hormone synthesis through inhibition of thyroid peroxidase and additionally decreases peripheral conversion of T4 to the more biologically active T3. Propranolol controls adrenergic manifestations such as tachycardia and may also reduce peripheral T4-to-T3 conversion at sufficiently high doses. Glucocorticoids similarly decrease peripheral conversion of T4 to T3 and provide

additional support in severe thyrotoxicosis. Inorganic iodine acutely inhibits the release of preformed thyroid hormone when administered after initiation of a thionamide [21,23]. In patients with trophoblastic disease, removal or control of the hCG-producing tissue is ultimately important because persistent trophoblastic activity may continue to stimulate thyroid function [20]. Therapeutic plasma exchange has been described as a rescue strategy in rare refractory cases in which severe thyrotoxicosis cannot be adequately controlled before an urgent intervention, although it is not routinely required [20].

The patient's age also deserves consideration. Advanced maternal age is associated with an increased incidence of molar pregnancy, and age ≥ 40 years remains one component of the FIGO-modified WHO prognostic scoring system [1,2,6–8]. However, age alone should not be used to predict persistent GTN or justify a particular intervention because prognosis depends on multiple factors, including antecedent pregnancy, interval from pregnancy, pretreatment hCG concentration, tumor size, and metastatic burden [1,2,16]. In perimenopausal women, the diagnostic process may be further complicated by nonspecific symptoms. In this case, nausea, vomiting, abdominal discomfort, irregular menstruation, and mild vaginal spotting were initially interpreted as dyspeptic or nonspecific complaints. The case therefore reinforces the importance of considering pregnancy-related trophoblastic disease even in women approaching menopause when clinical findings are accompanied by an unexpected positive pregnancy test or elevated serum hCG.

The role of hysterectomy in this patient also requires careful interpretation. GTN is generally highly chemosensitive, and contemporary guidelines recommend treatment according to FIGO stage and prognostic risk score [1–4,16]. Hysterectomy may have a role in selected patients who have completed childbearing, have substantial uterine disease or hemorrhage, or have specific histological subtypes in which surgery contributes substantially to disease control [1,3,4,16]. Therefore, TAH-BSO should not be presented as a universally preferred treatment solely on the basis of age greater than 40 years. In the present case, the patient's perimenopausal status, completed childbearing, and apparent uterine-confined disease may have contributed to the decision to perform hysterectomy; however, the source documentation did not provide sufficient information to establish the exact clinical rationale for surgery or for bilateral salpingo-oophorectomy. This limitation should be acknowledged rather than retrospectively assigning an indication that was not documented.

Histopathological examination demonstrated malignant trophoblastic proliferation with superficial myometrial invasion and atypical pleomorphic cells. These findings support malignant trophoblastic disease but are insufficient, based on the information available, to definitively classify the tumor as invasive mole, choriocarcinoma, PSTT, or ETT. Accurate distinction among these entities is clinically important because their biological behavior, β -hCG secretion, chemosensitivity, and preferred management differ substantially [17,18,24,25]. Immunohistochemical panels incorporating markers such as β -hCG, human placental lactogen (hPL), p63, cytokeratin, and Ki-67 can assist in distinguishing trophoblastic tumor subtypes. For example, PSTT typically demonstrates strong hPL expression and relative lack of p63 expression, whereas ETT commonly demonstrates p63 positivity; choriocarcinoma generally shows prominent β -hCG expression and a high proliferative index [17,24,25]. Because additional immunohistochemical characterization was not available in this case, the pathological diagnosis should remain descriptive and should not be extended to a specific GTN subtype without supporting evidence.

Serial β -hCG monitoring after surgery was particularly important in this patient. At postoperative week 2, β -hCG decreased to 3,111.4 mIU/mL, followed by a further decline

to 88.80 mIU/mL at week 4. The subsequent increase to 477.69 mIU/mL and later plateau between approximately 259.70 and 266.24 mIU/mL raised strong concern for persistent trophoblastic activity. According to contemporary FIGO recommendations, plateauing or rising serial hCG concentrations are central biochemical criteria for the diagnosis of post-molar or persistent GTN [1,2]. However, because the exact dates and complete sequence of all serial measurements were not available in the source documentation, the individual FIGO interval criteria cannot be retrospectively reconstructed with certainty. Accordingly, the postoperative pattern should be described as being consistent with persistent GTN, rather than claiming that every formal interval criterion was definitively documented. A graphical representation of serial β -hCG concentrations against time would further clarify the clinically important transition from initial biochemical response to secondary rise and plateau.

Alternative explanations for persistent low-level hCG should also be considered when appropriate. These include quiescent trophoblastic disease, pituitary hCG in perimenopausal women, and assay interference caused by heterophile antibodies, often termed "phantom hCG" [19]. In the present case, the initially markedly elevated β -hCG concentration, histologically demonstrated malignant trophoblastic proliferation with myometrial invasion, and clear postoperative changes in serial β -hCG make persistent trophoblastic disease clinically more plausible than isolated pituitary or assay-related hCG. Nevertheless, the absence of specific testing for assay interference represents another limitation, particularly when interpreting subsequent low-level hCG values.

The reported FIGO prognostic score of 3 places the patient in the low-risk GTN category. Contemporary recommendations generally advocate single-agent chemotherapy with methotrexate or actinomycin-D for low-risk GTN, with very high overall cure rates [1–4,16]. The available case documentation states that the patient subsequently received methotrexate and etoposide with leucovorin rescue. However, detailed information regarding the exact dosing schedule, number of cycles, sequence of agents, and rationale for this regimen was unavailable. Therefore, the treatment should be reported descriptively and should not be characterized as a standard single-agent regimen. The absence of detailed treatment documentation also prevents a meaningful comparison of this regimen with contemporary first-line recommendations for FIGO low-risk GTN.

Another important limitation is the absence of documented long-term follow-up. For GTN, therapeutic response cannot be determined solely from immediate clinical improvement; serial normalization of hCG and continued surveillance after treatment are essential for confirming remission and detecting recurrence [1–4]. Similarly, documentation of subsequent TSH and FT4 normalization would strengthen the proposed association between trophoblastic disease and thyrotoxicosis. In this case, detailed information regarding post-chemotherapy β -hCG concentrations, number of chemotherapy cycles, duration of surveillance, final thyroid status, and long-term clinical outcome was not available. These limitations should be explicitly acknowledged.

Overall, this case demonstrates the importance of a multidisciplinary approach to GTN complicated by severe thyrotoxicosis. Markedly elevated β -hCG may contribute to clinically significant thyroid stimulation, but alternative causes of hyperthyroidism should be considered when confirmatory endocrine testing is unavailable. Careful perioperative stabilization, appropriate histopathological characterization, FIGO-based risk assessment, and serial quantitative β -hCG surveillance are central to management. The postoperative secondary rise and plateau of β -hCG in this patient emphasize that hysterectomy does not eliminate the need for biochemical surveillance and that persistent trophoblastic activity may require additional systemic therapy.

Conclusion and Recommendations

This case highlights the importance of considering gestational trophoblastic neoplasia (GTN) in perimenopausal women presenting with atypical gastrointestinal or gynecological symptoms, particularly when accompanied by markedly elevated β -hCG concentrations. Severe thyrotoxicosis may occur in this setting, and β -hCG-mediated stimulation of the TSH receptor represents a plausible mechanism, especially in the absence of typical clinical features of Graves disease such as goiter or ophthalmopathy. However, alternative causes of hyperthyroidism should be considered when confirmatory endocrine investigations are unavailable.

The markedly elevated β -hCG concentration and severe thyrotoxicosis in this patient were associated with substantial perioperative risk and warranted preoperative endocrine stabilization before TAH-BSO. Although β -hCG levels initially declined after surgery, subsequent secondary elevation and plateau were consistent with persistent trophoblastic disease and prompted further systemic treatment. This case therefore emphasizes that surgical management does not eliminate the need for serial quantitative β -hCG surveillance.

Early recognition of GTN, appropriate management of severe thyrotoxicosis, accurate histopathological characterization, FIGO-based risk assessment, and continued biochemical monitoring are essential components of care. In patients with persistent or abnormal post-treatment β -hCG kinetics, timely evaluation and appropriate chemotherapy should be considered according to established GTN treatment guidelines. Long-term follow-up should include serial β -hCG measurements and reassessment of thyroid function to document disease remission and endocrine recovery.

This case highlights the importance of recognizing gestational trophoblastic neoplasia (GTN) with β -hCG-mediated hyperthyroidism in perimenopausal women, particularly because its clinical manifestations may mimic common perimenopausal or gastrointestinal conditions and may occur without classic signs of hyperthyroidism such as goiter or ophthalmopathy. The markedly elevated β -hCG level contributed to thyrotoxicosis and posed a significant perioperative risk, requiring appropriate preoperative medical management before TAH-BSO. Despite definitive surgery, serial β -hCG monitoring demonstrated a secondary rise followed by a plateau, fulfilling FIGO criteria for persistent GTN and necessitating chemotherapy. This case emphasizes the importance of early diagnosis, careful perioperative control of β -hCG-induced hyperthyroidism, histopathological confirmation, and continuous β -hCG surveillance to identify persistent disease and guide further treatment.

By integrating endocrine stabilization with prompt oncological intervention and meticulous biochemical surveillance, clinicians can achieve high cure rates and favorable outcomes in patients with even the most complex presentations of gestational trophoblastic neoplasia.

Statement on the Use of Artificial Intelligence

During the preparation of this manuscript, the authors used software solely to assist with the initial search and identification of potentially relevant literature and references. Artificial intelligence tools were not used to generate the manuscript content, perform data analysis, interpret the results, or formulate the conclusions. All references suggested or identified with the assistance of AI were independently verified by the authors through the original publications and/or academic databases. The authors take full responsibility for the accuracy, originality, integrity, citations, and final content of the manuscript.

Funding

This study received no external funding. All research-related expenses were borne by the authors. The Article Processing Charge (APC) was also covered by the authors.

Acknowledgments

The authors would like to express their sincere gratitude to the medical and nursing teams involved in the diagnosis, treatment, and perioperative management of the patient. The authors also thank the Department of Obstetrics and Gynecology, the pathology laboratory, and the radiology department for their valuable contributions to the diagnostic evaluation and management of this case. Special appreciation is extended to the supervising clinicians and academic mentors for their guidance and support during the preparation of this case report. Finally, the authors are grateful to the patient and her family for their cooperation and for providing consent for the use of relevant clinical information and images for academic and scientific purposes.

Conflict of Interest

The authors declare that there are no conflicts of interest related to this study or the preparation of this manuscript

Author Contributions

1. Nabila Kinantia Sarjono: Conceptualization, investigation, data curation, clinical data collection, literature review, manuscript drafting, visualization, and preparation of the original manuscript.
 2. Heru Priyanto: Supervision, validation, clinical expertise, critical revision of the manuscript, and final approval of the submitted version.
- All authors have read and approved the final version of the manuscript.

References

1. Ngan HYS, Seckl MJ, Berkowitz RS, Xiang Y, Golfier F, Sekharan PK, et al. Diagnosis and management of gestational trophoblastic disease: 2025 update. *Int J Gynaecol Obstet.* 2025;171(Suppl 1):78-86. doi:10.1002/ijgo.70275.
2. Ngan HYS, Seckl MJ, Horowitz N, Cheung ANY, Braga A, Sekharan PK, et al. FIGO staging for gestational trophoblastic neoplasia: 2026. *Int J Gynaecol Obstet.* 2026;174(3):1172-1180. doi:10.1002/ijgo.71229.
3. Soper JT. Gestational trophoblastic disease: current evaluation and management. *Obstet Gynecol.* 2021;137(2):355-370. doi:10.1097/AOG.0000000000004240.
4. Tidy J, Seckl M, Hancock BW. Management of gestational trophoblastic disease: Green-top Guideline No. 38. *BJOG.* 2021;128(3):e1-e27. doi:10.1111/1471-0528.16266.
5. Seckl MJ, Sebire NJ, Berkowitz RS. Gestational trophoblastic disease. *Lancet.* 2010;376(9742):717-729. doi:10.1016/S0140-6736(10)60280-2.
6. Lurain JR. Gestational trophoblastic disease I: epidemiology, pathology, clinical presentation and diagnosis of gestational trophoblastic disease, and management of hydatidiform mole. *Am J Obstet Gynecol.* 2010;203(6):531-539. doi:10.1016/j.ajog.2010.06.073.
7. Altieri A, Franceschi S, Ferlay J, Smith J, La Vecchia C. Epidemiology and aetiology of gestational trophoblastic diseases. *Lancet Oncol.* 2003;4(11):670-678. doi:10.1016/S1470-2045(03)01245-2.
8. Savage PM, Sita-Lumsden A, Dickson S, Iyer R, Everard J, Coleman RE, et al. The relationship of maternal age to molar pregnancy incidence, risks for chemotherapy

- and subsequent pregnancy outcome. *J Obstet Gynaecol.* 2013;33(4):406-411. doi:10.3109/01443615.2013.771159.
9. Walkington L, Webster J, Hancock BW, Everard J, Coleman RE. Hyperthyroidism and human chorionic gonadotrophin production in gestational trophoblastic disease. *Br J Cancer.* 2011;104(11):1665-1669. doi:10.1038/bjc.2011.139.
 10. Yoshimura M, Hershman JM. Thyrotropic action of human chorionic gonadotropin. *Thyroid.* 1995;5(5):425-434. doi:10.1089/thy.1995.5.425.
 11. Hershman JM. Human chorionic gonadotropin and the thyroid: hyperemesis gravidarum and trophoblastic tumors. *Thyroid.* 1999;9(7):653-657. doi:10.1089/thy.1999.9.653.
 12. Hershman JM. Physiological and pathological aspects of the effect of human chorionic gonadotropin on the thyroid. *Best Pract Res Clin Endocrinol Metab.* 2004;18(2):249-265. doi:10.1016/j.beem.2004.03.010.
 13. Yoshimura M, Pekary AE, Pang XP, Berg L, Goodwin TM, Hershman JM. Thyrotropic activity of basic isoelectric forms of human chorionic gonadotropin extracted from hydatidiform mole tissues. *J Clin Endocrinol Metab.* 1994;78(4):862-866. doi:10.1210/jcem.78.4.8157712.
 14. Alexander EK, Pearce EN, Brent GA, Brown RS, Chen H, Dosiou C, et al. 2017 guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and the postpartum. *Thyroid.* 2017;27(3):315-389. doi:10.1089/thy.2016.0457.
 15. Akamizu T, Satoh T, Isozaki O, Suzuki A, Wakino S, Iburi T, et al. Diagnostic criteria, clinical features, and incidence of thyroid storm based on nationwide surveys. *Thyroid.* 2012;22(7):661-679. doi:10.1089/thy.2011.0334.
 16. Horowitz NS, Eskander RN, Adelman MR, Burke W. Epidemiology, diagnosis, and treatment of gestational trophoblastic disease: a Society of Gynecologic Oncology evidence-based review and recommendation. *Gynecol Oncol.* 2021;163(3):605-613. doi:10.1016/j.ygyno.2021.10.003.
 17. Kaur B. Pathology of gestational trophoblastic disease (GTD). *Best Pract Res Clin Obstet Gynaecol.* 2021;74:3-28. doi:10.1016/j.bpobgyn.2021.02.005.
 18. Burkett WC, Soper JT. A review of current management of placental site trophoblastic tumor and epithelioid trophoblastic tumor. *Obstet Gynecol Surv.* 2022;77(2):101-110. doi:10.1097/OGX.0000000000000978.
 19. Oyatogun O, Sandhu M, Barata-Kirby S, Tuller E, Schust DJ. A rational diagnostic approach to the “phantom hCG” and other clinical scenarios in which a patient is thought to be pregnant but is not. *Ther Adv Reprod Health.* 2021;15:26334941211016412. doi:10.1177/26334941211016412.
 20. Pereira JVB, Lim T. Hyperthyroidism in gestational trophoblastic disease: a literature review. *Thyroid Res.* 2021;14:1. doi:10.1186/s13044-021-00092-3.
 21. Ross DS, Burch HB, Cooper DS, Greenlee MC, Laurberg P, Maia AL, et al. 2016 American Thyroid Association guidelines for diagnosis and management of hyperthyroidism and other causes of thyrotoxicosis. *Thyroid.* 2016;26(10):1343-1421. doi:10.1089/thy.2016.0229.
 22. Burch HB, Wartofsky L. Life-threatening thyrotoxicosis: thyroid storm. *Endocrinol Metab Clin North Am.* 1993;22(2):263-277. doi:10.1016/S0889-8529(18)30165-8.
 23. Satoh T, Isozaki O, Suzuki A, Wakino S, Iburi T, Tsuboi K, et al. 2016 guidelines for the management of thyroid storm from the Japan Thyroid Association and Japan Endocrine Society. *Endocr J.* 2016;63(12):1025-1064. doi:10.1507/endocrj.EJ16-0336.

24. Hui P. Gestational trophoblastic tumors: a timely review of diagnostic pathology. *Arch Pathol Lab Med.* 2019;143(1):65-74. doi:10.5858/arpa.2018-0234-RA.
25. Hancock BW, Tidy J. Placental site trophoblastic tumour and epithelioid trophoblastic tumour. *Best Pract Res Clin Obstet Gynaecol.* 2021;74:131-148. doi:10.1016/j.bpobgyn.2020.10.004.