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NAVIGATING THERAPY FOR HYPERTHYROIDISM IN LACTATION : A CASE REPORT AND REVIEW OF ANTITHYROID DRUG SAFETY

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ABSTRACT
Graves' disease is the leading cause of hyperthyroidism in women of reproductive age and may relapse in the postpartum period, when immune reactivation and the desire to continue breastfeeding complicate antithyroid drug selection. This case report aims to describe the therapeutic decision making process in a breastfeeding mother with Graves' hyperthyroidism and to provide practical insights that help bridge the gap between guideline recommendations and day to day clinical practice in navigating treatment options during lactation. Current guidelines indicate that methimazole at doses up to 20 mg per day can be used safely during breastfeeding. We report a 32-year-old woman with long-standing Graves' disease who experienced biochemical and clinical relapse two months postpartum, after discontinuing antithyroid therapy. At presentation, she was still breastfeeding her 9 month old infant. Hyperthyroidism was confirmed by markedly elevated free thyroxine and suppressed thyroid-stimulating hormone, in the context of diffuse goiter and prior ophthalmopathy, findings consistent with postpartum Graves' relapse rather than postpartum thyroiditis. Methimazole was reintroduced and titrated to 20 mg/day, with subsequent improvement in maternal symptoms and thyroid function, while breastfeeding was continued without clinical evidence of impaired growth or neurodevelopment in the infant. This case illustrates that methimazole at a daily dose of 20 mg can provide effective control of postpartum Graves' hyperthyroidism without necessitating interruption of breastfeeding, in line with international recommendations that classify low to moderate doses of MMI as safe during lactation. Careful monitoring of maternal thyroid status and individualized counselling are essential to balance disease control with maintenance of lactation.

Keywords: antithyroid drugs; graves' disease; hyperthyroidism; lactation; postpartum hyperthyroidism

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INTRODUCTION

Graves disease–related hyperthyroidism is the most common cause of hyperthyroidism in women of reproductive age and has been reported to complicate approximately 0.2% of pregnancies, with overt hyperthyroidism occurring in about 0.1–0.4% of all pregnancies. (Bhagat et al., 2023; Nguyen et al., 2018). Poorly controlled hyperthyroidism during pregnancy is associated with an increased risk of miscarriage, preeclampsia, preterm delivery, fetal growth restriction, low birth weight, congestive heart failure, and even thyroid storm, making timely diagnosis and appropriate management crucial (Ashkar et al., 2023; Bhagat et al., 2023; Nguyen et al., 2018).

The postpartum period, generally defined as the first 12 months after delivery, represents a distinct immunological phase characterized by an "immune rebound" phenomenon that may worsen or trigger recurrence of autoimmune thyroid disease, including Graves disease (Ashkar et al., 2023; Croce et al., 2019). Several longitudinal studies have shown that Graves activity tends to improve in the late third trimester but frequently exacerbates again after delivery, and pregnancy itself may increase relapse rates in women who had previously achieved remission after a full course of antithyroid drug therapy (Croce et al., 2019; Nguyen et al., 2018).

Breastfeeding is recognized as the optimal mode of infant nutrition, yet it poses specific challenges when the mother requires ongoing antithyroid drug (ATD) therapy for active Graves hyperthyroidism (Ashkar et al., 2023; Croce et al., 2019). Both methimazole and propylthiouracil (PTU) are known to be excreted into breast milk in small amounts; however, clinical evidence and current guidelines indicate that low to moderate doses of these agents are generally safe during lactation and do not impair thyroid function or intellectual development in breastfed infants.(Croce et al., 2019; Nguyen et al., 2018; Rind, 2021)

Guidelines from the American Thyroid Association (ATA) and the European Thyroid Association (ETA) recommend using the lowest effective dose in breastfeeding mothers, with commonly accepted upper limits of up to 20 mg/day for methimazole and 250–450 mg/day for PTU, administered immediately after breastfeeding and accompanied by routine clinical monitoring of infant growth and development (Ashkar et al., 2023; Croce et al., 2019). Nonetheless, choosing between methimazole and PTU during lactation remains complex, as clinicians must balance the teratogenic and embryopathic profile of methimazole, the hepatotoxic potential of PTU, the risk of maternal disease relapse, and the goal of maintaining breastfeeding (Bhagat et al., 2023; Croce et al., 2019; Nguyen et al., 2018).

In this context, case reports that illustrate therapeutic decision-making and long term outcomes in breastfeeding mothers with Graves hyperthyroidism provide valuable insights to bridge the gap between guideline recommendations and day to day clinical practice, particularly in settings with varying iodine status and healthcare resources (Ashkar et al., 2023; Croce et al., 2019). The present case report describes the treatment course of a breastfeeding mother with Graves disease who received methimazole in the postpartum period, along with a focused review of the safety of antithyroid drugs during lactation to support evidence based, patient centered management.

METHOD

This case report employed a descriptive design with a retrospective approach involving a single female patient with Graves disease who received antithyroid therapy during pregnancy and lactation. Clinical data were obtained from the patient's medical records at the Endocrinology Outpatient Clinic of RSUDZA, including structured history taking, physical examinations, disease course documentation, treatment regimens, and results of thyroid function tests (FT4 and TSH) from initial diagnosis through the postpartum and breastfeeding periods.

The history of antithyroid drug use (propylthiouracil and methimazole), dosage, duration of therapy, timing of discontinuation and re initiation, as well as the patient's clinical and biochemical responses, was systematically documented to delineate the dynamics of hyperthyroidism management during pregnancy and lactation. Breastfeeding status, the child's age, and continuation of breastfeeding were recorded to assess the relationship between antithyroid treatment choices and the maintenance of lactation, including general clinical monitoring of the infant based on the mother's clinical records.

In addition to the case description, a narrative literature review was conducted on the safety of antithyroid drugs in breastfeeding mothers by identifying scientific articles, clinical practice guidelines, and reviews addressing the use of propylthiouracil and methimazole during pregnancy and lactation, as well as dose limits considered compatible with breastfeeding. The literature search focused on the most recent recommendations regarding maximum doses during lactation, comparative safety profiles with respect to hepatotoxicity and other adverse effects, and evidence on drug transfer into breast milk and its impact on thyroid function and child development.

Patient identity was anonymized to preserve confidentiality, and preparation of this case report adhered to ethical principles for clinical case publication, including obtaining the patient's informed consent for the use of her clinical data in a scientific publication.

RESULT

Case Illustration

A 32-year-old woman, gravida 2 para 2, presented to the Department of Endocrinology with recurrent tremors that developed one week after discontinuing antithyroid therapy for approximately two months in the postpartum period after the birth of her second child. At presentation, she was still breastfeeding her 9-month-old infant. She had a history of hyperthyroidism since 2012, with progressively worsening tremors of the hands and body, palpitations, easy fatigability, exertional dyspnea, heat intolerance, excessive sweating, anxiety, sleep disturbance, and a 20-kg weight loss (from 60 kg to 40 kg), accompanied by neck enlargement and prominent eyes first noted in 2013.

She denied any history of diabetes, hypertension, or other autoimmune diseases, as well as a family history of thyroid disease, although several neighbors in the coastal area where she grew up reportedly had similar complaints. Her daily habits included frequent consumption of salty processed foods, acidic foods, and occasional carbonated beverages, as well as turmeric-based herbal preparations and vitamins obtained from traditional healers, while her husband was a smoker; her daily activities as a housewife were of moderate intensity.

Her hyperthyroid symptoms were first evaluated in mid-2013 when she presented with severe tremors and was found to have an FT4 level of 210 ng/dL and TSH of 0.004 µIU/mL, leading to a diagnosis of Graves disease and initiation of methimazole (thyrozol) 20 mg twice daily along with propranolol 10 mg once daily, with subsequent symptomatic improvement. The methimazole dose was gradually tapered to 10 mg twice daily and then 5 mg twice daily; however, in 2017 she discontinued medication because she felt well and experienced a relapse with FT4 >100 ng/dL and TSH 0.009 µIU/mL, prompting resumption of thyrozol 5 mg twice daily and propranolol 10 mg once daily until her symptoms improved.

During her second pregnancy in 2020, she continued antithyroid therapy, receiving PTU 100 mg twice daily in the first trimester, which was then switched to methimazole (thyrozol) 2.5 mg twice daily in the second and third trimesters, with thyroid function monitoring showing an FT4 of 0.92 ng/dL and a euthyroid state on 19 June 2020. After delivery, she stopped antithyroid medication for approximately two months due to difficulties accessing the hospital pharmacy; two months later, her tremors recurred and thyroid function testing on 3 May 2021 revealed an FT4 of 100 ng/dL, so the methimazole dose was increased to 10 mg twice daily while she continued breastfeeding.

On current physical examination, she appeared in fairly good general condition but fatigued with minimal exertion, with a blood pressure of 125/80 mmHg, heart rate of 108 beats per minute, respiratory rate of 24 breaths per minute, temperature of 36.5 °C, oxygen saturation of 99%, body weight of 40 kg, height of 158 cm, and a BMI of 16 kg/m², indicating undernutrition. Ocular examination showed improved exophthalmos without lid lag or lid retraction, while neck examination revealed a diffuse, non-tender enlargement of the thyroid gland measuring approximately 5×5 cm, without erythema, bruit, or cervical lymphadenopathy.

Cardiac examination demonstrated tachycardia with a louder S1 than S2 and no murmurs; the lungs were symmetric with vesicular breath sounds and no crackles or wheezing, and abdominal examination was unremarkable. In the upper extremities, there was a fine tremor on paper-holding test, warm acral temperature, palmar erythema, no pallor, and intermittent sweating; in the lower extremities, the acral parts were also warm without edema or pretibial myxedema.

The latest laboratory evaluation on 8 June 2021 showed an FT4 of 32.85 ng/dL with TSH 0.005 μIU/mL, indicating biochemically active hyperthyroidism despite partial clinical control with methimazole 20 mg/day during lactation. Given her long-standing symptom history, diffuse goiter, ophthalmopathy, a Wayne Index score of 25, and consistent biochemical profile, she was diagnosed as a case of Graves disease in the postpartum period while breastfeeding and was managed with methimazole 10 mg twice daily, within the dose range considered potentially compatible with breastfeeding in the context of antithyroid drug safety.

DISCUSSION

This case illustrates the clinical challenge of balancing control of Graves hyperthyroidism with lactation safety in a young woman entering the postpartum period with long standing Graves disease, multiple relapses after ATD withdrawal, and ongoing breastfeeding while receiving methimazole 20 mg/day. This clinical pattern is consistent with reports that pregnancy is often followed by a transient improvement in Graves disease due to an immunosuppressive state and a reduction in TRAb titers. However, this is subsequently accompanied by an increased risk of postpartum hyperthyroid relapse, both in women who continue antithyroid therapy and in those who have achieved remission after completing a full course of ATD treatment. These observations support the concept of the postpartum period as a "high-risk window" for the recurrence of autoimmune thyroid activity (Gheorghiu et al., 2021; Suzuki et al., 2025).

Other studies have shown that up to 45% of Graves disease in women of reproductive age may first manifest in the postpartum period and that postpartum relapse after ATD withdrawal can reach 84% among patients with prior long term remission (Croce et al., 2019). This pattern mirrors the clinical course of the present patient, who experienced multiple relapses after stopping ATD, including a relapse 2 months postpartum while breastfeeding, placing her within the classic spectrum of postpartum Graves disease with the added challenge of ensuring treatment safety during lactation. From a therapeutic perspective, the use of methimazole at a dose of 20 mg/day in this breastfeeding mother falls within the range supported by available lactation safety data, as demonstrated by studies showing that maternal methimazole doses of 5–20 mg/day do not adversely affect thyroid function or intellectual development in breastfed infants (Croce et al., 2019; Rind, 2021).

Croce et al. reported that approximately 0.1–0.2% of the maternal oral methimazole dose is excreted into breast milk, with no evidence of clinically relevant alterations in infant thyroid function at maternal doses of up to 20 mg/day. (Croce et al., 2019) The 2017 ATA and 2018 ETA guidelines, as cited by Croce and colleagues, state that methimazole doses up to 20 mg/day and PTU doses of 250–450 mg/day are compatible with breastfeeding, and recommend administering these drugs in divided doses immediately after nursing to minimize infant exposure (Alexander et al., 2017; Croce et al., 2019). Accordingly, the use of methimazole 10 mg twice daily in this patient aligns with internationally recognized safety thresholds and is supported by available lactation pharmacokinetic data.

Pathophysiologically, this case highlights postpartum immune dynamics in Graves disease. Pregnancy is characterized by a shift toward a Th2 dominant profile and expansion of regulatory T and B cells, whereas the postpartum period is marked by an "immune rebound" with restoration of Th1 predominance and increased B cell activation, which correlates with exacerbations of several autoimmune diseases, including autoimmune thyroid disorders, within 12 months of delivery (Croce et al., 2019; Lima et al., 2019). In Graves disease, the postpartum period acts as a precipitating rather than primary causal factor in genetically predisposed individuals, with postpartum onset cases tending to occur in younger women and more frequently in those with a family history of autoimmunity (Croce et al., 2019). Although this patient lacked a clear family history, her coastal upbringing with potential variability in iodine intake and passive smoke exposure from her husband represents additional environmental modulators of Graves risk and phenotype, in line with reports that iodine status and smoking influence Graves disease expression

(Croce et al., 2019; Xie et al., 2023).

An additional key consideration in the postpartum period is the high prevalence of postpartum thyroiditis (PPT) as a leading cause of thyrotoxicosis, necessitating careful differentiation from Graves relapse. Elevated TRAb levels and increased thyroid blood flow on Doppler provide high sensitivity for distinguishing postpartum Graves disease from destructive PPT. In this patient, the long standing Graves history, diffuse goiter, ophthalmopathy, persistent hyperthyroidism beyond 3 months postpartum, and a high Wayne score are compatible with postpartum Graves disease as described by Croce et al., rather than PPT, which typically has earlier onset (<3 months postpartum) and a brief thyrotoxic phase, thereby justifying continuation of ATD therapy, which is ineffective and potentially harmful in PPT but remains first line in Graves disease (Croce et al., 2019).

The clinical implications of this case span several domains. First, they underscore the need for close thyroid function monitoring during pregnancy and throughout the postpartum period, including in women with Graves disease in remission, since pregnancy after methimazole withdrawal increases relapse risk compared with nonpregnant women, with most relapses occurring within 18 months (Struja et al., 2017). Reflecting this, the 2017 ATA guidelines recommend TSH and FT4 monitoring not only in women with active Graves disease but also in those with a history of remitted Graves entering pregnancy or the postpartum period (Alexander et al., 2017). Second, careful ATD dose titration is crucial to avoid both uncontrolled hyperthyroidism and iatrogenic hypothyroidism; Gheorghiu et al. showed that in women on long term preconception ATD therapy, dose reduction and first trimester ATD withdrawal were feasible in approximately 40% of pregnancies and were associated with better pregnancy outcomes than in women diagnosed during pregnancy (Gheorghiu et al., 2021). In this case, delayed drug collection and abrupt ATD cessation immediately postpartum contributed to biochemical relapse (FT4 32.85 ng/dL), reinforcing the need for patient education and uninterrupted medication access during this high risk period.

Regarding ATD safety in pregnancy and lactation, the literature highlights distinct risk profiles for PTU and methimazole. Bhagat et al.'s systematic review of 10 case reports noted that methimazole/carbimazole is more frequently associated with a characteristic embryopathy (aplasia cutis, choanal atresia, omphalocele, tracheoesophageal fistula) when used in the first trimester, whereas PTU has fewer and generally milder malformations (Bhagat et al., 2023). Conversely, PTU is associated with a risk of severe maternal hepatotoxicity, and several reports have documented cases of severe liver failure linked to its use. These concerns have led to more restrictive recommendations on PTU administration, with guidance now suggesting that its use be limited to the first trimester, after which pregnant women should be switched to methimazole for treatment during the second and third trimesters (Dumitrascu et al., 2021; Liu et al., 2023). This strategy is mirrored in this case, where the patient received PTU 100 mg twice daily in the first trimester, was transitioned to low dose methimazole 2.5 mg twice daily in the second and third trimesters with achievement of euthyroidism (FT4 0.92 ng/dL), and subsequently to a moderate methimazole dose during lactation, consistent with the consensus that methimazole teratogenic risk is greatest in weeks 6–10 of gestation, after which prevention of maternal and fetal hypothyroidism becomes the primary focus(Dumitrascu et al., 2021; Gheorghiu et al., 2021).

In the context of breastfeeding, reports indicate that both PTU and methimazole are excreted into breast milk in small quantities and, with appropriate monitoring, do not cause thyroid dysfunction or developmental delay in infants. Earlier studies found that only about 0.1% of the maternal PTU dose enters breast milk, with maximum breast milk concentrations around 10% of maternal serum levels and no changes in infant thyroid parameters, while maternal methimazole doses of 5–20 mg/day result in milk excretion of roughly 0.1–0.2% of the oral dose and do not necessitate routine laboratory monitoring in infants with normal growth and development (Croce et al., 2019). On this basis, the 2018 ETA and 2017 ATA guidelines recommend that breastfeeding mothers on methimazole ≤20 mg/day or PTU ≤250‑450 mg/day may continue nursing without routine infant

thyroid testing, provided that the infant is clinically monitored and the drug is taken immediately after breastfeeding to reduce peak milk concentrations (Alexander et al., 2017; Kahaly et al., 2018). Within this framework, the choice of methimazole 20 mg/day in a mother breastfeeding a 9 month old infant represents a balanced compromise between adequate maternal disease control and infant safety.

A major strength of this case lies in its longitudinal documentation of Graves disease evolution from initial diagnosis through pregnancy, postpartum, and the lactation period, offering a concrete illustration of how guideline recommendations are operationalized in real world practice in a resource constrained setting. Croce et al. emphasize that many aspects of postpartum Graves disease, including immunologic triggers, predictors of relapse, and the role of iodine supplementation in women with Graves disease from iodine deficient regions, remain insufficiently studied and require large, prospective investigations (Croce et al., 2019). Gheorghiu et al. similarly highlight the limitations of small observational datasets and the need for national registries to evaluate ATD control strategies and long term child outcomes (Gheorghiu et al., 2021). A limitation of the present case is the absence of serial TRAb measurements and systematic monitoring of the infant's thyroid function, despite current recommendations to perform such testing when maternal TRAb levels are elevated or when moderate-to-high ATD doses are required until late pregnancy (Petca et al., 2023; Tzoraki et al., 2024). However, this situation reflects the reality of practice in many resource-limited healthcare centers, where clinical decisions must rely on population risk profiles, established lactation safety data, and rigorous clinical monitoring, rather than on extensive biomarker testing.

From a practical standpoint, this case supports several recommendations: (i) maintaining ATD therapy at the lowest effective dose during lactation in women with active Graves disease, without routinely advising breastfeeding cessation, provided methimazole doses remain ≤20 mg/day or PTU within established safety limits; (ii) avoiding abrupt ATD discontinuation in the early postpartum period, particularly in women with a history of relapse, and instead planning gradual tapering with regular FT4 and TSH monitoring; and (iii) reconsidering definitive therapy (radioiodine ablation or thyroidectomy) outside the lactation period for patients with recurrent relapses or ongoing need for medium to high ATD doses, in line with ETA 2018 recommendations for difficult to control Graves disease (Kahaly et al., 2018). At the same time, the growing body of evidence supporting the safety of low to moderate ATD doses during lactation provides a robust rationale for prioritizing breastfeeding while maintaining adequate maternal hyperthyroidism control, as underscored by Croce and Dumitrascu in their reviews of postpartum Graves disease and hyperthyroidism management in pregnancy and lactation (Croce et al., 2019; Dumitrascu et al., 2021).

CONCLUSION

This case underscores that methimazole 20 mg/day can effectively control Graves' hyperthyroidism in the postpartum period without requiring cessation of breastfeeding, provided that clinical and biochemical monitoring is carefully maintained. The report also highlights the need for heightened vigilance for Graves' relapse in the postpartum period and the importance of patient education to prevent abrupt discontinuation of antithyroid drugs, particularly in women with a history of recurrent relapse.

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