Thyroid Disease in Pregnancy and Postpartum

INTRODUCTION

This chapter discusses cases of pregnancy complicated by thyroid disease and thyroid test abnormalities, as well as thyroid problems after delivery. Thyroid diagnosis and treatment during pregnancy is more complex because there are two patients with whom to be concerned—the mother and the fetus. Diagnosis is more difficult because thyroid tests may be harder to interpret in this setting. Also, tests using radiation, such as the thyroid uptake and scan, cannot be safely performed on pregnant women. Treatment is more difficult because of concern about the effect of thyroid disease and medication on the fetus. Radioactive iodine (RAI) treatment is contraindicated during pregnancy.

Thyroid problems are also common in the months after delivery, and they are often missed. Following delivery, women may develop nonspecific symptoms, such as fatigue, depression, nervousness, and palpitations. These complaints may be the result of the stress of caring for a new infant and the major lifestyle changes that result. However, they may also result from thyroid dysfunction.

Postpartum hypothyroidism or hyperthyroidism occurs in up to 20% of women. It is often transient, but awareness and possible treatment may make a big difference to the patient. Often, the physician will feel that the complaints are the result of emotional problems, and the patient will either reject this diagnosis or feel unhappy about it. The diagnosis of an underlying and probably temporary thyroid disorder will relieve a lot of the patient’s stress even if treatment is not indicated. This chapter discusses several cases that demonstrate the types of thyroid problems that are seen in pregnancy and the postpartum period.

CASE 1

A 32-year-old woman was referred because of abnormal thyroid function tests. Her thyroid-stimulating hormone (TSH) was less than 0.03, total thyroxine (T₄) was 20 (4–12), and total triiodothyronine (T₃) was 274 (70–180). She was 16 weeks pregnant and had severe hyperemesis gravidarum with a 19-lb weight loss. She had noted shakiness and intermittent palpitations.
Physical examination revealed an acutely ill young woman who was weak and shaky. Pulse was 100 and blood pressure (BP) was 80/44. Her buccal mucosa was dry and her eyes were sunken. The thyroid was enlarged to about 1.5 times the normal size. She had no thyroid eye signs.

The following laboratory results were obtained:

- Free thyroxine (FT₄): 1.48 (0.8–1.8).
- Antithyroid peroxidase antibody was negative.
- Thyroid-stimulating immunoglobulin (TSI) was normal.

What Is Your Diagnosis?

The patient is clearly thyrotoxic. The differential diagnosis includes Graves’ disease and thyrotoxicosis of hyperemesis gravidarum. This is often a very difficult differential to make (see Case Discussion section). In this case, my working diagnosis was Graves’ disease.

How Would You Manage This Patient?

The patient was started on 100 mg of propylthiouracil (PTU) every 8 hours, and given parenteral hyperalimentation. One week later, she was seen by her obstetrician for jaundice and referred to a gastroenterologist. I was concerned that the jaundice might be a side effect of the PTU. Fortunately, she had not started the PTU yet because it was pending approval by Medicaid. The gastrointestinal consultant diagnosed fatty liver of pregnancy. The Medicaid approval came through and she started the PTU.

Clinical Course

The patient gained weight, her pulse slowed to 70 to 80, and the tremor cleared. Follow-up FT₃ and FT₄ were normal, although the TSH remained low. The PTU dose was gradually decreased to 50 mg twice daily. A TSI at 8 months of pregnancy was normal. She delivered a normal full-term infant.

Postpartum

The baby’s total T₄ at 1 d was 24.1 (upper-normal for that age). At 1 week, the baby’s total T₄ was 13.6, TSH was 1. The mother became clinically hyperthyroid and required an increase in PTU to 150 mg every 8 hours. She was continued on PTU for several months while awaiting Medicaid approval for RAI therapy. Eventually, she was treated with RAI and developed the usual post-RAI hypothyroidism. She is now euthyroid on replacement T₄. The baby is doing well.

Case Discussion

This challenging case demonstrates the difficulty in diagnosis of the etiology of hyperthyroidism in a pregnant woman. Making the correct diagnosis is obvi-
ously critical to appropriate treatment. The differential diagnosis is usually between transient hyperthyroidism of hyperemesis gravidarum (THHG) and Graves’ disease. THHG is caused by inappropriate secretion of human chorionic gonadotropin (HCG). HCG and TSH have the same α-subunit and different β-subunits. HCG is a mild thyroid stimulator, and high levels may produce hyperthyroidism. Graves’ disease is, of course, an autoimmune disease and is caused by immunoglobulins that stimulate the TSH receptors on thyroid cells. Hyperthyroidism is the second most common endocrine disease in pregnancy (diabetes is the first) and occurs in 1 in 500 pregnancies.

Graves’ disease is the more serious problem, and requires aggressive therapy to avoid complications in mother and child. THHG is usually a self-limited disease and may only require symptomatic therapy or observation. In the absence of Graves’ disease ophthalmopathy, the differential diagnosis is often difficult. Some clinical clues that point to Graves’ disease include a history of hyperthyroid symptoms prior to pregnancy, the presence of goiter, and exophthalmos and positive antibodies. In THHG, the severity of the hyperthyroidism is usually related to the severity of the vomiting, and the hyperthyroidism will usually spontaneously clear by the fourth or fifth month of pregnancy. A suppressed TSH may also be seen in normal pregnancy without thyroid disease, but in this case the patient will not have hyperthyroid symptoms, and the T₃ and T₄ will be normal.

This patient had severe hyperemesis and could well have had THHG. However, she had a goiter, and I made a working diagnosis of Graves’ disease. Antithyroid drugs (ATDs) are the treatment of choice in the pregnant Graves’ patient. She was started on PTU in a moderate dose, and the dose was tapered as she improved. It is important not to over treat and cause hypothyroidism, because hypothyroidism in the mother may produce goiter and hypothyroidism in the fetus. The ATD dose should be adjusted to keep the FT₄ in the upper normal range. Graves’ disease, like other autoimmune diseases, tends to improve during pregnancy, and the ATD can often be decreased and even discontinued in the latter part of pregnancy.

This patient delivered a normal infant. The baby was euthyroid and had no goiter. A TSI at 8 months of pregnancy was normal. The TSI should be measured in the last trimester. A significantly elevated TSI should alert the physician to the possibility of neonatal hyperthyroidism in the newborn. This is a serious problem that requires expert help from the endocrinologist and pediatrician.

My working diagnosis of Graves’ disease in the mother proved correct in this patient. The Graves’ disease persisted through pregnancy and became more severe after delivery. She required definitive therapy with RAI and has done well on replacement T₄. If she becomes pregnant again, a TSI should be done in early pregnancy. A significantly elevated TSI will alert the physician to the pos-
sibility of neonatal hyperthyroidism. The mother’s thyroid function should be monitored during pregnancy and the T₄ dosage adjusted to maintain a euthyroid state.

**What Can We Learn From This Case?**

- Consider hyperthyroidism in pregnancy, especially if the patient has a resting pulse over 100 and fails to gain weight despite good intake. Obtain FT₄ and TSH.
- Try to make differential diagnosis between Graves’ disease and the less serious THHG.
- Be aware that a suppressed TSH alone without symptoms and other findings of hyperthyroidism is common in normal pregnancies and requires no medication.
- Look for thyroid ophthalmopathy and goiter as signs that may point to Graves’ disease.
- In difficult cases, thyroid peroxidase (TPO) antibody and TSI testing may be helpful.
- If Graves’ disease is diagnosed, treatment with PTU or methimazole may be needed. Close monitoring is required to prevent maternal hypothyroidism from medication, which can result in fetal goiter and fetal hypothyroidism.
- In pregnant women with Graves’ disease, a TSI should be obtained in the last trimester. A significantly elevated TSI indicates that fetal or neonatal hyperthyroidism may occur.
- If treatment with an ATD is needed, keep FT₄ in upper third of the normal range, and try to decrease the dosage as pregnancy progresses. It may be possible to discontinue the drug in the last trimester.
- Be aware that autoimmune diseases, such as Graves’ disease, tend to improve in the last half of pregnancy and may flare up after delivery. Flare-ups can also occur in the first trimester.
- TSI should be monitored in the last trimester in all Graves’ disease patients, even those who have been treated prior to pregnancy and are euthyroid. TSI crosses the placental barrier and may cause fetal or neonatal hyperthyroidism.
- Think of hyperthyroidism in the fetus of a Graves’ disease mother if fetal tachycardia, growth retardation, or goiter on ultrasound are seen.

**CASE 2**

A 30-year-old woman was referred for thyroid evaluation. She was 12 weeks pregnant with her second child. She had noted fatigue, moodiness, and heat intolerance over the previous 2 months. She had constant nausea from morning sickness, but no vomiting. She had lost 5 lb over the previous 2 weeks and complained of headaches. She denied palpitations or tremor. She noted no change in the appearance of her eyes or in her vision. She had one child age 7 years and had no thyroid problems with that pregnancy or postpartum. However, she was found to have a goiter 4 years previously and was treated with T₄ for 3 months. The past several days she had felt better, less tired, but still moody. There was no family history of thyroid disease.
Physical examination revealed a pulse of 72 and BP of 110/70. The eyes showed bilateral stare without proptosis or lid lag and the extraocular movements appeared normal. The thyroid was bilaterally enlarged to about twice the normal size, firm, and without nodules. The examination was otherwise normal.

The following test results were obtained:

- TSH less than 0.03; FT₄ 1.17 (0.7–1.5); sedimentation rate, 18.
- TPO antibody, FT₃, and TSI were normal.

What Is Your Differential Diagnosis?

The differential diagnosis includes Graves’ disease, THHG, and low TSH of pregnancy. This patient could have THHG, however, the goiter and previous history of thyroid disease make Graves’ disease a more likely diagnosis. Suppressed TSH with normal T₄ is also a common finding in normal pregnancies, but these patients do not usually have a goiter or other evidence of thyroid disease. I saw this patient on a short locum assignment and was not able to follow her further. She probably had Graves’ disease.

CASE 3

A 26-year-old woman was referred because of a TSH of 0.14, total T₄ of 9.7 (4.5–12), and thyroid microsomal antibody elevated to 15 (<1). She was 6 months postpartum and had complained to her doctor that she could not lose the weight she had gained during pregnancy. She reported that she has been warmer than others at work. She felt otherwise well. Her only medication was a birth control pill.

On physical examination, the pulse was 68, BP was 124/72. There were no thyroid eye signs. The thyroid gland was diffusely enlarged to twice the normal size and rubbery in consistency. Examination was otherwise normal.

What Is Your Diagnosis?

The most likely diagnosis is postpartum thyroiditis (PPT) with mild or subclinical hyperthyroidism. Early Graves’ disease should be considered in the differential diagnosis.

Additional Testing? Treatment?

No additional testing or treatment is indicated at this point. Close follow-up is important.

Clinical Course

The patient returned 1 month later. She was no longer hot and felt well. Physical examination revealed that her thyroid had decreased in size to about 1.5 times the normal size. The TSH was now elevated to 46, FT₄ was 0.24 (0.75–2).
What’s Going On?

The patient has switched from borderline hyperthyroid to biochemically hypothyroid. In view of the degree of TSH and FT₄ abnormality, she was started on T₄. She returned 2 months later and reported a 6-lb weight loss. Her TSH was 1.42.

Final Diagnosis? Treatment Plan?

The final diagnosis is PPT.

Treatment Plan

Options for treatment include continuing T₄ or discontinuing T₄ with close follow-up to see if her thyroid has recovered. The majority of patients with PPT recover, whereas some go on to permanent hypothyroidism. Because she planned another pregnancy, I elected to continue therapy rather than risk hypothyroidism during pregnancy.

Case Summary

This 26-year-old woman presented 6 mo postpartum with mild heat intolerance and an enlarged thyroid gland. Her TSH was low with a normal T₄ and thyroid microsomal antibody was positive. The diagnosis was subclinical hyperthyroidism due to PPT. She then converted to hypothyroidism and was treated with T₄. Because she planned another pregnancy, the T₄ was continued to ensure a euthyroid state.

What Can We Learn From This Case?

• Consider thyroid disease in the postpartum period when the patient has vague complaints.
• Once the physician thinks about thyroid disease in this setting, the diagnosis can be easily ruled in or out with a TSH and FT₄.
• Postpartum thyroid dysfunction can present as either hyperthyroidism or hypothyroidism and can progress from one to the other.
• PPT is an autoimmune disease. The patient will return to a euthyroid state spontaneously in the majority of cases.
• Short-term treatment may be needed to relieve symptoms in some patients, whereas others can be followed without treatment.
• Whereas the majority of patients will return spontaneously to a euthyroid state, about 25% of patients will become permanently hypothyroid.
• Look for thyroid dysfunction in subsequent pregnancies.

CASE 4

A 28-year-old woman was referred because of heat intolerance and abnormal thyroid function tests. She had delivered twins 10 wk previously. Thyroid testing at 6 weeks postpartum revealed a TSH of 0.05, FT₄ of 2.45 (0.8–1.8), and FT₃ of
The patient developed PPT after the birth of her first child approximately 2 years previously. Approximately 5 months after her first delivery, she noted palpitations, nervousness, insomnia, and fatigue. Her thyroid was noted to be enlarged. Thyroid studies at that time revealed a TSH of less than 0.06 and total T4 of 10 (4.5–12). Over the next several weeks, these symptoms cleared and she noted the onset of severe fatigue. Repeat studies showed a TSH of 98, FT4 of 0.39, and radioactive iodine uptake (RAIU) of 2% (7–24). She was started on T4 and the dose was adjusted over the next several months to normalize her TSH. She was maintained on 0.112 mg of T4 daily until the present time. Family history was positive for thyroid disease in the patient’s mother. Physical examination currently revealed an enlarged thyroid gland and was otherwise negative.

**What Is Your Diagnosis?**

Recurrent PPT with probable hyperthyroidism

**Treatment**

T4 was discontinued. The patient was given a β-blocker as symptomatic therapy for her hyperthyroidism and asked to return with repeat studies off T4 in 1 month.

**Case Summary**

This young woman developed PPT with her previous pregnancy and again after delivering twins. Because she had been maintained on T4 after her first pregnancy, the thyroid tests were more difficult to evaluate. However, she was clinically hyperthyroid. The history of hyperthyroidism progressing to hypothyroidism with her previous pregnancy and a very low RAIU was compatible with PPT. It seemed likely that she had recurrent PPT with her second pregnancy, although an RAIU would be needed to rule out Graves’ disease. The appropriate course was to discontinue her T4, treat her hyperthyroidism symptomatically, and see her again in 1–2 months.

**What Can We Learn From This Case?**

- When PPT occurs after a pregnancy, it frequently recurs after subsequent pregnancies and the patient should be alerted to look for it.
- PPT can cause hyperthyroidism alone, hypothyroidism alone or, as in this case, progress from one to the other.
- The differential diagnosis is Graves’ disease and the correct test to make the diagnosis is the RAIU. The RAIU will usually be elevated in Graves’ disease and low in PPT.
- The hyperthyroidism of PPT may be treated symptomatically and followed because it tends to be self-limited, and the patient will usually either return to a euthyroid state or progress to hypothyroidism.
- PPT is an autoimmune disease and the TPO or microsomal antibody will often be positive.
CASE 5

A 27-year-old woman was referred to me because of abnormal thyroid function tests. She had delivered her third child about 8 months previously and there was no history of thyroid problems with her previous pregnancies. After her last delivery, she noted mood swings, fatigue, and heat intolerance along with a 15-lb weight gain. She was having regular menses. There was no family history of thyroid disease.

Physical examination revealed a pulse of 76 and BP of 114/72. No thyroid eye signs were noted. The thyroid gland was mildly enlarged. The remainder of the examination was normal.

The following laboratory studies were reviewed:

- The initial thyroid studies at 6 months postpartum showed a TSH of less than 0.005 and FT4 of 1.7 (0.8–1.8).
- Repeat studies 1 mo prior to this visit revealed a TSH of 2.84, FT4 of 0.8, and total T3 was normal.
- RAIU was 2.4% at 24 hours (7–24).
- Thyroid ultrasound had been reported as normal.

What Is Your Diagnosis?

The diagnosis is PPT with borderline or subclinical hyperthyroidism that had resolved and might be progressing toward hypothyroidism in view of the recent borderline low-normal FT4 with normal TSH.

Treatment

At the time of my evaluation, the patient was clinically euthyroid. She required no thyroid treatment but careful follow-up was required.

Case Summary

This 27-year-old woman had clinical and laboratory evidence of mild PPT disease. Her thyroid tests at 6 months postpartum were compatible with subclinical hyperthyroidism and the very low RAIU confirmed PPT as the etiology rather than Graves’ disease. Her TSH then normalized and the FT4 dropped to the lower edge of normal with low-normal total T3. She will require careful follow-up to see if she progresses to hypothyroidism or becomes euthyroid. I discussed all of this at length with her and her husband and told them what to look for. They were reassured that the thyroid problem was mild and likely would resolve over time.

What Can We Learn From This Case?

- This case of PPT was much milder than those discussed previously and might have been overlooked if the patient had not developed several nonspecific complaints.
• The test results included a low TSH and upper-normal FT$_4$ initially, which were compatible with subclinical or borderline hyperthyroidism. The very low RAIU confirmed the diagnosis of PPT rather than Graves’ disease.
• The follow-up tests showed a normal TSH and borderline low FT$_4$ suggesting that she might be edging toward hypothyroidism. The important point is that, when thyroid status is changing, the FT$_4$ will change faster than the TSH and may be a more valid reflection of current thyroid status. The TSH may take several weeks to equilibrate and reflect thyroid status. When thyroid status is relatively stable over time, the TSH is a more accurate guide to thyroid status.
• The patient will probably eventually become euthyroid, although the possibility of permanent hypothyroidism was discussed with her. She was also advised that thyroid disease may recur with future pregnancies.

**SUMMARY**

The cases discussed in this chapter demonstrate different clinical presentations of thyroid disease during pregnancy and in the postpartum period. Case 1 is a pregnant woman who was acutely ill. She presented with severe hyperemesis with dehydration and thyroid function tests compatible with hyperthyroidism. She required urgent treatment while the underlying cause of her hyperthyroidism was being determined. The difficulty in making the differential diagnosis between THHG and Graves’ disease is discussed. The diagnosis of Graves’ disease was eventually established and she was successfully treated.

The second patient presented with vague symptoms, an enlarged thyroid, and biochemical findings of subclinical hyperthyroidism. She was followed without treatment and subsequently developed clinical hypothyroidism that required treatment with T$_4$.

The third patient presented with overt hyperthyroidism several weeks after delivering twins. She had a history of PPT disease after her previous pregnancy. She was treated symptomatically and followed.

The last patient presented with nonspecific symptoms, an enlarged thyroid, and laboratory findings of subclinical hyperthyroidism. Her TSH normalized without treatment, but she requires follow-up. These cases demonstrate the importance of thinking about thyroid disease in pregnancy and the postpartum period, and checking thyroid tests in patients with nonspecific complaints.

**SELECTED SOURCES**