### TITLE OF CASE

Postpartum Thyroiditis: A Case Study

### AUTHORS OF CASE

*Please indicate corresponding author by* *

Desaree Litwiller

### SUMMARY

**Up to 150 words summarising the case presentation and outcome**

Patient is 34 y/o female presenting to ED with fever, tachycardia and mania. History is significant for type 1 DM and she is 7 weeks postpartum vaginal delivery without clinical complication.

On PE, patient is anxious, diaphoretic but cooperative. A fine tremor is observed and LE reflexes found to be hyper-responsive. All other ROS unremarkable. An extensive work-up was conducted. The only abnormal results appreciated included EKG with sinus tachycardia, a painless goiter and a thyroid panel consistent with clinical hyperthyroidism. Further testing included radioactive iodine uptake scan and found to be WNL. Patient was diagnosed with post-partum thyroiditis and immediate treatment began with IV propranolol. Dosing was titrated to 40 mg q6hrs until symptoms remitted, approximately three days post-admission.

Further testing later revealed the patient tested negative for TSH receptor antibodies and positive TPO antibodies, reinforcing her diagnosis of PPT. She continues to follow up with her endocrinologist biannually and currently remains euthyroid.

### BACKGROUND

**Why you think this case is important – why you decided to write it up**

Silent thyroiditis, more commonly referred to as postpartum thyroiditis (PPT), is a surprisingly common condition. Gaining insight into this condition can be (and was) a bit challenging. It may manifest in a number of ways and forms. In fact, the classic presentation of this condition actually occurs in less than 1/3 of those diagnosed.\(^1\)

Medically, much controversy exists with multiple aspects of PPT. *How should we manage PPT? Who’s at risk for PPT? Should we screen for it? Can we prevent it?* Currently there are no universally accepted answers to these questions, but this condition seems to be gaining much more popularity and consequently more insight.

Additionally, more and more scientists (and clinicians) are starting to speculate about the role of the thyroid and its hormones in postpartum depression (PPD). No conclusive studies have yet been thoroughly accepted, however, it seems research is proving effective management may provide a much lower occurrence of PPD.\(^3,7\)

I chose this case because of many reasons. Firstly, I realized how common this disorder can be and felt it was something that may be beneficial to teach to my class. Secondly, this particular case is a bit comical, which I felt would be something my classmates may find interesting. Finally, endocrinology is becoming more obviously my favorite branch of medicine, for this reason it was an extremely interesting case to investigate.

### CASE PRESENTATION

**Presenting features, medical/social/family history**

**Preface:** 34 y/o Caucasian female presents to the ED in a state of psychosis. She was first assessed by her
neighbor 1 hour prior running down her street in the nude while screaming “they” had eaten her baby. The police were called by a concerned neighbor and after arrival it was decided she would be transported to the nearest hospital via ambulance due to the nature of her behavior and the history obtained from the neighbor. The baby was discovered to be with a relative and family was notified. Soon after her arrival, husband and other family arrived to assist in initial history taking.

She now presents in the ED with fever, tachycardia and an obvious mental status change. (**08/14/09)

HPI:
- T. A. is a 34 y/o Caucasian female G1P1 hospitalized for acute onset of fever, tachycardia and a significant mental status change.
- Approximately 7 weeks prior, she gave birth to a healthy baby girl; uncomplicated vaginal delivery. The pregnancy was with no clinical complications; patient is not breast-feeding at this time.
- Hx of type 1 diabetes mellitus, controlled with insulin.
- Patient recently delivered normal baby girl during uncomplicated delivery 7 weeks before hospitalization; patient is not breast-feeding at this time.

PMH/PSH:
- Type I Diabetes Mellitus, well-controlled with insulin.
- Immunizations are current; has not received influenza vaccination this year.

Meds: Lantus 70 IU SC once daily

Allergies: NKDA

Family Hx:
- +Crohn’s Disease

Social Hx:
- Denies EtOH, tobacco, or illicit drug use.
- Currently unemployed.
- Married and denies home stress and/or domestic violence.

ROS:
- Gen: fever/chills/night sweats; (+) new onset of fatigue (attributed to postpartum and increase in responsibilities).
- Skin: c/o persistent diaphoresis and heat intolerance x 3 weeks.
- Cardiac: (+) heart palpitations, progressively more frequent over past 6 days. Denies CP
- Resp: Denies SOB.
- GI: +N/V; reports loose stools occurring multiple times/day since the delivery of her baby. Appetite also increased; last meal was approximately four hours prior.
- Otherwise, unremarkable.

PE:
- Gen: WD/WN middle-aged appearing adult in emotional distress with confusion and agitation.
- Skin: Diaphoretic. Pink, warm. No rashes, clubbing or petechiae noted.
- HEENT: Conjunctiva pink; sclera white. Pupils round, regular, equally reactive to light. EOMI. Necks supple with no LAD. Thyroid was approximately 2 times normal in size, symmetrically enlarged, firm, and non-tender. Carotids palpable bilaterally without bruits. No midline shift or JVD noted.
- CV: Tachycardia; rhythm regular. No murmurs appreciated.
- Lungs: CTA BL
- GI: Abdomen soft, non-tender and without guarding; (+) BSx4.
- EXT: No edema; 2+ peripheral pulses
INVESTIGATIONS *If relevant*

Laboratory Studies:

- **CBC**
  - Hgb: 12.9
  - Hct: 38.6%
  - **WBC: 14.8**
  - Plt: 210

- **BMP**
  - Na: 142
  - K: 3.6
  - Cl: 101
  - HCO$_3$: 24
  - BUN: 18
  - Cr: 1.0
  - Glucose: 129

- **Thyroid panel**
  - free thyroxine 24.5 (NL 4-13)
  - T3 resin uptake 36% (NL 25 – 35%)
  - TSH of <0.05 (NL 0.3-5.0)

- Troponin -**Neg**

- LFTs **WNL**

- UA -**Neg**

- Rapid Strep -**Neg**

- Monospot -**Neg**

- Blood Cultures

- EtOH level -**Neg**

- Toxicology Screen -**Neg**

- ESR -**Normal**

- TPO-Ab (+)

- HbA1c: 6.2%

*Subsequent Thyroid Bx performed and revealed diffuse, lymphocytic infiltration; pathology reports indicated strong evidence of PPT likely.*

Imaging Studies:

- **CXR -**Neg

- **ECG:** Sinus tachycardia; nml rythym

- Cranial CT -**Neg**

- Radioactive iodine uptake scan -**WNL**

*And later: ACTH stimulation test of the adrenocortical axis to r/o concurrent adrenal insufficiency was found to be negative.*

DIFFERENTIAL DIAGNOSIS *If relevant*

Initially, prior to lab results the differential diagnosis was substantial. Severe sepsis was high on the list despite the presence of a goiter. Postpartum psychosis was not considered apparently because of the high fever.

However, once results returned and showed hyperthyroidism, the differential was quickly focused to:

- Postpartum Thyroiditis
• Grave’s disease

Further studies distinguished between the two diseases by:
• (-) TSH receptor antibodies (neg in PPT and pos in Graves)
  o Grave’s disease characteristically positive for TSH receptor Ab.
• A normal/low radioactive iodine uptake RAI
  o High uptake found in Grave’s Disease
• No apparent exophthalmos
• (+) TPO-Ab

TREATMENT *If relevant*

• 1 L NS over 1 hour (replace volume depletion from fever)
• Propranolol
  o 0.5 mg IV q 10 minutes for 2 hours
  o 0.5 mg IV q 4 hours for approximately 36 hours
  o Titrated to 40 mg PO BID

OUTCOME AND FOLLOW-UP

Her hospital stay lasted 3 days and she was released once her symptoms had completely resolved on medication. Fortunately, no legal suits were filed.

She was seen by OBGYN doctor approximately 4 months after this episode interested in having an IUC placed. At this point, the patient was no longer taking propranolol as her thyroid levels normalized approximately 1 month prior. It was recommended that she see her endocrinologist every 6 months to assess her for permanent sequela of PPT, such as chronic hypothyroidism, as well as monitoring and controlling of her type 1 diabetes mellitus. The importance of her follow up is emphasized because approximately 25% of women who develop PPT suffer from chronic hypothyroidism.\(^{14,21}\)

The patient disclosed she was now taking fluoxetine 20 mg PO once daily for “mild blues.” It was also noted that her baby at that type was happy and healthy with no health issues or developmental delays.

DISCUSSION *including very brief review of similar published cases (how many similar cases have been published?)*

1. What is postpartum thyroiditis (PPT) and how may it present?
2. How is this disease managed, acutely as well as long-term?
3. Is screening for PPT efficient and/or beneficial? Furthermore, is it cost-effective? Similarly, how appropriate is screening thyroid function during pregnancy? (Could this have been prevented?)
4. Is there an association between postpartum thyroid dysfunction and postpartum depression?
5. So what can we do about it?

1. What is postpartum thyroiditis (PPT) and how may it present?

Thyroiditis means an inflammation of the thyroid gland. It refers to several disorders that cause an inflammation of the thyroid.\(^{12}\) Painless thyroiditis, which is also known as “silent” thyroiditis, is an autoimmune thyroid disease with a clinical course similar to subacute thyroiditis, except that there is little/no thyroid tenderness. When occurring in women after pregnancy (defined as up to 1 year following child birth), it is referred to as postpartum thyroiditis.\(^{10}\) Typically, patients have a brief phase of thyrotoxicosis (hyperthyroidism), followed by a course of hypothyroidism and then resolution. Often, however, only one phase is apparent.\(^{18}\) Major discrepancies exist as to the duration and time each phase presents, but generally it is accepted that thyrotoxicosis is initial and briefer in duration than hypothyroidism.
The condition is associated with the presence of thyroid peroxidise antibodies (TPO-Ab) antepartum and three times more common in women with type 1 diabetes mellitus. Symptoms range depending on what phase the patient is presenting in; oftentimes, patients are even asymptomatic and their condition may go undiagnosed. Most commonly, symptoms are subtle and this case provides an extreme instance of the disease.

Pathophysiology behind the disease is said to be an autoimmune attack on the thyroid gland, triggered by the physiological stressors induced by pregnancy and labor. The destruction facilitates an inflammatory response that ultimately results in the excessive release of stored hormones first inducing a phase of excess followed by an apparent deficient phase.

Diagnosis will typically begin with the observation of abnormal TSH levels. Further testing helps to aid in the differential diagnoses of subacute thyroiditis and Grave’s disease. Subacute thyroiditis is infectious in etiology and appears with a very tender and enlarged thyroid gland. In addition to the painless goiter, it can be distinguished from subacute thyroiditis by the normal ESR and the presence of TPO Ab. The diagnosis is differentiated from grave’s disease by the presence of TPO-Ab and lack of TSH-receptor Ab, as well as normal to low uptake visualized on a radioactive iodine uptake scan. Clinically, the absence of exopthalmos may also contribute to the distinction.

2. **How is this disease managed, acutely as well as long term?**

Typically, the majority of cases are transient and self-limited; resolving spontaneously. These cases will essentially not require treatment unless the patient is symptomatic. Although there are no controlled studies evaluating the optimal treatment for symptomatic PPT and thus no standard guidelines, many endocrinologists have agreed upon a few optimal treatment options that are generally accepted by most clinicians.

For symptomatic women presenting in the hyperthyroid phase, treatment recommended was propranolol or esmolol, titrated to achieve symptomatic relief. Symptoms may include palpitations, heat intolerance, and/or anxiety typical of hyperthyroidism. The duration of the therapy will typically not exceed 2 months, and the patient should be evaluated every 4 weeks to assess thyroid function. Keep in mind that antithyroid medications have no role in treatment as the excess thyroxine is secondary to the release of stored thyroid hormones after acute injury. There is no actual new hormone production and therefore medications that block new thyroid hormone formation are ineffective.

Treatment decisions for women in the hypothyroid phase of PPT depend on both the degree of hypothyroidism and whether the woman is attempting pregnancy. Women without symptoms and who are not planning a subsequent pregnancy and do not necessarily require intervention. Women with a TSH of 4 or greater who are either symptomatic or attempting to become pregnant should be treated with hormone replacement (thyroxine). It is important to treat prior to conception as it has been determined that deficient levels of thyroxine during the first trimester may be correlated with adverse pregnancy outcomes, such as higher incidence of miscarriage and mental retardation of the infant.

Additionally, it is important to follow-up with patients diagnosed with PPT. Up to 64% may develop a permanent and chronic form of hypothyroidism.

3. **Is screening for PPT efficient and/or beneficial? Furthermore, is it cost-effective? Similarly, how appropriate is screening thyroid function during pregnancy? (Could this have been prevented?)**

Screening thyroid function during and after pregnancy is very controversial.

**Benefits of screening:**
- Improve symptoms and thus quality of life of mothers or soon-to-be mothers.
- Early diagnosis of Grave’s disease may easily lead to remission and may also reduce incidence of
the disease in older age.\textsuperscript{3}

- Screening may also assist to alerting clinicians in potential risks for developing associated morbidities of PPT.
  - Subclinical hyperthyroidism has been associated with osteoporosis, cardiovascular morbidity and progression to overt thyrotoxicosis and thyroid failure.\textsuperscript{24}
  - The presence of thyroid autoantibodies in the first trimester of pregnancy is associated with an increased rate of spontaneous abortion.\textsuperscript{1}
  - Potential risk for postpartum depression? \textit{Further discussed shortly.}

**Drawbacks of screening:**

- Symptoms of the illness are often mild and brief; consequently treatment may not be necessary. When symptoms are more severe, these should be clinically recognized at which point testing would be indicated.
- Screening may not be cost-effective for a number of reasons, most notably:
  - There is no evidence that PPT can be prevented.
  - Treatment is usually not needed.

One thing, however, does appear to be equally agreed upon: certain women who are high risk for PPT (those with type I diabetes mellitus, previous autoimmune thyroid disease, or a strong family history of autoimmune thyroid disease) should be followed closely and monitored with the appropriate biochemical assays.\textsuperscript{14}

The arguments that favor screening for this disease make three important assumptions: 1) that the optimal screening strategy is known, 2) that treating women with postpartum thyroiditis would decrease the incidence or severity of postpartum depression, and 3) that treating postpartum thyroiditis would decrease the incidence of, or the symptoms associated with, long-term primary hypothyroidism. All of these stated assumptions have yet to be proven and even studied in some cases.\textsuperscript{3}

Fortunately, some clinical practical guidelines have been proposed from the Endocrine Society in regards to the management of thyroid dysfunction before and after pregnancy. A consensus was established after reviewing the related literature from the past 2 decades and are as follows:

**Recommendations:** \textsuperscript{1,23}

- There are insufficient data to recommend screening of all women for PPT. USPSTF level I.
- Women known to be TPO-Ab-positive should have a TSH performed at 3 and 6 months postpartum. USPSTF level A.
- The prevalence of PPT in women with type 1 DM is 3-fold greater than in the general population. Postpartum screening (TSH determination) is recommended for women with type 1 DM at 3 and 6 months postpartum. USPSTF level B.
- Women with a history of PPT have a markedly increased risk of developing permanent primary hypothyroidism in the 5- to 10-yr period following the episode of PPT. An annual TSH level should be performed in these women. USPSTF level A.
- Asymptomatic women with PPT who have a TSH above the reference range but less than 10U/ml and who are not planning a subsequent pregnancy do not necessarily require intervention, but should, if untreated, be reassessed in 4–8 wk. Symptomatic women and women with a TSH above normal and who are attempting pregnancy should be treated with levothyroxine. USPSTF level B.
- There is insufficient evidence to conclude whether an association exists between PPD and either PPT or thyroid antibody positivity (in women who did not develop PPT). USPSTF level I.
  - However, as hypothyroidism is a potentially reversible cause of depression, women with PPD should be screened for hypothyroidism and appropriately treated. USPSTF level B.

USPSTF levels: I=evidence is poor; B=evidence is fair; A=evidence is good;

4. Is there an association between postpartum thyroid dysfunction and postpartum depression (PPD)?
There have been a few studies that provide evidence of a correlation between PPT and PPD. A double-blind comparison was studied in Wales and examined different depression and anxiety scales of postpartum women. It was concluded that a significantly higher number of postpartum women testing positive to TPO-Ab were depressed as compared to women testing negative for thyroid antibodies.\textsuperscript{11} Another study from the Netherlands prospectively followed women during and after pregnancy and found that the presence of TPO-Ab early in pregnancy was associated with depression postpartum only at 4 and 12 weeks.\textsuperscript{13}

However, a number of studies have not been able to reproduce these results or produce results consistent with a clear correlation. So in conclusion, this certainly seems an issue to be further researched, as studies have failed to provide an agreeable stance on the existence of such an association.

In my opinion, many factors may contribute to such inconsistent results. The possibility that depression may simply be detected most often during the postpartum period may adversely affect the data. Women may feel more comfortable or feel more accepted to share their emotional feelings during this time and therefore the depressed diagnosis quantitatively rises. Additionally, it is clinically obvious and accepted that the thyroid hormone (or lack thereof) can have a substantial effect on mood and mental health. Levels during the antenatal and postpartum periods are substantially irregular, however physiologically still considered “normal” – however, what if these “normal” levels are in fact still producing symptoms such as depression in a portion of this population? How can you accurately determine the effect of only one of these variables without being sure that the other is completely absent? It is my feeling and personal speculation than that the situation cannot truly be a controlled environment (and thus a controlled study) because neither of the two variables, hormone levels & depressive feelings, can accurately be controlled.

5. \textbf{So what can we do about it?}

It would seem logical that managing thyroid dysfunction during pregnancy may have a positive effect. However, there are no reported associations between gestational thyroid dysfunction and PPT. Management of thyroid hormones during pregnancy does not seem to have an impact on the risk of developing PPT.

As explained previously, screening is indicated in high risk populations, such as patients with other autoimmune endocrine disorders, especially type 1 diabetes mellitus. Additionally, there has been some speculation that pregnant women with hyperemesis gravidarum have a transient hyperthyroidism during pregnancy and that it can be linked with the possibility of developing PPT after delivery.\textsuperscript{22}

Recent studies have been able to demonstrate promising interventions to prevent PPT in TPO-Ab positive women. Of particular interest is a recent study providing evidence of a lower incidence of PPT in women receiving selenomethionine 200 \( \mu \)g/d starting before 12 weeks gestation and continuing through postpartum. It was also discovered in this study that selenium supplementation may have a role in lowering TPO-Ab levels as well as decreasing the incidence of thyroid enlargement, which occurs in some women during the antenatal period.\textsuperscript{15}

It is still undetermined whether discontinuing Se after pregnancy will result in a return of thyroidism in these patients. Furthermore, optimal treatment duration postpartum will need to be investigated more extensively to make any real recommendations.

\textbf{LEARNING POINTS/TAKE HOME MESSAGES 3 to 5 bullet points}

- Never underestimate the power of thyroxine.

- PPT is a relatively common complication after pregnancy. Being able to recognize this condition can certainly be difficult, so it is important to be knowledgeable about the cost effective thyroid screening data as well as the differences in symptom presentation.
A multitude of controversy is packed within this topic. I felt compelled to lay out as much of the information as I competently could to assist my future colleagues with the basic knowledge base needed to form their own opinions and management choices if ever faced with such a situation.

It is imperative to remember the link that exists between all known autoimmune diseases. Remember, 1 out of 4 pregnant patients with type 1 diabetes mellitus will statistically develop PPT.

It is important to consider the role of the thyroid in a patient postpartum who is depressed within one year postpartum. Similarly, it is important to consider mood and feelings in patients with known thyroid dysfunction after delivery.

REFERENCES

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Title</th>
<th>Journal</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vanderpump MP, Tunbridge WM</td>
<td>2002</td>
<td>Epidemiology and prevention of clinical and subclinical hypothyroidism</td>
<td>Thyroid</td>
<td>839–847</td>
</tr>
</tbody>
</table>

Date: 1/11/09

PLEASE SAVE YOUR TEMPLATE WITH THE FOLLOWING FORMAT:

Author’s last name and date of submission, eg,

Smith_June_2008.doc