“34 Year Old Pregnant Woman with Hyperthyroidism and Hyperemesis”

Dr. Darji does not have any relevant financial relationships with any commercial interests.
ENDORAMA:
34 Year Old Pregnant Woman with Hyperthyroidism and Hyperemesis

Monika Darji
September 27, 2018
Objectives

• Review the differential diagnosis and evaluation of hyperthyroidism in pregnancy
• Discuss the role of hCG in transient hyperthyroidism of hyperemesis gravidarum
• Discuss familial gestational hyperthyroidism
Chief Complaint

34 year old G6P2032 pregnant woman at 8 weeks gestation presents with persistent nausea and vomiting
HPI

• Patient reports worsening nausea and vomiting and inability to tolerate PO for 2 days
• Denies any triggers or new foods
• Has been having issues with N/V for last 3 weeks leading to 2 hospital admissions and 2 ER visits
• Reports 7 lbs weight loss in the last few weeks
OB/GYN History

- G6P2032
- 1st pregnancy in 2003 -> NSVD
- 2nd pregnancy in 2012 -> c/b hyperemesis gravidarum, pregnancy terminated
- 3rd pregnancy in 2013 -> NSVD
- 4th pregnancy in 2015 c/b hyperemesis gravidarum and labs c/w hyperthyroidism, pregnancy terminated
- 5th pregnancy in 2016 c/b hyperemesis gravidarum, pregnancy terminated
- 6th pregnancy -> current
Additional history

- ROS: 7lb weight loss, palpitations, heat intolerance
  - Denies tremors, diaphoresis, diarrhea, muscle weakness, eye symptoms
- Past Medical History: asthma
- Past Surgical History: none
- Family History: thyroid disease in maternal grandmother
- Social History: married with 2 kids, works as patient care tech, denies smoking, alcohol, illicit drugs
Additional history

• Meds: albuterol
  • Discharged with Zofran, Compazine, Benadryl, B6, Pepcid after recent hospital stay for hyperemesis

• Allergies: Penicillin, shellfish and iodide containing products
Physical Exam

- Vitals: 61 kg, BMI 24, Temp 98.6, HR 85, RR 18, BP 123/73, SpO2 100%
- Constitutional: no acute distress
- HEENT: EOMI, no exophthalmos, no lid lag
- Neck: supple, no thyromegaly or thyroid nodules
- Cardiovascular: regular rate and rhythm
- Pulmonary/Chest: good respiratory effort, clear to auscultation bilaterally
  - Abdomen: soft, non-tender, nondistended
- Extremities: no edema
- Neurological: alert, oriented, 5/5 muscle strength in all four extremities, no tremor
- Skin: warm, dry
- Psychiatric: not agitated
### Admission Labs

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total protein</td>
<td>8.4</td>
<td>Ref: 4.9-8.4</td>
</tr>
<tr>
<td>Albumin</td>
<td>4.7</td>
<td>Ref: 3.5-5.5</td>
</tr>
<tr>
<td>Total bilirubin</td>
<td>0.6</td>
<td>Ref: 0.2-1.2</td>
</tr>
<tr>
<td>Ca</td>
<td>9.3</td>
<td></td>
</tr>
<tr>
<td>Anion gap</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Alkaline phosphatase</td>
<td>42</td>
<td></td>
</tr>
<tr>
<td>ALT</td>
<td>34</td>
<td></td>
</tr>
<tr>
<td>AST</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>TSH</td>
<td>0.01 (L)</td>
<td>Ref: 0.3-4.0</td>
</tr>
<tr>
<td>Free T4</td>
<td>2.3 (H)</td>
<td>Ref: 0.9-1.7</td>
</tr>
<tr>
<td>Total T4</td>
<td>16.5 (H)</td>
<td>Ref: 5-11.6</td>
</tr>
<tr>
<td>Free triiodothyronine</td>
<td>364</td>
<td>Ref: 230-420</td>
</tr>
<tr>
<td>Total triiodothyronine</td>
<td>149</td>
<td>Ref: 80-195</td>
</tr>
</tbody>
</table>

*Beta hCG 148,845, BHOB 1.97*
Previous Labs

• Patient was admitted in 2015 during her 4th pregnancy for hyperemesis gravidarum and was found to have hyperthyroidism

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH</td>
<td>&lt;0.01 (L)</td>
<td>0.3-4.0</td>
</tr>
<tr>
<td>Free T4</td>
<td>2.85 (H)</td>
<td>0.9-1.7</td>
</tr>
<tr>
<td>Total thyroxine</td>
<td>17.5 (H)</td>
<td>5-11.6</td>
</tr>
<tr>
<td>Total triiodothyronine</td>
<td>180</td>
<td>80-195</td>
</tr>
<tr>
<td>TSI negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TPO antibody</td>
<td>&lt;0.4</td>
<td></td>
</tr>
<tr>
<td>Thyroglobulin antibody</td>
<td>&lt;0.4</td>
<td></td>
</tr>
</tbody>
</table>
Additional history

• Patient followed up with Endocrinology in 2017 (between 5\textsuperscript{th} and 6\textsuperscript{th} pregnancy)
  • Asymptomatic
  • Labs showed:
    • TSH 1.04 \hspace{1cm} \text{Ref: 0.3-4.0}
    • Free T4 1.49 \hspace{1cm} \text{Ref: 0.9-1.7}
    • Triiodothyronine 112 \hspace{1cm} \text{Ref: 80-195}
Thyroid physiology in pregnancy
Pregnancy complications of maternal hyperthyroidism

• Fetal growth restriction
• Low birth weight
• Premature labor
• Spontaneous abortion
• Still birth
• Preeclampsia
Diagnosis of clinical hyperthyroidism

• Clinical manifestations and lab findings
  • Suppressed TSH <0.01 and free T4 and/or free T3 level or total T4 and/or total T3 exceeding the trimester specific normal range
Etiologies

• Graves’ disease
• hCG mediated hyperthyroidism
  • Gestational transient thyrotoxicosis
  • Hyperemesis gravidarum
  • Trophoblastic hyperthyroidism
  • Familial gestational hyperthyroidism
• Multinodular goiter
• Thyroiditis
Graves’ Disease – classic findings

- Presents with typical symptoms of hyperthyroidism – tachycardia, palpitations, tremors, diaphoresis, muscle weakness, weight loss, diarrhea
- Diffuse goiter
- Orbitopathy
- Presence of thyroid stimulating antibodies
- 0.1 to 1% of all pregnancies
Hyperemesis Gravidarum

• Nausea and vomiting in early pregnancy associated with 5% weight loss
• 0.1 to 0.2% of pregnancies
• Associated with higher serum hCG and estradiol concentrations than in normal pregnant women -> transient hyperthyroidism
  • Usually does not require treatment
  • Subsides as hCG production falls
Role of hCG

The Role of Chorionic Gonadotropin in Transient Hyperthyroidism of Hyperemesis Gravidarum*

THOMAS M. GOODWIN, MARTIN MONTORO, JORGE H. MESTMAN, A. EUGENE PEKARY, AND JEROME M. HERSHMAN

Departments of Obstetrics and Gynecology and Medicine, University of Southern California (T.M.G., M.M., J.H.M.), Los Angeles, California 90033; and Department of Medicine, West Los Angeles VA Medical Center (A.E.P., J.M.H.), University of California at Los Angeles School of Medicine, Los Angeles, California 90073
Goodwin et al.

• Investigated the role of hCG as a casual factor for hyperthyroidism in hyperemesis patients
• 2 groups – hyperemesis group and control group, controls matched for gestational age
• Findings:
  • Hyperemesis patients differed from controls in terms of hCG, TSH, free T4
  • Significant correlation between hCG concentration and degree of thyroid stimulation
Goodwin et al.

TABLE 1. Abnormal thyroid tests in 57 women with hyperemesis gravidarum

<table>
<thead>
<tr>
<th>Test</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH (mU/L)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Undetectable&lt;sup&gt;a&lt;/sup&gt;</td>
<td>17</td>
<td>30</td>
</tr>
<tr>
<td>Suppressed&lt;sup&gt;a&lt;/sup&gt;</td>
<td>34</td>
<td>60</td>
</tr>
<tr>
<td>Free T4 &gt; 23.2 nmol/L</td>
<td>26</td>
<td>46</td>
</tr>
<tr>
<td>Total T3 &gt; 2.69 nmol/L</td>
<td>25</td>
<td>44</td>
</tr>
<tr>
<td>Free T4 index &gt; 13.2</td>
<td>33</td>
<td>58</td>
</tr>
<tr>
<td>Free T3 index &gt; 225</td>
<td>6/51</td>
<td>12</td>
</tr>
<tr>
<td>TSH &lt; 0.4 or Free T4 &gt; 23.2</td>
<td>41</td>
<td>70</td>
</tr>
</tbody>
</table>

<sup>a</sup> Undetectable < 0.04; suppressed < 0.4.

TABLE 2. hCG and thyroid function in hyperemesis and controls, mean ± se

<table>
<thead>
<tr>
<th></th>
<th>Hyperemesis (n = 57)</th>
<th>Controls (n = 57)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>hCG (IU/ml)</td>
<td>97 ± 8</td>
<td>29 ± 2</td>
<td>0.001</td>
</tr>
<tr>
<td>TSH (mU/L)</td>
<td>0.63 ± 0.10</td>
<td>1.79 ± 0.18</td>
<td>0.001</td>
</tr>
<tr>
<td>Free T&lt;sub&gt;4&lt;/sub&gt; (nmol/L)</td>
<td>23.18 ± 1.82</td>
<td>20.10 ± 1.04</td>
<td>0.001</td>
</tr>
<tr>
<td>Total T&lt;sub&gt;3&lt;/sub&gt; (nmol/L)</td>
<td>3.40 ± 0.31</td>
<td>2.29 ± 0.11</td>
<td>0.01</td>
</tr>
<tr>
<td>Estradiol (pmol/L)</td>
<td>13,256 ± 1,145</td>
<td>9,625 ± 679</td>
<td>0.04</td>
</tr>
<tr>
<td>FRL (µg/L)</td>
<td>180.5 ± 13.6</td>
<td>65.1 ± 6.4</td>
<td>0.001</td>
</tr>
</tbody>
</table>

![Graph showing Iodide Uptake](image)
Goodwin et al.

- The degree of thyroid stimulation and concentration of hCG varied directly with severity of hyperemesis.
- More severe hyperemesis was associated with a greater degree of thyroid stimulation and higher concentration of hCG.
Goodwin et al.
• Estradiol found to be present in higher concentrations in hyperemesis patients
• May be related to the effect of hCG on steroidogenesis
• Hyperthyroidism -> increased SHBG -> increased estradiol
Tan et al.

BJOG: an International Journal of Obstetrics and Gynaecology

Transient hyperthyroidism of hyperemesis gravidarum

Jackie Y.L. Tan\textsuperscript{a,*}, Keh Chuan Loh\textsuperscript{b}, George S.H. Yeo\textsuperscript{c}, Yam Cheng Chee\textsuperscript{a}

Objective To characterise the clinical, biochemical and thyroid antibody profile in women with transient hyperthyroidism of hyperemesis gravidarum.

Design Prospective observational study.

Setting Hospital inpatient gynaecological ward.

Population Women admitted with hyperemesis gravidarum and found to have hyperthyroidism.

Methods Fifty-three women were admitted with hyperemesis gravidarum and were found to have hyperthyroidism. Each woman was examined for clinical signs of thyroid disease and underwent investigations including urea, creatinine, electrolytes, liver function test, thyroid antibody profile and serial thyroid function test until normalisation.

Main outcome measures Gestation at which thyroid function normalised, clinical and thyroid antibody
Tan et al.

• Prospective observational study
• 53 women with hyperemesis gravidarum who were found to have hyperthyroidism
  • 9 were lost to follow up
  • 39 were diagnosed with transient hyperthyroidism of hyperemesis gravidarum
  • 5 were diagnosed with Graves’ disease
Tan et al. findings

- Clinically overt hyperthyroidism usually absent
- Thyroid antibodies usually negative
- Thyroid function normalizes by middle of second trimester without anti-thyroid treatment
  - Free T4 normalized by 15 weeks of gestation
  - TSH remained suppressed until 19 weeks of gestation
Tan et al.

Fig. 2. Percentage of TSH <0.1 mIU/L by gestation.
Hyperemesis vs Graves’

- Severe vomiting with weight loss
- Absence of goiter and ophthalmopathy
- Absence of common signs and symptoms of hyperthyroidism like tachycardia, muscle weakness, tremor
- Free T4 usually only mildly elevated and serum T3 usually not elevated
- Absence of thyroid antibodies
- Resolves by second trimester. Graves’ disease can occasionally resolve during pregnancy
Familial gestational hyperthyroidism

- Few case reports describing recurrent gestational hyperthyroidism 2/2 mutant TSH receptor

Brief Report

Severe Gestational Hyperthyroidism Can Be Due to a Mutant TSH Receptor with Enhanced Sensitivity to HCG

Jerome M. Hershman

Familial gestational hyperthyroidism

• Rodien et al. case describes a patient with hyperemesis and signs and symptoms of hyperthyroidism
  • Recurrent gestational hyperthyroidism and hyperemesis
  • Normal hCG level for pregnancy
• Missense mutation in the extracellular domain of TSH receptor
  • Lysine replaced by arginine at position 183
  • Results in hypersensitivity of the TSH receptor to hCG despite normal hCG levels for pregnancy
Familial gestational hyperthyroidism

• Hershman et al. similarly described a case with gestational hyperthyroidism and hyperemesis
  • Patient required treatment with antithyroid drugs
  • Hyperthyroidism persisted throughout pregnancy
Back to our patient

• Patient was admitted for hyperemesis and started on antiemetics
  • Given IV fluids and electrolytes replaced
  • Zofran, Compazine, Tigan, Benadryl, B6, Pepcid
  • Started on methylprednisolone 16 mg q8h given minimal improvement in nausea on above regimen
• On day 3 of hospital stay, patient decided to terminate the pregnancy given severe hyperemesis, multiple admissions for hyperemesis, and other social issues
Back to our patient

• Pt was not started on any antithyroid medications as hyperthyroidism was thought to be transient
• Considered TSH receptor mutation testing but patient deferred
• 7/23/18 – pt had surgical abortion
• No-showed to Endocrinology follow up appointment
Conclusion

• Transient hyperthyroidism of hyperemesis gravidarum is usually mild, does not require treatment, and subsides by second trimester.
• Hyperemesis is associated with higher levels of hCG which correlates with degree of thyroid stimulation.
• Graves’ disease can be distinguished from transient hyperthyroidism by presence of goiter, orbitopathy, thyroid antibodies, absence of severe vomiting.
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