Full term infant with abnormal newborn screen

Stelios Mantis, MD
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Initial Presentation

CC: Full term 4 day old LGA infant female with abnormal thyroid newborn screen.

HPI: Pt was born term to healthy 32 y.o G1P1001 mom at OSH. Pt suffered a clavicle fx during NSVD. In OSH nursery, pt became hypoglycemic (40s) and septic w/u was undertaken. While at OSH on DOL #4 NBS returned TSH 189 uIU/ml (less than 20) Total T4: 10.6 ug/dl (8-23).
Initial Presentation

Fam Hx: Hispanic origin, no DM or thyroid disorders. Mom did not have gestational DM

Past med & Birth Hx: LGA, NSVD, hyperbilirubinemia, phototherapy, poor feeding. NG feeds.

Meds: MVI (finished amp & cefotax)
Initial Presentation

ROS: difficulty feeding, started on NG feeds due to poor PO intake. No rashes, birthmarks, midline defects, hernias, (unsure of hearing screen), + torticollis. OSH repeated labs on DOL 5: TSH 600 mcu/ml. Pt then transferred to U of C.
Exam

Temp 36.7 C Pulse 160 RR: 26 BP: 70/37
Wt: 4.25 kg (90\textsuperscript{th}) Length: 50 cm (50\textsuperscript{th})
Gen: jaundiced, sleeping, not easily arousable
HEENT: mild scleral icterus, milia, Ant fonanelle: open 3.5 cm
   Neck: no goiter, no palpable thyroid, prominent SCM
CV: RRR, no murmur
Lungs: CTAB
Abd: soft NT ND, no hernia
Extr: difficulty moving L arm,
Differential Dx

Congenital Hypothyroidism (elevated TSH)

Thyroid Dysgenesis
athyreosis
ectopic thyroid
hypoplasia
Hemithyroidea

TSH Resistance

Dyshormonogenesis
Na-I symporter defect
Organification defect
Thyroglobulin synthesis defect
Deiodination defect

Transient hypothyroidism
Iodine contamination
Antithyroid drugs
Maternal antibodies
DUOX-2 mutation
TSH: 817.25 mcu/ml (0.3-4)
Free T4: 0.34 ng/dl (0.9-1.7)
Total T4: 3 mcg/dl (5-11.6)
Total T3: 65 ng/dl (80-195)
Tg: 1ng/dl
TPO and Tg antibodies: neg
US: No visualized thyroid (DOL 7)
Tc scan: No thyroid tissue visualized (DOL 7)
<table>
<thead>
<tr>
<th>CAUSE</th>
<th>TSH</th>
<th>T4</th>
<th>Goiter</th>
<th>Tc scan</th>
<th>US</th>
</tr>
</thead>
<tbody>
<tr>
<td>Athyreosis</td>
<td>Increased</td>
<td>Decreased</td>
<td>No</td>
<td>No uptake</td>
<td>No gland</td>
</tr>
<tr>
<td>Ectopic Thyroid</td>
<td>Increased</td>
<td>Decreased</td>
<td>No</td>
<td>+ uptake</td>
<td>No gland (at thyroid bed)</td>
</tr>
<tr>
<td>TSH receptor defect</td>
<td>Increased</td>
<td>Decreased</td>
<td>No</td>
<td>No uptake</td>
<td>Small gland</td>
</tr>
<tr>
<td>Na-I symport defect</td>
<td>Increased</td>
<td>Decreased</td>
<td>Yes</td>
<td>No Uptake</td>
<td>Enlarged gland</td>
</tr>
<tr>
<td>Organification defect</td>
<td>Increased</td>
<td>Decreased</td>
<td>Yes</td>
<td>+ uptake</td>
<td>Enlarged gland</td>
</tr>
<tr>
<td>Thyroglobulin synthesis defect</td>
<td>Increased</td>
<td>Decreased</td>
<td>Yes</td>
<td>+ uptake</td>
<td>Enlarged gland</td>
</tr>
<tr>
<td>Deiodination defect</td>
<td>Increased</td>
<td>Decreased</td>
<td>Yes</td>
<td>+ Uptake</td>
<td>Enlarged gland</td>
</tr>
<tr>
<td>Central Hypothyroidism</td>
<td>Low-Nl</td>
<td>Decreased</td>
<td>No</td>
<td>+ uptake</td>
<td>Small gland</td>
</tr>
<tr>
<td>Transient</td>
<td>Increased</td>
<td>Low-Nl</td>
<td>Possible if due to Iodine deficiency or exposed to goitrogen</td>
<td>+ uptake (unless TSH receptor blocking antibodies present)</td>
<td>Normal gland</td>
</tr>
</tbody>
</table>
Congenital Hypothyroidism

-most frequent congenital endocrine disorder

-Most NBS use TSH elevation as indicator of primary hypothyroidism (threshold at 15-25Mu/l)

-early measurement leads to high false +

-prevalence is 1:3,500 births; Hispanics affected more at 1:2000 births; 2:1 female to male ratio
Congenital Hypothyroidism

- Screening methods: Primary TSH w Backup T4: May miss TBG deficiency, Hypothalamic-pituitary hypothyroidism and hypothyroxinemia w delayed TSH surge;
- Primary T4 w Backup TSH: May miss delayed TSH elevation w initial normal T4
- Ideal method is Primary TSH + T4 measurements
Clinical Management

Initial Work-up:
Detailed hx and PE (especially maternal hx)
Refer to peds endo
Recheck TSH and FT4
Thyroid US and/or Tc (Tc scan may be performed even on Tx if TSH is over 30).

Treatment:  10-15 mcg/kg daily

Monitoring:
Recheck TSH FT4 in 2-4 wks after therapy initiated
Recheck TSH FT4 every 1-2 months in 1st 6 months
Recheck TSH FT4 every 3-4 months between 6 months and 3 yrs of age

Assess Permanence of Congenital Hypothyroidism (CH)
If initial US showed ectopic or absent gland CH is permanent
IF initial TSH <50 mU/L and no incr in TSH after newborn period, trial off therapy at 3 yrs
If TSH increases off therapy consider permanent CH.
Treatment

• Initial dose LT4 10-15 mcg/kg/day; remind parents not to administer with soy formulae, Fe or fiber supplements. OK to give in 1-2 ml of water or formulae.

• Goal of therapy is to normalize T4 within 2 wks and TSH within 1 month.

• TSH normalization may be slow due to relative pituitary resistance despite nl T4. (TSH ref range for infants between 2-6 wks: 1.7-9.1 mU/L)

• More appropriate to use T4 to titrate dose.

• Keep T4 levels in upper half of nl limits
Cognitive Development in CH

• Prior to NBS, 5-6 month delay in Tx showed decr IQ of 5-6 points/month
• Study done in 2000 indicated there was not a linear effect and most IQ points lost were early on in extrauterine life.
• Early high dose Tx (10-15 mcg/day) eliminates negative impact of severe vs mild CH on IQ.
Back to our baby

<table>
<thead>
<tr>
<th></th>
<th>3-12-10</th>
<th>3-29-10</th>
<th>5-4-10</th>
<th>6-15-10</th>
<th>8-11-10</th>
<th>11-17-10</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TSH (mIU/ml)</strong></td>
<td>817.25</td>
<td>3.72</td>
<td>1.74</td>
<td>9.54</td>
<td>2.21</td>
<td>4.85</td>
</tr>
<tr>
<td><strong>Free T4 (ng/dl)</strong></td>
<td>0.34</td>
<td>4.5</td>
<td>2.43</td>
<td>1.53</td>
<td>2.00</td>
<td>1.84</td>
</tr>
<tr>
<td><strong>Dose LT4 (mcg)</strong></td>
<td>50</td>
<td>37.5 (held 3 days)</td>
<td>37.5 alternating 25</td>
<td>37.5</td>
<td>37.5</td>
<td>37.5</td>
</tr>
</tbody>
</table>
Back to our baby

- Pt received PT for torticollis
- Meeting all developmental milestones.
- Now almost 2 years, began walking at 11 months, first words at 1 yr. No formal evaluation by Early Intervention.
References

