Full term infant with abnormal newborn screen

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March 15, 2012

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^{th}) Length: 50 cm (50^{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

U of C Studies DOL 5

TSH: 817.25 mcu/ml (0.3-4

Free T4: 0.34 ng/dl (0.9-1.7)

Started on LT4
50 mcg

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 viualized (DOL 7)

CAUSE	TSH	T4	Goiter	Tc scan	US
Athyreosis	Increased	Decreased	No	No uptake	No gland
Ectopic Thyroid	Increased	Decreased	No	+ uptake Usually at base of tongue	No gland (at thyroid bed)
TSH receptor defect	Increased	Decreased	No	No uptake	Small gland
Na-I symport defect	Increased	Decreased	Yes	No Uptake	Enlarged gland
Organification defect	Increased	Decreased	Yes	+ uptake	Enlarged gland
Thyroglobulin synthesis defect	Increased	Decreased	Yes	+ uptake	Enlarged gland
Deiodination defect	Increased	Decreased	Yes	+ Uptake	Enlarged gland
Central Hypothyroidism	Low-Nl	Decreased	No	+ uptake	Small gland
Transient	Increased	Low-nl	Possible if due to Iodine deficiency or exposed to goitregen	+ uptake (unless TSH receptor blocking antibodies present)	Normal gland

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 w 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

	3-12-10	3-29-10	5-4-10	6-15-10	8-11-10	11-17-10
TSH (mIU/ml)	817.25	3.72	1.74	9.54	2.21	4.85
Free T4 (ng/dl)	0.34	4.5	2.43	1.53	2.00	1.84
Dose LT4 (mcg)	50	37.5 (held 3 days)	37.5 alternating 25	37.5	37.5	37.5

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

- Brown R *et al.* Update of Newborn Screening and Therapy for Congenital Hypothyroidism. *Pediatrics* 2006; 117;2290-2303.
- Gruters, A. Update on the Management of Congenital Hypothyroidism. *Hormone Research* 2007;6 (suppl 5):107-111.
- Editorial. Journal of Pediatrics March 2000 Volume 136 Number 3. The importance of early management in optimizing IQ in infants with congenital hypothryoidism.