PEDIATRIC THYROID SURGERY
A Multidisciplinary Approach
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Daniel Kwon MD
4/1/2020

It’s Going to be Okay

#1 On the West Coast

#4 In the Country
**CHLA Thyroid Team**

- Daniel Kwon, MD - H&N Surgery
- Juliana Austin, MD - Pediatric Endocrinology
- Gabriel Gomez, MD - Pediatric ENT
- Diagnostic Radiology/Interventional Radiology
- Medical Oncology
- Pathology/Cytopathology
- Nuclear Medicine
- Data scientists / Database

**Outline**

- Background / Indications
  - Benign Disease
  - Endocrinopathy
  - Nodules/Malignancy
- Work-up of Thyroid Nodules
  - US and FNA
  - Pediatric considerations
- Thyroid Cancer
  - Nerve Monitoring, show how to modify ET tube for small kids
  - Calcium Mgmt
  - Neck Dissections
- Adjuvant therapy Radioactive Iodine
- Genetic Syndromes
- Case Presentation

**Indications for Pediatric Thyroid Surgery**

- Thyroid Cancer (~50%)
- Goiter (~20%)
- Graves/Toxic Nodules (20%)
- Other (~10%)
  - 4th branchial cleft cysts
  - Prophylactic
  - Intrathyroidal thymic tissue → surgery not needed

**Intrathyroidal thymic tissue**

- Can Mimic Malignancy
- In young Children
- Version of Ectopic thymus
  - 3rd/4th Branchial Pouches
  - Inadequate descent embryologically

**Intrathyroidal thymic tissue:**

- Pathology/FNA: Lymphocytes and Hassall’s Corpuscles
- Don't do unnecessary surgery
- It will regress
**Graves’ Disease**

- Most Common Cause of Hyperthyroidism in Children
- Caused by antibodies to the thyrotropin receptor
- Presentation: goiter, poor weight gain, behavioral changes, restlessness, headaches, sleep disturbances, anxiety, and heat intolerance, **exophthalmos**
- ↓ TSH, ↑ Free T4, + TSH-Receptor Antibodies

**Graves’s Disease**

- Treatment: Non-surgical
  - Beta-blockers
  - Anti-thyroidal Drugs: Methimazole, Propylthiouracil
    - May be poorly tolerated: autoimmune reactions, liver failure, leukopenia
    - Remission less common than in adults (<25%)
  - Radioactive Iodine Ablation
    - For Children >10 yo
  - Endocrinologist →

**Graves’s Disease**

- Treatment: Surgical
  - Total or near-total thyroidectomy
  - Euthyroid state preferable
  - Beta-blockade (adrenergic symptoms)
  - Iodine pre-treatment (KI/SSKI/Lugol’s) may be used
    - Decrease vascularity/intraoperative bleeding
    - Wolff-Chaikoff Effect: temporary effect

**Toxic Nodules**

- Another Hyperthyroid State
  - Adults Often Treated with RAI
  - Surgery usually recommended
    - RAI may be mutagenic for surrounding tissue
    - Some series described high rates of incidental malignancies

**Fourth Branchial Cleft Cyst**

- Not Thyroid Pathology...
  - Fistula Course (often incomplete): Pyriform Sinus → Pierce Cricothyroid Membrane → Deep to SLN and Superficial to RLN
  - Left Thyroid Lobectomy maybe required for dissection

**Prophylactic Thyroidectomy**

- MEN2A
  - Before Age 5 yo (ATA H category)
  - Start Calcitonin Screen q6 months (ATA MOD)
- MEN2B
  - Before Age 1 yo (ATA HST category)
PEDIATRIC THYROID NODULES

What is the Incidence of Thyroid Nodules in Children by Ultrasound?

A. 0.5-5%
B. 25-35%
C. 55-65% (upper limit of adult incidence)
D. >75%

What is the Incidence of Cancer in Pediatric Thyroid Nodules?

A. 5% (adult)
B. 25%
C. 50%
D. 75%

ATA Management of Thyroid Nodules
Background:
- <1% of all pediatric malignancies are thyroid cancer (2.5% in adults)
  - BUT: Adolescents: 8th most common cancer, 2nd for females
- Carcinoma 5x more likely in females (3x in adult women)
- 20-25% incidence in thyroid nodules (vs 5-10%)
- Increasing incidence in all Stages of pediatric thyroid cancer
  - SEER data

Risk Factors:
- Radiation exposures
  - Younger children are particularly sensitive
  - Often survivors of other childhood cancers
- Iodine deficiency
- Family Hx
- Autoimmune thyroiditis

Hereditary Tumor Syndromes:
- APC Associated Polyposis (Familial Adenomatous Polyposis, Gardner and Turcot)
- DICER1 Syndrome
- PTEN hamartoma syndrome (Cowden Syndrome)
- Werner Syndrome
- Carney Complex
- ....

Guiding Differences in Evaluation and Management
- Higher likelihood of malignancy
- Unique pathogenesis (gene rearrangements vs point mutations)
- More judicious use of RAI
- Relative lack of data

- High Definition Ultrasound
  - US features rather than size

- Higher incidence of lymph node metastasis, pulmonary metastasis, extra-thyroidal extension
- Improved outcomes (Disease specific survival, Progression free survival)
- Different tumor genetic profiles:
  - Kids: RET/rearrangements
  - Adults: Point mutations BRAF
  - Pediatric PTC more RAI sensitive
• Adult TIRADS grading systems have mixed results
  - Lim-Dunham et al., Am J Roentgenology. 2019
  - Richman et al., Radiology. 2019
  - Martinez-Rios et al., Pediatric Radiology. 2018

• FNA
  – Should always be US guided
  – Anesthesia?
    - Moudgil Et al
    – 71/86, 83% required conscious sedation/general anesthesia
    – Avg age 14y
    • This plays a factor on surveillance and prospect of repeat FNAs

• Cytopathology
  – Described using Bethesda system
  – Common Language
  – However different ROM rates have been shown

<table>
<thead>
<tr>
<th>Bethesda Classification System (2017)</th>
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<tbody>
<tr>
<td>Diagnostic category</td>
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<tr>
<td>--------------------------------------</td>
</tr>
<tr>
<td>Non-Diagnostic</td>
</tr>
<tr>
<td>Benign</td>
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<tr>
<td>Atypical Lesion of Undetermined Significance</td>
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<td>Suspicious Lesion or Suspicious for a Follicular Neoplasm</td>
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<td>Malignant</td>
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• What is the Pediatric Rate of Malignancy in each category?

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<th>Adult Malignancy Rate</th>
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<tr>
<td>I (Non-Diagnostic)</td>
<td>11%</td>
<td>4%</td>
</tr>
<tr>
<td>II (Benign)</td>
<td>0.7%</td>
<td>1%</td>
</tr>
<tr>
<td>III (Atyp)</td>
<td>44%</td>
<td>22%</td>
</tr>
<tr>
<td>IV (Atyp)</td>
<td>71%</td>
<td>28%</td>
</tr>
<tr>
<td>V (Suspicious)</td>
<td>73%</td>
<td>68%</td>
</tr>
<tr>
<td>VI (Malignant)</td>
<td>97%</td>
<td>95%</td>
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Note: Data from Cherella et al.
**Thyroid Cancer: Evaluation**

- What is the Pediatric Rate of Malignancy in each category?

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- Molecular Testing
  - Shows promise as with adults
  - Unique genetic profiles
  - Need more data

**Thyroid Cancer: Evaluation**

**Thyroid Cancer: Adults vs Peds**

- Lower threshold for investigation
  - Any “suspicious nodule”
  - Diffuse enlargement
- Lower threshold for thyroidectomy
  - Toxic nodules
  - Indeterminate nodules
  - Growing nodules

**Pediatric Surgical Management**

- Surgeon is central to thyroid disease
  - More Hemi thyroidectomies for any suspicious nodules
  - More Total thyroidectomies for any malignancy
  - More Neck Dissections

**Thyroid Cancer: Adults vs Peds**

- More aggressive surgery
  - Total Thyroidectomy vs Lobectomy
    - Higher incidence of multifocal/bilateral disease
  - Central Neck Dissection
    - Higher incidence of metastasis
    - May help avoid RAI
Thyroid Cancer: Adults vs Peds

- No validated staging system in children (AJCC, AMES, MACIS)
- ATA recommends 3-tier Pediatric Staging
  - Low risk: intrathyroidal tumor, “minimal” N1a or less
  - Intermediate risk: “extensive” N1a - N1b
  - High risk: “extensive” N1b, ETE, distant mets

THYROIDECTOMY

Surgery Video

Pediatric Thyroidectomy

- ATA Principles of Pediatric Thyroid Cancer
  1. Surgery outcome must beat Cancer outcome
     - <2% mortality
  2. Avoid Complications
     - Voice/Swallow
     - Hypoparathyroidism
     - Psycho-social
     - Secondary Malignancy

Pediatric Thyroidectomy

- Technique similar to adult
  - Para thyroids are even smaller
    - (higher rate of HypoPara)
  - Beware of Thymus in level 6 dissection
- Avoid drains or non-absorbable sutures
- Central Neck Dissection more commonly performed
- Remote Access Techniques not commonly used in children

Pediatric Thyroidectomy

- Rapid Frozen Analysis for Indeterminate Cytology
  - Not useful for follicular tumors
  - May help avoid secondary surgery
Pediatric Thyroidectomy

- RLN Monitoring
  - Medtronic NIM tube (Largest tube is 5.0 (7.8mm O.D) or 6.0)
  - Neurovision/Dragonfly surface electrodes wrapped ET tube
  - Use needle electrodes placed near vocal cords (sticker/hookwire)
- ATA guidelines Recommend For:
  - Revision Cases/High Risk Cases
  - Alone Scope those with complaints

HypoParathyroidism

- Post-op HypoPTH, ~30% of patients
  - Numbers in literature range widely
  - % in cancer cases are higher
- Permanent HypoPTH ~1-3%
  - Calcium dependent
- CHLA Thyroid Cancer: ~80% / <1%
  - Increased risk in young patients, concomitant neck dissection, graves

- Various post-op Calcium replacement regimens described
  - Standard dose vs PTH driven
- Unique Challenges in Children
  - Recurrent Lab Draws
  - High Dose Oral Supplementation
- CHLA
  - Standard routine postoperative calcium, calcitriol

Adjuvant Therapy

- Radioactive Iodine
  - Historically used routinely in all cases for thyroid remnant ablation
  - Clear indication for distant/pulmonary metastases
  - No consensus for intermediate risk cases

- TSH Suppression
  - Based on risk profile
  - Generally normalized after long term remission
  - Poorly studied
  - Principal: TSH stimulates both normal thyroid tissue and malignant thyroid tissue, so suppressing will reduce chance of recurrence

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Short-term and long-term risks of 131I therapy</th>
</tr>
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<tbody>
<tr>
<td><strong>Short Term</strong></td>
<td><strong>Long Term</strong></td>
</tr>
<tr>
<td>Salivary, xerostomia, dental caries, stomatitis, oculu-dryness, naso-airway duct obstruction</td>
<td>Lifelong xerostomia, dental caries, swallowing difficulty, malignancy</td>
</tr>
<tr>
<td>Gonadal injury, transient amenorrhea, and menstrual irregularities</td>
<td>Increase in infertility, miscarriage, birth defects</td>
</tr>
<tr>
<td>Acute bone marrow suppression</td>
<td>Rare, long-term bone marrow suppression</td>
</tr>
<tr>
<td>Increased risk of secondary malignancy, increased mortality</td>
<td>Pulmonary fibrosis</td>
</tr>
</tbody>
</table>
Adjuvant Therapy

- Tyrosine Kinase Inhibitors / Systemic Therapy
  - Reserved for iodine refractory progressive disease
  - Very rarely used
  - Poorly studied

CHLA Thyroid Team

- How we do it: The CHLA / USC Experience

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CHLA Thyroid Team

- One of few high-volume interdisciplinary pediatric thyroid surgery centers
  - ~50-70 cases per year
  - Pediatric thyroidectomy database

Pre-op / Evaluation

- All referrals screened through Dr. Austin, the leader and “gate-keeper”
- All nodules/surgical cases have in-house high resolution US with concurrent US-FNA under GA
- All cases reviewed at multi-disciplinary thyroid conference / tumor board
- Consultation at multi-disciplinary TNC clinic

Surgery / Peri-operative

- 2-attending surgery (Peds ENT and Adult H&N ENT)
- Nerve monitoring with neuro-diagnostics staff
- Intra-operative rapid PTH
- If admitted, cared for by specialized Pediatric Hospitalist Team with ENT and Endocrine following
CHLA Thyroid Team

Post-op
- ~3 month post-operative staging (Tg, TgAb, scans)
- Re-presented at Thyroid Conference
- Initial surveillance at TNC clinic then Ped Endocrine clinic long-term

Importance of Thyroid Centers


<table>
<thead>
<tr>
<th>Complication (%)</th>
<th>General</th>
<th>Endocrine</th>
<th>Duration of stay (days)</th>
<th>Cost ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>8.7</td>
<td>1.0</td>
<td>1.3</td>
<td>12,471</td>
</tr>
<tr>
<td></td>
<td>32.6</td>
<td>13.3</td>
<td>5.9</td>
<td>20,004</td>
</tr>
<tr>
<td></td>
<td>30.2</td>
<td>3.8</td>
<td>3.8</td>
<td>18,014</td>
</tr>
</tbody>
</table>

Importance of Thyroid Centers

- Thyroid disease (all comers) often treated with surgery
- Pediatric thyroid cancer often presents with greater burden of disease but with excellent prognosis
- Multi-disciplinary, high-volume care offer best outcomes
- More pediatric specific data is required
- Management guidelines will continue to evolve

Summary

GOAT

Dennis Maceri, MD
Questions?

14 yo Hispanic Male

- Presented with lower neck swelling x 6 months
- What else do you want to know

14yo Hispanic Male

- Slowly growing, Hyper/Hypothyroidism, Dysphagia/SOB, prior infections, Discharge, Constitutional symptoms, Trauma, prior Med/Surgical hx
- Extensive ROS
  - “Blurry vision sometimes”
- Famhx: Negative for any malignancies or tumors
- Allergies: None

What do you do next?
Labs?
- TSH, Free T4
- Calcitonin
- Thyroid and Neck US
- CT Neck?

FNA:
- Results: Medullary Thyroid Carcinoma
- Refer to Heme Onc, Genetics, Ophthalmology, Endocrine
- Present at Multi Disciplinary Tumor Board

Anything else needed prior to surgery?

Rule out concomitant Pheochromocytoma/Metastatic Disease
- Urine Methanephrines
- PET CT
- If found, Pheochromocytoma

Txt Total Thyroidectomy, Bilateral Central and Lateral Neck Dissections, Tongue Biopsy (confirmed neuromas)
- Calcitonin : 3286→64

Sources