Pediatric Thyroid Disease:
So you found a nodule – now what?

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"If a surgeon should be so foolhardy as to undertake it... every step he takes will be enrobed with difficulty, every stroke of his knife will be followed by a torrent of blood and lucky it would be for him if his victim lives long enough to enable him to finish his horrid butchery.

No honest and sensible surgeon would ever engage in it."
- Samuel Gross, 1848

"The extirpation of the thyroid gland for goiter typifies perhaps better than any other operation the supreme triumph of the surgeon’s art."
- William Halsted

Overview
- Background
  - Embryology and Anatomy
  - Endocrine Function
- Exam and Treatment
  - ATA Guidelines
  - Workup
- Management of Differentiated Thyroid Carcinoma
  - Papillary
  - Follicular
  - Medullary

Presenter Disclosures

- Consultant/Speakers bureaus: No Disclosures
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- Off-label uses: No Disclosures
**Background**

- Embryology
  - Developed from the median and lateral anlagen
  - Thyroid follicular cells form at 4th to 5th gestational week
  - Descends to inferior neck from the foramen cecum

**Anatomy**

- Thyroid gland overlies the trachea in the anterior neck
- Attachment to the airway via Berry's ligament

**Endocrine Function**

**Physical Exam**

- Evaluate for asymmetry or visible gland
- Palpation of central and lateral neck
- Observe gland with swallow
- Consider auscultation of the gland
- Assess voice quality / strength
Cervical Lymph Nodes
- Levels of the neck
- Patterns of nodal spread

Beyond thyroid nodules...

Lingual Thyroid
- Painless, firm mass in the midline neck
- Moves with deglutition or tongue protrusion
- May become infected (typically aerobic and anaerobic oral flora)
- <1% risk if concomitant thyroid carcinoma

Thyroglossal Duct Cyst
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Autoimmune Thyroiditis

- Graves' disease
  - Elevated TSH
  - Thyroid with increased gland vascularity
  - Proptosis
  - Symptoms of hyperthyroidism
    - Agitation, increased appetite, weight loss, tremor, heat intolerance...

- Treatment
  - Anti-thyroid medications (methimazole, PTU)
  - RAI ablation
  - Total thyroidectomy

Autoimmune Thyroiditis

- Hashimoto's Thyroiditis
  - Elevated anti TPO antibodies
  - May be hyperthyroid in early stages
  - Eventually hypothyroidism with gland involution
  - Multinodular gland with reactive lymphadenopathy

The Incidental Nodule

- Thyroid nodules uncommon in children
  - 1-1.5% of young children
  - 13% of adolescents

Balancing Act

- Early Diagnosis
- Effective Treatment
- Unnecessary Workup
- Side Effects
- Surgical Complications
Bethesda System

- FNA cytology divided into six major groups
- Adequate sample requires six follicular groups with at least 10-15 cells per group
- Ideally from two separate aspirates

<table>
<thead>
<tr>
<th>Category</th>
<th>Meaning</th>
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<tbody>
<tr>
<td>I</td>
<td>Non-diagnostic or inadequate</td>
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<tr>
<td>II</td>
<td>Benign</td>
</tr>
<tr>
<td>III</td>
<td>Atypical follicular lesion of undetermined significance</td>
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<tr>
<td>IV</td>
<td>Follicular neoplasm or suspicious for follicular neoplasm</td>
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<tr>
<td>V</td>
<td>Suspicious for malignancy</td>
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<tr>
<td>VI</td>
<td>Malignant</td>
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Pediatric Thyroid Cancer Management

- Increased risk of nodule with malignancy
  - 22-26% in children vs 5-10% in adults
- Earlier nodal spread
- Propensity for extrathyroidal tumor extension
- Increased risk of distant metastatic disease
  - 25% with pulmonary metastases
- Can be stable for many years
- Generally excellent progression free survival and low disease specific mortality

Are All Ages Equal?

- Tendency towards increased recurrence risk in younger population < 10 to 15 years of age in retrospective review
- Potentially due to less aggressive surgery in younger patients

Imaging

- Ultrasound of the central / lateral neck
- Consider CT
  - Suspect local invasion if fixed clinically or vocal cord paralysis preop
  - Superior mediastinal and retropharyngeal involvement
  - Contrast may require delay of RAI by 2-3 months
- PNA for suspicious cervical nodes and consider Tg washing
- CXR or Chest CT for significant nodal disease
- No role for routine bone scan or PET-CT

TI-RADS
Stratifying Risk

• Low risk
  • Disease confined to the thyroid, N0 or incidental
disease N1a disease in a small number of lymph
  nodes (microscopic)

• Intermediate Risk
  • Extensive central neck disease or minimal lateral
  neck disease. Minimal ETE likely falls into this
  group.

• High Risk
  • Locally invasive tumor or extensive lateral neck
  disease.

AJCC Staging (8th Edition)

Papillary Thyroid Carcinoma

• May present with diffuse infiltrative form involving the
  gland without discrete nodularity

• Appropriate surgery is total thyroidectomy (30% risk of
  bilateral disease). Consider ipsilateral elective central neck
  dissection.

• More extensive surgery decreased risk of local
  recurrence in one long term study with 40 year follow
  up from 35% to 6%.

• Also allows for RAI and Tg monitoring post op.

Follicular Thyroid Carcinoma

• Early hematogenous spread

• Treatment with thyroid lobectomy alone may be adequate
  given lower rate of multifocal / bilateral disease

• Total thyroidectomy for tumors > 4cm or significant
  vascular invasion (multiple foci)
Radioactive Iodine Therapy

- Adjuvant treatment for microscopic disease
- Side effects include sialadenitis, gonadal damage, bone marrow suppression
- Risk of a second malignancy at doses >200mCi

Medullary Thyroid Carcinoma

- Genetic Mutations
  - BRAF: Uncommon in children, more frequent in adults, may allow for targeted therapy (TKI)
  - RET: More common in pediatric population, less risk of dedifferentiation, association with MEN syndrome
  - PTEN

Genetic Mutations

- Screening
  - Syndromes such as Werner, APC-associated polyposis, PTEN hamartoma may be at increased risk of thyroid cancer
  - Annual physical exam recommended for high risk patients
  - Consider imaging for palpable nodule, cervical LAD or thyroid asymmetry on physical exam
**Surveillance**

- I\(^{131}\) scan at 12 weeks post operatively
- Surveillance ultrasound at 6 months then 6-12 months depending on risk. May have delayed recurrence beyond 7-10 years from treatment
- TSH suppression (goal 0.5 -2.0)

**Conclusions**

- Thyroid issues in children may include congenital abnormalities and endocrine dysfunction
- Pediatric nodules should be worked up with appropriate imaging with consideration of biopsy given the higher risk of malignancy
- Appropriate medical and surgical treatment for differentiated thyroid cancer should follow ATA guidelines