Multidisciplinary Approach to Pediatric Thyroid Cancer: Nuclear Medicine Considerations

HELEN R. NADEL MD
FRCPC(Diag Rad, Nuc Med) ABR (Ped CAQ) ABNM
Pediatric Radiologist and Nuclear Medicine Physician
Head, Division of Nuclear Medicine, Department of Radiology
British Columbia Children’s Hospital
Associate Professor of Radiology
University of British Columbia
Vancouver, British Columbia, Canada

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Disclosures

- Member of Board of Directors of SNMMI 2013–16
- Member of Board of Directors of the American Board of Nuclear Medicine 2010–2017
- No Financial Disclosures
Objectives

ATA Pediatric Recommendations pertaining to:

- Thyroid Ultrasound
- Body Imaging
- I-123 Scintigraphy with SPECT/CT
- FDG PET/CT
Thyroid Carcinoma

- Traditional approach in past was to follow adult guidelines
- 2015 ATA Guidelines task force
Thyroid Carcinoma

- Papillary thyroid carcinoma (PTC)
- Follicular thyroid carcinoma (FTC)
- Hurthle cell including Medullary thyroid carcinoma (MTC)
- Anaplastic
Well-differentiated Thyroid Carcinoma—DTC

- Arise from follicular cells that produce thyroid hormone
- Include papillary and follicular
- Papillary most common – 95% in children
- Are iodine-avid
DTC

- PTC Most common in adults and children
- Increasing incidence in adults and children
- Incidence increases with age
- Age less than 10 years age < 1/million/yr
- Age 10-14 years 3.5/ million/yr
- Age 15-19 years 15.4/million/yr
- Age 25-29 years 60.8 cases/million/yr
Pediatric Thyroid Carcinoma

- Advanced disease at diagnosis
- 60–90% regional node involvement
- More distant disease
- Bone mets <5%
- Lung mets at diagnosis 10–20%
<table>
<thead>
<tr>
<th>Thyroid Nodules</th>
<th>Adults</th>
<th>Children</th>
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<tbody>
<tr>
<td>Incidence</td>
<td>10% in young adults; &gt;50% in those &gt;60 years</td>
<td>1%-5 %</td>
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<tr>
<td>Percent harboring cancer</td>
<td>5%-14%</td>
<td>26%</td>
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<tr>
<td>Size criteria for FNA</td>
<td>&gt;1-1.5 cm</td>
<td>Based on ultrasound characteristics and clinical context rather than size alone</td>
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**Autonomously functioning nodules**

| Cancer risk | 3% | 30% (associated incidental DTC) |
| Management | 1-131 radiotherapy, ethanol ablation, or surgical resection | Surgical resection (lobectomy + isthmusectomy) |

**Frequency of pathologic subtypes**

| PTC | 70%-80% | >90% |
| FTC | 15%-25% | <10% |
| Medullary thyroid cancer | 5%-8% | Rare |
| Anaplastic | 4%-10% | Rare |

**Tumor focality**

| Multifocal disease | 30% | 40%-65% |
| Bilateral disease | 33% | 30% |

**Tumor size**

| Newly diagnosed, >4 cm | 15% | 36% |
| Newly diagnosed, <1 cm | 22% | 9% |

**Frequency at presentation**

| Cervical lymph node metastases | 30%-40% | 60%-80% |
| Distant metastases | 2%-14% | 20%-25%, almost always lung |
| Lung metastases | 1%-7% | 20% |

**Survival**

| Overall (at 20 years) | 90% | 98% |
| In those with distant metastases | 40% at 5 years, 20% at 10 years | 96%-100% at 5 and 10 years |
| Recurrence rate, PTC (age at diagnosis) | 20% (20-50 years) | 40% (<20 years) |

**Genetics**

| Prevalence of gene rearrangements | Lower | Higher |
| BRAF mutations | Common (36%-83%) | Rare |
| RET/PTC rearrangements | Less common | More common |

Parisi et al, Seminars in Nuclear Medicine, Volume 46, Issue 2, 147 – 164
Thyroid Ultrasound

- Cystic vs solid
- Size and number of nodules
- Cervical adenopathy
Thyroid Nodules - US

- **Benign**
  - Homogeneous
  - Translucent halo
  - No internal calcifications

- **Malignant**
  - Indistinct margins
  - Variable echotexture
  - Increased blood flow
  - Microcalcifications
Thyroid Ultrasound

- Comprehensive neck ultrasound
- Doppler assessment
- Compartment analysis
**Equipment:** High-frequency linear array probe.

- **Positioning:** Hyperextension of neck.

- **Primary lesion:** Assess size, multiplicity, margin, invasion of deep structures.

- **Central compartment lymph nodes (level 6):** Scan from submental area to sternal notch. Scan three distinct areas: pretracheal, right paratracheal, and left paratracheal. Turn head away from side of interest to image tracheoesophageal groove. Angle transducer inferiorly to examine mediastinum.

- **Lateral compartment lymph nodes (levels 2, 3, and 4):** Scan from mandible to clavicle. Angle transducer inferiorly at clavicle to image infraclavicular nodes at base of level 4.

- **Posterior compartment lymph nodes (level 5):** Sweep laterally along clavicle to posterior border of sternocleidomastoid muscle, then trace posterior border superiorly to mastoid process.
Preoperative CT Neck and Chest or MR Neck

- Large fixed mass
- Vocal cord paralysis
- Bulky metastatic nodes
- Suspected tracheal or esophageal invasion
TNM Classification
Post Surgery

- **Low Risk:**
  - **NO** disease confined to thyroid gland with no regional node met
  - **NX** regional nodes not assessed
  - **N1a** incidental micrometastasis
Intermediate Risk:

- **N1a** mets to level VI nodes
- **N1b** mets to unilateral, bilateral, contralateral level I-VI nodes and low risk for distant mets but at risk for incomplete node resection/persistent cervical disease
High Risk:

- N1b Regional extensive disease
- T4 tumors local invasive disease
- At risk for incomplete resection, persistent disease, distant mets
WB I-123 Imaging

- Low risk: not indicated, follow with US and TSH- suppressed Tg only
- Intermediate and High risk: WB I-123 uptake and staging scan and TSH stimulated Tg measurement
Post-operative I-123 Staging

- to assess for persistent locoregional disease
- to identify if patients likely to benefit from I-131 treatment
- to identify if patients likely to benefit from additional therapy
- Correlate with thyroglobulin levels
I-123 Whole body Post Operative Staging

- 12 weeks post op
- D/C LT4 2-4 weeks
- rTSH stimulation - increases iodine retention in the remaining thyroid tissue and disease
TSH Stimulation

- Remnant ablation
- Monitoring for persistent / recurrent disease with Iodine WBS
- $TSH > 30 \text{ mU/L}$
- Thyroxine withdrawal
- $\text{rhTSH stimulation}$
Recombinant human thyrotropin Thyrogen®

- rhTSH useful if cannot tolerate hypothyroidism
- If cannot generate elevated TSH
- Thyroxine stopped 1 day prior to rhTSH injection and restarted 1 day after I-131 therapy
- Treat with rhTSH on Mon and Tues and Scan Wed
- Treat Wed or Thursday
Preparation—blood work

- CBC
- Serum calcium
- Serum thyroglobulin when hypothyroid or after rhTSH
- Serum creatinine
I-123 Uptake and Scan Preparation

- Low iodine diet
- Patient and family given literature to read regarding Iodine treatment radiation protection requirements
- Confirm that treatment guidelines can be met with respect to travel and home conditions
I-123 Thyroid Scan

- Uptake greater than 3%
- If cervical uptake outside thyroid bed +/- distant mets
- Should perform CT or if possible SPECT/CT
- Surgical treatment may be indicated
I-131 Treatment

- Residual disease not amenable to surgery
- Iodine-avid distant metastatic disease
- Pulmonary metastases
I-131 Treatment

- Low risk DTC not recommended for adults
- May still be recommended for children
- Children have more high risk disease
- Children have higher risk of DTC recurrence
- Challenges of long-term follow-up
- Decreases recurrence in children with DTC who have residual disease
I-131 Therapy—Intermediate and High Risk Disease

- Not indicated if
  - no or minimal I-123 uptake <1%
  - Stimulated Tg < 2 ng/ml unless T4 disease or known microscopic cervical disease

- Indicated if
  - Stimulated Tg 2-10 or >10 ng/ml
  - Distant mets but no cervical disease
I-131 Therapy

- Higher doses I-131 required in children for treatment vs remnant ablation
- Empirical dosing vs dosimetry
- 30–200 mCi (1.1–7.4 GBq) depending on disease burden, and initial vs follow-up treatment
- adjusted for body weight
- 7 day post treatment scan
- Informed consent
- Serum Beta HCG test in females 8 years of age and older
- Radiation protection issues including travel and living arrangements post therapy
- Discharge instructions
• 8 year old girl with thyroid ca
• Post surgical evaluation
I-123 diagnostic scan

I-131 7 day post ablation scan
I-131 7 day post ablation SPECT/CT

activity in normal thymus
Thyroglossal Duct Remnant
9 year old with previous resection of her right lobe thyroid elsewhere for follicular thyroid ca, then underwent completion thyroidectomy

Surgeon requested I thyroid scan

I-123 wholebody scan performed 6 weeks post thyroidectomy

RAI=3%
- Residual left lobe present
- Some activity in right side neck
- Repeat surgery to left side neck done after this scan
- Did not re-operate on right side as too much scar tissue

Post 30 mCi ablative scan
No additional lesions seen
16 year old female with previously resected papillary thyroid ca and post surgical I-131 therapy done elsewhere. Now presents for evaluation of possible neck node seen on ultrasound. Post recombinant TSH stimulated wholebody I-123 scan. Thyroglobulin is normal.
Two small lymph nodes resected with help of gamma probe
No tumor found
Case

- 13 year old male with Papillary Thyroid Carcinoma
- TNM Stage: T4N1bM0
- ATA Risk Classification: Intermediate
- Pathology: Papillary Thyroid carcinoma of right lobe, with extensive microscopic involvement of left lobe and isthmus, positive margins, extensive soft tissue invasion, positive nodes
- Clinical testing: Ultrasound and I-123 whole body scan consistent with diagnosis
- Treatment:
  - I-131 100 mCi at time of initial diagnosis
  - I-131 150 mCi at time of metastatic relapse
Personalized Oncogenomic Assessment

- Specific question for POG:
  - Young age for this malignancy and resistant to usual first line therapy
  - Did POG testing reveal a specific pathway that could be targeted with medication if there is future recurrence?
  - Note that POG was undertaken now, rather than in the event of refractory disease or future recurrence, because it is unlikely there would be tissue obtained again in these events
Uptake 1%

Tx 100mCI I-131

Increased Tg >1000

Tx 150 mCI I-131
At the time for POG

- TNM Stage: TXN1bM1
- Biopsy sites: Bilateral and central neck compartments
- Biopsy again showed Papillary Thyroid Carcinoma
- Treatment receive between the time of biopsy and the presentation: Received a second course of radioactive iodine (I131) treatment of 150 millicuries. Too soon to assess radiographic response.
- Patient not enrolled on another trial

Next treatment in mind:

- If there is recurrence or insufficient response after this most recent treatment, plan would be for further radioactive iodine, and possibly external beam radiation
Presentation:

14 year old healthy female with R thyroid enlargement X years. Clinically euthyroid

HPH- 0

FH-0

U/S- 2012
+ Left neck nodes normal
FNA- Nov 2015

Cytopathology:
Papillary ca
Dec. 2015

Total Thyroidectomy +

Right modified lymph node dissection (levels 2,3,4,6)

Pathology:

Papillary ca- usual variety*

Diffuse in right & left gland

Lymph nodes levels 2,3,4,6 metastatic papillary ca

(1 Parathyroid)
Rx- $^{131}$I

Feb 2016- RAI & scan
- negligible update

PET- Aug 2016
Bilateral disease
FDG PET/CT

- Iodine negative disease
- Rising thyroglobulin
June & Sept 2016

June 2016-
Bilateral lymph node sampling
Right 2 a
Left 3

Path: R & L- metastatic papillary ca

Sept- lymph node dissections-
Right level 2
Left levels 3,4,5,2a & b, 6

Path:
5,6- neg-ve for ca
2,3,4, 2a & b- pos+ve for ca
Nov 2016 Patient was retreated with $^{131}I$ ablation.
Multidisciplinary approach of thyroid nodules at BCCH

April 7, 2016
This document is only intended to propose the usual process whereby a patient with a thyroid nodule/surgical thyroid issue would be managed at BCCH. Considering the number of steps involved in the diagnosis and follow up of a patient with thyroid malignancy, it is suggested that the patient be referred to Pediatric Surgery/Endocrinology at BCCH for diagnosis confirmation or for management early in the process.

First referral for isolated nodule rarely sent to Oncology but secondary malignancies are usually first recognized in Oncology.

Initial testing may duplicate initial community testing as necessary. The scope and nature of investigations will depend on the presentation and context.

FNA biopsy is obtained under Rx guidance, specimens must be sent to BCCA and results must be sent to referring MD (as it is not entered in Cerner).

Benign nodules:
- Referral to surgery will usually take place because of increase in size of the nodule, cosmetic concerns, change in FNA results.

Malignant nodules:
- Surgery will usually be performed early on as it is an obvious management approach and its extent will have been guided by imaging and clinical.
- Endocrinology is responsible for diagnostic investigations (MEN, other genetic conditions), F/U imaging, order recombinant TSH as necessary, liaise with Nuclear Medicine (Dr Nadel) and primary F/U of the patient after surgery.
- Oncology will systematically be involved in case discussion, BCCA presentation, registration of the patient. Referral of the patient to Oncology may not be systematic but will take place in case of MEN, secondary malignancy, family history.
Request for presentation at BCCA tumor board

BC CANCER AGENCY
Vancouver Cancer Center

DOCTOR’S ORDERS FOR
CONFERENCE
Outside Vancouver Cancer Center: Fax to Conference Clerk at 604-877-6013
Otherwise deliver to conference clerk

Conference

DATE OF ORDERS: Date Preferred for Conference: Unit Clerk

WORKING DIAGNOSIS:

REASON FOR CONFERENCE:
Patient To Attend: Y N Presenter:
Oncologist:
Notify: Telephone No:

CLINICAL HISTORY: [ ] New Patient Staging

DIAGNOSTIC IMAGING: Radiologist to present the following imaging studies:

<table>
<thead>
<tr>
<th>EXAMINATIONS</th>
<th>D/M/Y</th>
<th>PLACE</th>
<th>X-RAY # *</th>
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PATHOLOGY: Pathologist to present the following pathology:

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<thead>
<tr>
<th>TEST/SITE</th>
<th>D/M/Y</th>
<th>PLACE</th>
<th>PATH#*</th>
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PET SCAN: PET Scan Staff to present the following PET Scan studies:

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<tr>
<th>TEST/SITE</th>
<th>D/M/Y</th>
<th>PLACE</th>
<th>PET study #*</th>
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<tr>
<td>1. PET Scan</td>
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<td>2. PET Scan</td>
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OTHER REPORTS: Unit Code

1. Unit Code
2. Unit Code

DOCTOR’S SIGNATURE: Nurse Signature

* All requested exams will be reviewed at conference. For additional formal review a separate request is required.

Revised 10 May 2007
1. Thyrogen order (fillable form available at [link to form]):
2. Thyrogen monograph:
   [link to monograph]
Objectives

ATA Pediatric Recommendations pertaining to:

- Thyroid Ultrasound
- Body Imaging
- I-123 Scintigraphy with SPECT/CT
- FDG PET/CT
ACKNOWLEDGMENTS:
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Dr Meg Parisi
Dr Adina Alazraki