THYROID NODULES & CANCER

What Next?

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Etiology of Thyroid Nodules

- Multinodular goiter (colloid adenoma)
- Hashimoto thyroiditis
- Cysts: colloid, simple, or hemorrhagic
- Follicular adenoma
  - Macrofollicular
  - Microfollicular
- Hurthle–cell adenoma

- Papillary carcinoma
- Follicular carcinoma
- Medullary carcinoma
- Anaplastic carcinoma
- Primary thyroid lymphoma
- Metastatic carcinoma (breast, renal cell, melanoma, others)
Epidemiology of Thyroid Nodules

- Prevalence increases with age and in women greater than men
- Autopsy surveys 37% to 57% of patients had thyroid nodules
HOW TO FIND THYROID NODULES?

- Avoid random screening
- Thyroid nodules common but are commonly benign——Try not to open a can of worms
HISTORY

- Medical History = thyroid disorder? History of radiation exposure or treatment other than x-rays, particularly in childhood.
- Surgical History = thyroid surgery or biopsy? reason for the surgery?
- Allergies = adverse response to thyroid medication or to iodine
- Medication = any type of thyroid medication T3, T4, thyroid booster; taking iodine, kelp or seaweed
- Social History = smoking hx
- Family History = thyroid related disease familial or genetic
Family History

Benign thyroid disease is common in families; In areas of endemic goiter or iodine deficiency

Ask about thyroid cancer? Patient may need to investigate

Thyroid cancer in the family is of particular importance in Aggressive thyroid cancer such as Medullary Thyroid Carcinoma, but Papillary carcinoma can also be familial
PHYSICAL EXAMINATION

• Routine physical to check findings relating to thyroid nodules

• Heart = high or low heart rate, abnormal rhythm

• Neurology = deep tendon reflexes brisk or delayed

• Eye evaluation = thyroid eye disease

• This type of information could lead to underlying thyroid nodules
24 YO FEMALE

- Fatigue, weakness, Depression
- Constipation, weight gain
- Slow reflex relaxation (pseudomyotonia), peri-orbital edema, cool skin, hypertension
- Coarse skin and dry hair
- Bradycardia
- Thyroid small without nodule on physical examination or midline incision above the suprasternal notch
33 YO MALE

- Nervous, insomnia, diaphoresis, palpitations, weight loss, tremor, loose + frequent stool, heat intolerance, emotional

- Tachycardia, thyroid bruit, goiter, warm damp skin, vitiligo, proptosis
PHYSICAL EXAM
THYROID

- Patient position upright, use dominant hand palpation anteriorly for irregularity or distinct nodule, firmness, tenderness to palpation. This is done at rest and with patient swallowing a sip of water. Patient to sit up straight, chin slightly down. Check for abnormal lymph nodes upright and supine.

- Patient position supine dominant hand palpation at rest and with swallowing. Some lesions more easily palpated supine. Consider palpating each lobe reaching across the patient.
WHEN TO SCREEN WITH ULTRASOUND?

Screen with history of external radiation, particularly in childhood. Chernobyl risk higher cancer rates in children.

Family history of thyroid cancer. Ask this question? Papillary cancer, FH MEN; Of greater importance aggressive familial thyroid cancer such as Medullary thyroid cancer. Most are Not familial/genetic. Most MTC is random or sporadic.

Other imaging such as MRI or CT may see thyroid lesions, but Ultrasound should be performed once identified as the imaging test of choice for anatomy. Lesions lighting up on PET should be imaged by ultrasound and are at a high risk for malignancy.
NECK SYMPTOMS

- Patient may have compressive symptoms
- Most patients have no symptoms related to thyroid nodules, but that does not exclude the need for evaluation and treatment of thyroid nodules
- No symptoms and a normal TSH does not change the need for additional evaluation.
SOLITARY NODULE VS MNG

- Each nodule has its own significance

- Solitary nodules are not to be considered more suspicious than multiple lesions

- Often what appears to be a solitary lesion on physical exam is multiple lesions on ultrasound
LABORATORY

- TSH is the 1st lab of choice in a patient with thyroid nodularity
- If the TSH is abnormal, consider testing of Free T4 and, if hyperthyroid, consider T3 measurement
- If hyperthyroid and with thyroid nodules, nuclear thyroid scan is recommended
- Measuring thyroglobulin is not likely helpful for the general evaluation of thyroid nodularity
THYROID SCAN  11 May 2000 at 11:55

markers

2hr. uptake = 2.05
24hr uptake = 3.07
ULTRASOUND FEATURES ASSOCIATED WITH DECREASED RISK OF THYROID CARCINOMA

- Hyperchoic
- Large, coarse calcifications
- Peripheral vascularity
- Comet tail shadowing (colloid nodule)
- Egg shell calcification
WHICH NODULE TO BIOPSY ON ULTRASOUND PATTERN?

- Hypoechoic
- Microcalcification
- Central vascularity
- Irregular border
- Incomplete halo
- Nodule taller than wide
- Nodule enlargement
Fig. 2. Strength of indication for fine-needle aspiration (FNA) biopsy of thyroid nodules on the basis of ultrasonography (US) findings.
NODULE SIZE INDICATION FOR FNA

- Solid hypoechoic nodules (palpable or nonpalpable) measuring >1 cm
- Solid nodules that are isoechoic or hyperechoic, measuring ≥ 1.5 cm
- Mixed cystic-solid nodules without suspicious features on ultrasound, measuring ≥2.0 cm
- FNA biopsy for all nodules >5 mm in high-risk patients
- Purely cystic nodules (no mural component) does not require a biopsy
ELASTOGRAPHY

- This imaging process may be helpful after further studies
- This addresses the concept of the harder the lesion the more suspicious
- Some nodules such as calcified nodules are not amenable to this process
BETHESDA SYSTEM FOR THYROID FNA CYTOPATHOLOGY

• Is the specimen adequate?

• 6 groups of follicular cells with 10 cells per group

• Colloid is a benign finding, predominately colloid biopsies are usually benign, macrofollicular
• Non diagnostic or unsatisfactory

• Benign (Vast majority)

• Atypia of undetermined significance or Follicular lesion of undetermined significance

• Follicular neoplasm or suspicious for follicular neoplasm

• Suspicious for malignancy

• Malignancy
MICROFOLLICULAR OR CELLULAR ADENOMA

- Represents a unique diagnostic problem
- Differ from follicular carcinomas only by their lack of capsular or vascular invasion, which cannot be seen on FNA. Must be seen on thyroidectomy pathology
- Microfollicular lesions are usually excised to exclude cancer
- Autonomous microfollicular nodules are not likely to be cancer
- Consider molecular markers such as BRAF for indeterminate cytology
Thyroid cancer types

- Papillary thyroid carcinoma is most common
- Follicular thyroid carcinoma is more rare
- Hurthle cell carcinoma is a potentially more aggressive sub-type of follicular carcinoma
- Medullary thyroid carcinoma
- Anaplastic thyroid carcinoma
- Thyroid lymphoma
Well Differentiated Thyroid Carcinoma

- Papillary and follicular + hurthle cell
- Papillary is the least aggressive
- Treatment is total thyroidectomy
- Ablative treatment can be considered with radioactive iodine based on size, invasiveness, nodes, stage
Thyroidectomy

• Total thyroidectomy if cancer diagnosis is clear
• Total thyroidectomy if bilateral nodules or bilateral disease otherwise
• Pre-operative neck ultrasound for lymph node evaluation
• Lymph node evaluation for nodes that are round, calcification, absent hilum, irregular
LYMPH NODE BIOPSY OF SUSPICIOUS NODE

- FNA of lymph node for cytology

- Washout of the biopsy syringe with saline to measure Thyroglobulin at USC

- Thyroglobulin should Not be measurable in a non-metastatic lymph node

- May need neck dissection vs thyroidectomy only
### TNM staging system for thyroid cancer

<table>
<thead>
<tr>
<th>Primary tumor (T)*</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td>Primary tumor cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor 2 cm or less in greatest dimension limited to the thyroid</td>
</tr>
<tr>
<td>T1a</td>
<td>Tumor 1 cm or less, limited to the thyroid</td>
</tr>
<tr>
<td>T1b</td>
<td>Tumor more than 1 cm but not more than 2 cm in greatest dimension, limited to the thyroid</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor more than 2 cm but not more than 4 cm in greatest dimension limited to the thyroid</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor more than 4 cm in greatest dimension limited to the thyroid or any tumor with minimal extrathyroid extension (eg, extension to sternothyroid muscle or perithyroid soft tissues)</td>
</tr>
<tr>
<td>T4a</td>
<td>Moderately advanced disease</td>
</tr>
<tr>
<td></td>
<td>Tumor of any size extending beyond the thyroid capsule to invade subcutaneous soft tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve</td>
</tr>
<tr>
<td>T4b</td>
<td>Very advanced disease</td>
</tr>
<tr>
<td></td>
<td>Tumor invades prevertebral fascia or encases carotid artery or mediastinal vessels</td>
</tr>
</tbody>
</table>

**All anaplastic carcinomas are considered T4 tumors**

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>T4a</td>
<td>Intrathyroidal anaplastic carcinoma</td>
</tr>
<tr>
<td>T4b</td>
<td>Anaplastic carcinoma with gross extrathyroid extension</td>
</tr>
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</table>

### Regional lymph nodes (N)*

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>NX</td>
<td>Regional lymph nodes cannot be assessed</td>
</tr>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>Regional lymph node metastasis</td>
</tr>
<tr>
<td>N1a</td>
<td>Metastasis to Level VI (pretracheal, paratracheal, and prelaryngeal/Delphian lymph nodes)</td>
</tr>
<tr>
<td>N1b</td>
<td>Metastasis to unilateral, bilateral, or contralateral cervical (Levels I, II, III, IV, or V) or retropharyngeal or superior mediastinal lymph nodes (Level VII)</td>
</tr>
</tbody>
</table>

### Distant metastasis (M)

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
<td>No distant metastasis</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastasis</td>
</tr>
<tr>
<td>Papillary or follicular (differentiated)</td>
<td>45 years</td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>---------</td>
</tr>
<tr>
<td><strong>Under 45 years</strong></td>
<td></td>
</tr>
<tr>
<td>Stage I</td>
<td>Any T</td>
</tr>
<tr>
<td>Stage II</td>
<td>Any T</td>
</tr>
<tr>
<td><strong>45 years and older</strong></td>
<td></td>
</tr>
<tr>
<td>Stage I</td>
<td>T1</td>
</tr>
<tr>
<td>Stage II</td>
<td>T2</td>
</tr>
<tr>
<td>Stage III</td>
<td>T3</td>
</tr>
<tr>
<td></td>
<td>T1</td>
</tr>
<tr>
<td></td>
<td>T2</td>
</tr>
<tr>
<td></td>
<td>T3</td>
</tr>
<tr>
<td>Stage IVA</td>
<td>T4a</td>
</tr>
<tr>
<td></td>
<td>T4a</td>
</tr>
<tr>
<td></td>
<td>T1</td>
</tr>
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<td></td>
<td>T2</td>
</tr>
<tr>
<td></td>
<td>T3</td>
</tr>
<tr>
<td></td>
<td>T4a</td>
</tr>
<tr>
<td>Stage IVC</td>
<td>T4b</td>
</tr>
<tr>
<td>Stage IVC</td>
<td>Any T</td>
</tr>
</tbody>
</table>
1. Distant metastases
2. Gross extrathyroidal extension of the tumor regardless of tumor size
3. Primary tumor size >4 cm even in the absence of other higher risk features
### Table 5. Major Factors Impacting Decision Making in Radioiodine Remnant Ablation

<table>
<thead>
<tr>
<th>Factors</th>
<th>Description</th>
<th>Expected benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Decreased risk of death</td>
<td>Decreased risk of recurrence</td>
</tr>
<tr>
<td><strong>T1</strong></td>
<td>1 cm or less, intrathyroidal or microscopic multifocal</td>
<td>No</td>
</tr>
<tr>
<td>1–2 cm, intrathyroidal</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td><strong>T2</strong></td>
<td>&gt;2–4 cm, intrathyroidal</td>
<td>No</td>
</tr>
<tr>
<td><strong>T3</strong></td>
<td>&gt;4 cm</td>
<td>No</td>
</tr>
<tr>
<td>&lt;45 years old</td>
<td>No</td>
<td>Conflicting dataa</td>
</tr>
<tr>
<td>≥45 years old</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Any size, any age, minimal extrathyroidal extension</td>
<td>No</td>
<td>Inadequate dataa</td>
</tr>
<tr>
<td><strong>T4</strong></td>
<td>Any size with gross extrathyroidal extension</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Nx,N0</strong></td>
<td>No metastatic nodes documented</td>
<td>No</td>
</tr>
<tr>
<td><strong>N1</strong></td>
<td>&lt;45 years old</td>
<td>No</td>
</tr>
<tr>
<td>&gt;45 years old</td>
<td>Conflicting dataa</td>
<td>Conflicting dataa</td>
</tr>
<tr>
<td><strong>M1</strong></td>
<td>Distant metastasis present</td>
<td>Yes</td>
</tr>
</tbody>
</table>

*Because of either conflicting or inadequate data, we cannot recommend either for or against RAI ablation for this entire subgroup. However, selected patients within this subgroup with higher risk features may benefit from RAI ablation (see modifying factors in the text).
RADIOACTIVE IODINE IN WELL DIFFERENTIATED THYROID CARCINOMA

• This is given while the patient is on a low iodine diet for at least 2 weeks

• Recombinant Thyrotropin can be used while the patient is on thyroid hormone

• Thyroid hormone withdrawal can be used to drive up the TSH to a value of 30 or greater

• The goal is for any remaining thyroid tissue to be starving for iodine due to low iodine diet low thyroid function

• This is Only helpful in Well Differentiated Thyroid Carcinoma
Radioactive Iodine

- Radiation precautions are necessary to protect others that may be near the patient.
- Avoid pregnant women and young children.
- Sleeping alone and otherwise at a several feet distance from other people.
- Follow-up with a total body nuclear scan.
THYROID HORMONE SUPPRESSION THERAPY IN THYROID CANCER

- TSH suppression was associated with improved progression-free survival in high-risk papillary cancer patients.

- Stage I and II the serum TSH concentration should be at or slightly below the lower reference range 0.1 to 0.4 mU/L.

- Stage II disease and higher with distant metastases, the serum TSH should be less than 0.1 mU/L.

- Other than Thyroid Cancer, No reason for suppression of TSH and it raises the risk of arrhythmia.
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