Approach to Thyroid Nodule

Asal Alqum
Thyroid Nodule

• **Discrete** lesion within the thyroid gland that is radiologically distinct from the surrounding parenchyma

• Non palpable nodules detected on US or other anatomic imaging are termed incidentally discovered nodules or “incidentalomas”
Thyroid Nodule - prevalence

• Thyroid nodules are common
• Prevalence 1-5%
• Prevalence on high resolution U/S 20-68%
• Thyroid sonograms in a clinical study, 22% of thyroid glands contained solitary and 45% contained multiple thyroid nodules
• Risk of cancer in Clinically detected thyroid nodules 6-15%
## Thyroid Nodules - Causes

<table>
<thead>
<tr>
<th>BENIGN (95%)</th>
<th>MALIGNANT (5%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multinodular (sporadic) goitre</td>
<td>Papillary carcinoma</td>
</tr>
<tr>
<td>Hashimoto’s (chronic lymphocytic thyroiditis)</td>
<td>Follicular carcinoma</td>
</tr>
<tr>
<td>Cysts: colloid, simple, or hemorrhagic</td>
<td>Minimally or widely invasive</td>
</tr>
<tr>
<td>Follicular adenomas</td>
<td>Hurthle-cell (oxyphilic) type</td>
</tr>
<tr>
<td>Macrofollicular adenomas</td>
<td>Medullary carcinoma</td>
</tr>
<tr>
<td>Microfollicular or cellular adenomas</td>
<td>Anaplastic carcinoma</td>
</tr>
<tr>
<td>Hurthle-cell (oxyphil-cell) adenomas</td>
<td>Primary thyroid lymphoma</td>
</tr>
<tr>
<td>Macro- or microfollicular patterns</td>
<td>Metastatic carcinoma (breast, renal cell, lung, others)</td>
</tr>
</tbody>
</table>
Thyroid nodule found clinically or incidentally on imaging

TSH, thyroid ultrasound

TSH normal or elevated*

Radionuclide thyroid scan
Measure FT4, T3

Nodule is nonfunctional

Meets sonographic criteria for FNA?
Yes
FNA
No
MonitorΔ

Nodule is functioning

FT4 and T3 normal
Observe in most cases◊

Subclinical hyperthyroidism

FT4 and/or T3 high
Treat◊

Overt hyperthyroidism
Thyroid Nodule - Clinical History

• Symptoms of hyper and hypothyroidism should be explored
• Factors suggesting malignancy in a thyroid nodule:

  Hx of previous irradiation
  Recent onset and rapid growth
  Pain
  Family history of thyroid CA
  MEN 2a or 2b
  Age <20 or >60 (indicates poor prognosis)
  Male gender

  Compressive or invasive symptoms: dyspnea, dysphagia, hoarseness
Thyroid Nodule – Physical examination

- Moves up with swallowing
- Size
- Surface
- Consistency
- Border
- Tenderness
- Thrill
- Percussion over manubrum sterni
- Relation to surrounding structures: fixity, carotid pulse
- Cervical lymphadenopathy
Thyroid Nodule – Physical examination

• Physical findings suggesting malignancy:
  - Firm
  - Fixed
  - Irregular
  - Cervical lymphadenopathy
  - Vocal cord paralysis
Recommended management of thyroid nodules

Patient with thyroid nodule

- TSH
  - TSH-N or \( \uparrow \)
    - Ultrasound to assess need for FNA
      - Doesn’t meet criteria
        - Monitor
        - Nondiagnostic
          - Repeat (US-FNA)
        - Papillary cancer
          - Surgery
      - Meets criteria
        - Fine needle aspiration
          - Suspicious for malignancy
            - Surgery
          - Macrofollicular
            - Follow
          - Follicular neoplasm (microfollicular)
            - Follicular lesion or atypia of undetermined significance
              - Repeat fine needle aspiration after 3 to 6 months or earlier
    - TSH-\( \downarrow \)
      - Radioisotope scan and ultrasound
        - Cold
          - Observation
        - Hot
          - Treatment in overt hyperthyroidism and selected cases of subclinical hyperthyroidism
Thyroid Nodule – Labs

- CBC, ESR for inflammatory or infectious thyroiditis
- TFT most patients are euthyroid
- Antibodies
- Serum calcitonin
- 24-hour urine for metanephrines and catecholamines
- Serum calcium
- Serum Tg

Correlates with iodine intake and the size of the thyroid gland rather than with the nature or function of the nodule

Seldom used in nodule diagnosis

Extremely elevated levels may suggest thyroid metastasis.

Diffuse high uptake: Grave’s • Diffuse low uptake: Hashimoto’s • Multiple areas of high uptake: nodular goiter • Single “hot” nodule: adenoma • Single “cold” nodule: Possible cancer • Most cancers do not make hormone • About 10% cold nodules are malignant
Thyroid Nodule – Radiography

• Not routinely done

• May show:
  - Tracheal deviation or compression
  - Pulmonary metastasis
  - Calcifications
Thyroid Nodule – Ultrasound

- Thyroid sonography with survey of the cervical lymph nodes should be performed in all patients with known or suspected thyroid nodules.

- Is there truly a nodule?
- How large is the nodule?
- What is the nodule’s pattern of ultrasound imaging characteristics?
- Is suspicious cervical lymphadenopathy present?
- Cystic or solid?
- Is the nodule located posteriorly in the thyroid gland?
- Extracapsular growth?
Thyroid Nodule – Ultrasound

• **High** risk of thyroid CA
  - Hypoechoic
  - Irregular margins
  - Microcalcifications
  - Rim calcifications
  - Central vascularity
  - Taller than wide shape
  - Extrathyroidal extension

• **Low** risk of thyroid CA
  - Hyperechoic
  - Large, coarse calcifications
  - Peripheral vascularity
  - Spongiform appearance
<table>
<thead>
<tr>
<th>Sonographic pattern</th>
<th>Ultrasound features</th>
<th>Estimated risk of malignancy</th>
<th>Consider biopsy (FNA size cutoff, largest dimension)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High suspicion</td>
<td>Solid hypoechoic nodule or solid hypoechoic component of a partially cystic nodule</td>
<td>&gt;70 to 90%*</td>
<td>Recommend FNA at &gt;1 cm</td>
</tr>
<tr>
<td></td>
<td>WITH one or more of the following features: irregular margins (infiltrative,</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>microlobulated), microcalcifications, taller than wide shape, rim calcifications</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>WITH small extrusive soft tissue component, evidence of extrathyroidal extension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermediate suspicion</td>
<td>Hypoechoic solid nodule with smooth margins WITHOUT microcalcifications,</td>
<td>10 to 20%</td>
<td>Recommend FNA at &gt;1 cm</td>
</tr>
<tr>
<td></td>
<td>extrathyroidal extension, or taller than wide shape</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low suspicion</td>
<td>Isoechoic or hyperechoic solid nodule, or partially cystic nodule with eccentric</td>
<td>5 to 10%</td>
<td>Recommend FNA at &gt;1.5 cm</td>
</tr>
<tr>
<td></td>
<td>solid areas, WITHOUT microcalcification, irregular margin or extrathyroidal</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>extension, or taller than wide shape</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very low suspension</td>
<td>Spongiform or partially cystic nodules WITHOUT any of the sonographic features</td>
<td>&lt;3%</td>
<td>Consider FNA at &gt;2 cm</td>
</tr>
<tr>
<td></td>
<td>described in low, intermediate, or high suspicion patterns</td>
<td></td>
<td>Observation without FNA is also a reasonable option</td>
</tr>
<tr>
<td>Benign</td>
<td>Purely cystic nodules (no solid component)</td>
<td>&lt;1%</td>
<td>No biopsy</td>
</tr>
</tbody>
</table>
Thyroid Nodule – CT, MRI and PET scan

• Usually unnecessary
• Useful in determining:
  • Substernal extension
  • Identifying cervical and mediastinal adenopathy
  • Evaluating relationship of thyroid lesion to adjacent structures (trachea, esophagus)
• PET: use if Tg positive with unknown tumor location
Thyroid Nodule – FNA

- FNA is the procedure of choice in the evaluation of thyroid nodules, when clinically indicated.
- Minimally invasive
- Improved diagnostic accuracy
- Specificity: 72 - 98%, sensitivity: 65 - 98%
- Can confirm: papillary, medullary, anaplastic thyroid cancers, lymphoma and metastases
Thyroid Nodule - FNA

• Limitations:

Cannot distinguish follicular adenoma from carcinoma

Cannot distinguish Hurthle cell adenoma from Hurthle cell carcinoma

FNAC is less reliable in patients who have history of head and neck irradiation or family history of thyroid cancer due to higher likelihood of multifocal lesions and occult cancer
Thyroid Nodule – FNA

• Recommendations:
  ✓ Nodules >1cm in greatest dimension with high suspicion sonographic pattern
  ✓ Nodules >1cm in greatest dimension with intermediate suspicion sonographic pattern
  ✓ Nodules >1.5cm in greatest dimension with low suspicion sonographic pattern
  ✓ Nodules >2cm in greatest dimension with very low suspicion sonographic pattern
Thyroid Nodule – FNA

• Bethesda System for Reporting Thyroid Cytopathology:

<table>
<thead>
<tr>
<th>Diagnostic category</th>
<th>Risk of malignancy (%)</th>
<th>Usual management</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Nondiagnostic or unsatisfactory</td>
<td></td>
<td>Repeat FNA with ultrasound guidance</td>
</tr>
<tr>
<td>II. Benign</td>
<td>0–3</td>
<td>Clinical follow-up</td>
</tr>
<tr>
<td>III. Atypia of undetermined significance or follicular lesion of undetermined significance</td>
<td>5–15</td>
<td>Repeat FNA</td>
</tr>
<tr>
<td>IV. Follicular neoplasms or suspicious for a follicular neoplasm</td>
<td>15–30</td>
<td>Surgical lobectomy</td>
</tr>
<tr>
<td>V. Suspicious for malignancy</td>
<td>60–75</td>
<td>Near-total thyroidectomy or surgical lobectomy</td>
</tr>
<tr>
<td>VI. Malignant</td>
<td>97–99</td>
<td>Near-total thyroidectomy</td>
</tr>
</tbody>
</table>
Thyroid cyst

• Simple thyroid cysts resolve with aspiration in about 75% of cases

• Surgical indications (Hemithyroidectomy):
  * Persist after three attempts at aspiration
  * Cysts >4cm in diameter
  * Complex cysts with solid and cystic components (higher incidence of malignancy, 15%)
Thyroid cancer

- 90% are well differentiated (papillary or follicular) with favorable prognosis
- **Papillary (most common 85-90%)**
- Follicular (5-10%)
- Medullary (7%)
- Hurthle cell cancer (3%)
- Anaplastic (1%)
- Lymphoma (1%)
Papillary Thyroid Cancer

- More often in women, 30-40 years

- Mets: cervical lymph nodes

- Good prognosis: 10 year survival exceeds 90%

- Histological characteristics: papillary projections, orphan annie nuceli, psammoma bodies

- Three key pathology findings: Psammoma bodies, Nuclear grooves, Orphan Annie’s Eye Nuclei

- Diagnosis made by nuclear findings

Increased risk with prior radiation exposure
Psammoma body: Appearance on fine needle aspirate of the thyroid

Fine needle aspirate of a papillary carcinoma of the thyroid showing a psammoma body. The laminations can best be appreciated under the microscope by moving the depth of focus.
Papillary thyroid cancer: Findings on fine needle aspirate

Fine needle aspirate of a thyroid nodule showing papillary cancer. The cells and nuclei are large, and their cytoplasm has a "ground glass" appearance. Nucleoli are prominent and the nuclei have clefts, grooves, and "holes" due to intranuclear cytoplasmic inclusions ("Orphan Annie eyes").
Papillary cancer– Management

• The American Thyroid Association (ATA)- 2015

• Thyroid cancer thyroid cancer <1 cm
  • without extra thyroidal extension
  • and no lymphnodes
  Initial surgical procedure ➔ thyroid lobectomy (hemithyroidectomy)

• Thyroid cancer >1 cm and <4 cm
  • without extrathyroidal extension
  • and without clinical evidence of any lymph node metastases
  Initial surgical procedure can be either total thyroidectomy or thyroid lobectomy
Papillary cancer - Management

• Thyroid cancer >4 cm:
  ± extrathyroidal extension
  clinically apparent mets disease to nodes
  distant sites \rightarrow total thyroidectomy

• Any tumor size and history of childhood head and neck radiation do total thyroidectomy

• Follow Tg level postop if total thyroidectomy for tumor recurrence
Lateral aberrant thyroid

• Almost always denotes a cervical lymph node that has been invaded by metastatic cancer.

• Papillary carcinoma is most common associated with lateral aberrant thyroid.
Follicular Thyroid Cancer

• More common in women with mean age of 50 years
• Malignant proliferation of follicles surrounded by a fibrous capsule with invasion through the capsule
• Entire capsule must be examined microscopically, needs surgical specimen (lobectomy)
• Metastasis generally occurs hematogenously
  10% have distant mets at time of diagnosis: lung, brain, liver

Management same as papillary thyroid cancer
Follicular lesions: Appearance on fine needle aspirate of a thyroid nodule

Multiple fine needle aspiration specimens from thyroid nodules revealing microfollicles in syncytia with nuclear atypia and little or no colloid.
Hurthle cell cancer

- **Subtype** of follicular thyroid cancer
- **More aggressive** than classic follicular neoplasms
- **Diagnosis**: needs surgical specimen for definitive diagnosis, FNA cannot distinguish
Hurthle cell cancer

• Hurthle cell cancer differ from Follicular Carcinomas in:
  1) More often **multifocal and bilateral** (about 30%)
  2) Usually **do not take up RAI** (about 5%)
  3) More likely to **metastasize to local nodes** (25%) and **distant sites**
  4) Associated with **higher mortality rate** (about 20% at 10 years)

• Same management
Hurthle cell lesion: Appearance on fine needle aspirate of a thyroid nodule

Fine-needle aspiration biopsy specimen showing mostly eosinophilic oxyphilic cells with abundant cytoplasm and round or oval nuclei with prominent nucleoli.
Medullary thyroid cancer

- Malignant proliferation of **parafollicular C cells**
  - Neuroendocrine cells secrete calcitonin
  - Inactive at normal physiological levels
- 75% sporadic, 25% inherited
  - 10% with sporadic and all with inherited have bilateral or multifocal
- Associated with **RET proto-oncogene and MEN II syndromes**
- Spread is both **lymphatic and hematogenous**

With malignancy -> hypocalcemia
- Amyloid deposits in thyroid
Medullary carcinoma of the thyroid: Findings on fine needle aspirate

Fine needle aspirate with immunostaining for calcitonin in medullary carcinoma of the thyroid. The nuclei of the tumor cells are placed eccentrically, and are larger and more pleomorphic than those of normal follicular cells. Immunocytologic staining for calcitonin is positive (brown staining which is best seen at the arrow). The background contains many red cells that nonspecifically take up the stain.
Medullary thyroid cancer

- Preoperative evaluation:
  - **Serum calcitonin** (prognostic, baseline, recurrence)
  - CEA
  - Genetic testing for germline RET mutations
  - Biochemical evaluation for coexisting tumors (esp. pheochromocytoma and parathyroid diseases)
Medullary thyroid cancer

- **MTC confined to the neck, No ultrasound evidence of cervical lymphnode involvement** → total thyroidectomy with bilateral dissection of the central lymph node compartment without lateral neck dissection

- For patients with **evidence of central cervical lymphnode involvement**, dissection of the involved lateral neck compartment is also performed

- **Follow up:** Calcitonin, 2-3 months after surgery to detect the presence of residual thyroid disease
Medullary thyroid cancer

• Prophylactic Thyroidectomy in RET mutation cancers

MEN 2a  before 5 years
MEN 2b  before 1 year
Anaplastic Thyroid Cancer

- Undifferentiated malignant tumor of the thyroid
- More common in patients older than 60
- 75% of patients have distant metastasis: lung, brain, liver, adrenals
- Often invades local structures
- Treatment: usually palliative
- Poor prognosis

Occurs in elderly • Highly malignant - invades local tissues • Dysphagia (esophagus) • Hoarseness (recurrent laryngeal nerve) • Dyspnea (trachea) • Don’t confuse with Riedel’s (“rock hard” thyroid/young pt) • Poor prognosis • Pathology: Undifferentiated cells
Lymphoma

• Female predominance
• More common by age 70
• Most commonly non-Hodgkin type
• Associated with hashimoto thyroiditis
• Treatment: radiation and chemotherapy
Prognostic indicators in PTC

✓ Classify patients into **LOW RISK** and **HIGH RISK** groups

  AGES scoring system

  **Age, Grade, Extrathyroidal invasion and Size.**

  - **LOW RISK** patients are
    - Young <40 years
    - Well differentiated tumor
    - No mets
    - Small primary lesions (<4cm)
  
  - **HIGH RISH** include
    - Older >40 years
    - Poorly differentiated tumor
    - Distant metastasis
    - Large primary lesion >4cm
Types of Thyroidectomies

- **a)** Total thyroidectomy
- **b)** Semi thyroidectomy
- **c)** Subtotal thyroidectomy
- **d)** Near-total thyroidectomy
Types of Thyroidectomies

• **Total thyroidectomy:**
  Complete removal of all visible thyroid tissue

• **Near total thyroidectomy:**
  Both lobes are excised except for less than 2 gm near the RLN & parathyroid glands

• **Subtotal thyroidectomy:**
  Leaves a rim of thyroid tissue bilaterally

• **Hemithyroidectomy:**
  Removal of one lobe with or without the isthmus
Thyroidectomy - Complications

• Immediate complications
  • HEMORRHAGE
  • INFECTION
  • RECURRENT LARYNGEAL NERVE PALSY
  • THYROID CRISES OR STORM
  • RESPIRATORY OBSTRUCTION
  • PARATHYROID INSUFFICIENCY OR TETANY

• Late complications
  • THYROID INSUFFIENCY
  • RECURRENT THYROTOXICOSIS
  • PROGRESSIVE EXOPHTHALMOS
  • HYPERTROPHIC SCAR OR KELOID.