Thyroid Nodules

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Objectives

• Discuss the significance of incidental thyroid nodules
• Identify the indications for thyroid biopsy
• Describe the management and monitoring of thyroid nodules
Epidemiology of Thyroid Nodule

• Prevalence increases with age and in women more than men
• Age less than 30, men & women 2%
• Age 45 to 50, men 12% and women 14%
• Age 55 and older, men 14% and women 18%
Benign Causes of Thyroid Nodules

- Multinodular goiter (colloid adenoma)
- Hashimoto thyroiditis
- Cysts: colloid, simple, or hemorrhagic
- Follicular adenoma
  - Macrofollicular
  - Microfollicular
- Hurthle-cell adenoma
Malignant Causes of Thyroid Nodules

- Thyroid follicular epithelial-derived cancers:
  - Papillary thyroid carcinoma
  - Follicular thyroid carcinoma
  - Anaplastic thyroid carcinoma
- Medullary thyroid cancer
  - Familial, part of MEN2 syndrome
- Primary thyroid lymphoma
- Metastatic carcinoma
  - Breast, renal, melanoma, and colon
Thyroid Nodule Evaluation

- History
- Physical Examination
- Laboratory Testing
- Thyroid Ultrasound
- Fine Needle Aspiration Biopsy
History

- Childhood head and neck irradiation
- Total body irradiation for bone marrow transplantation
- Family history of thyroid cancer or thyroid cancer syndromes (multiple endocrine neoplasia 2, familial polyposis, or Cowden syndrome)
- Rapid growth of a neck mass
Physical Examination

• A fixed, hard mass
• Cervical lymphadenopathy
• Vocal cord paralysis
• Obstructive signs and symptoms
Laboratory Testing

• Laboratory testing is helpful to evaluate the function of the gland and not for malignance.

• Serum TSH:
  – it should be done on all patient

• Calcitonin level:
  – is not indicated for routine thyroid nodule evaluation if no other risk factors for medullary thyroid carcinoma exist

• TPO antibody, thyroglobulin antibody
  – It is not helpful in initial nodule evaluation
Normal TSH

• Normal TSH is the most common scenario
• Biopsy is indicated if patient meet the ultrasound criteria
Elevated TSH

• Evaluate for hypothyroidism
• Biopsy is still indication if ultrasound meet the criteria
• Thyroiditis can present as pseudo-nodule
Suppressed TSH

• It indicates overt or subclinical hyperthyroidism
• Thyroid scintigraphy (RAI uptake and scan) should be performed next
• Cold nodule should be biopsied
Thyroid Ultrasonography

• Thyroid ultrasound should be performed in all patients with a suspected thyroid nodule or nodular goiter on physical examination or with nodules incidentally noted on other imaging studies (carotid ultrasound, CT, MRI, or FDG-PET scan)

• Do not rely on thyroid ultrasound to diagnose cancer or to select patients for surgery

• Ultrasound findings can be used to select nodules for FNA biopsy
RAI Uptake and Scan

• Test used to determine the functional status of a nodule
• Only useful in patients with hyperthyroidism on laboratory testing
• It should not be done to evaluate thyroid nodules in patient with normal or elevated TSH
RAI Uptake and Scan

• Non-functional nodule or cold nodule
  – uptake is less than surrounding thyroid tissue, nodule requires FNA biopsy

• Autonomous nodule or hot nodule
  – uptake is greater than surrounding thyroid tissue with no suppressed uptake in the rest of the gland, nodule does not require FNA biopsy
RAI Uptake and Scan

• Indeterminate Nodule
  – uptake is the same as surrounding thyroid tissue
  – can represent either small non-functioning nodules anterior or posterior to normally functioning thyroid tissue or autonomous nodules that do not produce sufficient thyroid hormone to suppress the surrounding thyroid tissue
  – Indeterminate nodules require FNA biopsy
Factors Associated with an Increased Risk of Thyroid Nodules

• Iodine deficiency
• Smoking, especially in areas of mild iodine deficiency
• Alcohol consumption is associated with thyroid enlargement, more so in women
• IGF-I levels — associated with nodules in men and goiter in both men and women
• Uterine fibroids — in one report, women with fibroids had a twofold increase risk
Ultrasound Features Associated with Low Risk of Thyroid Carcinoma

- Hyperchoic
- Large, coarse calcifications
- Peripheral vascularity
- Colloid nodule
- Egg shell calcification
Ultrasound Features Associated with an **Increased Risk** of Thyroid Carcinoma

- Hypoechoic
- Microcalcification
- Central vascularity
- Irregular border
- Incomplete halo
- Nodule is taller than wide
- Documented enlargement of the nodule
Indication for FNA Biopsy

- Hypoechoic nodules measuring >1 cm
- Hypoechoic nodules measuring >0.5 cm in high risk patients
- Isoechoic or hyperechoic nodules measuring ≥ 1.5 cm
- Mixed cystic-solid nodules without suspicious features on ultrasound measuring ≥2.0 cm
- Purely cystic nodules (no mural component) do not require a biopsy
High-Risk History

• History of thyroid cancer in one or more first degree relatives
• History of external beam radiation as a child
• Exposure to ionizing radiation in childhood or adolescence
• Prior hemithyroidectomy with discovery of thyroid cancer
• FDG avidity on PET scanning
• MEN2/FMTC-associated RET proto-oncogene mutation
• Calcitonin >100 pg/mL
FNA Pathology Result

- Benign:
  - Macrofollicular lesion
  - Thyroiditis
- Malignant
- Indeterminate:
  - Microfollicular lesion
  - Suspicious lesion
  - Follicular lesion of undetermined significance
  - Hurthle cell lesion
Management of Benign Thyroid Nodules

• Thyroid ultrasound in 6 to 12 months after the initial diagnosis to monitor nodule size then once a year
• Re-biopsy if nodule:
  – Increased in diameter by more than 20%, or
  – Changed in texture, or
  – New symptoms attributed to the nodule
• Re-biopsy of thyroid nodules that are unchanged is not indicated
Management of Benign Thyroid Nodules

• Thyroid hormone suppressive therapy is not effective in majority of benign thyroid nodule
• Thyroid hormone suppressive therapy proven benefit in:
  – Patients with elevated TSH (upper normal range or sub clinical hypothyroidism)
  – Patients with history of radiation exposure during childhood
Management of Malignant Nodules

• 5% of thyroid nodules are cancerous in the general population
• Thyroidectomy is the standard of care for differentiated thyroid carcinoma
• Good prognosis for differentiated thyroid carcinoma with overall 20 years survival of 90%
Prevalence of Thyroid Cancer in Patients with Thyroid Nodule is Higher in Certain Populations

- Children
- Men
- Adults less than 30 years or over 60 years old
- Patients with a history of head & neck irradiation
- Patients with a family history of thyroid cancer
Classification of Thyroid Malignancy

• Thyroid follicular epithelial-derived cancers:
  – Papillary thyroid carcinoma
  – Follicular thyroid carcinoma
  – Anaplastic thyroid carcinoma
• Medullary thyroid cancer
  – Familial, part of MEN2 syndrome
• Primary thyroid lymphoma
• Metastatic carcinoma
  – Breast, renal, melanoma, and colon
Management of Indeterminate Nodules

• 10 to 15% of thyroid nodule biopsy are indeterminate
• Risk of malignancy 34%
• Thyroidectomy
• Repeat FNA and check aspirate for gene testing to decrease thyroidectomy for benign nodules
FNA for Specific Gene Mutation

- Papillary and medullary thyroid cancers harbor RAS, RET, and BRAF genetic mutations
- Follicular thyroid cancers harbor translocations and fusions of certain genes (PAX 8 and PPAR-gamma)
- The above test helps as rule-in test (100% PPV) but not sensitive enough to rule out malignancy
Afirma Gene Expression Classifier

• The Afirma Gene Expression Classifier has been validated to identify benign nodules (NPV >95%)
• Reclassifies indeterminate FNAs as benign or suspicious
• High NPV helps in identifying benign nodule with high confidence
Questions?