Radiological Diagnosis and Treatment of Papillary Thyroid Carcinoma

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Presentation Outline

• Overview
  – Epidemiology
  – Anatomy

• CT scan in Thyroid CA

• Ultrasonography and Ultrasound-guided FNAB

• Scintigrapy

• Nuclear Medicine
  – Post-operative Radioiodine Ablation
  – Follow-up WBS and ablation Tx

• PET and PET-CT
Overview of Papillary Carcinoma

- **Incidence**
  - ~210,000 in 2005; 2.5:1 F/M
  - 75% of Thyroid tumors, ~1% of US malignancies

- **Typical presentation:** Solitary thyroid Nodule

- **Prognosis**
  - All comers: cancer-related mortality of 6%
  - Risk Factors (AMES)
    - Age (>40 in men, 50 in women)
    - Mets (outside of neck)
    - Extent—soft tissue invasion (5x)
    - Size (2-3.9cm =6%, 4-6.9cm = 16%, >7cm = 50%)

- **Metastases**
  - Local Nodes 80%
    - Half microscopic
    - Not diagnostic
  - Local invasion
    - Soft tissue 5-35%
    - Vascular: 5-10%
  - Distant
    - 10% of patients
    - Lung (2/3), Bone (1/4), other

http://www.georgetown.edu/dml/educ/path/cpc/endo_thyroid/09.html
Anatomy of the Thyroid

- Composed of two lateral lobes connected by an isthmus with variable presence of a pyramidal lobe

- Isthmus rests at 2nd-4th laryngeal cartilages
  - Superior poles can rise normally to the level of the larynx
  - Inferior poles can descend to 5th-6th laryngeal cartilage
  - Exact size, location of thyroid tissue somewhat variable

- Dimensions of lateral lobes: normally 4-8cm long, 1.5-2cm wide, and less than 2-2.5cm deep

- Thyroid is bound anteriorly by the infrahyoid, laterally by sternothyroid muscles (and carotid sheath), posteriorly by the larynx, and medially by the larynx and inferior constrictor.
Brief Anatomy of the Neck (Ant. View)

Thyroid
- Pyramid
- Isthmus
- Lateral Lobes

Arteries
- Brachiocephalic
  - Occasional thyroid ima (or from arch)
- Common Carotid
- External Carotid
  - Superior Thyroid artery

Nerve
- Vagus
- Recurrent Laryngeal

Strap Muscles
- Thyrohyoid
- Cricothyroid
- Sternothyroid, Infrahyoid (anterior)

Airway
- Larynx
- Trachea

Veins
- Internal Jugular
  - Drains superior, middle thyroid veins
- Brachiocephalic
  - Usually drains inferior thyroid veins (variable)

Our Patient AS is an 83 y/o woman with a history of coronary artery disease complaining of >2yrs cough + “need to clear throat,” occasional difficulty swallowing that has been getting slightly worse over time.
Patient AS: Barium Swallow

Barium Swallow

Round, smooth, extrinsic indentation

Esophagus is deviated to the right and slightly anteriorly over 2-3cm

Ddx R Lower Neck Mass

• Thyroid Nodule
• Lymph node enlargement
  • Infection, lymphoma, inflammatory (sarcoid), mets
• Tracheal masses
• Soft tissue tumors

What follow-up imaging is indicated?
Enlarged R thyroid w/ 2x3cm heterogeneous mid-thyroid nodule

* Normal Appearance of Thyroid Tissue on CT

Small round hypodense L lower pole lesion w/ nearby small semi-calcified nodule (both <1cm)
CT in Thyroid Carcinoma I: Determination of Likely Thyroid Lesion

Signs of Thyroid Origin

- Anatomic continuity
  - Local spread of tumor more common than distant metastasis
- Superior mediastinal mass (usually anterior)
  - Ddx: Teratoma, thymoma, thyroid, (terrible) lymphoma
- Deviation of trachea, esophagus
  - Large thyroid lesions have significant mass effect
- Focal calcification, heterogeneity (iodine, cysts)
- High HU (~100)
- Increased density after contrast bolus
- Prolonged contrast enhancement
CT in Thyroid Carcinoma II: Evaluation of Known Thyroid Lesion

Indications for CT in Thyroid Carcinoma

- Generally indicated in thyroid masses >3cm
- Characterization of laryngeal/tracheal or esophageal invasion
- Assess blood vessel, nerve involvement for surg. planning
- Detection of local metastases
  - Most useful post-surgery and radioiodide ablation for mets that are not iodine avid
- Detection of non-local metastases

Notes

- Contrast should not be given before scintigraphy, TSH evaluation, or shortly before radioiodide WBS/ablation
- CT is not sensitive or specific for determining malignancy of intrinsic thyroid nodules
Our Patient AS was sent to Ultrasound for further characterization and likely biopsy of thyroid nodules
Thyroid Ultrasonography I

- **Technique**
  - 5-15MHz high resolution transducer
  - Patient lies supine w/ neck hyperextended

- **Indications**
  - Characterize/verify physical exam findings
  - Search for nodules in high risk population (radiation exposure)
  - Follow up multinodular disease
  - Detect recurrent tumor post-operatively
  - Guidance of fine needle aspiration biopsy (FNAB)
  - Guidance of ETOH ablation

- **Why not a screening tool?**
  - Diagnostic yield low
  - Time consuming
  - Morbidity, patient anxiety involved (FNAB)
  - Relatively low morbidity, mortality of thyroid CA in current practice
Thyroid Ultrasonography II
Nodule Characterization

Pathological Ddx thyroid nodule:
- Colloid Nodule
- Adenoma
  - Adenomatous hyperplasia of thyroid
  - Follicular adenoma
  - Parathyroid adenoma
- Thyroid Carcinoma
  - Papillary, follicular, anaplastic, medullary, Hurthle cell
- Cyst
  - Simple Thyroid cyst (uncommon)
  - Degenerating adenoma or necrotic carcinoma
- Metastasis (very uncommon)

US Features of nodules:
- Internal Consistency
- Echogenicity
- Margin Regularity
- Presence of macro- or micro-calcifications
- Peripheral Sonolucent Halo
- Presence & distribution of blood-flow signals
US: Benign Features

- Homogeneous hyperechogenicity (<1% malignant) or isoechogenicity with regular lucent halo
- Cystic lesion with no solid mass present (rare)
- Lack of vascularization (especially central)
- Multinodularity of lesions
  - Less of an effect than previously thought (improved detection?)
  - Dominant lesion in multinodular goiter carries same risk as single nod
- Eggshell calcification
- Hypo- or isoechoic w/distal enhancement +/- lateral acoustic shadowing
- Regular Margins

2 Demonstration Patients with enlarged thyroids containing multiple small nodules by physical exams
US: Suspicious Features

- Irregular or poorly defined margins
- Microcalcifications
  - <2mm in diameter
  - Psammomas
- Same-side lymphadenopathy
- Invasion of adjacent structures
- Significant *vascularization*
  - Esp. central or chaotic
- Hypoechogenic solid lesions with incomplete/irregular halo and w/o distal enhancement

**Mildly increased Risk**

- Other calcifications (non-eggshell)
- **Heterogeneous internal structure**
- Complex cystic lesions

2 demonstration patients evaluated for nodules noted on physical examination. Neither of these nodules were the ones initially noted. Both turned out to be papillary carcinoma.
Patient AS: Ultrasound Results

Rt mid 2.5 X 2.1cm nodule

- Heterogeneous structure, echogenicity
- Incomplete halo
- Microcalcifications
- Poorly defined superior margin

Lt Lower 1.5 X 1cm nodule

- Small nodule w/ fairly large calcifications & posterior shadowing
- Neighboring hypoechogenic region (cystic appearing) w/ solid portion along medial wall
- Clear margins
Ultrasound-guided FNAB

Ultrasound accuracy
• 90% of biopsied nodules benign → current practice has low specificity

Indications
• Any nodule with more than one suspicious sign
• Any solitary nodule
• Dominant nodule in multinodular goiter
• Incidentalomas? Controversial

Not indicated
• Benign-appearing non-dominant nodules
• “Hot nodules” by Thyroid scintigraphy
  - This study of uptake w/ I-123 done less frequently for nodules unless patient has low TSH (suggesting hyperfunctioning thyroid).

Patient AS -- FNAB

This patient presented with a large neck nodule. Scintigraphy with 300Mci I-123 revealed a cold nodule in the right lower lobe.
Patient AS Follow-up

• Both right mid-lobe nodule and left thyroid nodule were positive for papillary carcinoma.

• The patient has been recommended for surgical consultation, and has begun her pre-operative work-up.
Introduction: Patient AJ

Our Second Patient, AJ, is a 42 year-old woman with a history of type II DM and a new finding of multinodular thyroid on physical examination.
Patient AJ: Thyroid Ultrasound

Right-sided 17 x 12mm Nodule
- Isoechoic
- Distal enhancement
- Lateral acoustic shadowing
- Clear halo
- Slight heterogeneity
- Avascular
- Clear margins

FNAB Diagnosis: C/w mixed micro- & macrofollicular lesion

Left-sided 15 x 6mm Nodule
- Hypoechoic
- Clear Margins
- No acoustic shadowing or distal enhancement
- No halo
- Chaotic hypervascular pattern

FNAB Diagnosis: Papillary Ca
Patient 2: CXR and Chest CT

Small concerning lesions in R lower lobe on CXR → Neck & Chest CT for further characterization

Chest CT Results:

- No mediastinal, hilar, axillary lymphadenopathy
- Small bilateral subpleural noncalcified nodules measuring 3, 4, & 6mm
- Ddx: Metastatic Disease, non-specific nodules
Multiple Pulmonary Micronodules on CXR and CT

Companion Patient 1: 64 y/o woman initially p/w Hx of hoarseness, neck discomfort, now s/p thyroidectomy, pre-op for further tumor debulking

- Substernal anterior-superior mediastinal mass extending into neck & causing tracheal displacement
- Diffuse pulmonary micronodules (<5mm) w/ occasional macronodular met

Ddx Diffuse micronodules w/ near-random distribution:

- Metastases (especially thyroid!)
- Miliary TB
- Miliary Sarcoidosis
- Disseminated Histiocytosis
Patient AJ: Total Thyroidectomy

Findings

- Direct sternohyoid invasion
- 7/28 nodes positive for malignant tumor
  - All visually involved lymph nodes dissected
- Uncomplicated Re-implantation of parathyroid gland

The Patient was referred to Nuclear Medicine for radioiodine ablation
Radionuclide Ablation I: Uses

Indications

- Post total thyroidectomy for thyroid carcinoma
  - All patients >45
  - All patients with primary tumor >1.5cm at resection
  - All patients with any sign of extra-thyroid disease

Justification

- Allows destruction of residual thyroid tissue
- Can identify and potentially treat previously unknown metastases
- Clears normal thyroid tissue to allow follow-up whole body scans
  - Normal thyroid uptake very strong compared to tumor uptake, so recurrence cannot be monitored by radionuclide scanning without thyroidectomy and ablation
- Improves value of thyroglobulin measurement
  - An increase in thyroglobulin levels after radionuclide ablation is a highly specific marker for recurrence
Radionuclide Ablation II : Method

Administration of $^{131}\text{I}$
- Beta-emitter – 190keV betas – 90% absorbed within 0.8mm of source
- Some gamma emission (fortunate for detection)

Induction of thyroid & tumor uptake
- TSH > 25mU/L – 2 strategies: iodine withdrawal, rhTSH

Scanning prior to ablation
- Can be useful for dosimetry
- Must avoid “stunning”
  - Reduction in uptake due to radiation injury
- Small doses (1.3-1.5mCi) of I-123 now generally used, but 3-5mCi I-131 works as well

Scanning post-ablation
- Always obtain scan within a week post-ablation
- Generally most sensitive indicator of metastatic disease.
Radioiodide Whole Body Scan

Companion Patient 2: 57 y/o male w/ poorly differentiated papillary CA s/p total thyroidectomy

- Residual thyroid tissue or cervical lymph nodes noted in resection cavity
- Normal uptake seen in salivary glands, liver, kidneys, bladder
- Patient went on to have negative follow-up radioiodide scans

I-123 scan (pre-ablation) I-131 (post ablation)
Patient AJ: Radioiodine Whole body Scan
Six Days Post-Ablation

- Two well-defined foci of uptake within the lower neck
  - c/w residual thyroid tissue or lymph node involvement

- Multiple bilateral foci of uptake within the lungs
  - c/w metastases
The patient is now 3 months post-ablation. She will undergo another I-123 scan and ablation (if necessary) in the next few months.
Follow-up Radionuclide Scans and Ablations I: Indications and Limitations

Indications

- Repeat scan in all patients with post-operative ablation every 6-12 months until two negative scans (97% relapse-free survival)
- Repeat ablation if any abnormal uptake sites

Limitations

- Limited tumor uptake
  - Poorly differentiated tumor
  - Tumor Progression / Response
- Large foci
  - <1cm lymph mets 76% treated in 3 rounds, 20% in larger
  
  Suggests large focus Tx w/ surgical resection or radiation therapy
Follow-up Radionuclide Scans and Ablations II: Complications and Prognosis

Favorable Prognostic Variables
- Age (<40)
- Extent of tumor
  - Lack of visualization on standard radiographs
  - Micronodular vs. macronodular
- Differentiation of tumor
- I-131 uptake
- Lack of 18-FDG uptake

Complications
- Nausea, gastric pain, neck edema, sialadenitis
- Transient impairment of spermatogenesis, transient ovarian failure
- Mildly increased risk salivary gland tumors, other tumor types

Bottom Line: 10 yr Survival
- Complete response – 93%
- Incomplete response – 14%

Age<40 w/ micronodular mets: 96% 10 year survival
Age>40 w/macronodular mets: 7% 10 year survival
Other: 63% 10 year survival
Axial fused PET/CT at baseline and follow-up in a patient with suspected recurrent thyroid cancer and rising thyroglobulin level. Abnormal FDG uptake is seen in the sternum on both scans.

From Fukui et al., Seminars in Ultrasound, CT, and MRI, 24(2), 2003.

What is PET-CT?

- Co-registered F-18 fluorodeoxyglucose (FDG) positron emission scan and CT imaging
  - PET-FDG scan for increased glucose uptake is specific for recurrent neoplasm
  - CT co-registration gives increased utility to low-resolution PET scan
    - Better structural resolution to guide therapy
    - Of particular utility in small spaces like the neck
PET-CT – The New Player for Bad Actors

Indications

• High risk patients to scan for metastases
  – E.g. Companion patient 2 (age, poorly differentiated CA)

• Thyroglobulin positive patients w/ neg. I-131 WBS
  – PET scanning with 18-FDG has been shown to be highly sensitive (~85%) in pts with negative I-131 scans → poorly differentiated CAs

• Prognosis and staging of metastatic disease
• Determine relationship of tumor to vital structures, guiding planned biopsy, resection, or radiation tx
• Monitoring Response to therapy

Limitations

• Not sensitive to all thyroid carcinomas
• Non-therapeutic
• Limited Scanner Resolution
  – Misses lesions smaller than 1cm unless extensive uptake
• Requires interval of 4 months after radiation therapy
Review of Imaging Modalities in Papillary Thyroid Cancer

• **CT**
  - Determines extent of soft-tissue invasion, distant metastases
  - Normally indicated in persons with nodules >3cm, abnormalities on pre-op plain-film

• **Ultrasonography**
  - Mainstay for intrinsic nodule characterization
  - Provides guidance for fine-needle aspiration biopsy → diagnostic method of choice

• **Scintigraphy**
  - Determines nodule iodine uptake
  - Indicated in persons with low TSH

• **Radionuclide WBS, ablation**
  - Therapeutic treatment for distant mets, recurrent disease
  - Allows visualization of functional tumor burden in well-differentiated cancers

• **PET-CT**
  - New tool for staging and monitoring of high risk patients with poorly differentiated disease
References

15. Sherman S. Overview of Papillary Thyroid Carcinoma. UptoDate Online, 2006.
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