Overcoming “Thyrophobia”: A Guide to Diagnostics in Thyroid Surgical Pathology

Papillary Thyroid Carcinoma Variants

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Thyroid Carcinoma:

- Papillary Carcinoma
- Follicular Carcinoma
- Poorly Differentiated Carcinoma
- Undifferentiated (Anaplastic) Carcinoma
- Medullary Carcinoma
- Mixed Medullary and Follicular Cell Carcinoma
- Squamous Cell Carcinoma
- Mucoepidermoid Carcinoma
- Sclerosing Mucoepidermoid Carcinoma with Eosinophilia
- Mucinous Carcinoma
- Spindle Cell Tumor with Thymus-like Differentiation
- Carcinoma Showing Thymus-like Differentiation
Papillary thyroid carcinoma is the most common type of endocrine malignancy
Papillary Thyroid Carcinoma

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Papillary Thyroid Carcinoma

Distinct nuclear morphology

1. Nuclear elongation/oval to box-shaped nuclei
2. Nuclear enlargement
3. Nuclear clearing: “Orphan Annie eyes”
4. Nuclear membrane irregularities
5. Nuclear pseudoinclusion
6. Nuclear crowding/overlapping
7. Intranuclear grooves
“DISTINCT NUCLEAR MORPHOLOGY”

- Lymphocytic thyroiditis
- Autoimmune thyroiditis
- Graves Disease
- Post-fine needle aspiration changes
- Processing artifacts

- Hyalinizing trabecular tumor
- Solid cell nests
- Adenoma and carcinoma, oncocytic type
Papillary Thyroid Carcinoma

• Prognostic features:
  – Certain clinical and pathologic features portend a higher risk for tumor recurrence and cancer-related mortality.
  – The most important are:
    • age at diagnosis
    • size of the primary tumor
    • presence of soft tissue invasion or distant metastases
Papillary Thyroid Carcinoma

- Poor prognostic features:
  - multifocal disease
  - bilateral or mediastinal lymph node involvement
  - male gender
  - delay in primary surgical therapy > 1 yr after detection of nodule
  - aggressive histologic subtype
• Papillary Thyroid Carcinoma
  – Follicular Variant
  – Macrofollicular Variant
  – Oncocytic Variant
  – Clear Cell Variant
  – Diffuse Sclerosing Variant
  – Tall Cell Variant
  – Columnar Cell Variant
  – Solid Variant
  – Cribriform Morular Variant
  – Papillary Carcinoma with Fasciitis-like Stroma
  – Papillary Carcinoma with Focal Insular Component
  – Papillary Carcinoma with Squamous Cell and Mucoepidermoid Carcinoma
  – Papillary Carcinoma with Spindle and Giant Cell Carcinoma
  – Combined Papillary and Medullary Carcinoma
  – Papillary Microcarcinoma
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MACROFOLLICULAR VARIANT OF PAPILLARY THYROID CARCINOMA

- Among the rarest or underdiagnosed of papillary carcinoma variants
- Requires strict histologic criteria to diagnose
- Low rate of LN metastasis
- Confused with colloid or hyperplastic nodules
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PAPILLARY THYROID CARCINOMA

Clear cell variant:
- Described in the early 1980s
- Predominantly females, 6th-7th decade
- Often behave like follicular variant/follicular carcinoma
- Distinguished from renal cell carcinoma and other mets via TTF1 or thyroglobulin staining

Histologic Features:
- Clear cytoplasm
- Features of classical variant and oncocytic change
- Often encapsulated (like follicular variant)
- May have tall cell/columnar cell features
- Focally prominent nucleoli
- Grooves/pseudoinclusions
- More likely vascular invasion than lymph node mets
Case

- 28 yo female presents at an outside hospital for excision of a 1 cm thyroid nodule
- No prior medical history
Case

• 64 yo female presents with a thyroid mass and a lytic lesion of the humerus
Final Pathologic Diagnosis

PAPILLARY THYROID CARCINOMA, CLEAR CELL VARIANT, ENCAPSULATED (5.0 cm, by report), with a focally solid and insular growth pattern worrisome for evolution in the direction of POORLY DIFFERENTIATED THYROID CARCINOMA
Follow Up

- Thyroid excised in 12/2008
- 3/09 – Humerus met excised
- 9/09 – Shoulder met excised
- 10/09 – PET shows sternum mass, T10 mass, numerous lung mets, uptake in in the right and left thyroid beds
- 1/10 – FNA of right axillary node positive for met thyroid cancer
- 10/10 – Left distal tib/fib fx, likely met
### PAPILLARY THYROID CARCINOMA

#### Oncocytic variant:
- Grossly mahogany brown (as in renal oncocyto mas)
- Tumors often present with lymph node involvement (about 50%)
- Multifocal disease (about 35%)
- Disease free survival (about 75% at 6 years)

#### Histologic Features:
- Papillary architecture
- Oncocytic with focally prominent nucleoli
- Other changes associated with papillary thyroid carcinoma – crowding, nuclear enlargement, clearing, pseudoinclusions
- Psammoma bodies (about 33%)
PAPILLARY THYROID CARCINOMA

Solid variant:
- Largest study at Mayo Clinic (Nikiforov, 2001)
- 20 cases of 756 (3%)  
- Females 3:1
- Mean 35 yo
- F/U 6-32 yrs (10% dead (2), 1@ 7 yrs, 1@10 yrs; 10% lung mets (2))

Histologic Features:
- 70% solid growth pattern
- Largely unencapsulated with infiltrative edges
- Small areas of micropapillary/follicular structure
- Characteristic papillary carcinoma nuclear features
- Grooves, irregular nuclear contours, nuclear clearing, and pseudoinclusions
- Not to be confused with poorly differentiated carcinoma
Overall Summary

• Variants of Papillary Thyroid Carcinoma
  – In young patients, be aware of associated syndromes to point clinicians toward additional diagnoses
  – Most variants have excellent outcomes (excellent)
  – Newer variants have outcomes data pending
  – Distinguishing variants useful for identifying metastases and clinical behavior