Papillary Thyroid Carcinoma: Aggressive Variants

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Papillary Thyroid Carcinoma

- Follicular Variant
- Macrofollicular Variant
- Classical Variant
- Oncocytic Variant
- Clear Cell Variant
- Solid Variant
- Hobnail Variant
- Papillary Microcarcinoma
- Warthin-like Variant
- Tall Cell Variant
- Columnar Cell Variant
- Cribriform Morular Variant
- Diffuse Sclerosing Variant
Papillary Thyroid Carcinoma: Aggressive Variants

1. Papillary Thyroid Carcinoma, Tall Cell Variant
2. Papillary Thyroid Carcinoma, Diffuse Sclerosing Variant
3. Papillary Thyroid Carcinoma with Prominent Hobnail Features
Papillary Thyroid Carcinoma

Papillary Thyroid Carcinoma, Tall Cell Variant
Papillary Thyroid Carcinoma, Tall Cell Variant

• Aggressive variant of papillary thyroid carcinoma predominantly composed of cells with height 3x their width and characteristic nuclear features and pink cytoplasm with well defined membranes

• Represents 4-19% of all PTC
  • Average age: 55 years
  • Predominance in males
Papillary Thyroid Carcinoma, Tall Cell Variant

- Rapidly enlarging thyroid mass
- Patients present with symptoms related to involvement of surrounding structures
- May be fixed due to involvement of surrounding structures
- Distant metastases are frequent
Papillary Thyroid Carcinoma, Tall Cell Variant

Gross Features:
- Tumors are large >4cm
- Infiltrative growth pattern
- Usually solid firm lesions
  - Pale tan to white
- Extrathyroidal extension may be identified
Papillary Thyroid Carcinoma, Tall Cell Variant

Histology:
• Papillary, trabecular, and cord-like patterns
• Follicular structures are rare
• >50% cells have height 3x their width
  • Abundant eosinophilic cytoplasm
• Well-defined cytoplasmic borders
• Abundant intranuclear pseudoinclusions
Papillary

Solid/Follicular

Low Power Clue: Ample Pink Cytoplasm
Cord-like pattern “Tram-tracking”

Low Power Clue: Ample Pink Cytoplasm

High Power Clue: Well-defined cytoplasmic borders and Intranuclear pseudoinclusions
Papillary Thyroid Carcinoma, Tall Cell Variant

Intranuclear pseudoinclusions are more common in this variant than any other variant
Papillary Thyroid Carcinoma, Tall Cell Variant

- Necrosis is commonly seen
- Lymphovascular invasion is very common
- Extrathyroidal extension is commonly seen in invasive tumors
Papillary Thyroid Carcinoma, Tall Cell Variant

Immunohistochemistry

- TTF-1
- Thyroglobulin
- PAX8
- Cyclin D-1
- HBME-1
- Galectin 3
- BRAF in ~70-80% cases
BRAF
HBME1
Galectin 3
BRAF
Papillary Thyroid Carcinoma, Tall Cell Variant

Molecular Genetics

• **BRAFV600E** point mutation:
  – In 70-80% of tumors
  – Associated with vascular invasion, distant metastases and extrathyroidal extension

• **RET/PTC** rearrangement not present
A Practical Approach

• Aggressive variant of papillary thyroid carcinoma: extensive lymphovascular invasion
• Widely known to be underdiagnosed...
• Identification of cell characteristics is crucial for diagnosis!
Papillary Thyroid Carcinoma, Tall Cell Variant

Differential Diagnosis

• PTC, columnar cell variant
• PTC, classical variant
• Follicular oncocytic carcinoma
• PTC, Warthin-like variant
• PTC, hobnail variant
Unusual Variants of Papillary Thyroid Carcinoma

Papillary Thyroid Carcinoma, Diffuse Sclerosing Variant
Diffuse Sclerosing Variant of Papillary Thyroid Carcinoma

- Young patients
- Evidence of autoimmune disease
- Diffuse involvement of one or both lobes
  - Background of lymphocytic thyroiditis
    - Firm white sclerotic mass
    - Early lymph node involvement
- Lung metastases at presentation ~25%
Diffuse Sclerosing Variant of Papillary Thyroid Carcinoma

- Tumors are usually very large: Average 5.8 cm
  - Diffusely involves gland
  - No obvious encapsulation
- Lobulated, nodular, and multifocal
  - Hard and firm masses
  - Pale grey
  - Gritty cut surface
- Cystic changes may be present
Papillary Thyroid Carcinoma, Diffuse Sclerosing Variant

Characterized by:

• Papillary, follicular and tall cell variant components
  • Dense sclerosis
  • Extensive squamous metaplasia
• Patchy to dense lymphocytic infiltrate
  • Numerous psammoma bodies
• Marked lymphatic spread of tumor
• Infiltration into perithyroidal soft tissues
Lymph node metastasis
Diffuse Sclerosing Variant of Papillary Thyroid Carcinoma

Immunohistochemistry:
• TTF1
• PAX8
• HBME1
• BRAF
• p63
• CK5/6
• CD5
• S100
Diffuse Sclerosing Variant of Papillary Thyroid Carcinoma

CK5/6
Diffuse Sclerosing Variant of Papillary Thyroid Carcinoma

A Practical Approach

• Large and firm tan masses
• Mixed histology: papillary, follicular, and tall cell variant components
  • Lymphocytic infiltrate
  • Dense sclerosis
• Extensive squamous metaplasia
  • Intrathyroidal spread
Diffuse Sclerosing Variant of Papillary Thyroid Carcinoma

Molecular Genetics

*RET/PTC1* rearrangements in ~30% of cases

– Younger patients

*RET/PTC3* ~10%

*BRAFV600E* point mutation:

– In ~40-60% of tumors

– Found in older patients

– Associated with vascular invasion, distant metastases and extrathyroidal extension
Diffuse Sclerosing Variant of Papillary Thyroid Carcinoma

Differential Diagnosis

- Lymphocytic thyroiditis
- PTC, classical variant
- Squamous cell carcinoma
- Mucoepidermoid carcinoma
  - Metastases
  - Lymphoma
Papillary Thyroid Carcinoma: Aggressive Variants

Papillary Thyroid Carcinoma with Prominent Hobnail Features
Papillary Thyroid Carcinoma with Prominent Hobnail Features

• Papillary thyroid carcinoma characterized by loss of cellular polarity/cohesiveness, with hobnail features in >30% of neoplastic cells

• Rare, likely 1% of all PTC cases

• Mean age: 57.6 years
  • 3F:1M
Papillary Thyroid Carcinoma with Prominent Hobnail Features

**Macroscopy**

- Multifocal, involving both lobes,
- Infiltrative,
- Large ~ 4 cm
Papillary Thyroid Carcinoma with Prominent Hobnail Features

**Histological Features**

- Architectural patterns:
  - Papillary pattern
    - Variably sized papillae with prominent vascular core lined by 1-4 cells thick hobnail cells
  - Follicular pattern
    - Variably sized follicles with no colloid lined by hobnail cells
  - Clustered pattern
    - Clusters of hobnail cells
Papillary Thyroid Carcinoma with Prominent Hobnail Features

Cytological features

• Hobnail cells with dense eosinophilic cytoplasm
• Well defined cell membranes
Papillary Thyroid Carcinoma with Prominent Hobnail Features

**Histological features**

- Nuclei are located in the apical portion
- Severe nuclear atypia
- Nuclear features of PTC are focal
  - Irregular nuclear membranes/pseudo-inclusions
  - Nuclear enlargement and overlapping
Papillary Thyroid Carcinoma with Prominent Hobnail Features

**Histological features**

- Loosely and individually arranged neoplastic cells
- Colloid is minimal and usually absent
Papillary Thyroid Carcinoma with Prominent Hobnail Features

Histological features

- Psammoma bodies are rare
- Necrosis may be present
- Lymphovascular invasion always present
Papillary Thyroid Carcinoma with Prominent Hobnail Features

Immunohistochemistry

- Thyroglobulin (focal)
  - TTF1
  - CK19
  - HBME-1
  - EMA
  - P53
Papillary Thyroid Carcinoma with Prominent Hobnail Features

Molecular Genetics

• **BRAF V600E** mutation are identified in >50% cases
  – Associated with vascular invasion, lymph node metastases, and extrathyroidal extension

• **RET/PTC** gene rearrangement are negative
Thank you!