Parathyroid Pathology

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Disclosures

I have nothing to disclose

Objectives

1. Review the pathologic features of parathyroid hyperplasia, adenoma and carcinoma.

2. Describe the role of immunohistochemistry in evaluation of histologically abnormal parathyroid tissue.

The normal parathyroid

- Normal parathyroid = 4 mm x 3 mm, 30 mg
- Normal epithelial cellularity is 60% (40% fat)
- Complete absence of fat is abnormal
  - fat is scant in normal children
  - fat content reflects total body adiposity
The normal parathyroid

One basic cell type, chief cell

Variants more common in hyperfunctioning glands:
- Oxyphil cell - granular eosinophilic cytoplasm
- Water clear cell - abundant optically clear cytoplasm

Primary Hyperparathyroidism

- 85% parathyroid adenoma
- 14% parathyroid hyperplasia
- 1% parathyroid carcinoma
Parathyroid adenoma

- Women > Men, 3:1
- Etiology: Sporadic, MEN syndrome, radiation exposure
- Histology:
  - Well-circumscribed to vague hypercellular nodule devoid of stromal adipocytes
  - 60% show a thin rim of normal or compressed parathyroid tissue at the periphery

Parathyroid adenoma

- Tumor cells in sheets, acini, or follicles, with round regular nuclei or "endocrine atypia"
- Dominant follicular pattern can be mistaken for follicular thyroid carcinoma

Parathyroid adenoma

Follicular pattern

- Parathyroid forming follicles containing granular eosinophilic material can make distinction between parathyroid and thyroid difficult on frozen section
- PTH is specific for parathyroid
- TTF-1 is specific for thyroid follicular epithelium
Parathyroid adenoma

- Areas of fibrosis, hemorrhage, infarction, or cystic change are not necessarily worrisome

Parathyroid hyperplasia

- Hyperplasia of chief cells with uneven enlargement of all glands and marked reduction in parenchymal fat
  - Isolated
  - Familial
  - MEN1, MEN2a
  - Hyperparathyroidism-jaw tumor syndrome
Parathyroid hyperplasia

- Distinction between primary and secondary hyperplasia depends on clinical and laboratory findings, not histology
- “Water-clear hyperplasia,” a rare non-familial form of hyperplasia of cells with abundant clear cytoplasm

Adenoma or hyperplasia?

Adenoma vs. Hyperplasia

- Distinction between adenoma and hyperplasia depends on findings in the remaining glands
Adenoma vs. Hyperplasia?

- Some are histologically diagnosed as adenomas, malignant nature is only manifest due to metastasis years later

Parathyroid carcinoma

- Affects patients younger than adenomas
- Clinical clues
  - Severe hypercalcemia
    - rarely non-functional
  - Simultaneous renal colic (26%) and bone pain or fracture (73%)
  - Palpable mass in the neck

Parathyroid carcinoma
**Histologic diagnosis**

<table>
<thead>
<tr>
<th>Absolute criteria</th>
<th>Features associated with malignancy</th>
</tr>
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<tbody>
<tr>
<td>Invasion into surrounding tissues</td>
<td>Broad fibrous bands splitting tumor nodules (90%)</td>
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<tr>
<td>Regional or distant metastasis</td>
<td>Capsular invasion (67%)</td>
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<td></td>
<td>Vascular invasion (12%)</td>
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<td></td>
<td>Readily identifiable mitotic figures (81%)</td>
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<td>Diffuse cellular atypia</td>
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<td>Coagulative tumor necrosis</td>
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**Absolute criteria**

- Invasion of normal tissue
- Tumor metastasis to bone
**Tumor metastasis to lung**

- **Broad fibrotic bands**

- **Capsular invasion**

**Relative criteria**
Vascular invasion

Increased mitotic rate

Atypical mitosis

Nuclear pleomorphism
**Coagulative “tumor-type” necrosis**

- Atypical parathyroid adenoma
  - Few (1-2), inconclusive features of malignancy
  - Acknowledges the grey areas in the spectrum of parathyroid tumors and difficulty predicting clinical outcome based on histologic features
  - Patients should be followed with regular serum calcium

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**Can immunohistochemical stains help?**

- Total loss of parafibromin is highly specific for parathyroid carcinoma (only 1/3 of cases)
- Strong positivity for galectin-3 is very sensitive for parathyroid carcinoma

**Parafibromin**

- Positive = benign or malignant
- Negative = malignant
Galectin-3

Positive = supports malignancy

In practice

- Usual results are positive for both parafibromin and galectin-3, this pattern is equivocal for malignancy and does not resolve the dilemma

What about FNA?

Utility of FNA

- Assessment of % fat is not possible
- Most features diagnostic of malignancy are not apparent on FNA
- Parathyroid and thyroid epithelium are cytologically similar
**Utility of FNA**

- Parathyroid tissue can be distinguished from thyroid tissue if a needle rinse specimen is sent for PTH analysis at the time of biopsy.

**Conclusions**

1. Parathyroid hyperplasia, adenoma and carcinoma are all characterized by hypercellularity and histologic features can be ambiguous.

2. Correlation with operative findings is imperative and communication of such clinical information to the pathologist can facilitate timely and accurate diagnosis.

3. Immunohistochemistry has limited utility, but can be helpful in a subset of problematic cases.

Thank you!