The suspicious thyroid nodule

A case for total thyroidectomy

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Overview

1. Background – Nodular thyroid disease
2. Diagnosis – HPI, U/S, FNA
3. Staging
4. Workup
5. Therapy
6. Treatment protocol
Nodular thyroid disease

Incidence

• 100/100,000 per year
• 300,000 new nodules in US in 2007
• 10% lifetime probability

Prevalence

• Palpation: 3-7%
• U/S : 20-76%
• Autopsy: 50%

∼5% possibility of malignancy

Regardless of size
Risk Factors

- Male
- Extremes of age: <20 or >70
- Head/neck radiation exposure
- Family history of PTC, MTC
- Genetic predisposition
  - MEN2, Cowden disease, Gardner’s Syndrome
- Enlarging and/or fixed nodule
- Cervical adenopathy
- Objective hoarseness, ipsilateral RLN paralysis
Workup

- TSH
- Ultrasound
- Fine needle aspiration
- CT/MRI
Ultrasonography

Indications
• Palpable nodule
• MNG
• History of neck radiation
• Family history of MTC, MEN2, PTC, genetic disorders
• Unexplained cervical adenopathy

Advantages
• Non-invasive
• Identify nodules or adenopathy not apparent on PE or radionuclide scanning
• Combination of features may predict malignancy
• Interval growth
Ultrasonography

Disadvantages

- Low sensitivity/PPV
- Not standardized
- Adjunctive only

→ a guide to further study

Gharib, H. Thyroid nodules: clinical importance, assessment, and treatment. Endocrin Metab Clin N Am

<table>
<thead>
<tr>
<th>US feature</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
<th>Positive predictive value, %</th>
<th>Negative predictive value, %</th>
<th>Relative risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microcalcifications</td>
<td>26.1–59.1</td>
<td>85.8–95.0</td>
<td>24.3–70.7</td>
<td>41.8–94.2</td>
<td>4.97</td>
</tr>
<tr>
<td>Hypoechogeticity</td>
<td>26.5–87.1</td>
<td>43.4–94.3</td>
<td>11.4–68.4</td>
<td>73.5–93.8</td>
<td>1.92</td>
</tr>
<tr>
<td>Irregular margins or no halo</td>
<td>17.4–77.5</td>
<td>38.9–85.0</td>
<td>9.3–60.0</td>
<td>38.9–97.8</td>
<td>16.83</td>
</tr>
<tr>
<td>Solid</td>
<td>69.0–75.0</td>
<td>52.5–55.9</td>
<td>15.6–27.0</td>
<td>88.0–92.1</td>
<td>4.2*</td>
</tr>
<tr>
<td>Intranodule vascularity</td>
<td>54.3–74.2</td>
<td>78.6–80.8</td>
<td>24.0–41.9</td>
<td>85.7–97.4</td>
<td>14.29</td>
</tr>
<tr>
<td>More tall than wide</td>
<td>32.7</td>
<td>92.5</td>
<td>66.7</td>
<td>74.8</td>
<td>10.5*</td>
</tr>
</tbody>
</table>

Fig. 4. Calcifications in thyroid nodules in two patients. (A) Nodule with a hypoechoic pattern and multiple fine calcifications. FNA biopsy showed papillary thyroid carcinoma, which was confirmed at surgery. (B) Transverse view of the right thyroid lobe showing a solid nodule with scattered calcifications suggestive of cancer. FNA biopsy results suggested medullary thyroid carcinoma, which was confirmed at thyroidectomy.
Fine needle aspiration

Practice guidelines of
American Thyroid Association
and
National Comprehensive Cancer Network

FNA should be used as the initial diagnostic test because of its superior diagnostic reliability and cost effectiveness before thyroid scintigraphy and ultrasonography.
Fine needle aspiration

- Benign – 70%
- Malignant – 5%
- Suspicious – 10%
  - Follicular
  - Hurthle cell
  - Papillary
- Unsatisfactory – 15%

Fine needle aspiration

For diagnostic specimens:

<table>
<thead>
<tr>
<th>Feature</th>
<th>Mean</th>
<th>Range</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity, %</td>
<td>83</td>
<td>65–98</td>
<td>Likelihood that patient who has disease has positive test results</td>
</tr>
<tr>
<td>Specificity, %</td>
<td>92</td>
<td>72–100</td>
<td>Likelihood that patient without disease has negative test results</td>
</tr>
<tr>
<td>Positive predictive value, %</td>
<td>75</td>
<td>50–96</td>
<td>Fraction of patients who have positive test who have disease</td>
</tr>
<tr>
<td>False-negative rate, %</td>
<td>5</td>
<td>1–11</td>
<td>FNA negative; histology positive for cancer</td>
</tr>
<tr>
<td>False-positive rate, %</td>
<td>5</td>
<td>0–7</td>
<td>FNA positive; histology negative for cancer</td>
</tr>
</tbody>
</table>

Abbreviation: FNA, fine-needle aspiration.


Gharib, H. Thyroid nodules: clinical importance, assessment, and treatment. Endocrin Metab Clin N Am
Fine needle aspiration of the thyroid and correlation with histopathology in a contemporary series of 240 patients

- Frozen section failed to diagnose follicular ca
- Age, sex, history of rads, number of nodules all failed to indicate high risk
- Nodule size >2cm was only factor to confer increased risk of malignancy

<table>
<thead>
<tr>
<th>Histopathologic diagnoses in 100 patients with indeterminate fine-needle aspiration biopsy (FNA) results</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. patients (%)</td>
</tr>
<tr>
<td>Follicular neoplasm</td>
</tr>
<tr>
<td>Total no. patients</td>
</tr>
<tr>
<td>Malignant on histopathology</td>
</tr>
<tr>
<td>Papillary</td>
</tr>
<tr>
<td>Follicular</td>
</tr>
<tr>
<td>Hurthle cell</td>
</tr>
<tr>
<td>Benign on histopathology</td>
</tr>
<tr>
<td>Multinodular goiter</td>
</tr>
<tr>
<td>Follicular adenoma</td>
</tr>
<tr>
<td>Chronic thyroiditis</td>
</tr>
<tr>
<td>Hurthle cell adenoma</td>
</tr>
<tr>
<td>Colloid nodule</td>
</tr>
</tbody>
</table>

* Incidental papillary thyroid carcinoma was reported in 5 patients with follicular adenoma and 1 patient with chronic thyroiditis.
† Incidental follicular thyroid carcinoma was reported in the contralateral thyroid lobe.
### Staging and risk assessment

<table>
<thead>
<tr>
<th>System</th>
<th>Group</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGES</td>
<td>Mayo Clinic, Rochester</td>
<td>Hay et al. (1987)</td>
</tr>
<tr>
<td>TNM</td>
<td>International Union Against Cancer</td>
<td>Hermanek (1987)</td>
</tr>
<tr>
<td>AMES</td>
<td>Lahey Clinic, MA</td>
<td>Cady &amp; Rossi (1988)</td>
</tr>
<tr>
<td>DAMES</td>
<td>Karolinska Hospital, Sweden</td>
<td>Pasieka et al (1992)</td>
</tr>
<tr>
<td>MACIS</td>
<td>Mayo Clinic, Rochester</td>
<td>Hay et al. (1993)</td>
</tr>
</tbody>
</table>

A, age; G, grade; E, tumor extent (local invasion, **distant mets**); S, size; T, tumor size; N, nodal involvement; M, mets; D, DNA ploidy; C, completeness of resection; I, local invasion
## Extent of resection

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Removal of</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partial</td>
<td>Nodule + margin of nl tissue</td>
<td>Benign lesions</td>
</tr>
<tr>
<td>Subtotal</td>
<td>More than ½ thyroid gland and isthmus</td>
<td>Benign lesions</td>
</tr>
<tr>
<td>Lobectomy</td>
<td>One entire lobe and isthmus</td>
<td>Initial treatment for indeterminate nodules?</td>
</tr>
<tr>
<td>Near total</td>
<td>Lobectomy, isthmectomy and subtotal resection contralateral lobe with &lt;10% remnant</td>
<td>Malignancy</td>
</tr>
<tr>
<td>Total</td>
<td>Both lobes and isthmus</td>
<td>Malignancy</td>
</tr>
</tbody>
</table>
Benign lesions

Clinical and ultrasound follow-up every 1-2 years in absence of:

- Worrisome PE findings
  - Fixation
  - Cervical lymphadenopathy
- Ipsilateral RLN palsy
- Rapid enlargement
- Airway/esophageal compromise
- Unacceptable cosmesis
Malignant lesions

• 98% are well differentiated

→ Follicular
  • Papillary thyroid carcinoma + variants
  • Follicular thyroid carcinoma
  • Hurthle cell carcinoma

→ Parafollicular
  • Medullary thyroid carcinoma

• Remainder are undifferentiated tumors, lymphoma, or metastases
Differentiated Thyroid Carcinoma

Why thyroidectomy?

No prospective randomized trial

Restrospective analysis:

- Mazzaferri et al., Armed Forces data of 576 pts with papillary thyroid cancer and median follow up >10yrs
  Recurrence rates **19.2%** vs **10.9%** (p<0.01) for lobectomy vs. total thyroidectomy
  Cause specific mortality 1.5% and 0.6% (p>0.05)

- Grant et al., MACIS scoring for papillary thyroid cancer with median follow up >22 yrs
  No significant difference in mortality or distant mets
  Local recurrence and nodal mets after lobectomy **14% & 19%** vs. **2% & 6%** after total thyroidectomy (p<0.0001)
Differentiated Thyroid Carcinoma

Why thyroidectomy?

1. Lower recurrence rates
Lower recurrence

- Large retrospective analyses by Mazzaferri, Hay, DeGroot
  - 5-10% recurrence rate in opposite lobe
  - long term recurrence 30% (lobectomy)
  - long term recurrence 1% (NTT + RAI)
- 30% of pts with recurrence will die from the disease, 50% if in central neck
- Highest frequency of pulmonary mets
  - 11% for lobectomy
  - 1.3% for TT + RAI

Differentiated Thyroid Carcinoma

Why thyroidectomy?

1. Lower recurrence rates
2. Multifocal disease
Multifocal disease

• Papillary carcinoma bilateral in 30-85%
• Follicular carcinoma multicentric in 23%
• Individual tumors may arise in a background of genetic susceptibility, NOT always via intraglandular spread


Differentiated Thyroid Carcinoma

Why thyroidectomy?

1. Lower recurrence rates
2. Multifocal disease
3. Safety of thyroidectomy
Safety of thyroidectomy

Cross sectional analysis of 5,860 pts who underwent thyroid surgery in Maryland

- Highest vol surgeons showed equivalent complication rates for lobectomy vs. TT
- Length of stay and hospital charges decreased with increasing surgical experience

<table>
<thead>
<tr>
<th>Outcome, by surgeon volume group (cases/yr)</th>
<th>Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lobectomy</td>
</tr>
<tr>
<td>Complications (%)</td>
<td>7.7</td>
</tr>
<tr>
<td>1–9 cases</td>
<td></td>
</tr>
<tr>
<td>10–29 cases</td>
<td>5.8</td>
</tr>
<tr>
<td>30–100 cases</td>
<td>5.6</td>
</tr>
<tr>
<td>&gt;100 cases</td>
<td>6.2 ref</td>
</tr>
<tr>
<td>Length of stay (Days)</td>
<td>1.7***</td>
</tr>
<tr>
<td>1-9 cases</td>
<td></td>
</tr>
<tr>
<td>10–29 cases</td>
<td>1.6***</td>
</tr>
<tr>
<td>30–100 cases</td>
<td>1.5**</td>
</tr>
<tr>
<td>&gt;100 cases</td>
<td>1.3 ref</td>
</tr>
<tr>
<td>Hospital charges ($)</td>
<td>3,652</td>
</tr>
<tr>
<td>1–9 cases</td>
<td></td>
</tr>
<tr>
<td>10–29 cases</td>
<td>3,428***</td>
</tr>
<tr>
<td>30–100 cases</td>
<td>3,313***</td>
</tr>
<tr>
<td>&gt;100 cases</td>
<td>3,718 ref</td>
</tr>
</tbody>
</table>

Outcomes adjusted for surgeon volume and patient age, comorbidities, hospital volume, and time period.

ref = reference category.

*P < 0.05.

**P < 0.01.

***P < 0.001.

Differentiated Thyroid Carcinoma

Why thyroidectomy?

1. Lower recurrence rates
2. Multifocal disease
3. Safety of thyroidectomy
4. Radioactive iodine
Radioactive Iodine

- Normal thyroid tissue more iodine avid than DTC
- Removal of excess thyroid tissue decreases dose of $^{131}$I, increases likelihood of successful ablation
- RAI ablates residual thyroid and metastatic disease in 75% pts after NTT or TT
Differentiated Thyroid Carcinoma

Why thyroidectomy?

1. Lower recurrence rates
2. Multifocal disease
3. Safety of thyroidectomy
4. Radioactive iodine
5. Thyroglobulin surveilance
6. Risk of de-differentiation – 1%
7. Thyroid suppression therapy
The suspicious thyroid nodule

**Why thyroidectomy?**

- No definitive pre-operative staging
- Intra-OP frozen section only helpful for PTC
- Majority of suspicious PTC will be malignant
- Significant proportion of disease is multifocal
- Even if nodule is benign, 5-10% will develop contralateral nodules
- Even in lowest risk DTC, anything less than NTT shows decreased survival
References


Another Video Captured by Blackdog