Making Sense of Thyroid Nodules in Primary Care

Friday, Nov 23, 2012
Question 1

42 y/o male with no active medical problems. During a periodic health exam you find a thyroid nodule.

What information do you want from the patient?

1) Family history
2) Recent growth of nodule
3) Vocal changes
4) All of the above

Answer: 4
Question 2

What is the next step in laboratory work up?
1) Serum thyroglobulin
2) TSH
3) T4 and T3
4) All of the above

Answer: 2
Question 3

If the TSH is normal, what is the next step?

1) Radioactive thyroid scan
2) Thyroid ultrasound
3) Fine needle aspiration (FNA)
4) Refer to surgeon

Answer: 2
Question 4

40 years old female with 2cm thyroid nodule. What result on FNA would be most useful preoperatively?

1) Colloid
2) Hurthle cells
3) Follicular cells
4) Papillary

Answer: 4
Question 5

54 female with 1.8 cm lesion in left thyroid on ultrasound. Normal TSH. FNA: 75% Hurthle cells. What is next step in management?

1) Total thyriodectomy
2) Left hemithyroidectomy
3) I 131 ablation
4) FU U/S in 6 month

Answer: 2
Question 6

10 year old with 2cm left thyroid lesion at lower lobe. What the best management?

1) Total thyriodectomy
2) Left hemithyroidectomy
3) I-131 ablation
4) Follow up ultrasound in 6 month

Answer: 2
Question 7

Which is the most common histological type of thyroid cancer?

1) Hurthle cell
2) Follicular
3) Papillary
4) Medullary

Answer: 3
A 35 y/o female had a hemithyroidectomy for a well differentiated thyroid cancer and has been discharged to your care from the thyroid clinic on replacement L-T4. Regarding follow-up care, which of the following are not required?

1) Thyroglobulin
2) TSH
3) Ultrasound
4) Neck examination

Answer: 1
Thyroid Nodule

- 4%-7% of adults in North America have palpable thyroid nodules (Mazzaferri, 1993, Vander, 1968)
- 19-60% population have U/S detectable nodules
- After childhood radiation-30%-50% chance of a thyroid nodule to be malignant (Goldman, 1996)
- Benign nodules occur most frequently in women of 20-40 years (M:F=1:5) (Campbell, 1989)
- 5%-10% of these are malignant (Campbell, 1989)
- Men have a higher risk of malignant nodule
Canadian Cancer Statistics 2010

- 7th most common non-skin cancer
- 1.3% of all cancers in males & 4.7% in females
- Accounts for 0.2% of all cancer deaths in males and 0.3% in females
- 1:81.3 women will develop thyroid cancer & 1:1160 will die from it
Risk Factors

• History of thyroid cancer in $\geq 1^{st}$ degree relatives
• Jewish descent
• History of external beam radiation/ionizing radiation in childhood or adolescence (2%/yr)
• History of FAP and Cowden’s syndrome
• Hashimoto’s thyroiditis
• Male gender
• Iodine intake
• RET proto-oncogene mutation
Classification of Malignant Thyroid Neoplasms

- Papillary carcinoma
  - Encapsulated
  - Classical
  - Follicular variant
  - Tall cell
  - Diffuse sclerosing
- Follicular carcinoma
  - Minimally invasive
  - Overtly invasive
- Hurthle cell carcinoma
- Anaplastic carcinoma
  - Giant cell
  - Small cell
- Medullary Carcinoma
- Miscellaneous
  - Lymphoma
  - Sarcoma
  - Squamous cell carcinoma
  - Mucoepidermoid carcinoma
  - Clear cell tumors
  - Plasma cell tumors
- Metastatic
  - Direct extension
  - Kidney
  - Colon
  - Melanoma
# Histological Types

<table>
<thead>
<tr>
<th></th>
<th>Papillary</th>
<th>Follicular</th>
<th>Hurthle Cell</th>
<th>MTC</th>
<th>ATC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Frequency</strong></td>
<td>70-80%</td>
<td>10-15%</td>
<td>3-4%</td>
<td>4-5%</td>
<td>1-4%</td>
</tr>
<tr>
<td><strong>Mean Age</strong></td>
<td>35 yrs</td>
<td>39 yrs</td>
<td>61 yrs</td>
<td>SMTC-50</td>
<td>71 yrs</td>
</tr>
<tr>
<td><strong>F:M</strong></td>
<td>4:1</td>
<td>2:1-4:1</td>
<td>2:1</td>
<td>3:2</td>
<td>1.5-2:1</td>
</tr>
<tr>
<td><strong>Neck LN</strong></td>
<td>33-45%</td>
<td>5-20%</td>
<td>30%</td>
<td>50%</td>
<td>25%</td>
</tr>
<tr>
<td><strong>Metastasis</strong></td>
<td>10%</td>
<td>25%</td>
<td>35%</td>
<td>5-15%</td>
<td>15-50%</td>
</tr>
<tr>
<td><strong>10 yr surv.</strong></td>
<td>93%</td>
<td>85%</td>
<td>76%</td>
<td>75%</td>
<td>&lt; 10%</td>
</tr>
</tbody>
</table>
TCSS Based on Pathology (N= 2310)

Pathak et al 2012

p<0.001

Proportional Cause Specific Survival

Months After Diagnosis

HISTOLOGICAL TYPE
- PAPILLARY
- FOLLICULAR
- HURTHLE CELL VARIANT
- POORLY DIFFERENTIATED
- MEDULLARY
- ANAPLASTIC

Pathak et al 2012
Presenting Symptoms

- 50% asymptomatic; < 1% hyperthyroid
- Solitary thyroid nodule
- Rapidly enlarging goitre
- Stridor due to tracheal compression
- Hemoptysis- Tracheal invasion
- Dysphagia- Esophageal compression
- Hoarseness - Vocal cord palsy
- Cervical lymphadenopathy
- Metastases
SOLITARY THYROID NODULE

OBSERVE

Enlarged 13%

Reduced 23%

Same 34%

NP; US + 19%

Disappear 11%

Kuma et al, WJS 1992
Features of Malignancy

- Male patient
- Age < 14 years or > 65 years
- Past history of ionizing radiation
- Past/Family history of thyroid cancer
- Rapid/ Sudden increase in size
- Nodule > 4 cm in size, solid/partly cystic
- Clinically hard, fixed or recurrent nodule
- Pressure effects & vocal cord paralysis
- Neck node metastases
- Distant metastases
Ultrasound

- Best method of determining the volume of a nodule (Rojeski, 1985)
- 90% accuracy in categorizing nodules as solid, cystic, or mixed (Rojeski, 1985)
- Non-invasive, inexpensive & widely available
- Helps to assess difficult necks & localize nodule
- Directs biopsy for difficult to palpate or deep-seated nodules
- Long term follow-up of thyroid nodules
Ultrasound

- **Discern solid/cystic & dominant/solitary nodules**
- **Cervical lymphadenopathy (pre-operative staging)**
  - Rounded shape, Hypoechogenicity, Loss of fatty hilus, Peripheral vascularity, Calcification, Cystic change

- **Identify features of malignancy**
  - Microcalcifications
  - Hypoechogenecity of a solid nodule
  - Intranodular hypervascularity
  - Taller than wide on transverse view
  - Infiltrative margins/ Extrathyroidal extension

(Lyschick et al, *Radiology* 2005)
<table>
<thead>
<tr>
<th><strong>Sonographic/clinical features</strong></th>
<th><strong>Recommended nodule threshold size for FNA</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High-risk history</strong></td>
<td></td>
</tr>
<tr>
<td>Nodule WITH suspicious features</td>
<td>&gt;5mm (A)</td>
</tr>
<tr>
<td>Nodule WITHOUT suspicious features</td>
<td>&gt;5mm (I)</td>
</tr>
<tr>
<td><strong>Abnormal cervical lymph nodes</strong></td>
<td>All (A)</td>
</tr>
<tr>
<td><strong>Microcalcifications present in nodule</strong></td>
<td>≥1cm (B)</td>
</tr>
<tr>
<td><strong>Solid nodule</strong></td>
<td></td>
</tr>
<tr>
<td>AND hypoechoic</td>
<td>&gt;1cm (B)</td>
</tr>
<tr>
<td>AND iso- or hyperechoic</td>
<td>≥1–1.5cm (C)</td>
</tr>
<tr>
<td><strong>Mixed cystic–solid nodule</strong></td>
<td></td>
</tr>
<tr>
<td>WITH any suspicious features</td>
<td>≥1.5–2cm (B)</td>
</tr>
<tr>
<td>WITHOUT suspicious features</td>
<td>≥2.0 cm (C)</td>
</tr>
<tr>
<td><strong>Spongiform nodule</strong> (multiple microcystic components)</td>
<td>≥2.0cm (C)</td>
</tr>
<tr>
<td><strong>Purely cystic nodule</strong></td>
<td>FNA not indicated (E)</td>
</tr>
</tbody>
</table>

ATA Guidelines 2010
• An air-filled 10 cc syringe with its plunger already retracted is attached to the 25-gauge needle.
• The nodule is immobilized with the index and middle fingers or thumb of the other hand.
• The needle is moved back & forth several times with a rapid, gentle, stabbing motion.
• The needle contents are immediately expelled onto clean glass slides for thin, evenly spread smears.
• At least 2, preferably, 3 punctures be performed.
• The presence of at least six follicular cell groups, each containing 10–15 cells derived from at least two aspirates of a nodule
THYROID NODULE

FNA

- Carcinoma 4% (1-10%)
  - 100% malignant
- Suggestive 10% (5-23%)
  - 20-30% malignant
- Benign 70% (53-90%)
  - <1% malignant
- Inadequate 17% (15-20%)
- Cyst 15-25%

Hossein and Goellner (1993)

Sensitivity: 65-98%  Specificity: 72-100%  Accuracy: 70-90%

False positive: 3 - 6%  False negative: 1 - 6% (Mazzeferri, 1993)
FNA: Bethesda Classification

<table>
<thead>
<tr>
<th>Category</th>
<th>Risk Of Malignancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-diagnostic</td>
<td>Unsatisfactory</td>
</tr>
<tr>
<td>Benign</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Atypia of undetermined significance*</td>
<td>5-10%</td>
</tr>
<tr>
<td>Neoplasm (Suspicious for neoplasm)</td>
<td>20-30%</td>
</tr>
<tr>
<td>Suspicious for malignancy</td>
<td>50-75%</td>
</tr>
<tr>
<td>Malignant</td>
<td>100%</td>
</tr>
</tbody>
</table>

*Indeterminate follicular lesions, R/O neoplasm, atypical follicular lesion, cellular follicular lesion

Layfield LJ et al  2009
PTC- FNA & Histology
Thyroid Cyst

- 15-25% of all thyroid nodules are cystic
- Simple cysts- re-aspirate with U/S guidance (3m)
- Haemorrhagic colloidal nodules
- Cystic parathyroid tumors
- Necrotic papillary cancers (15%)
- Recurrent cystic benign thyroid nodules should be considered for surgical removal or PEI based on compressive symptoms & cosmetic concerns

ATA Guidelines 2010
Thyroid Nodule

FNAC

Non Diagnostic

Repeat FNAC with USG

Core needle biopsy for Lymphoma, ATC

Surgery (solid / partially cystic)
THYROID NODULE → FNAC → Benign → F/U U/S 6-18 mths X 3-5 yrs

- Resolution
- Stable or enlarging
  - ? TSH suppression
  - Repeat FNA/Surgery
Outcome of TSH Suppression

- “Benefit” or “lack of benefit” not clear
- Cystic lesion does not reduce in size
- 16% of malignant nodules are suppressible
- Only 21% of benign nodules are suppressible
- Provides little use in distinguishing benign from malignant nodules. *(Geopfert, 1998)*

- Hence current recommendations: observation alone *(Castro et al 2000)*
THYROID NODULE

FNAC

Atypia of undetermined significance

Repeat FNA in 3-6 months

Molecular markers → Suspicious

Surgery
Surgery

H/o radiation, Rapid growth, Compression, Hurthle cell neoplasm

THYROID NODULE

FNAC

Neoplasm

No significant clinical features

Close observation with repeat FNAC, Scan

Surgery
Follicular Adenomas

- Colloidal nodule and macro-follicular adenoma: No malignant potential
- Micro-follicular – 5%
- Hurthle cell adenoma – 5 – 15%
- Embryonal adenoma – 25%
Radioactive Thyroid Scan

• Radioactive scan is **not** indicated in all clinically euthyroid patients with a STN

• Malignancy is found in 17% of cold nodules, 13% of warm nodules and 4% of hot nodules (Campbell and Pillsbury 1989)

• Thyroid scan is used to assess residual thyroid following previous surgery

• I-123 or Tc-99 used
Time to demonstrate physical exam and FNA
SURGICAL OPTIONS

Stell and Maran 2002
Management of Primary WDTC

Hemi thyroidectomy
Low risk-Age <45 years
Size< 1cm
Intrathyroidal
Unilateral
Incidentaloma/microca
Minimally invasive FTC

Total thyroidectomy
High risk-Age >45 years
Size > 1cm
Extra-thyroidal spread
Bilateral-Prior radiation
Metastasis
Widely invasive FTC

Completion thyroidectomy usually offered for > 1cm WDTC
Rationale for Total Thyroidectomy

- 30%-87.5% of papillary carcinomas involve opposite lobe *(Hirabayashi, 1961, Russell, 1983)*
- 7%-10% develop recurrence in opposite lobe *(Soh, 1996)*
- Lower recurrence rates, possibly increased survival *(Mazzaferri, 1991)*
- Facilitates earlier detection of recurrent or metastatic carcinoma with radio-iodine & thyroglobulin *(Soh, 1996)*
- Facilitates treatment of recurrent or metastatic carcinoma with radio-iodine *(Soh, 1996)*
- Residual DTC can dedifferentiate to ATC
What problems do you anticipate?

- Hemorrhage
- Wound infection
- Superior laryngeal nerve injury
- VC paralysis (1-2%)- Unilateral/Bilateral
- Hypocalcemia- Transient /Permanent (3-5%)
- Hypothyroidism
- Pneumothorax (uncommon)
Landmarks for RLN

- Cricothyroid joint
- Berry’s ligament
- Zuckerkanndl’s tubercle
- Inferior thyroid artery
- Tracheo-esophageal groove
## Anatomy of RLN

<table>
<thead>
<tr>
<th></th>
<th>Right</th>
<th>Left</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length in cm</td>
<td>5-6</td>
<td>12</td>
</tr>
<tr>
<td>Non recurrent Laryngeal Nerve</td>
<td>0.5%</td>
<td>0.04%</td>
</tr>
<tr>
<td>Single trunk divides into branches</td>
<td>30.1%</td>
<td>30.6%</td>
</tr>
<tr>
<td>Runs deep to Inferior thyroid Art.</td>
<td>25%</td>
<td>50%</td>
</tr>
<tr>
<td>Runs through the branches of ITA</td>
<td>50%</td>
<td>35%</td>
</tr>
<tr>
<td>Runs superficial to ITA</td>
<td>25%</td>
<td>15%</td>
</tr>
</tbody>
</table>
Factors Contributing to RLN Palsy

- Abnormal anatomy
- Revision surgeries (3.6% versus 0.6%)
- Surgeon inexperience (1.4%-0.6%)
- Extent of resection (1.3% versus 0.7%)
- Nature of disease (0.2%– 25.0%)
  - Malignancy
  - Substernal goiter

(Dralle H et al, Surgery 2004)
Follow up

• **Loco-regional**
  Examination of the neck at least once/year

• **Distant Metastasis**

• **Annual blood work**
  Serum TSH to confirm suppression
  Serum thyroglobulin (Tg)/ Anti Tg Antibodies

• **Imaging** - ?Neck ?? Distant Metastasis
What is the role of TSH suppression?

- TSH suppression beneficial in Ca thyroid
- 27% reduction in risk of adverse outcome
- **High risk pts:** Total TSH suppression
- **Low risk pts:** Partial TSH suppression?
- **Careful monitoring in**
  - Post-menopausal females
  - Elderly
  - Pre-existing cardiac ailment
How much thyroxine to give?

Starting Dose: 2 µgm / kg / day (age < 60 years)
1.6 – 1.8 µgm / kg / day (age > 60 years)

Normal: 0.4– 4.6 mU/L
Partial Suppression: 0.1 – 0.4 mU/L
Total Suppression: < 0.1 mU/L
Points to remember in WDTC

• Primary treatment is surgery. Extent of surgery varies
• Goal of surgery is safe resection of all gross disease
• In North America, total thyroidectomy is usually recommended for >1 cm WDTC
• Ipsilateral hemithyroidectomy with TSH suppression is an alternative for low risk WDTC
• Elective node dissection is usually not needed
• Preservation of functioning RLN and parathyroids
• Metastatic DTC are aggressively treated
Points to remember

• TC represent diverse histology and behavior
• Age is an important prognostic factor
• Risk stratification important in management
• Total thyroidectomy recommended for >1 cm
• Elective node dissection is not needed in DTC
• Metastatic DTC are aggressively treated
• Suppress TSH in DTC & replace T4 in MTC
• 75-80% LN micro metastasis in clinical MTC
Thank You!