EVALUATION OF THYROID NODULES IN PRIMARY CARE

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DISCLOSURES

• PA Sadler does not intend to discuss the use of any off-label use/unapproved drugs or devices
• Employee of Janssen Pharmaceuticals
• PA Sadler has no conflicts of interest related to this topic

OBJECTIVES

• Review the typical presentation of thyroid nodules in clinical practice
• Identify what diagnostic tests to order to work up a suspected thyroid nodule
• Understand the prognostic significance of different ultrasound findings and their implications for further testing/referral
A 2.0 CM CYSTIC AND SOLID NODULE WITH SPONGIFORM APPEARANCE IS MORE SUSPICIOUS FOR THYROID CA THAN A 2.0 CM NODULE THAT IS UNIFORMLY SOLID (TRUE OR FALSE)

1. True
2. False

Correct answer is 2

A 35 YO ASYMPTOMATIC FEMALE IS FOUND TO HAVE A SOLITARY 2.0 CM SOLID, MARKEDLY HYPOECHOIC NODULE WITH MICROCALCIFICATIONS ON THYROID ULTRASOUND. THE TSH IS NORMAL. THE MOST APPROPRIATE NEXT STEP WOULD BE TO:

1. Reassure, repeat US 6-12 months
2. Order an FNA
3. Refer for surgery
4. Order thyroid uptake and scan

Correct answer is 2

THYROID ANATOMY
THYROID NODULES DON'T USUALLY PRESENT LIKE THIS

THYROID NODULES USUALLY PRESENT LIKE THIS
• Found incidentally on other imaging
• Carotid US
• CT/MRI of neck
• Picked up during routine physical exam
• Patient notices lump in neck

THYROID NODULE/CA OVERVIEW
• Using US 19 - 68% of randomly selected adults have thyroid nodules
• More common in women and elderly
• 2009 - 37,200 cases of thyroid cancer diagnosed
• 2014 - 63,000 cases of thyroid cancer diagnosed
• Mortality rates unchanged despite the increase in thyroid cancer incidence

Causes of Thyroid Nodules

- Benign nodular goiter
- Chronic lymphocytic thyroiditis (Hashimoto’s)
- Simple or hemorrhagic cysts
- Toxic autonomous nodule
- Follicular neoplasm
- Subacute thyroiditis
- Papillary carcinoma – most common
- Follicular carcinoma
- Medullary carcinoma
- Anaplastic carcinoma
- Primary thyroid lymphoma
- Metastatic tumors

CLINICAL FACTORS SUGGESTING INCREASED RISK OF MALIGNANT POTENTIAL

- History of head and neck irradiation (<25 yrs ago)
- Family history of MTC, MEN 2, PTC, Familial Polyposis coli, Cowden dz, Gardner syndrome
- Age <50, >70
- Female sex
- Firm or hard consistency
- Fixed nodule
- Palpable cervical adenopathy
- Persistent dysphonia, dysphagia, or dyspnea

HOW TO WORK UP THYROID NODULES

1) Check TSH
   - If low consider I-123 uptake or scan to rule out toxic nodule(s). (Check FT4, T3)
   - If normal or high-normal order US exam. (For high TSH check FT4, TSH if necessary)
   - A single, non-stimulated serum calcitonin measurement if medullary thyroid carcinoma is suspected due to FNA results or + family history (MEN or MTC).
2) Order Thyroid US exam. Based on results:
   - Reassure patient – no follow-up needed
   - Reassure patient – arrange follow-up exam
   - Refer for FNA
3) Refer for FNA if indicated. Based on results:
   - Arrange appropriate referral or follow-up
   - Refer for Surgery
THYROID NODULE WORK-UP
(ATA GUIDELINES)

ULTRASOUND FACTORS SUGGESTING MALIGNANCY
• Taller than wide
• Microcalcifications
• Irregular margins
• Solid – marked hypoechoicinity
• Suspicious cervical lymphadenopathy
• Taller than wide in transverse view
• Extra-capular extension
• Interrupted rim calcification
• Location of Nodule?
  • Upper pole

QUALITY OF THE ULTRASOUND
• Experience varies widely: What to look for?
  • Documented details of nodule characteristics
    • Size, location, solid, cystic, mixed
    • Hypoechoic/hyperchoic
    • Margins, calcifications, vascularity
    • Taller than wide, extra-thyroidal extension
  • Mention of presence or absence of adenopathy
  • Clear report with guidance regarding next steps – [FNA, repeat US, no further f/u needed]
  • Follow-up – a rapidly growing or changing nodule is more suspicious (change in US characteristics is more prognostic than change in size)
PATTERN APPROACH (ATA)

ACR – TI-RADS

FINE NEEDLE ASPIRATION

(Ultrasound guided FNA is standard of care)
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(Ultrasound guided FNA is standard of care)

• Best means of evaluating a thyroid nodule.
• For solitary nodule the diagnostic procedure of choice
• If multiple nodules, choose high risk nodules for sampling based on suspicious characteristics, not size
• ACR – recommends sampling not more than 2 nodules with the most suspicious findings based on point totals
• Dependent on an experienced cytopathologist

THYROID US BASICS

• Normal
  • Transverse

THYROID US BASICS

• Normal
  • Long axis
CASE 1

- A 40-yr-old female had an incidental finding of a thyroid nodule on a CT exam of the neck after a MVA. An US was ordered and found a 1-cm cystic nodule in the left upper pole. No cervical adenopathy was detected, and recent TSH was WNL.

PATTERN APPROACH (ATA)

ACR – TI-RADS

Source: ACR Nodule Report 2017
CASE 1

• Pure Cystic Nodule
  • ATA: Benign, < 1% Risk
  • No FNA (but may aspirate fluid if symptomatic)
  • TI-RADS = 0 pts (No FNA)
  • No follow-up recommended
  • Reassure patient

CASE 2

• 64 yo female was found to have a lump on physical exam in the left thyroid lobe. TSH was normal. Thyroid US revealed a 2.3x1.4x1.8 cm partially cystic and solid nodule with spongiform appearance. No cervical adenopathy was identified.

PATTERN APPROACH (ATA)
CASE 2

- Spongiform Nodule
  - ATA: Very low suspicion, < 3% Risk
  - FNA if ≥ 2.0 cm
  - TI-RADS = 3 pts (mildly suspicious)
  - FNA if ≥ 2.5 cm
  - Follow-up if ≥ 1.5 cm
  - Can send for FNA based on ATA criteria or arrange repeat US in 1, 3, 5 yrs based on ACR criteria and FNA if ≥ 2.5 cm at any follow-up

NODULE CHARACTERISTICS

- ATA: Solid hypoechoic, regular margins
- Intermediate suspicion
- 10-20%
- FNA ≥ 1 cm

- TI-RADS = 4 pts
- (FNA if ≥ 1.5 cm)
ATA: FNA FOR LOW RISK PATIENTS W/O ABNORMAL LNS

• Solid Hypoechoic nodule = intermediate risk 10-20%
• If < 1 cm can reassure and repeat US in 12 months, then if 1 cm and/or more importantly, develops new suspicious features → FNA.
• If repeat US are stable for several years, then may no longer need to follow this nodule
• TI-RADS = 4 pts moderately suspicious (FNA if ≥ 1.5 cm) Follow-up. Repeat US at 1, 3 and 5 yrs.

NODULE CHARACTERISTICS

• ATA: Solid hypoechoic w/Microcalcifications
  High suspicion
  > 70-90%
  FNA if ≥ 1 cm
  (punctate echogenic Foci)
  TI-RADS = 7 pts (Highly Suspicious)
  (FNA if ≥ 1 cm)

NODULE CHARACTERISTICS

• ATA: Solid iso/hyperechoic
  • Regular Margins –
  • Low suspicion
  • 5-10%
  • FNA if ≥ 1.5 cm
  • TI-RADS = 3 pts
  • Mildly suspicious
  • (FNA ≥ 2.5 cm)
NODULE CHARACTERISTICS

• ATA: Solid Hypoechoic
• Lobulated Margins
• Calcifications
• High suspicion
• >70-90% Risk
• FNA if ≥ 1 cm
• TI-RADS = 9 pts
• Highly suspicious
• (FNA ≥ 1 cm)

NODULE CHARACTERISTICS

• ATA: Solid Hypoechoic-Taller than Wide (transverse view)
• High suspicion
• >70-90% Risk
• FNA ≥ 1 cm
• TI-RADS = 7 pts
• Highly suspicious
• (FNA > 1 cm)

NODULE CHARACTERISTICS

• ATA: Extra-capsular invasion
• High suspicion
• >70-90% Risk
• FNA ≥ 1 cm
• TI-RADS = 7 pts
• Highly suspicious
• (FNA ≥ 1 cm)
NODULE CHARACTERISTICS
• Lumpy Bumpy Thyroid – benign pattern
• No need for FNA

LYMPH NODE CHARACTERISTICS
• Normal
  • Transverse view
  • A/T ratio > 2
• Abnormal
  • A/T ratio < 2

CASE 3: KERI
• 22 yo female presents with left sided nodule on routine exam
• Ultrasound order by PCP: 1.8 cm solid hypoechoic nodule in the left lower pole with irreg. margins
• On exam, the left sided nodule is firm, non-tender
• TSH and TPO antibodies are normal
• Here in my office with very anxious mother
CASE: KERI

HOW WOULD YOU PROCEED?

• 1) refer immediately to surgeon
• 2) US guided FNA of left thyroid nodule
• 3) Observe and repeat US in 6 months
• 4) Give thyroid hormone to suppress the nodule and repeat US in 6 months

Correct answer: 2

ACR – TI-RADS
FNA FOR LOW RISK PATIENTS W/O ABNORMAL LNS

- ATA: Hypoechoic solid ≥ 1.0 cm + irreg. margins
- High suspicion pattern (70-90% risk)
- FNA if ≥ 1.0 cm
- TI-RADS = 6 pts – moderately suspicious (FNA if > 1.5 cm)

CASE 3: KERI

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- FNA: Suspicious for Papillary Thyroid Carcinoma
- Suspected metastatic lymph nodes throughout left neck
- Plan: Total Thyroidectomy with left neck dissection, postoperative RAI and total body scan
THYROID CANCER

- Five types
  - Papillary: 60-80% of all cases; slow growing
  - Follicular: 15-30%. More aggressive than papillary
  - Medullary: 2-10%. Familial, associated with MEN II
  - Anaplastic: (rare) Most aggressive of all; 20% five year survival. Differentiates into small and giant cell. Death within 6 months if giant cell
  - Thyroid Lymphoma: 4-10% usually women over 50 with Hashimoto’s thyroiditis. Rapid growing neck mass

CASE 4: RICK

- 42 yo male 2.5 cm nodule in left thyroid lobe
  - Solid hypoechoic; well defined border; no other suspicious features
  - Visible, firm, moves well
  - FNA 4 years ago = benign cytology
  - Yearly US exams stable
  - Pt. with young children, continues to worry
  - Last US one year ago - no change
WHAT WOULD YOU DO NEXT?

1. Repeat US
2. Repeat US guided FNA
3. Refer for surgery
4. Reassure – repeat US in one year

Correct answer: 2

BENIGN CYTOLOGY HAS LOW RISK FOR MALIGNANCY

<table>
<thead>
<tr>
<th>Cytology Type</th>
<th>Risk of Malignancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-diagnostic</td>
<td>1-4%</td>
</tr>
<tr>
<td>Benign</td>
<td>0-3%</td>
</tr>
<tr>
<td>AUS/FLUS</td>
<td>5-15%</td>
</tr>
<tr>
<td>Follicular neoplasm</td>
<td>15-30%</td>
</tr>
<tr>
<td>Suspicious for malignancy</td>
<td>60 to 75%</td>
</tr>
<tr>
<td>Malignant</td>
<td>97.99%</td>
</tr>
</tbody>
</table>

False negative rate 5% (range 14-31%)

FOLLOW-UP OF CYTOLOGICALLY BENIGN NODULES

Growth = > 50% increase in volume or > 20% increase in 2 of 3 dimensions (min 2 mm)
However growth not related to malignancy

CASE 4: RICK

• Repeat US guided FNA reveals cytology c/w papillary thyroid carcinoma
• Referred for surgical removal
• If 2 US guided FNA’s are benign the risk of malignancy is virtually zero.
  • **Always listen to the patient**

TI-RADS – FOLLOW UP OF NODULES TOO SMALL TO MEET FNA CRITERIA

• Mildly to Moderately suspicious – repeat US at 1, 3 and 5 yrs
• Highly suspicious – US yearly for 5 yrs
• Caveats – Abnormal cervical lymph nodes in the presence of a thyroid nodule dramatically increases risk of malignancy regardless of size
• ATA – Recommends repeat of FNA within a year for highly suspicious nodules with benign cytology on initial FNA.
SUMMARY

• Thyroid nodules are common and most are benign
• Initial work-up includes TSH, Ultrasound
• Identify suspicious nodules based on patterns or TI-RADS
• USG-FNA should be performed on suspicious nodules
• Follow-up determined by risk category of nodule
• Timely referral to specialist for high-risk nodules

A 2.0 cm cystic and solid nodule with spongiform appearance is more suspicious for thyroid CA than a 2.0 cm nodule that is uniformly solid (true or false)

Post Test Question 1
1. True
2. False
Correct answer is 2

A 35 yo asymptomatic female is found to have a solitary 2.0 cm solid, markedly hypoechogenic nodule with microcalcifications on thyroid ultrasound. The TSH is normal. The most appropriate next step would be to:

1. Reassure, repeat US 6-12 months
2. Order an FNA
3. Refer for surgery
4. Order thyroid uptake and scan

Post Test Question 2
1. Reassure, repeat US 6-12 months
2. Order an FNA
3. Refer for surgery
4. Order thyroid uptake and scan
Correct answer is 2
RESOURCES

- www.thyroid.org - American Thyroid Association
  2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer
- www.aace.com – American Association of Clinical Endocrinologists
  Medical Guidelines for Clinical Practice for the Diagnosis and Management of Thyroid Nodules – 2016 Update
- ACR Thyroid Imaging, Reporting and Data System (TI-RADS) / Am Coll Radiol 2017;14:587-595