ULTRASOUND EVALUATION OF HYPERPARATHYROIDISM

Endocrine University - 2016

AACE-ACE-MAYO CLINIC

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OBJECTIVES

1. Why use US for localization?
2. Review the US findings and features of parathyroid adenomas and locations
3. When to consider FNA biopsy?
4. Review the potential problems associated with biopsy and how to avoid them?
**Historical perspectives**

1850–1900  Parathyroid glands discovered Sir Owen (Indian Rhino)
1877  In man - Uppsala anatomist - Ivar Sandström
1891  Bone disease - von Recklinghausen
1900–1925  Tetany after parathyroidectomy Gley and Bothy
1925  Active gland extract purified- Collip
1925–1950s  Pathophysiology of Hyper- and hypoparathyroidism- Virchow, Erdhim and Albright
1925  Mandl first parathyroid surgery - enlarged parathyroid tumor
1929  Bone mass increase in rats - Paradox (largely ignored)
1970s  Hormone structure and synthesis.
1970s  Multichannel analyzers – led to detection of hypercalcemia fortuitously – apparent increase in incidence
1980’s – 90’s – Tc99MIBI
Minimally invasive surgeries, the pendulum is swinging back

The success of minimal invasive surgery hinges on **LOCALIZATION**
Hyperparathyroidism

- Most common cause of hypercalcemia
- 1 in 500-1000 population.
- 1.5% incidence in postmenopausal population
  - Most are “asymptomatic”
  - Detected by multi-channel chemistry screening
  - “Asymptomatic” patients may improve after surgery
- Female:Male = 3:1
- 85 – 90 % single adenoma
  - Multiple Adenomas in 2-4%
  - Remainder - Hyperplasia
WHY SHOULD ENDOCRINOLOGISTS PERFORM US FOR PARATHYROID DISEASE?

Cost & Time effective
Point of contact service – Improves quality
Single adenoma in most cases, therefore localization makes sense
Endocrinologists identify, treat and follow these patients
No radiation involved, simple equipment and it is readily available
Reasons to Perform Ultrasound in Hyperparathyroidism

• Locate parathyroid adenoma
  • Guide surgery
  • Allow Minimally Invasive Parathyroidectomy

• Identify coexisting thyroid disease
  • Thyroid nodules
  • 2-6% incidence of thyroid cancer

• Ethanol ablation in select patients
## Indications for surgery

<table>
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<tr>
<th>Parameter</th>
<th>2002</th>
<th>2009</th>
<th>2014</th>
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<tbody>
<tr>
<td>Serum calcium</td>
<td>&gt;1 mg</td>
<td>&gt;1 mg</td>
<td>&gt;1 mg</td>
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<tr>
<td>Urine calcium</td>
<td>&gt;400 mg /day</td>
<td>Not recommended</td>
<td>&gt;400 mg /day &amp; nephro-lithiasis or risk</td>
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<tr>
<td>Creatinine clearance</td>
<td>Reduction of 30% or more</td>
<td>&lt;60 ml/min</td>
<td>&lt;60 ml /min</td>
</tr>
<tr>
<td>BMD-DXA</td>
<td>T score &lt;-2.5 at any site</td>
<td>T score &lt;-2.5 Same plus previous fracture</td>
<td>T score &lt;-2.5 any site and vertebral fracture by other imaging</td>
</tr>
<tr>
<td>Age</td>
<td>&lt;50 years</td>
<td>&lt;50 years</td>
<td>&lt;50 years</td>
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US of parathyroid adenomas

- US is a localization study and therefore should not be applied prior to making a firm biochemical diagnosis of primary HPT.
- Rule out FHH (Familial hypocalciuric hypercalcemia) prior to US study by calculating urine Fractional Excretion of Urine Calcium (<1% or <0.01):
  \[
  \left( \frac{U_{\text{calcium}}}{S_{\text{calcium}}} \right) / \left( \frac{U_{\text{cr}}}{S_{\text{cr}}} \right)
  \]
BIOCHEMICAL DIAGNOSIS – Serum Calcium, PTH and Urine calcium
Essential to establish biochemical diagnosis first, prior to imaging or therapy

Establish need for therapy

Localization studies – Neck US, (TC99MIBI, 4D CT)
Surgical, ETOH ablation or medical treatment
Minimally invasive surgery

ADVANTAGES
- Most patients with PHPT have single adenomas that are easily accessible, in the vicinity of the thyroid gland
- Shortened hospital stay (same day surgery)
- Speedier recovery

DISADVANTAGES
- Requires accurate preoperative localization
- Requires intra-operative confirmation of successful removal (e.g. intra-operative rapid PTH, gamma probe)
- Associated thyroid disease may go unrecognized unless adequate pre-operative thyroid US.
Localization techniques

**Tc $^{99}$ MIBI**
- Later studies suggest 75% sensitivity
- Evaluation of thyroid gland not possible
- Protocol and institution dependent
- Less operator dependent
- Useful in intra-thoracic and posteriorly located PAS

**Ultrasound**
- Greater sensitivity
- Lower cost
- No ionizing radiation
- Less time for examination
- Evaluation of thyroid possible
- Operator dependent
- Non-operator dependent limitations: posterior and intrathoracic locations

**4D CT**
- Not practical in most centers
- High radiation exposure
Equipment requirement

- Transducers capable of multiple frequency is ideal
- Lower frequency has better depth penetration
- Most commonly used 7-10mHz
- Higher frequency transducers provide better visualization of superficial structures
- Patient positioning is critical
Proper patient positioning

Adequate extension of the neck is essential with pillows placed under the shoulders.
Embryological anatomy of parathyroid glands - The brachial pouches

Inferior pair undertake a longer migratory route along with the thymus gland

Superior pair are more likely to be intra-thyroidal
Develop along with C-cells
Superior Parathyroid - Anatomic distribution and variations

- Mid portion of the thyroid lobe - Typical location
- Upper pole of the thyroid
- Para-esophageal
- Carotid Sheath

1% 10% 77% 11%
INFERIOR PARATHYROID – Anatomical variations

- Undescended - Above ITA: 2%
- Inferior pole of thyroid: 3%
- Thyro-thymic ligament: 56%
- Mediastinal: 26%
- Inferior pole: 9%
How common is ectopic location of adenomas?

- Autopsy series Greece - 942 cadavers, 5% had supernumerary glands, 2% had 3 glands, 8.5% were ectopic within the neck, 0.2% intra-thyroidal and 6% were within the mediastinum.

- Ectopic gland frequency varies from 5-20%.

- What is the reason for this wide variation?
Ultrasound Characteristics of Parathyroid Adenoma

- Hypoechoic texture in relation to the thyroid
- Homogenously-hypoechoic
- Variable Shapes
  - Conforms to surrounding structures
- Adjacent to but separate from posterior thyroid
  - May indent the posterior capsule
  - Echogenic line of separation from the thyroid capsule
- Vascular pedicle from polar artery
Anatomical relationship of inferior PA – Panoramic view

- Larynx
- Thyroid nodule within right thyroid lobe
- Inferior parathyroid adenoma
- RCC
- LIJ
- LCC
- SCM
- RIJ

Thyroid nodule within right thyroid lobe

Inferior parathyroid adenoma
Parathyroid Adenoma

Transverse View
Indentation

Cranio-caudal axis
ECHOGENIC LINE

NOTE THE INDENTATION OF THE THYROID CAPSULE

Cranio-caudal
TE groove lesions

- Smaller, posterior located lesion is usually hard to be seen with US
- More mobile
- Valsalva, cough, movement of neck can also ‘bring out’ the lesion into vision
Mobile TE groove
right upper adenoma
Small TE groove upper lesion
T-E groove left upper mimicking esophagus
99 Tc MIBI negative, tracheo-esophageal groove
Linear lesions
Vascular pedicle / flow
VASCULAR PEDI CLE

thyroid

PA
VASCULAR PEDIICLE

PA
Vascular pedicle
Polar Artery
Coincidental thyroid pathology
MNG/FVPCT and PA
Multiple lesions / hyperplasia

- Relatively uncommon in general population – 15%
- ESRD – 50% or more chance that multiple glands are involved
- MEN 1 – multi-gland hyperplasia
- Limited role for localization in ESRD and MEN 1 patients
Parathyroid Hyperplasia
Multiple lesions
Hyperplasia - ? intrathyroidal
Unusual appearance or location
Thyro-thymic ligament – superior mediastinal
Thyro-thymic lig
Vascular sheath
Intra thyroidal – note absence of echogenic line of separation
Intra-thyroidal PA
Bilobed - Partial intrathyroidal

Cranio-caudal
Cystic parathyroid adenoma
PTH - >50,000 pg/ml

Cystic lesion
Large superior gland adenoma
- Partial cystic degeneration
UG FNAB – Parathyroid adenomas

Dr. John Doppman (NIH) – 1980’s
Dr. Valcavi: US and scan of 75 patients
Positive ultrasound in 71 patients
Positive UG FNAB – PTH in 59 patients
44/45 patients positive at surgery
PPV 97.5%
(PPV 83.7% with sestamibi scan)
Biopsy

- The more typical a lesion appears, less the necessity for biopsy
- Caution in patients on warfarin or anti-platelet agents
- Use 27 g needles
- One or two attempts, using rotation of the syringe & aspiration
- Avoid jabbing technique
Parathyroid FNA

- Avoid vigorous jabbing and multiple passes
- Avoid puncture of posterior capsule
- Fewer passes, one to two - rotate and aspirate

- Parathyroid lesions yield bloody tap
- ‘Dry’ tap – usually a LN
Parathyroid FNA

Indications:
- More imaging typical features – no FNA
- Unusual location
- Intrathyroidal
- Failed surgery
- Multiple lesions (FNA the less typical appearing lesion)
- Prior to ETOH ablation

Contraindications:
- Jaw Tumor syndrome CDC-73
- Family history of jaw tumors+PHPT
- Relative – anticoagulation
- Obscuration by blood vessels
- Respiratory excursions
- Morbid obesity
How to process parathyroid FNA specimen?
Perform FNA – 27 g needle one or two passes
- Make one or two smears
- Rinse the syringe and needle into 1 cc saline
- Ideally, spin and separate supernatant fluid
- Freeze fluid prior to transportation to lab
- Save the cell pellet, this serves as a duplicate specimen
- If the PTH FNA level is low, submit the smears for cytological analysis
Cytology of Parathyroid Aspirates

- Cytology is not useful in the identification of PA
- Thyroid follicular cells and colloid can be seen
- But recommend at least 1-2 smears to be made
  - Save the slides until PTH results become available
  - If PTH level from the syringe washing is elevated, discard slide.
    Only perform cytology in cases with negative PTH analysis

What is the rationale to making smears?
- Small but finite probability that lesion is a pathological lymphnode as a result of coincidental cancers.

When to suspect Parathyroid carcinoma?

- Acute, massive calcium elevation
- Massive elevation of PTH
- Palpable mass
- Jaw tumor history
- US findings – non specific – But, suspect when tumors are large
- Calcification
Parathyroid Cancer – US Features

- Lesions > 15 mm - 8/69 carcinoma
  - Usually felt to be <1% of cases with PHPT
- Strongly suggesting cancer:
  Infiltration or calcification (100% PPV)
- Strongly suggesting benign adenoma:
  Homogeneous, absence of suspicious vascularity, absence of thick capsule (96.7- 100% NPV)

US features of malignancy in the preoperative diagnosis of parathyroid cancer: A retrospective analysis of parathyroid tumours larger than 15 mm. Sidhu PS et al, Eur Radiol May 2011
Ultrasound in Hyperparathyroidism

Conclusions

- Useful in preoperative localization of parathyroid adenoma and hyperplasia
  - Biochemical diagnosis should be established prior to imaging
- Understanding the anatomical variations in the location of parathyroid glands is essential.
- Proper patient positioning to effect neck extension improves the sensitivity and quality of the study.
- PAs are extrathyroidal, hypoechoic, often with a vascular pedicle
- FNAB for PTH analysis improves specificity
  - Biopsy should only be performed after acquiring sufficient expertise and in select cases using fewer attempts (1-2) with fine bore needles (27g needles)