Thyroid FNA
Key Cytology and Histology for “Clinicians”

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Faculty/Presenter Disclosure

• Faculty: [Zubair Baloch, MD, PhD]

• Relationships with commercial interests: None
Objectives of Thyroid FNA

• Recognize *specific* diagnostic entities
• Provide meaningful, management oriented *diagnosis*
• Potential utilization of ancillary techniques
# Thyroid FNA

### Bethesda Classification Scheme

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<th>Diagnostic Category</th>
<th>Risk of Malignancy (%)</th>
<th>Usual Management</th>
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<tbody>
<tr>
<td>Non-diagnostic or Unsatisfactory</td>
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<td>Repeat FNA with ultrasound guidance</td>
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<tr>
<td>Benign</td>
<td>0-3%</td>
<td>Clinical follow-up</td>
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<tr>
<td><strong>Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance (AUS/FLUS)</strong></td>
<td>~ 5-15%</td>
<td>Repeat FNA</td>
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<tr>
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<td>97-99%</td>
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Easy-Breezy Thyroid Pathology

Concordant Ultrasound Features, FNA cytomorphology & Histologic Follow-up
Nodular Goiter

Colloid: Generally abundant. **Follicular cells** Variable morphology

**Oncocytes, Macrophages**

**Degeneration/regeneration:** Calcification, stromal proliferation, mitoses
Chronic Lymphocytic Thyroiditis

Oncocytes
Lymphocytes: In the background & infiltrating the cell groups
Papillary Thyroid Carcinoma

Nuclear features – Major Diagnostic Features
Elongation, chromatin clearing, Nuclear membrane irregularities Intranuclear grooves Inclusions Small peripheral nucleoli
Not so easy - Head Scratching
Everyday Thyroid Cytopathology

*Indeterminate Lesions*

*Or*

*Indeterminate Pathologist?*
## Thyroid FNA

**Bethesda Classification Scheme**

**The Bethesda System for Reporting Thyroid Cytopathology:**
*Implied Risk of Malignancy and Recommended Clinical Management*

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Diagnosis Follicular Neoplasm

80% Benign on Surgical Excision
Diagnosis
Follicular Lesion / Neoplasms
“Microfollicles” in FNA Specimens

*Microfollicles = Neoplasm*
Is It That Easy

Don’t Think So
Microfollicles

• Inter-observer Agreement on Microfollicles
  – Renshaw AA et al. (Arch Pathol Lab Med 2006)
  – 12 cytopathologists were shown 45 small groups of follicular cells
    • 20 Microfollicles
    • 7 Macrofollicles
    • 18 Indeterminate
  – <15 cells arranged in circle that is at least two-thirds complete, should be classified as microfollicles.
Microfollicles

• Mowschenson PM et al (Surgery 1994)
• FNA of normal thyroid tissue may result in the misdiagnosis of micro-follicular lesions
  – 42 cases
    • 9 unremarkable
    • 18 microfollicular
    • 3 mixed macromicrofollicular
    • 1 Hurthle cell
    • 1 Papillary carcinoma
The Atypical Category

The Dreaded AUS/FLUS
Lets Talk About FLUS/AUS
Responsible Factors

• History
  – TFT’s, H/O prior FNA
• Ultrasound features
  – Cystic vs. solid
• Operator – sampling
• Adequacy
• Cytology Preparation
• Interpretation
• Surgical follow-up – ? Gold standard
The so Called Gold Standard
Case-1
Case 1

Thyroid Experts Diagnoses
The Cytopathologists Gold Standard

Diagnoses:
Hyperplastic nodule – Benign
or
Follicular Adenoma – Benign
or
Follicular Variant of Papillary Thyroid Carcinoma - Malignant
Case 1 - Sampling

Benign

Malignant
Case 2

Lesional Morphology

Benign

Atypical Architecture
Case 3

History of Prior FNA-
Making Sense of Atypia

Markedly Atypical Cells
Case 4: Inadequate History

52-year-old woman. Ultrasound – Left thyroid lobe occupied by a predominantly ill-defined hypoechoic structure – suspicious for anaplastic carcinoma

Original Diagnosis
Suspicious for Anaplastic Carcinoma

More History
Transient symptomatic hyperthyroidism (TSH – 0.03) followed by hypothyroidism.
Current medication:
Synthroid

Second opinion Dx
Suspect sub-acute thyroiditis
Surgical excision of left lobe
Dealing with AUS/FLUS
The Dreaded Call From the Clinician

Too Many FLUS Cases
What is going on?
# HUP Experience

<table>
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<tr>
<th>Year</th>
<th>% of Total Non-Gyn Cases</th>
<th>Cases Diagnosed as AUS/FLUS</th>
<th>% of Total Thyroid FNA Biopsied at HUP</th>
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<tr>
<td>2009</td>
<td>8.5%</td>
<td>96</td>
<td>10.5%</td>
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<tr>
<td>2010</td>
<td>7.84%</td>
<td>88</td>
<td>9%</td>
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<tr>
<td>2011</td>
<td>8.9%</td>
<td>89</td>
<td>8%</td>
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How to Relay
The AUS/FLUS Diagnosis

*Explain, Explain & Explain*
HUP Experience

- AUS/FLUS cases are further sub-classified into Following subcategories (SC):
  - SC1 - favor benign, however, a follicular neoplasm (FN) could not be excluded due to increased cellularity
  - SC2 - specimens with focal nuclear overlapping and crowding
  - SC3 - scant specimens with focal nuclear overlapping and crowding
  - SC4 - specimens with focal nuclear overlapping and crowding in a background of lymphocytic thyroiditis
  - SC5 - few cells with features suspicious for papillary thyroid cancer (PTC)
  - SC6 - specimens in which a FN cannot be excluded (with miscellaneous morphologic descriptors).
Malignancy Rate by AUS-FLUS Subtype

SC1
SC2
SC3
SC4
SC5
SC6
What I have Learned so Far

• Thyroid FNA diagnoses vary among pathologist
• History and Sampling is as important as the Interpretation
• AUS/FLUS is a useful category
  – Rates
  – Follow-up
  – Ancillary testing
Modern Approach
A Gentle Mix of Old and New

Nothing is 100%
My View

- History
- Clinical features; TFT’s
- Ultrasound Characteristics
- Cytologic Interpretation (have you talked to your pathologist)
- Ancillary Studies
  - Which pass(es) are being selected for molecular studies
  - Selected cases
  - Test selection
  - Test results vs. cytologic interpretation
- Histologic follow-up
He described thyroid nodules/enlargements as “this tumor, which is called Elephant of the throat, is a large tumor which commonly occurs in women and is of congenital and acquired types. The congenital type is incurable, whereas, the acquired type is of two types: one resembles sebaceous cyst and other as an arterial aneurysm which is dangerous to incise, so never apply knife to it unless the tumor is small”.

Abu-al Qasim (936-1013 AD)
Kitab al-Tasrif