Thyroid follicular neoplasms in cytology

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Lecture overview

• importance of FNAB in assessing thyroid lesions
• follicular thyroid neoplasms
• other follicular-patterned thyroid lesions in cytology and difficulties in their differentiation
• how is The Bethesda system for reporting thyroid cytopathology (TBSRTC) dealing with follicular-patterned lesions
• the role of ancillary techniques
Importance of FNAB in assessing thyroid lesions

- palpable thyroid nodule in 4-10% of the population
- US detected thyroid nodule in up to 27% of the population
- majority benign (app. 1% malignant)
- FNAB is most accurate and cost effective method for triage and management of the patients with thyroid nodules (diagnostic accuracy from 80 to > 95% for representative samples)
- FNAB could be diagnostic (papillary, medullary carcinoma,...) or screening test (follicular carcinoma)
Follicular neoplasms

• include: - follicular adenoma (FA)
  - follicular carcinoma (FC)
• diagnosis of FC based strictly on histological criteria (vascular/capsular invasion)
Follicular adenoma (FA)

• encapsulated benign neoplasm
• several different histomorphologic growth patterns (usually uniform architecture in a single lesion)
• morphologic diversity is the cause for overlapping cytologic patterns in some cases of nodular goiter, follicular adenoma and follicular carcinoma
Morphologic variants of FA

- conventional:
  - macrofollicular (colloid)
  - normofollicular (simple)
  - microfollicular
  - trabecular/solid
- oncocytic
- hyalinizing trabecular
- FA with clear cell change
- FA with papillary hyperplasia
- atypical
Microfollicular growth pattern

• architecture
  - syncytial tissue fragments (mostly follicular pattern)

• follicular cells characteristics:
  - uniformly enlarged nuclei
  - fine to coarsely granular chromatin, no nucleoli

• background:
  - scant to absent colloid

DD: well differentiated follicular carcinoma
Trabecular/solid growth pattern

• architecture
  - syncytial tissue fragments with mostly trabecular pattern
  - crowding & overlapping of nuclei
• follicular cells characteristics:
  - variably enlarged, sometimes pleomorphic nuclei
  - fine to coarsely granular chromatin, no nucleoli
• background:
  - scant to absent colloid

DD: well differentiated follicular carcinoma
Macrofollicular (colloid) growth pattern

• architecture
  - regular follicles
  - monolayered sheets with honeycomb pattern
• follicular cells characteristics:
  - small picnotic nuclei
• background:
  - abundant colloid
  - bare nuclei of follicular cells

DD: nodular goiter
Normofollicular growth pattern

• **architecture**
  - syncytial tissue fragments
  - regular follicles
  - monolayered sheets with honeycomb pattern

• **follicular cells characteristics:**
  - normal sized or slightly enlarged nuclei
  - granular, evenly distributed chromatin, no nucleoli

• **background:**
  - variable amount of colloid

**DD:** nodular goiter
Follicular carcinoma

- presence of capsular or vascular invasion essential for the diagnosis of FC
- different morphologic patterns
- poorly differentiated FC pose no diagnostic problem
- well differentiated FC has overlapping morphologic features with FA
Well differentiated FC

• architecture
  - syncytial tissue fragments with or without follicular pattern
  - crowding & overlapping of nuclei
  - irregular follicles
• follicular cells characteristics:
  - enlarged, round to oval, uniform or pleomorphic nuclei
  - fine to coarsely granular chromatin, micro and macro nucleoli
  - more cytoplasm than cells of FA, poorly defined cell borders
• background:
  - clean, scant or absent colloid

DD: follicular adenoma, FVPC
Poorly differentiated FC

- **architecture**
  - syncytial tissue fragments of malignant cells with or without follicular pattern, solid areas
  - crowding & overlapping of nuclei

- **follicular cells characteristics:**
  - larger than in WDFC, pleomorphic
  - large round nuclei, coarsely granular chromatin, parachromatin clearing, nucleoli
  - pale to dense cytoplasm

- **background:**
  - absent colloid, sometimes necrosis
Follicular patterned thyroid lesions

- the most common type of thyroid FNA specimens
- lesions with follicular pattern:
  - neoplasms:
    - follicular adenoma
    - follicular carcinoma
    - follicular variant of papillary carcinoma
  - non-neoplastic lesions:
    - nodular goiter (nodular hyperplasia)
Follicular variant of papillary carcinoma

- **architecture:**
  - syncytial tissue fragments
  - microfollicles
- **follicular cells characteristics:**
  - enlarged nuclei
  - pale chromatin
  - micronucleoli
  - nuclear grooves & pseudoinclusions
- **background:**
  - dense colloid
  - multinucleated giant cells
Nodular goiter (nodular hyperplasia)

- **architecture:**
  - monolayerd tissue fragments with honeycomb pattern
  - regular follicles
  - pseudopapillary tissue fragments
  - single cells

- **follicular cells characteristics:**
  - small round uniform nuclei
  - compact to finely granular chromatin

- **background:**
  - colloid (variable amount, even absent)
Morphological features that can help in the differentiation of follicular lesions

• amount of colloid
• architectural pattern of tissue fragments
• size and shape of follicular cell nuclei
• changes in chromatin pattern
The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC)

Recommended diagnostic categories:
• nondiagnostic or nonsatisfactory
• benign
• atypia of undetermined significance or follicular lesion of undetermined significance
• follicular neoplasm or suspicious for follicular neoplasm
• suspicious for malignancy
• malignant
The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC)

Advantages:
- standardisation of cytology reports
- each diagnostic category carries the information of:
  - malignancy risk
  - recommended clinical management
- facilitates communication among cytopathologists and clinicians
- facilitates cytologic-histologic correlation
Ancillary techniques in evaluating follicular lesions

- Not very useful:
  - immunohistochemistry:
    HBME-1, CD 57, Lactoferrin (malignant vs benign thyroid neoplasms)
  - DNA ploidy

- Promising:
  - molecular techniques:
    - for detecting somatic mutations (RAS mutations, PAX8/PPARG1 rearrangement)
    - for gene expression profiling (microarrays)
Conclusions

• Follicular thyroid lesions are difficult to evaluate from cytology samples because of variety of their morphological pictures which sometimes overlap between several entities.

• TBSRTC enables the standardisation of the thyroid cytology reports, which facilitates the communication between cytologist and referral physician and improve patients care.

• Cytology will remain a screening and not a diagnostic test for follicular carcinoma until ancillary techniques will be developed that would enable the differentiation between benign thyroid nodules and FC.