Cytology of the thyroid gland

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Staining

- no definite recommendation
- 3 options
- 1. Papanicolaou – excellent nuclear features
  - x wet fixation needed
- 2. May-Grünwald-Giemsa – drying out at room temperature, less nuclear details, better cytoplasmic features and other structures
- 3. haematoxylin-eosin
Evaluation

- all smears, whole area (periphery!!!)
- morphologic features in context - synthesis of information
- CAVE! - under- or overdiagnosis based on a single morphologic detail
- close clinico-pathologic cooperation is a must!
- limitations of the method - FNAC is not supposed to replace histology
- second opinion, ancilliary techniques
Criteria of adequacy

- variable at different institutions
- 5-6 cell groups, 10-15 follicular cells each
- 10 cell groups, 20 follicular cells each
- counting of cells = limited evaluation
- "benign structures only, amount of material is limited"
- repeat the aspiration
The Bethesda system

- unified terminology
- categories I – VI
- simplification of the message to a clinician
I. Nondiagnostic or Unsatisfactory
   Cyst fluid only
   Virtually acellular specimen
   Other (obscuring blood, clotting artifact, etc.)

II. Benign
    Consistent with a benign follicular nodule (includes adenomatoid nodule, colloid nodule, etc.)
    Consistent with lymphocytic (Hashimoto) thyroiditis in the proper clinical context
    Consistent with granulomatous (subacute) thyroiditis
    Other

III. Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance

IV. Follicular Neoplasm or Suspicious for a Follicular Neoplasm
    specify if Hürthle cell (oncocytic) type

V. Suspicious for Malignancy
    Suspicious for papillary carcinoma
    Suspicious for medullary carcinoma
    Suspicious for metastatic carcinoma
    Suspicious for lymphoma
    Other

VI. Malignant
    Papillary thyroid carcinoma
    Poorly differentiated carcinoma
    Medullary thyroid carcinoma
    Undifferentiated (anaplastic) carcinoma
    Squamous cell carcinoma
    Carcinoma with mixed features (specify)
    Metastatic carcinoma
    Non-Hodgkin lymphoma
    Other
<table>
<thead>
<tr>
<th>Diagnostic category</th>
<th>Risk of malignancy(%)</th>
<th>Usual management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nondiagnostic or Unsatisfactory</td>
<td>b</td>
<td>Repeat FNA with ultrasound guidance</td>
</tr>
<tr>
<td>Benign</td>
<td>0–3</td>
<td>Clinical follow-up</td>
</tr>
<tr>
<td>Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance</td>
<td>~5–15&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Repeat FNA</td>
</tr>
<tr>
<td>Follicular Neoplasm or Suspicious for a Follicular Neoplasm</td>
<td>15–30</td>
<td>Surgical lobectomy</td>
</tr>
<tr>
<td>Suspicious for Malignancy</td>
<td>60–75</td>
<td>Near-total thyroidectomy or surgical lobectomy&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Malignant</td>
<td>97–99</td>
<td>Near-total thyroidectomy&lt;sup&gt;d&lt;/sup&gt;</td>
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Other
Non-diagnostic smears

- missing small nodule
- abnormal structure of the lesion (cystic, highly vascularized or regressively changed nodules)
- non-diagnostic aspirations 1,6 - 21% cases
- our current series 6,6%
Hyperplastic goiter

- any enlargement, variable etiology
- diffuse goiter (homogenous, no nodular rearrangement)
- children – virtually always diffuse goiter
- variable proliferative activity
- selection of populations with different features, somatic mutations
- hyperplastic nodules – nodular goiter
Colloid goiter - diffuse and nodular

- variable cellularity of smears
- abundant colloid, mosaic pattern
- hyperfunction - anisokaryosis, vacuolization of cytoplasm, "lace-like margin"
- macrofollicular - large flat fragments and sheets
- non-transparent tissue-fragments
- regressive change - nuclear shrinkage, vacuoles, granules of hemosiderin
- siderophages, foamy histiocytes, cholesterol crystals
Subacute thyroiditis (de Quervain)

- viral etiology, heredity (antigen HLA-B35)
- follows acute respiratory infection
- may be unilateral (single lobe)
- solitary nodule!
Cytologic features

- moderate cellularity
- cellular debris, small amounts of colloid, regressive changes of follicular cells
- lymphocytes, neutrophils and macrophages
- epithelioid cells - „wavy" nuclei
- granulomas
- multinucleated giant cells (reaction to colloid)
- not specific for subacute thyroiditis !!!
# Autoimmune thyroiditis

## Thyroiditis

<table>
<thead>
<tr>
<th>Thyroiditis</th>
<th>Clin.course</th>
<th>Characteristic features</th>
</tr>
</thead>
<tbody>
<tr>
<td>with goiter (Hashimoto)</td>
<td>chronic</td>
<td>goiter, lymphoid infiltrate, oncocytic transformation of follicular cells, fibrosis</td>
</tr>
<tr>
<td>atrophic (primary hypothyroidism)</td>
<td>chronic</td>
<td>atrophy, fibrosis</td>
</tr>
<tr>
<td>juvenile</td>
<td>chronic</td>
<td>lymphocytic infiltrate</td>
</tr>
<tr>
<td>focal lymphocytic</td>
<td>self-limited</td>
<td>present in 20% of goiters at autopsy</td>
</tr>
<tr>
<td>post-partum</td>
<td>transient</td>
<td>small goiter, lymphocytic infiltrate</td>
</tr>
<tr>
<td>silent</td>
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Hashimoto thyroiditis

- goiter, variable size and character
- small changes of thyroid size (fast progression - susp. of malignancy)
- clinical symptoms of hypothyroidism
- US - hypoechoic, inhomogenous structure
Diffuse toxic goiter
(Graves-Basedow disease)

- most frequent cause of thyroid hyperfunction
- organ specific autoimmune disorder
- autoantibodies against TSH receptor
- thyroid growth + increased production of T3, T4
- indication for FNAC = nodule
- 40% of GB goiters
- Ca in 3.5% of GB goiters
- probability of malignancy of nodule = 11%
Cytologic features

- high cellularity
- minimal amount of colloid
- follicular cells in small and middle-sized groups, moderate cohesivity
- marginal vacuoles at periphery
- background with small amount of mature lymphocytes
Papillary carcinoma

- most frequent thyroid malignancy (65-80%)
- derived from follicular cells
- tumor papillae and/or specific nuclear features
- F:M = 2-3:1, any age
- microCa more frequent in males!
More aggressive behavior

- tall cell PC
- columnar cell PC
- diffuse sclerosing PC

Less aggressive

- encapsulated PC
- papillary microcarcinoma
Typical cytologic features of PC

- high cellularity
- increased N/C ratio
- intranuclear pseudoinclusions – higher frequency
- multinucleated giant cells without presence of lymphoid elements
- thick colloid (chewing-gum like)
- intranuclear grooves
- papillary fragments
- psammoma bodies
Follicular neoplasms

- Hyperplastic nodule
- Follicular adenoma
- Atypical follicular adenoma (UMP)
- Follicular carcinoma
  - minimally invasive – without vascular i.
  - minimally invasive – with vascular i.
  - widely invasive
- Follicular variant of PC
- Follicular variant of medullary carcinoma
- Mixed tumors
There are no reliable cytologic criteria, distinguishing benign and malignant follicular tumors
Follicular carcinoma

- malignant counterpart of follicular adenoma
- more frequent in elderly and in regions with iodine deficiency
- Europe 27%
- USA 10%
Follicular carcinoma

- invasion
- transcapsular invasion
  and/or
- vascular invasion

- minimally invasive FC (without or with vascular invasion)
- widely invasive FC
Biologic behavior

- different from PC
- hematogenous spread, metastases into bones, brain and lungs
- ras mutations
Cytologic features of follicular neoplasia

- high cellularity
- low cohesivness of cells
- microfollicular formations (rosette-like)
- dense colloid in microfollicles
- absence of colloid in the background
- nuclear anisomorphy (no prognostic significance)
Oncocytic (Hürtle cell) tumors

- >75% of oncocytes (Askanazy, oxyphillic or Hürtle cells)
- abundant mitochondriae
- oncocytic adenoma
- oncocytic carcinoma - follicular
  - papillary
  (oncocytic variant of PC)
Anaplastic (undifferentiated) carcinoma

- USA 1.7%, Germany 3.6%
- M:F = 1.5:1
- max. 7. decenium
- rapidly growing mass
- extrathyroidal spread
- necrosis, calcifications, bone formation
Anaplastic carcinoma

- large cells, variation of size and shape, bizarre nuclei, multinucleated cells
- mitotic and apoptotic activity
- vascular invasion
- histologic types: squamous giant-cell
- spindle-cell (sarcomatoid)
- frequently mixed features
- high cellularity
- absence of colloid
- necrotic debris and neutrophills
- poorly cohesive cell groups
- large polygonal cells
- spindle cells
- bi- or multinucleated cells
Medullary thyroid carcinoma (MTC)

- relatively rare
- sporadic
- hereditary syndromes (25%) - MEN 2A, MEN 2B, FMC
- typical growth pattern x atypical manifestations
- unusual features small cell
  - giant cell
  - squamous cell
  - amphicrine
  - mucinous
  - pigmented
  - follicular
  - oncocytic
- Moderately to highly cellular smears
- Poorly cohesive cells, absence of colloid
- Fragments of amyloid (1/4 cases)
- Round, oval, triangular, spindle cells
Thyroid lymphomas

- relatively rare
- 2% of extranodal lymphomas
- 5% of all thyroid malignancies
- max. in 7. decade
- M:F = 3:1
- thyroid enlargement, growth of nodule
- virtually always in the background of HT
- non-Hodgkin ML, 98% B cells
- high-grade transformation from MALT-lymphoma
Secondary neoplasms

- rare (autoptic series 24%, bioptical series – significantly less)
- direct growth (larynx, hypopharynx, esophagus)
- hematogenous – tumor generalization
- solitary metastasis, long time span
- serious diagnostic problem
- renal, lung, breast, GIT ca, melanoma