Forpath Workshop 24 Jan. 2009
Update in Thyroid Tumours
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Summary of today

1. Macroscopy
2. Benign lesions
   2.1 Endocrine Organ
   2.2 Terminology
   2.3 AD Nodule v FA
   2.4 Thyroiditis
   2.5 Atypia in benign lesions
   2.6 Lymph node containing thyroid tissue
3. Malignant Lesions
   3.1 General remarks
   3.2 Hurthle diff.
   3.3 FC and FT-UMP
   3.4 PTC
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   3.6 Pitfalls
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Summary of Part 1 bis

3.11 IHC
3.12 TNM
3.13 Meta
3.14 HTT
3.15 Conclusions of the first part
1. Macroscopy

Isthmus should be sectioned in the sagittal plane.


Figure 3  Where possible, the thyroid gland should be sectioned horizontally as demonstrated above.

Ink the surface of the specimen.

Isthmic margin

Surgical pathology Dissection
An Illustrated Guide
Second edition
W.H. Westra et al.
Springer
Serially sectioned from superior to inferior.
Always take the whole capsule if it is a thick capsule!

sections may be further divided into quadrants.
More specific sectioning of a nodule to capture the whole capsule. Like an orange.
1. **Macroscopy**

- Cross sections of lobes and sagittal sections of isthmus
- Nodules with a capsule *and* special looking nodules: many biopsies especially from the capsule
2.1 The Thyroid is an Endocrine Organ

- In endocrine organs, the presence of cellular atypia is not necessarily indicative of malignancy. Rather, large atypical cells are commonly found in reactive conditions and benign tumours, and often merely reflect hyperfunction.

  *Seminars in Diagnostic Pathology, Vol 12, no 1, 1995*

- There are more mitoses in benign thyroid disease than in malignant thyroid disease.

  *Simoes, Paris 2006*
2.2 If benign: Terminology, ...?

Diagnostic equals

- Adenomatous goiter
- Colloid goiter
- Nodular goiter
- Adenomatous hyperplasia
- ....
2.3 **Adenomatous nodule**

**AJSP vol 26 no 11, 2002**

- 1. Incomplete capsule: always
- 2. Variable sized follicles: always
- 3. Coarse papillary configuration: very often (Sanderson Polster)
- 4. Abundant edematous or hyalinized stroma may be possible
- 5. Chronic inflammatory cell infiltrate sometimes
- 6. Degenerative changes: very often
- 7. Frequent multiple
2.3 Follicular Adenoma WHO

- 1. Complete capsule of variable thickness
- 2. Architectural pattern and cytological features are different from the surrounding tissue
- 3. Architectural: follicular, trabecular
- 4. Cells: cuboidal, columnar, polygonal and often with dark round nuclei. Enlarged hyperchromatic nuclei may be present
- 5. 60% are monoclonal!
2.3 Follicular adenoma WHO

- 6. Central portion due to delayed fixation with large and pale nuclei
- 7. Mitotic figures are rare
- 8. Often richly vascular
- 9. Focal myxoid change, subcapsular
- 10. Secondary changes: edema, fibrosis, hyalinization, haemorrhage, calcification, cartilaginous metaplasia, cyst formation, infarction, ..
- 11. Recurrence rate is very high
2.3 Follicular adenoma versus Adenomatoid nodule(s)

- FA: Growth pattern:
  - normofolliculair
  - macrofolliculair
  - microfolliculair

- FA: Clear capsule
  - Adenomatoid nodules lack a well defined capsule
  - Adenomatoid nodules: follicules are similar to those in the surrounding tissue.
2.3 Special types of FA

- Fetal adenoma (micro-, trabecular)
- Signet ring cell follicular adenoma
- Mucinous follicular adenoma
- Lipoadenoma
- Clear cell follicular adenoma
- Toxic adenoma (tall cells)
- Oncocytic adenoma
  - (Adenomatoid oncocytic nodules often occur in Hashimoto Thyroiditis)
- Follicular adenoma with papillary hyperplasia
FA ... follicular ... variant

Ref. WHO
FA Embryonal

Ref. WHO
Signet ring variant FA

Ref. WHO
Mucinous variant FA

Ref. WHO
Clear cell variant FA

Ref. WHO
Papillary Hyperplasia FA

Ref. WHO
FA vascular rich with spindle cells

Ref. WHO
Myxoid variant of FA

Ref. WHO
Follicular Adenoma with bizarre nuclei

- Small groups of monstrous tumor cells with enlarged hyperchromatic nuclei within an otherwise typical follicular adenoma
Follicular thyroid adenoma *versus* Parathyroid adenoma

- Arising within the thyroid gland or not
- Microfollicular, clear cell or oncocytic type cells
- Presence of water clear cells
- Chromogranine positivity and parathyroid hormone positivity
Parathyroid Adenoma
2.4 Thyroiditis

2. Granulomatous thyroiditis of de Quervain
3. Palpation thyroiditis (Granulomatous)
4. Silent focal lymphocytic thyroiditis
5. Post partum thyroiditis
2.4 Thyroiditis

- Riedel’s thyroiditis: extensive fibrosis extends to the adjacent muscle with sharp demarcation between affected area and normal areas, granulomatous changes in vessels.

- DD 1. Paucicellular Anaplastic (Undifferentiated) Thyroid Carcinoma of the elderly
- DD 2. PTC with fasciitis like stroma
- DD 3. PTC with extensive fibrosis or Diffuse sclerosing variant. Most are TG negative
2.5 Cytologic appearance in thyroiditis. Atypia is not malignancy


www.jclinpath.com
Nuclear clearing resembling Orphan Annie nuclei: 15%

Nuclear grooves and pseudonuclear inclusions focally in 8%

Cytologic atypia in 7% (nuclear enlargement, multinucleation, nuclear pleomorphism with prominent nucleoli)

Mitoses in 6% ,1/10 HPF

Psammoma bodies focally in 4%

Muscle infiltration in 1%

Two cases with thyroid in lymph node sinuses
2.6 Lymph nodes (cervical) containing thyroid tissue

- May represent heterotopic thyroid tissue or metastatic carcinoma - evaluate with extreme caution
2.6 Heterotopic thyroid

- Small aggregate of follicles with no attributes of papillary carcinoma after detailed examination (i.e. no atypical nuclei, no papillary architecture, no psammoma bodies), and limited to capsule/periphery of one or two lymph nodes
Ectopic thyroid follicles in cervical lymph node have normal architecture and cytology and appear as a small cluster in nodal capsule.
3. Thyroid Carcinoma
3.1 Thyroid Carcinoma

- 1% of all malignancies
- 8th place of malignancies of women
- 80% is PTC
- Increasing

Arch Pathol Lab Med 30 July 2006, p 1057
Thyroid Carcinoma: WHO book on Endocrine Tumours, 3rd edition, 2004

1. Follicular carcinoma  FC
2. Papillary carcinoma  PTC
3. Medullary carcinoma  Med. Ca
4. Poorly differentiated ca  PDC
5. Undifferentiated ca  UDC

...
3.2 (Hürthle cell carcinoma)

- Doesn’t exist anymore as a separate entity. (WHO 2004)
- *Hürthle cell variant* ...
- *... with Hürthle cell differentiation*
- Alle entities benign or malignant
Course on Thyroid Pathology

Paris, June 15-16, 2006
Prof. Manuel Roberto Simoes
Normal cell → Carcinogenic hit → Initiated cell → MtDNA alteration → Carcinoma with "secondary" oxyphilia
3.3 Follicular carcinoma
3.3 Follicular Ca

Arch Pathol Lab Med vol 130 july 2006 p 984

**Vessel and/or capsular invasion.**

- Vascular invasion within the tumor: not significant
- No capsule is no Fol. Ca!
  - (Cave Widely invasive FC)-
- A thin, fine capsule is (probably) not a Fol. Ca.
- CD 34 or an other vascular markers are useless
- Invasion of one vessel is very rare
- Cave torn of capsule (J. Rosai)
  Tumor herniation through a torn capsule simulating capsular invasion)

Histopathology;2006,49,107-120
3.3 Carcinoma

- Is trabecular, solid, microfollicular (fetal) and NOT macrofollicular or normofollicular.
- Macrofollicular growth pattern is probably FV-PTC (Follicular Variant of Papillary Carcinoma).
- FTC peak: 60-70 year older age group.
- If there is any inflammation it is probably not FC but PTC. No lymphoid infiltrate in FC and near always in PTC.
Vascular invasion

- Should be assessed in vessels located within or beyond the capsule
- Plugs of tumor cells floating within vascular lumens unattached to the vessel wall do not qualify for vascular invasion.

CAVE: Reactive vascular proliferation

Rosai in Histopathology, 49, 107-120, 2006: Pitfalls in thyroid tumour pathology
Vascular invasion, bis.

- To qualify for vascular invasion the tumor cells should be covered by a partial or full layer of endothelium.
- Some authors will accept nonendothelialized tumor thrombi as evidence of vascular invasion if they are attached to the vessel wall.
Capsular breakthrough

- Penetration of tumour through the whole capsule, deflecting the collagen fibres of the capsule.
- Contact of tumour with the surrounding non-neoplastic thyroid tissue.
- A concomitant vascular invasion is not required even if metastasis are already present.
- Tumour foci within the capsule are not sufficient for the diagnosis. They represent, most likely, tumour trapping and distortion by fibrosis.
Small nodules found outside the tumour capsule showing a similar morphology to the main tumour mass should not be regarded as capsular invasion.

Free floating islands of tumour cells present within the capsule without connection with the tumour mass should not be regarded as capsular invasion.
More sections to find the breakthrough
Torn capsule of a follicular adenoma with herniation of tumour tissue simulating capsular invasion. (J Rosai)

Histopathology, 2006, 49, 107-120
Worrisome Histologic Alterations Following Fine Needle Aspiration (Livolsi)

Ref. WHO
3.3 Anatomic forms of FC

- **Minimally invasive MI-FC/ Low Grade**
  1. With or without capsular invasion
  2. With limited vascular invasion (≤4 Vessels involved)
- **Widely invasive FC/ Intermediate Grade**
- With extensive vascular invasion (≥4 Vessels involved) No capsule anymore
3.3 Variants of FC

- Hurtle cell
- Clear cell
- Cave clear cell adenoma does also exist!
FC Mushroom

Paris 2006
Section near a mushroom

Capsule

Pseudocapsule
Minimally invasive follicular carcinoma—the invasive tongue of tumour has completely penetrated the capsule of the neoplasm

J Rosai: Vascular invasion is more important than capsular invasion

Paris 2006
FC Minimal capsular invasion

Ref. WHO
Hurtle cell variant of FC

Ref. WHO
FC Vascular invasion

Ref. WHO
FC Vascular invasion

Ref. WHO
Vascular Invasion in FC

Ref. WHO
FC Capsular and vascular invasion

Ref. WHO
Case nr. 19

Paris 2006
Widely invasive FC
Mimics of vascular invasion

Endothelial proliferation

Kaposi sarcoma like

Histopathology 2006, 49, 107-120
Benign vs Malignant
Adenoma versus Foll. Carcinoma

- Adenoma
- Follicular Tumor with Unknown Malignant Potential
- Folliculair Carcinoma
3.3 Follicular tumour of uncertain potential  FT UMP

- Doubt about vascular invasion and/or capsular invasion.
- Take many blocks of the whole capsule.
3.4 PTC

Papillary Thyroid Carcinoma
PTC is the most common thyroid carcinoma. Its prognosis is extremely good. The most common single prognostic factor is age. 
Histopathology 2001, 39, p 536.

PTC is not conventionally regarded as having any associated benign or premalignant lesion.

PTC is a low grade tumour
3.4 PTC

- **Multicentric disease**

  This multicentricity is thought to be one cause of recurrences in patients treated by lobectomy.

  - If the lesion is found incidentally, reoperation is not required.

  - Arch Pathol Lab Med vol 130 July 2006
3.4 PTC variants

- Microcarcinoma: smaller than 1 cm.
- Encapsulated (Lindsay tumour)
- FV PTC (Encapsulated or not)
- Solid (Most frequent in Childhood)
- Trabecular
- Diffuse sclerosing variant
- Tall cell variant
- Columnar cell variant (Separate entity?)
- Oncocytic variant with lymphoid stroma, Whartin like
- Hurtle cell variant / Clear cell variant
3.4 PTC variants bis

- Diffuse Follicular Variant
- Macrofollicular variant (more than 50 % macrofollicles)
- Cystic variant of PTC
- PTC with Exuberant nodular fasciitis like stroma
- Multifocal Pap T Ca
- Cribriform (morular) variant
- Multinodular variant
- PTC with focal insular component
- PTC with lipomatous stroma
3.4 PTC with worse prognosis

- Tall cell variant (not in childhood!). If 30% of cells are tall cells it is a tall cell variant.
- Solid variant.
- Diffuse sclerosing variant (Often with huge squamous metaplasia) Children and young adults cave S100 positivity due to many FDC cells.
- Columnar cell variant.
- Diffuse follicular variant.
- Oncocytic? NO because no separate entity.
3.4 PTC

- Follicles are frequently present
- Tubulo Papillar pattern also a frequent form of presentation
- Patterns: Less common: microglandular, guirlande, cribriform, anastomosing, tubular, trabecular.
- 50% contain multinucleate histiocytes (Fletcher)
- Psammoma bodies also in Hashimoto
- Often abundant sclerotic or fibrotic with calcification and/or ossification.
3.4 PTC Nuclei

- **NOT Malignant:**
  Dispersed cells with PTC nuclei: Hashimoto, Goiter.
  Intermingled with normal cells.

- **Malignant:**
  Clusters with PTC nuclei: PTC.
  All of the same family.
Classic Nuclear features of Papillary Thyroid Carcinoma (PTC)

- Nuclear optical clarity
- Nuclear grooves
- Sharply delineated nuclear membranes
- Intranuclear cytoplasmic protrusions
- Nuclear overlapping
- Elongated nuclei, oval nuclei (a normal nucleus is as big as an erythrocyte)
- Eccentric nucleoli
- ...
Some PTC’s may not exhibit all the characteristic nuclear features while FA and FC exhibit focal clear or grooved nuclei.

Scattered large hyperchromatic cells are very uncommon in PTC. No grooves, no oval nuclei, ...
Most important criteria for the diagnosis of FV PTC, % = cases with this features

- Cytoplasmic invagination into nucleus 25%
- Abundant nuclear grooves 100%
- Ground glass nuclei 97%
- Psammoma bodies 16%
- Enlarged overlapping nuclei 98%
- Irregular shaped nuclei 100%
Less important criteria
% = cases with this features

- Dark staining colloid 86%
- Irregular contours of follicles 64%
- Scalloping of colloid 58%
- Elongated follicles 80%
- Multinucleated macrophages in lumen of follicles 13%
PTC: Orphan Anny and overlap

Paris 2006
Bubble artefacts lack a delimiting nuclear membrane

Paris 2006
PTC Papillarity

Ref. WHO
PTC: clear nuclei, grooves

Ref. WHO
PTC Basophilic colloid

Ref. WHO
Macrofollicular variant of FV-PTC

- Only focal distribution of diagnostic nuclear features
Macrofollicular variant PTC

Ref. WHO
Columnar cell carcinoma: variant of PTC or separate entity?

- Endometrial carcinoma or colonic carcinoma look
- DD Tall cell variant of PTC
- Striking nuclear pseudostratification
- Nuclear Hyperchromatism
- No PTC nuclei – Tall cell variant: PTC nuclei
- No oxyphilic change in cytoplasm
Columnar cell variant

Diagnostic histopathology 14:5,2008, p 236-243
PTC Columnar cell variant, subnuclear vacuolisation

Ref. WHO
Tall cell variant Pap Ca

- Cells whose length is at least 3 times their width (for some authors 2 times)
- Abundant eosinophilic cytoplasm (DD with Columnar cell variant)
- Higher incidence of extra thyroid disease
- CD 15 pos, EMA positive
- Dedifferentiate like conventional PTC into Spindle ca, Squamous ca or Undifferentiated ca (Anaplastic ca)
Tall cell variant PTC

Ref. WHO
Tall cell variant

Diagnostic histopathology 14:5, 2008, p 236-243
Diffuse sclerosing variant with microcalcifications

Ref. WHO
Diffuse sclerosing variant of PTC

Diagnostic histopathology 14:5, 2008, p 236-243
PTC with squamous metaplasia

Ref. WHO
PTC Clear cell variant

Ref. WHO
Micro PTC

Ref. WHO
Solid PTC

Ref. WHO
DD Solid growth

- FC
- PDC
- UC
- Med Ca
- CASTLE (with thymus like elements)
- Parathyroid Carcinoma
- Lymphoma
- Metastatic carcinoma
- MucoEpidermoid Carcinoma
- Solid PTC
Graves

Histopathology 2006, 49, 107-120.

Hashimoto

PTC
Follicular adenoma’s can exhibit clear or even grooved nuclei!

Encapsulated PTC: prognosis is so good with lobectomy effecting cure in almost all cases. There is little consequence of mistaking it for a benign lesion.
If PTC nuclei are concentrated in one of the nodules and tend to form one or several “microcarcinoma’s” then we make the diagnosis of FV PTC for the whole nodule.

Take home lesson: Even if one is seeing a lesion resembling a “fetal” follicular adenoma one should look carefully for the nuclear features.
Nuclear Bubbles - Clearing

- Artefact due to underfixation
Tissue reaction PTC

- Exuberant nodular fasciitis-like stromal reaction to PTC obscuring the neoplastic nature of the process
FV-PTC “The real problem “

- Nodule with a single zone of PTC nuclei is a FV PTC
- There is an abrupt change in nuclear morphology compared with the surrounding benign portion.
- Sometimes very difficult to recognize
Follicular Variant of Papillary Carcinoma, FV PTC

Ref. WHO
FV PTC: three subtypes

- Encapsulated
- Poorly circumscribed
- Diffuse, multinodular
1. Nuclear clearing in it may be very focal
2. Nuclear clearing is clonal and subcapsular
3. Follicular neoplasm: nuclei are round, smaller often centrally located clearing due to poor fixation, and change has a diffuse edge.

Histopathology 48, 6 May 2006 p 629
Diffuse variant of FV PTC
“A trap”

- Replaces the whole thyroid
- No edge to the tumor
- No normal thyroid to compare with
Calcification

- Calcified nodule: always decalcification because there are often small PT CA.
Psammoma bodies

- Typical of PTC
- Often when Hurtle cell differentiation: psammoma like bodies
- Hashimoto thyroiditis
- Many in diffuse sclerosing variant of PTC
Small foci of PTC nuclei in benign lesions is not restricted to follicular adenoma’s.

Also Hashimoto’s thyroiditis and nodular (adenomatous) goiter.

If large, clear, irregular nuclei are rare and do not form clusters we do not go beyond the diagnosis of goiter.
Follicular patterned, encapsulated neoplasms

- Adenoma
- Minimally invasive follicular ca
- Follicular variant of PTC
3.5 Well differentiated tumour of uncertain malignant potential

- Follicular architecture and cytology suspicious for papillary carcinoma
- **No** capsule and/or vascular invasion. **Not** suspicious for vascular and/or capsular invasion.
Well differentiated carcinoma

- Capsular and/or vascular invasion
- Cytology is unclear for Pap CA but suspicious for Pap Ca
- Fol. Ca has no lymphocytic infiltrate whatsoever. PTC has always more or less lymphocytic infiltrate
Capsule /Vascular ?

FT UMP

Pap Ca Cyto ?
But
No Capsular breakthrough and
No Vascular Invasion

Clear (proven) Capsule /Vascular invasion But Pap Ca Cyto ?

WD T UMP

WD Ca
Unknown malignant potential UMP

- Follicular Tumour (FT) UMP Capsular breakthrough and/or vascular invasion?
- Well Differentiated Tumour (WDT) UMP PTC cytology in doubt and no capsular or vascular doubt
- Well differentiated carcinoma if there is clear vascular invasion and/or capsular breakthrough but there is doubt about the PTC cytology
WD Carcinoma

- Well differentiated carcinoma if there is clear vascular invasion and/or capsular breakthrough but there is doubt about the PTC cytology.
3.6 Pitfalls
Histopathology 49, 107-120

- Tumour herniation through a capsule
- Reactive vascular proliferation simulating vascular invasion
- Pseudo infiltration of skeletal muscle
- Parasitic noduli simulating metastatic thyroid ca
3.7 Prognosis PTC and FC

- Women have a better prognosis
- With age prognosis get worse
- Before 45 year prognosis is much much better (Man 40 years, Women 50 years)
- Every 10 year prognosis decreases significantly
- Extrathyroid extension or more than 5 cm diameter make them high risk
Prognostic factors in papillary and follicular thyroid carcinoma

- Completeness of surgery and responsiveness to radioactive iodine

A – Age
M – Distant metastases
E – Extrathyroid extension
S – Size of the tumours

Still debatable: aneuploidy (D...AMES), vascular invasion and molecular features (MIB1, p53)
3.8 Medullary Carcinoma: Intermediate grade

- 80% have amyloid, 20% have no amyloid
- Small proportion is calcitonin negative
- Chromo and Synapto and CEA are usually positive
- C cell Hyperplasia is not Med ca
- C cells are most frequent in the lateral regions of the upper poles of the thyroid
- In young and old persons there are C cell aggregates
- Neuroendocrine nuclei instead of PTC nuclei or small nuclei of FC
Med. Ca

- Familial form versus occasional form
- Always genetic counseling
- There is no anaplastic med. Ca. (Undifferentiated)
- DD Meta carcinoid lung
Histological Patterns of Medullary Carcinoma
(UsCAP Short Courses 2004)

- Epithelial (nested)
- Spindled
- Mixed spindle and epithelial
- Papillary
- **Follicular**
- Glandular
- Giant cell
- Small cell
- Clear cell
- Oncocytic
- Squamous
- HTT like
- Carcinoid like
- Pseudo angiosarcoma
- Pigmented
- Neuroblastoma like
- Paraganglion like
- ...

...
Med. Ca

Ref. WHO
Med. CA insular pattern

Ref. WHO
Med. Ca Pseudopapillary pattern

Ref. WHO
Med. Ca vacuolated cells

Ref. WHO
Spindled cell growth pattern of Med. Ca

Ref. WHO
Oncocytic variant of medullary carcinoma. Note the amphophilic staining quality of the cytoplasm and the fibrohyaline bands

Ref. WHO
IHC Med Ca

- Calcitonin
- CEA
- Serotonin
- Bombesin
- Synaptophysin
- Chromogranin (Cave parathyroid adenoma)
- ACTH
- Some are calcitonin negative
Soares et al, Virchows Arch 444:572, 2004

- Follicular ca
  - Poorly diff ca
    - Undifferentiated
  - Poorly diff ca
  - Papillary ca

- Without recognisable FC or PTC/ De novo

- De Novo
3.9 PDC

Poorly Differentiated Thyroid Carcinoma

Intermediate grade
Poorly Differentiated Carcinoma of thyroid

- Reviews of large numbers of thyroid carcinomas have often included examples of carcinomas that are recognizable as originating from follicular epithelium (often with evidence of coexistent papillary or follicular carcinoma), but with some notable differences: moderate to high rates of mitotic activity, composed of solid masses or trabeculae of relatively uniform epithelial cells, tiny follicles present in varying numbers, regions of acute necrosis, and more aggressive than the usual well-differentiated carcinomas.
These tumors generally lack the usual histologic features and exceptional aggressiveness of anaplastic carcinomas, but they are neither typical follicular nor papillary carcinomas.
Criteria for PDC (majority of the tumor)
- All three -

1. Presence of solid/trabecular/insular growth pattern, alone or in combination
2. Absence of the conventional nuclear features of PTC even if criterium 1 is met!
3. Presence of at least one of the following features: convoluted nuclei/mitotic activity more than 3/10 HPF, tumour necrosis
Convoluted nuclei: small round hyperchromatic nuclei with convolutions of the nuclear membrane (raisin like contour, occasional grooves)

Weaker positivity for TG and TTF1, sometimes dotlike paranuclear

If PTC nuclei: PTC with necrosis, PTC with trabecular growth pattern, ...

De novo or from PTC or FC
FIGURE 1. Diagnostic criteria for poorly differentiated thyroid carcinomas.
Insular PDC

Ref. WHO
PDC trabecular with vascular invasion

Ref. WHO
PDC Trabecular

Ref. WHO
Trabecular Growth

- HTT
- Med ca
- FC
- PTC
Solid PD C

Ref. WHO
PDC transformation to UDC

Ref. WHO
Convoluted nuclei

The Turin proposal
3.10. Undifferentiated (Anaplastic) Ca
High grade

- 1. Large pleomorphic giant cells resembling osteoclasts with cellular tissue septae, may have cavernous blood filled sinuses (Osteoclasts are CD 68 pos)
- 2. Spindle cells resembling sarcoma (Vim pos)
- 3. Squamoid
- 4. Paucicellular variant EMA pos, Ker pos.
  P53 positive
UDC Spindle cell

Ref. WHO
UDC Giant cell

Ref. WHO
Paucicellular UDC

Ref. WHO
Fibrosis

- Riedel’s
- Paucicellular anaplastic TC
- Micro PTC
- After ischemic necrosis, regeneration with atypia
- Diffuse sclerosing variant of PTC (TG negative)
3.11 Other Malignant tumours

- Squamous cell carcinoma
- Mucoepidermoid carcinoma
- Sclerosing mucoepidermoid carcinoma with eosinophilia
- Mucinous carcinoma
- Carcinoma with thymus-like differentiation (CASTLE) (AJSP 30, 8, Aug. 2006)
- Soft tissue: Often SFT
- Angiosarcoma which is also high grade
Other bis

- Teratoma
- Lymphoma and plasmocytoma low grade is MALT and high grade is Diffuse B lymphoma
- Ectopic thymoma
- Smooth muscle tumours
- Angiosarcoma
- PNST
- Paraganglioma
- FDC
- Langerhans cell histiocytosis
### 3.12 IHC- WHO Book

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<tr>
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<th>Ki67</th>
<th>Bcl2</th>
<th>Bcl1</th>
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<td>Normal</td>
<td>&lt;5%</td>
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<td>Well Diff.</td>
<td>&lt;10%</td>
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<td>Poorly</td>
<td>10-30%</td>
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<td>Anaplastic</td>
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Chromogranin

- Med Ca
- Solid cell nest
- Parathyroid adenoma
- Meta from Carcinoid lung
TG

- Note: macrophages may contain thyroglobulin in lymph nodes draining thyroid tumors (J Clin Pathol 2001;54:314)
- TG is well known to diffuse through local tissues resulting in artefactual staining that can hamper the diagnosis.
IHC

- CK 7 Neg and CK 20 Neg.
- CK 7 may be positive
- DD HCC, Lung (small cell), Prostate, RCC, Squamous cell CA, ...
3.13 TNM and Clinical Stage

- I  Intrathyroidal
- II  Cervical adenopathy
- III Locally invasive disease
- IV Distant metastases
TNM

- T1 2 cm or less limited to the thyroid
- T2 more 2cm; less than 4 cm limited to the thyroid
- T3 more than 4 cm or extra thyroid extension
- T4a subcutaneous, larynx, trachea, esophagus or nervus recurrens
- T4b invades prevertrebral fascia, carotid artery or mediastinal vessels
TNM stadia

- Thyroid TNM is the only that brings AGE into account
  - Papillary or Follicular Ca, Not Med. Ca
- Under 45 years: Stage 1, Any T, Any N, M0
- Under 45 years: Stage 2, Any T, Any N, M1 Papillary or Follicular Ca
If older than 45 years: All anaplastic carcinoma’s (undifferentiated) are considered T4

- T4a intrathyroid
- T4b extrathyroid
TNM

- N1a to level 4 pre or para tracheal
- N1b cervical or superior mediastinal
3.14 Metastases

- Fol. Ca
  - Lungs and Bones
- PTC
  - Lymph nodes. Thyroid tissue in a lymph node is near always a metastasis and it is a metastasis of PTC! (cfr. supra: normal thyroid in lymph nodes)
- A cystic lesion with only slight atypia of the comumunar cells in it, in the neck is often a metastatic PTC!
Cystic Meta of PTC
Meta’s to the Thyroid

- RCC
- Lobular breast
- Mucinous ca of digestive tract
- Squamous cell ca of digestive tract
- All sorts
Hyalinizing trabecular adenoma

- Fibrous capsule
- Trabecular arrangement of columns of cells in parallel arrays.
- Sparse mitotic figures.
- Occasional grooving, clearing and inclusions
- Minimal capsular and vascular invasion possible
- No medullary carcinoma.
- DD encapsulated PTCA Excellent prognosis of both.
HTT
HTT
HTT
Before coffee: test

AJSP, 30, 2, feb. 2006
Classic PTC

Tall cell variant

PTC with Psammoma bodies

Follicular variant of PTC
Thank You!!!!

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Coffee or questions?