FNAC of epithelial borderline and in situ lesions of the breast

FNAC of microcalcifications

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Lesions included

- Ductal carcinoma in situ (DCIS)
  - High grade
  - Non-high grade
- Atypical ductal hyperplasia (ADH)
- Columnar cell lesions (CLL), including flat atypia
- Lobular neoplasia
  - Atypical lobular hyperplasia (ALH)
  - Lobular carcinoma in situ (classical)
  - Pleomorphic lobular carcinoma in situ
Breast lesions associated with radiological microcalcifications

- Atrophy, inflammatory lesions
- Benign non-tumour conditions
  - Adenosis
  - UDH (usual ductal hyperplasia)
- Benign tumours
  - papilloma
  - fibroadenoma
  - adenomyoepithelioma
- Borderline proliferative lesions (= columnar cell lesions)
- PLCIS
- Ductal carcinoma in situ
- Invasive lesions
Ductal carcinoma in situ (WHO definition)

• A neoplastic proliferation of epithelial cells confined to the mammary ductal-lobular system
• A subtle to marked cytological atypia
• An inherent but not necessarily obligate tendency for progression to invasive breast cancer
(Histologic) growth pattern subtypes of DCIS

- Solid
- Cribriform
- Micropapillary
- Papillary
- Comedo
- Non-comedo
- Apocrine
- Signet ring type
- Clear cell type
- Flat/”clinging”

All subtypes are reflected in the cytological specimens
(Histological) grading of DCIS

• Depends primarily on the nuclear atypia

• Low nuclear grade
  – Small monomorphc cells (growing in arcades, micropapillae, cribiform or solid patterns)

• Intermediate grade
  – Cells with mild to moderate variability in shape, size, chromatin pattern and variably prominent nucleoli
  – Comedo type necrosis may be present

• High nuclear grade
  – Highly atypical cells
Grading of DCIS


- Cytological grading of DCIS
  - high grade DCIS – G3 (irrespective of growth pattern as well as comedo type necrosis or not): > 2 x RBC
  - non-high grade DCIS: < 2 x RBC
  - comedo type necrosis seen: G2

- Concordance with histology 95 %
In a setting of mammographic microcalcifications WITHOUT a tumour

the following features are characteristic of high grade DCIS:
Threedimensional solid or cribriform aggregates
Nuclei > 2 x RBC
Comedo type necrosis
Occasionally papillary or micropapillary
Variable number of single cell component

Note also the microcalcifications!
Dissociation in single cells is (still) a criterion of malignancy,

- But it is NOT a feature of invasiveness
Diagnostic considerations high nuclear grade DCIS

- Some cases of IDC grade 3 may present cytologically with necrosis and microcalcifications on FNAC, but the radiology will be that of a tumour
- A few DCIS may be tumour-forming (-8% with radiological mass or asymmetry)
- Palpable tumours with cytologic characteristics like DCIS are invasive in 97% of the cases
- Microinvasion will not be sampled
- Invasive lesions not recognised radiologically will not have been sampled and about 20% of radiological DCIS will have an invasive component in the surgical specimen
- Single cells are not a feature of invasion
DCIS varia

• In a setting of microcalcifications without tumour a diagnosis of high grade DCIS may be given
• The question is not «invasive OR in situ», but «is there an invasive component in addition to the DCIS?»
• The larger the extent of high grade DCIS, the larger the risk of an additional invasive component

• In a setting of radiological tumor, approx 97 % of the lesions are invasive (with or without an in situ component)
In a setting of microcalcifications without tumor, the following is characteristic of a none-high grade DCIS (low and intermediate grades)
Very large three-dimensional aggregates; solid, cribriform and often more cohesive than high grade lesions.
Cell monotony
Micropapillary groups
True papillary structures
Monolayer (two-dimensional) sheets

+micropapillary
Variable number of single cells
Microcalcifications
Occasional comedo type necrosis
Low to moderate/intermediate nuclear atypia
Diagnostic pitfalls and considerations in low- and intermediate-grade DCIS

• The cytological criteria overlap with epithelial hyperplasia with and without atypia (ADH, columnar cell lesions)
  - A diagnosis suggestive of non-high grade DCIS should ONLY result in a diagnostic biopsy for confirmation, never mastectomy or ALND
• Some of the lesions might appear deceivingly monotonous, in contrast to some benign, hyperplastic lesions with a polymorphous cell pattern
• Numerous single cells are not indicative of an invasive lesion
• Myoepithelial cell nuclei on the epithelial groups are no «proof» of a benign lesion.
• Pure subtypes as to growth pattern is virtually non-exisent
Diagnostic categories low grade DCIS

• Equivocal
• C3-C4
• proliferative with low grade atypia
• suspicious for low grade DCIS/ADH
Columnar cell lesions (WHO)

• CCC and CCL are lesions of the terminal-duct lobular unit (TDLU)
  – enlarged, variably diated acini lined by columnar epithelial cells

• Flat epithelial atypia is a neoplastic alteration of the TDLU
  – replacement of the native epithelial cells by one to several layers of a single epithelial cell type showing low-grade (monomorphic) cytological atypia

• Radiologically seen as grouped microcalcifications
Cytological features of the columnar cell lesions have not been published in the cytological literature, but .......
Monolayer sheets, microcalcifications and debris
Crowded palisading strips
Complex sheet/aggregate
Secretoric debris/mucous material, macrophages, microcalcifications
CLL diagnostics and pitfalls/caveats

• The full spectrum of cytologic features is not known
• The entity of CLL harbor a continuous spectrum of architectural and cellular/nuclear changes from «benign» to «flat atypia»
• Myoepithelial cells/nuclei are often absent
• None or low grade nuclear atypia
• Is a risk lesion for simultaneous
  – ILC
  – TUB
  – LCIS/ALH
  – Low grade DCIS/ADH
• Risk of over- and underdiagnosis
• Reporting category: proliferative, with or without atypia, and with a recommendation of biopsy
Example CLL

- 65 yrs
- Group of microcalcifications 1 cm
- US-guided FNAC
Lobular neoplasia – lobular carcinoma in situ

• several variants of lobular carcinoma in situ (LCIS) have been recognized
  – classical type
  – **pleomorphic LCIS (PLCIS)**
  – LCIS with Comedo Necrosis
  – carcinoma in situ with mixed ductal and lobular features
  – clear cell variant
  – signet ring cell variant
Pleomorphic lobular carcinoma in situ (PLCIS)

Sneige N et al. Mod Pathol 2002

- Cells appear dyshesive
- More pleomorphism than in “classical” LCIS
- Usually abundant cytoplasm
- Cytoplasm may appear eosinophilic or granular (apocrine appearance)
- Comedo type necrosis and microcalifications common
PLCIS

- radiologically they appear as suspicious microcalcifications (almost always present)
- can be difficult to differentiate from ductal carcinoma in situ (on histology)
  - The dyshesive appearance of the cells is helpful in making this diagnosis,
  - lack of E-cadherin
Immunophenotype of PLCIS

- ER/PgR positive
- E-cadherin negative
- may show HER2 protein overexpression/gene amplification (particularly if associated with invasive carcinoma)
- may show p53 positivity
- moderate to high Ki67 labeling index
Cytologic features of PLCIS

• Solid three-dimensional aggregates
• Dyscohesive with loosely cohesive cells and often abundant single cells
• Variable, but often abundant cytoplasm; often granular and eosinophilic
• Distinct cellular pleomorphism with variable cellular size and shape
• Often plasmacytoid
• Cytoplasmic vacuoles more common in PLCIS than in DCIS
• Distinct nuclear pleomorphism with nuclear size up in the range of high grade DCIS (> 2x RBC)
• Comedo type necrosis and microcalcification AS IN DCIS
Cell dissociation and pleomorphism
Comedo necrosis and microcalcifications
Microcalcification
Solid, threedimensional aggregates and myoepithelial cells
Cytoplasmic vacuoles and amount of cytoplasm
PAP and ThinPrep morphology
Which means:

• Nuclear features, amount and appearance of cytoplasm, dissociation and pleomorphism are not distinguishable from high nuclear grade DCIS

• *No cytomorphological feature(s) that definitely separates PLCIS and high grade DCIS*
If you consider PLCIS: E-cadherin ICC
Diagnostic considerations PLCIS

• Obviously malignant cells
• Radiological microcalcification without tumour, suspicious of high grade DCIS
• Total overlap with cytological criteria of high grade DCIS
• Perhaps more plasmacytoid in appearance and with more cytoplasm than most DCIS
• Cytoplasmic vacuoles more common than in DCIS
• Nuclear size > 2 x RBC, but usually not very much larger
• Previously diagnosed as DCIS in histology and cytology

• As of today: no difference in treatment
End of session!