Diagnostic pitfalls in breast FNAC
Topics included

• “Atypical” fibroadenomas
  – Cellular/proliferative
  – Myoepithelial cell hyperplasia
• FA vs low grade phyllodes tumour
• FA vs low grade (ductal) carcinomas
• Adenomyoepithelioma
• Mucinous lesions
• Cell dissociation
• Metastases
Atypical fibroadenoma

- A lesion with some, but not all of the characteristic features of FA
- In addition one or more cytomorphological features that may be suspicious of malignancy
- < 10 % of FA are diagnosed cytologically as “atypical”
- > 80 % of “atypical” FA are histologically benign
FA with unusual ductal hyperplasia
We “accept” quite some nuclear and other changes within the diagnosis of an ordinary FA

- Enlarged nuclei
- Distinct nucleolus, especially if focal
- Some dyscohesion
- High cellularity
What is too much atypia?

• The whole or a large part of the cell population show cellular atypia
  – distinct or even prominent nucleolus
  – increased n/c-ratio
  – irregular nuclear contour
  – crowding
• Increased dyscohesion with a distinct population of single (epithelial) cells, occasionally dominant
• Increased cellularity
• Few naked nuclei
Diagnostic aid(s) in favor of benign

• Atypia is focal
• Patients usually < 40 yrs
• A concomitant benign component
  – epithelial
  – stromal
  – naked nuclei
• Radiologically benign consistent with FA
• May be not use the smallest needles, because stromal fragments and larger epithelial sheets might not be present (use 0.7 mm needle ?).
Myoepithelial cell hyperplasia

- Might present with a large single cell population with preserved cytoplasm
- A nucleolus might be present
- NO chromatin abnormalities, i.e. uniform chromatin structure
- Some anisonucleosis might be seen
- Is hardly ever noticed on histology
- A true DCIS of myoepithelial cell type is exceedingly rare
What are the reasons for cellular atypia in FA?

- Hormonal (influence most pronounced in the secretory menstrual phase)
- Focal secretory activity
- Inflammatory response (e.g., in the menstrual phase)
- Metaplasia
- True/genuine preneoplastic atypia
True carcinomas originating in FA

- Rare!
- Mainly older women
- Most reported seem to be LCIS
- DCIS and IDC may occur
FA versus low grade carcinomas

• Cellular, proliferative FA with enlarged nuclei and distinct nucleolus
• Cellular dissociation
  – genuine
  – artefact (smearing)
• Evenly distributed chromatin, evt with a peripheral enhancement consistent with (increased) proliferative activity
• NB look for presence of typical myxoid stromal fragments and/or naked nuclei
• 3% of breast FNAC cases diagnosed as carcinoma were histologically FA (Benoit JL et al. Fibroadenoma of the Breast: Diagnostic Pitfalls of Fine-Needle Aspiration. Diagn Cytopathol 1992; 8(6): 643-7).
Phyllodes tumour

- Circumscribed, fibroepithelial neoplasm resembling fibroadenoma
- Double-layered epithelial component hypercellular stromal/mesenchymal component which in combination elaborate leaf-like structures

- Benign/borderline/malignant (WHO)

- In the recent literature:
  - Low grade PT (benign + most borderline)
  - High grade PT

- Variable stromal cellularity, overgrowth, atypia and mitoses
- Heterologous elements and necrosis in malignant cases
FA versus low grade phyllodes tumour

- Cytological findings are at best indicative!
- Size, demarcation of and cellularity of stromal fragments
- **Single spindle cells**
- Epithelial component of little significance
- Age of patient (generally 20 yrs older than the mean age of FA)
- Clinical history, rapid growth?
- Radiology (?)
- Size of tumour
Adenomyoepithelioma

- Usually a solitary mass
- < 10 mm – several cm; median size 2.5 cm
- Radiologically round with somewhat fuzzy margins
- Histologically a dual cell population of epithelial and myoepithelial cells, fibrous septa with hyalinisation
- Malignancy can occur in both populations: either as single component or both simultaneously
Histological features adenomyoepithelioma
Cytological findings in adenomyoepithelioma

- A dual cell population of both epithelial and spindled cells
- Mild to moderate nuclear pleomorphism
- Occasional intranuclear cytoplasmic vacuoles
- Naked bipolar cells
- Metachromatic, fibrillary myxoid material
- No necrosis or mitoses
- Metachromatic, basal membrane-like globules may be present
Differential diagnoses adenomyoepithelioma

• There may be a distinct cellular pleomorphism which may lead to a false suspicious or false malignant diagnosis of carcinoma

• Presence of basal membran-like globules may mimic findings in adenoid-cystic carcinoma

• Adenomyoepithelial carcinoma looks like a ductal carcinoma on cytology
Mucinous lesions (stromal or epithelial compartment)

- Fibrocystic changes (FCC)
- Myxoid fibroadenoma (and phyllodes tumour)
- Adenoid-cystic carcinoma
- Matrix-producing metaplastic ca.
- PEK med myxoid stroma
- Pleomorphic adenoma

- Mucocele-like lesions (MLL)
  - Benign-nodular mucinosis, injected (foreign) mucin-like material
  - Associated with ADH, CCL
  - Associated with DCIS, flat atypia
  - Associated with invasive mucinous carcinoma

- Mucinous cystadenocarcinoma
- Invasive mucinous carcinoma
- Mixed mucinous – ductal carcinoma
- Metastasis from mucinous carcinoma, usually colorectal origin
Mucin in fibrocystic changes

Torill Sauer, Akershus University Hospital, Norway
Mucocele-like NOS
Myxoid fibroadenoma
Loss of cohesion i cytological specimens

- Benign lesions that may present with a single cell component
  - Fibroadenoma
  - Papilloma
  - Adenomyoepithelioma
  - Complex sclerosing lesion
- Dyscohesion in preinvasive lesions
  - Atypical lobular hyperplasia (ALH)
  - Lobular carcinoma in situ (LCIS)
  - DCIS
  - Some columnar cell lesions, including flat atypia
- All malignant/invasive lesions
Which means

• Some benign lesions may present with a single cell component (myoepithelial cell hyperplasia!)

• In the vast majority though, loss of cohesion is a feature of neoplastic cells,

BUT

☑️ It is NOT a feature of invasiveness, both lobular neoplasias and DCIS will present with a single cell population

DCIS G1
Metastases

• Metastatic lesions in the breast are uncommon and make up about 3% of all tumors in the breast.
• Most of them are metastases from the contralateral breast
• Less than 0.5% will represent metastases from a primary tumor outside the breast
• They are often located superficially, but cannot be differentiated from a primary breast tumor on clinical appearance
• They often occur as palpable round tumors, firm and freely movable with no fixation of the overlying skin or the underlying pectoral muscle.
• There is no nipple discharge.
Clinical relevance of diagnosis

• Metastatic tumors in the breast require treatment according to origin and type of tumor
• Important to recognize these lesions in FNAC in order to avoid unnecessary mastectomy or non-relevant chemotherapy
• Many of the patients will have a previous history of a non-mammary malignancy
• Up to 1/3 of the metastatic lesions may present themselves primarily in the breast without any other known primary
Radiological findings

- Radiologically there may be a single or multiple nodules that tend to have the same size on palpation and mammography.
- Mammography typically show a circumscribed, round nodule with slightly irregular margins.
- There is usually no microcalcification or spiculation.
- Microcalcification may occur, but usually as psammoma bodies in metastatic ovarian carcinomas as well as in metastatic lesions from the lung and the thyroid.
Origo of metastases

• Malignant lymphoma/leukemia and malignant melanomas are the most common non-epithelial metastases

• Lung, ovaries, kidney, thyroid, cervix, stomach, colon and prostate are the most common origins of epithelial malignancies.

• From own (previous) institution
  – Metastatic lesions in the breast are far more common in men (23.3 % vs 0.46 %) than in women
  – Lung is the most common origin (41.7 %)
  – Primary tumour unknown at the time of FNAC in 38.9%
  – Primary tumour remained unknown in 5/36 = 13.9 % of cases
  – 88 % of carcinomas are high-grade (G3)
  – totally 6317 malignant FNAC in the breast during 1990 – 2007: 9 ML(0,1 %), 3 MM, 1 MFH (male) and 34 metastatic carcinomas

Torill Sauer, Akershus University Hospital, Norway
When should we suspect that a tumour in the breast is metastatic and not primary?

- RARELY!

- Unusual clinical and/or radiological presentation should alert us
- Unusual cellular morphology
- (very) high nuclear atypia
- Male patient
Varia

- Mamma lactans
- Granulomatous mastitis
- Fat necrosis
- Florid gynecomastia
- Microglandular adenosis vs tubular carcinoma
Unknown case

- 48yrs
- ILC G2 (9 mm diameter) in the right breast one year ago (BCT with free resection margins and negative SN)
- a MR control (due to dense breast tissue) revealed two tumours in the left breast
- Both lesions identified with post-MR US:
  - One consistent with FA
  - One suspicious for malignancy (6-7 mm in diameter)
- US-guided FNAC of both lesions
Wash-out curve
WHAT IS YOUR DIAGNOSIS?
Still confused? But definitely on a higher level!

Faroe Islands July 2014
<table>
<thead>
<tr>
<th></th>
<th>Fibrocystic Change</th>
<th>Mucocele-Like Lesion</th>
<th>Myxoid Fibroadenoma</th>
<th>Colloid Carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cellularity Pattern</strong></td>
<td>0 to 3+</td>
<td>Mostly 0 or 1+; rarely 2+</td>
<td>3+</td>
<td>2+ to 3+</td>
</tr>
<tr>
<td></td>
<td>Cohesive epithelial cell clusters associated with myoepithelial cells</td>
<td>Presence and amount of an epithelial component directly proportional to the degree of hyperplasia within the MLL; pattern similar to that for FCC</td>
<td>Staghorn epithelial clusters, stromal fragments, and numerous oval bare nuclei</td>
<td>Highly variable from cohesive sheets, 3-dimensional balls, to predominance of single epithelial cells</td>
</tr>
<tr>
<td><strong>Atypia</strong></td>
<td>No</td>
<td>No</td>
<td>Mild atypia and dissociation are usual</td>
<td>1+ to 2+; if high nuclear grade (3+), suspect ductal carcinoma, NOS type</td>
</tr>
<tr>
<td><strong>Background</strong></td>
<td>Oval bare nuclei and macrophages present; no stromal fragments</td>
<td>Similar to that for FCC</td>
<td>Numerous oval bare nuclei; stromal fragments</td>
<td>No oval bare nuclei; no stromal fragments; prominent thin-walled capillaries present</td>
</tr>
<tr>
<td><strong>Nature of mucinous material</strong></td>
<td>Wispy or colloid-like; positive for mucicarmine, PAS, alcian blue</td>
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<td>Strandy; negative for mucicarmine; positive for PAS, alcian blue</td>
<td>Wispy or colloid-like; positive for mucicarmine, PAS, alcian blue</td>
</tr>
<tr>
<td><strong>Association of mucinos material with other smear components</strong></td>
<td>Similar to MLL</td>
<td>Mostly acellular mucin; mucin may contain rare macrophages, apocrine cells, and benign ductal epithelial cells</td>
<td>Epithelial cells, stromal fragments, and oval bare nuclei float in mucin</td>
<td>Malignant epithelial cells and thin capillaries float in mucin singly and in clusters</td>
</tr>
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