Flat Epithelial Atypia

Richard Owings, M.D.

University of Arkansas for Medical Sciences
Department of Pathology
• Flat epithelial atypia can be a difficult lesion
• May be a subtle diagnosis
• Lots of changes in the breast
• Numerous previous names and different descriptions
• Patient management is ambiguous.
Why so difficult

• Often occurs around definitively neoplastic lesions.
• Often occurs in the setting other columnar cell and proliferative lesions.
• Relative interpretation of “atypia” and “flat”
Flat epithelial atypia

“A presumably neoplastic intraductal alteration characterized by replacement of the native epithelial cells by a single or 3-5 layers of mildly atypical cells.”
Histologic criteria

• Enlarged ductules or lobules
• Normal epithelial cells replaced by 1-4 cell layers of cytological atypical cells which are usually monomorphc
• The glands typically have rounded contours
• No complex architecture (Flat)
• Attenuated myoepithelial cells
• Atypia is small, round, and monomorphc
Clinical significance

• Low grade non-obligate pre-neoplastic lesion

• Association with other lesions
  – Atypical ductal hyperplasia
  – Lobular neoplasia
  – Low grade ductal carcinoma in situ (cribiform and micropapillary types)
  – Low grade invasive carcinoma (Tubular carcinoma)

• FEA lesions are typically excised following diagnosis by biopsy.

• Excision may demonstrate a worse lesion.
“At least some columnar cell lesions, particularly FEA, are neoplastic proliferations that may well represent either a precursor to, or at least the earliest morphologic manifestation of, a low grade DCIS as well as a precursor to invasive carcinoma.”

Excisions following FEA on CNB

• ADH was found in 17.3% (37/214 cases) of “pure” FEA cases on the first set of biopsy levels by cutting 3 additional levels.

• A worse lesion (ADH, DCIS, LN) was found in 23 of 35 (67%) follow up excisions after complete submission.

• 14% of patients with FEA only on CNB may have DCIS or invasive carcinoma (5/35) on excision.

• Similar to ADH on CNB.

Excisions following FEA on CNB

• 3/15 (20%) patients with FEA only by CNB were found to have worse lesions.
  – 1 was DCIS and 2 were IDC
  – Not correlated to residual microcalcifications

• 6/46 (16%) patients with ADH only by CNB were found to have DCIS.

FEA-Molecular

• Clonally and molecularly related to ADH, lobular neoplasia, and low grade tubular carcinoma
• Similar chromosomal aberrations most commonly involving chromosomes 11q and 16q
• FEA colliding or merging into a low grade DCIS has similar chromosomal aberrations
Differential Diagnosis

• From a trainee perspective, FEA, columnar cell lesions, and ADH are probably the most difficult to understand.

• This is likely due recognizing “atypia”
  – Separating benign from atypial is difficult
  – Lots of things are “atypical” (both benign and malignant)
  – Instead we have to recognize these lesions as neoplastic
“Atypical” looking breast lesions/Differential diagnosis

- Myoepithelial hyperplasia
- Fibrocystic change (low power cysts)
- Usual ductal hyperplasia
- Columnar cell lesions without atypia
- Apocrine metaplasia
- Lactation changes
- Blunt duct adenosis
- Flat ductal carcinoma in situ
Interobserver variability

• Most studies have shown good reproducibility
  – Typically compared after brief tutorial with digitized images.
  – Little variability in separating ADH, DCIS, and normal breast
  – Most variable lesions were those classified as columnar cell lesion with and without atypia.


Management

- FEA on CNB is usually followed by excision.
- Size of the core biopsy
  - Upgrade rate in cases of ADH is inversely proportional to core size (14 g to 11 g).
- Complete removal of microcalcifications
  - Adjacent foci of DCIS or invasive carcinoma without calcifications has been documented
- Follow up MRI
- Clinical features such as age, size of lesion, patient desires
Closing remarks

• FEA can be a tricky lesion due in a large part to its history, evolving terminology, and place in the classification system.

• The low grade end of any classification system can be difficult

• Separating FEA from other proliferative lesion
  – Over calling benign lesions

• Separating more malignant lesions from FEA.
  – Under calling malignant lesions
Closing remarks
Flat Epithelial Atypia

Richard Owings, M.D.

University of Arkansas for Medical Science
Little Rock, Ar