Case study 1

Rie Horii, M.D., Ph.D.
Division of Pathology
Cancer Institute Hospital,
Japanese Foundation for Cancer Research
Present illness:
A 50 y.o. premenopausal woman was found abnormal mammogram results and referred to Cancer Institute Hospital.

Physical findings:
No mass palpable in either bilateral breasts nor bilateral axillary fosses. No nipple discharge.

Family history of breast and ovarian cancer: none
Past history of breast disease: none
Gravitates: three times, Parturition: twice
Mammogram at the initial visit
Right outer upper area
Amorphous grouped calcifications in scope of 5 x 4mm
Category 3-2 according to the Japanese MMG Guideline
Ultrasound at the initial visit

Bilateral breast cysts (Mastopathy)
Stereo-guided vacuum assisted breast biopsy
(Mammotome™ biopsy)

- 5 samples of 11 gauge needle biopsy
- Micro-calcifications were confirmed at 3 of 5 samples.
- Micro-mark was inserted.
Pathological findings of biopsy specimens
Stereo-guided vacuum assisted breast biopsy
(Mammotome™ biopsy)

- 5 samples of 11 gauge needle biopsy

- Micro-calcifications were confirmed at 3 of 5 samples.

- Micro-mark was inserted.
Micro-calcification

Original magnification: Objective lens X2
Atypical in situ lesion with micro-calcifications
A terminal duct-lobular unit with distended acini and secretory luminal contents. The spaces are lined by one to three layers of monotonous atypical cells.
These cells are columnar and have eosinophilic cytoplasm and oval nucleus with mild atypia. Cytoplasmic snouts are evident. The myoepithelium is indistinct. This lesion was comparable to flat epithelial atypia (FEA) according to the WHO histological classification.
Stereo-guided vacuum assisted breast biopsy (Mammotome™ biopsy)

- 5 samples of 11 gauge needle biopsy
- Micro-calcifications were confirmed at 3 of 5 samples.
- Micro-mark was inserted.
Original magnification: Objective lens X2
Atypical in situ lesion
A solid growth of monotonous atypical cells fills the duct lumen. A few micro-lumens are evident.
These cells are cuboidal and have relatively abundant cytoplasm and oval nucleus with mild atypia. The myoepithelium is evident. This lesion was comparable to atypical ductal hyperplasia (ADH) according to the WHO histological classification.
Stereo-guided vacuum assisted breast biopsy (Mammotome™ biopsy)

- 5 samples of 11 gauge needle biopsy
- Micro-calcifications were confirmed at 3 of 5 samples.
- Micro-mark was inserted.
Atypical in situ lesion with micro-calcifications
Original magnification: Objective lens X10
A solid growth of atypical cells expands acini of a lobule.
These cells show mild atypia and loss of cohesion. This lesion was comparable to atypical lobular hyperplasia (ALH) according to the WHO histological classification.
Our diagnosis of the biopsy specimens

Atypical in situ lesion of the breast.

WHO histological classification
- Flat epithelial atypia (FEA)
- Atypical ductal hyperplasia (ADH)
- Atypical lobular hyperplasia (ALH)

Comments:
Benignity or malignancy cannot be determined. Periodic follow up is needed.
1 year follow up

MMG: No change

US: Right outer upper area
Low echoic lesion, 5mm in diameter
Suspicious of concentrate cyst
2 years follow up

MMG: No change
US: Low echoic lesion, 7mm in diameter
(Is growth present?)
2 years follow up

US-guided aspiration biopsy cytology was performed to the low echoic lesion in the upper outer area of the right breast. Cytological diagnosis is suspicious of malignancy.
Preoperative MRI

Multiple small nodules are segmentally located near a micro-mark.

Suspicions of DCIS or micro-invasive breast cancer.
Operation

Right partial mastectomy with sentinel lymph node biopsy was performed.

Sentinel lymph nodes showed negative for cancer by frozen sections during the surgery.
Axillary lymph nodes dissection was omitted.
Specimen mammography of the partial mastectomy material

Peripheral site

Micro-calcifications

Micro-mark

Nipple site
Whole material is pathologically examined by 5 mm wide serial section.
Pathological findings of surgical materials
Our diagnosis of the surgical materials

Noninvasive mixed ductal and lobular carcinoma of the breast.
Original magnification: Objective lens X10
US-detected lesion shows histological findings of noninvasive ductal carcinoma, cribriform type.
Cancer cells show the cribriform structure.
Loupe image of the representative section

Subcutaneous fat

Surgical margin

Carcinoma in situ
Two distinct morphological patterns are seen in this area: noninvasive ductal carcinoma on the left and lobular carcinoma in situ on the right. Transitional zone between ductal and lobular carcinoma is seen on the center.
Noninvasive ductal carcinoma, flat type.
Noninvasive ductal carcinoma, flat type.
Noninvasive ductal carcinoma

Flat type

Cribiform type

Original magnification: Objective lens X40
Cancer cells have relatively abundant cytoplasm, round to oval shaped nucleus and show tubular formations.
Lobular carcinoma in situ with a micro-calcification
Loosely cohesive cancer cells proliferate beneath the native epithelial cell’s lining (pagetoid growth pattern).
Original magnification: Objective lens X10
Transitional zone between ductal and lobular carcinoma with micro-calcifications
Histological structure of this area resembles those of lobular carcinoma in situ, but cancer cells appear more adherent than typical lobular carcinoma in situ.
Noninvasive mixed ductal and lobular carcinoma

Two distinct morphological patterns are seen in this area: lobular carcinoma in situ on the right and transitional zone on the left. Lobular carcinoma cells show negative staining for E-Cadherin.
Surgical margin: negative for cancer.
No lymph node metastasis
No adjuvant therapy

The patient is now alive without any recurrence 4 years after the surgery.
Review of pathological findings of biopsy specimens
Our diagnosis of the biopsy specimens

1. Flat epithelial atypia
2. Atypical ductal hyperplasia
3. Atypical lobular hyperplasia

Atypical in situ lesion of the breast
Biopsy specimen
Flat epithelial atypia

Surgical specimen
Noninvasive ductal carcinoma, flat type

Original magnification: Objective lens X40
Pathological findings of FEA resemble those of noninvasive ductal carcinoma, flat type.
Biopsy specimen
Atypical lobular hyperplasia

Surgical specimen
Lobular carcinoma in situ

Original magnification: Objective lens X40
Pathological findings of ALH resemble those of lobular carcinoma in situ.
Biopsy specimen
Atypical ductal hyperplasia

Biopsy specimen
Flat epithelial atypia

Original magnification: Objective lens X40
Cytological findings of ADH resemble those of FEA.
Lesions which were diagnosed as atypical in situ lesion in the biopsy specimens could be parts of noninvasive carcinoma.
Discussion points for the case

(A) Pathological diagnosis of this case
   - Surgical specimen
   - Biopsy specimen

(B) Management of this case after needle biopsy
Our diagnosis of the surgical materials

Noninvasive mixed ductal and lobular carcinoma of the breast.
Discussion (A): Surgical specimen

- What would be your diagnosis of the surgical specimen?

- What would be your terminology of noninvasive carcinoma which have both ductal and lobular components?
Our diagnosis of the biopsy specimens

1. Flat epithelial atypia
2. Atypical ductal hyperplasia
3. Atypical lobular hyperplasia
Discussion (A) : Biopsy specimen

- What would be your diagnosis of the biopsy specimen?

- After seeing the surgical specimen, did you change your diagnosis of the biopsy specimen?

- What would be your terminology of these lesions?
Mixed ductal and lobular carcinoma

Noninvasive carcinoma
- Noninvasive ductal carcinoma
- Lobular carcinoma in situ

Invasive carcinoma
- Invasive and/or noninvasive ductal carcinoma
- Invasive and/or noninvasive lobular carcinoma
Mixed ductal and lobular carcinoma

Mixed ductal and lobular carcinoma often contains noninvasive ductal carcinoma, flat type and lobular carcinoma in situ.

When only these components are sampled by a needle biopsy, pathological diagnosis of mixed ductal and lobular carcinoma is difficult.

Mixed ductal and lobular carcinoma should be considered, when both FEA and ALH are seen in a needle biopsy specimen.
Discussion (B):
Management of this case after needle biopsy

When atypical in situ lesion was found in needle biopsy specimen

- Excision?
- Re-needle biopsy?
- Follow up?
  by MMG or US?
  Interval?
  Indication for re-biopsy?