ICD-O-3
Carcinoma, infiltrating duct, NOS
8500/3 12/8/10
lw

TSS

Path Site code: breast, upper outer quadrant C50.4
CQCF Site: breast, NOS C50.9

SPECIMENS:

A. WLE RIGHT BREAST NEEDLE LOCALIZATION
B. LEFT SIMPLE MASTECTOMY
C. SENTINEL LYMPH NODE #1 LEFT AXILLA
D. SENTINEL LYMPH NODE #2 LEFT AXILLA
E. SENTINEL LYMPH NODE #3 LEFT AXILLA
F. SENTINEL LYMPH NODE #4 LEFT AXILLA
G. SENTINEL LYMPH NODE #5 LEFT AXILLA

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G. SENTINEL LYMPH NODE #5 LEFT AXILLA

INTRAOPERATIVE CONSULTATION DIAGNOSIS:

TPC, D, E, F, G: Sentinel lymph nodes #1-5, biopsies: No tumor seen.
By Drcalled to Dr. a

GROSS DESCRIPTION:

A. WLE RIGHT BREAST NEEDLE LOCALIZATION
Received fresh labeled with the patient's name and "WLE right breast needle localization excision atypical hyperplasia, single-ant, double lateral, triple superior" is a 28 gm oriented wide local excision breast specimen, 6.0 cm from superior to inferior, 4.0 cm from lateral to medial and 2.0 cm from anterior to posterior, with needle localization wire and attached radiograph. The specimen is inked as follows: superior-red, inferior-orange, medial-green, lateral-yellow, anterior-blue, posterior-black. The specimen is serially sectioned from lateral to medial into 6 slices; slice 1 being most lateral, slice 6 being most medial to reveal multiple gray-white nodular areas, the largest of which measures 0.9 cm in greatest dimension and is located 0.3 cm from the anterior margin. The entire specimen is submitted as follows:

A1-A3: lateral margin perpendicular sections taken from superior to inferior slice 1
A4: superior margin slice 2
A5: anterior and posterior margin slice 2
A6: inferior margin slice 2
A7: superior margin slice 3
A8: anterior and deep margin slice 3
A9: inferior margin slice 3
A10: superior margin slice 4
A11: anterior and deep margins slice 4
A12: inferior margin slice 4
A13: superior margin slice 5
A14: anterior and deep margin slice 5
A15: inferior margin slice 5
A16-A17: medial margin perpendicular sections submitted sequentially from superior to inferior slice 6

B. LEFT SIMPLE MASTECTOMY
Received fresh labeled with the patient's name and "left simple mastectomy, stitch in axilla" is a 560 g, 21 x 20 x 3 cm mastectomy with an 11 x 5.7 cm skin ellipse with 0.5 cm well healed scar in the lower outer quadrant, 1.5 cm areola, and a 1 cm everted nipple. Inked as follows: superior anterior = blue, inferior anterior = orange, deep margin = black. The specimen is serially sectioned revealing a 2.5 x 2.3 x 1.7 cm well-circumscribed firm tan mass in the upper outer quadrant that is 1.5 cm from the deep margin. A portion of tumor is submitted for tissue procurement. In the lower outer quadarnt, there is a 1.2 x 1.0 x 0.6 cm hemorrhagic biopsy site, 3.7 cm from the mass. 0.3 cm lateral to the biopsy site is a firm tan nodule, 1.3 cm in diameter. One lymph node is identified near the axillary stitch.
Representatively submitted:

B1-B6: mass from upper outer quadrant
B7-B9: area of biopsy
B10: nodule near biopsy site
B11: upper inner quadrant
B12: upper outer quadrant
B13: lower outer quadrant
B14: lower inner quadrant
B15-B16: areas of possible calcification from upper outer quadrant
B17-B18: nipple
B19: possible axillary lymph nodes

C. SENTINEL LYMPH NODE #1, LEFT AXILLA

Received fresh are 2 tan-pink lymph nodes, 2.0 x 0.9 x 0.9 cm and 0.5 x 0.4 x 0.3 cm. The specimen is serially sectioned and 2 touch preps are taken. The specimen is submitted entirely as follows:
C1: 1 lymph node
C2: 1 lymph node

D. SENTINEL LYMPH NODE #2, LEFT AXILLA
Received fresh is a tan-pink lymph node, 1.0 x 0.6 x 0.6 cm. The specimen is serially sectioned and touch preps are taken. Toto D1.

E. SENTINEL LYMPH NODE #3, LEFT AXILLA
Received fresh is a tan-pink lymph node, 0.3 x 0.2 x 0.2 cm. The specimen is bisected and touch preps are taken. Toto E1.

F. SENTINEL LYMPH NODE #4, LEFT AXILLA
Received fresh is a tan-pink lymph node, 1.4 x 0.8 x 0.2 cm. The specimen is serially sectioned and touch preps are taken. Specimen is submitted entirely in cassette F1.

G. SENTINEL LYMPH NODE #5, LEFT AXILLA
Received fresh is a tan-pink lymph node, 1.8 x 1.0 x 1.0 cm. The specimen is serially sectioned and touch preps are taken and the specimen is submitted entirely in cassette G1.

RESULTS:

SUMMARY OF IMMUNOHISTOCHEMISTRY/SPECIAL STAINS

Material: Block B4
Population: Tumor Cells

Stain/Marker:	Result:	Comment:
ECADHERIN	Positive	

The interpretation of the above immunohistochemistry stain or stains is guided by published results in the medical literature, provided package information from the manufacturer and by internal review of staining performance and assay validation within the Immunohistochemistry Laboratory. The use of one or more reagents in the above tests is regulated as an analyte specific reagent (ASR). These tests were developed and their performance characteristic determined by the . . They have not been cleared or approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary.

DIAGNOSIS:

A. BREAST, RIGHT, NEEDLE LOCALIZATION WIDE LOCAL EXCISION:
- LOBULAR CARCINOMA IN SITU.
- SMALL INTRADUCTAL PAPILLOMA, RADIAL SCAR, FLORID USUAL DUCTAL HYPERPLASIA, COLUMNAR CELL LESIONS, EXTENSIVE SCLEROSING ADENOSIS, DUCT ECTASIA, AND MICROCALCIFICATIONS.
- FOCAL PREVIOUS BIOPSY SITE CHANGES (SEE NOTE).

NOTE: Focal previous biopsy site changes are present in slide A5.

B. BREAST, LEFT, MASTECTOMY:
- INVASIVE DUCTAL CARCINOMA.
  - SBR GRADE 2.
  - 2.5 CM IN GREATEST DIMENSION.
  - MARGINS, NEGATIVE FOR CARCINOMA.
- EXTENSIVE DUCTAL CARCINOMA IN SITU (DCIS), SOLID AND CRIBRIFORM TYPES, NUCLEAR GRADES 2 & 3, WITH COMEDO NECROSIS AND MICROCALCIFICATIONS, INVOLVING LOBULES.
  - DCIS IS FOCALLY WITHIN 1 MM OF THE ANTERIOR-SUPERIOR MARGIN.
  - DCIS IS PRESENT IN UPPER OUTER AND LOWER OUTER QUADRANTS.
- NIPPLE, NEGATIVE FOR CARCINOMA.
- ONE LYMPH NODE, NEGATIVE FOR CARCINOMA (0/1).

NOTE: Three biopsy sites were identified, associated with the tumor, a fibroadenoma and hemorrhage.

C. SENTINEL LYMPH NODE #1, LEFT AXILLA, BIOPSY:
- TWO LYMPH NODES, NEGATIVE FOR CARCINOMA (0/2).

D. SENTINEL LYMPH NODE #2, LEFT AXILLA, BIOPSY:
- ONE LYMPH NODE, NEGATIVE FOR CARCINOMA (0/1).

E. SENTINEL LYMPH NODE #3, LEFT AXILLA, BIOPSY:
- ONE LYMPH NODE, NEGATIVE FOR CARCINOMA (0/1).

F. SENTINEL LYMPH NODE #4, LEFT AXILLA, BIOPSY:
- MICROMETASTATIC CARCINOMA (1.1 MILLIMETERS) TO ONE LYMPH NODE (1/1) (SEE NOTE).

NOTE: The touch prep was reviewed and shows no evidence of carcinoma.

G. SENTINEL LYMPH NODE #5, LEFT AXILLA, BIOPSY:
- ONE LYMPH NODE, NEGATIVE FOR CARCINOMA (0/1).

SYNOPTIC REPORT - BREAST
Specimen Type: Mastectomy
Needle Localization: No
Laterality: Left
Invasive tumor: Present
Multifocality: No
WHO CLASSIFICATION
Invasive ductal carcinoma, NOS 8500/3
Tumor size: 2.5cm
Tumor site: Upper outer quadrant
Margins: Negative
Distance from closest margin: 0.6cm
anterior
Tubular score: 3
Nuclear grade: 2
Mitotic score: 1
Modified Scarff Bloom Richardson Grade: 2
Necrosis: Absent
Vascular/Lymphatic Invasion: None identified
Lymph nodes: Sentinel lymph node only
Lymph node status: Positive 1 / 7
Micrometastases: Yes
Non-neoplastic areas: fibroadenoma, columnar cell change

DCIS present
Margins uninvolved by DCIS:
DCIS Quantity: Estimate 40%
DCIS type: Solid
Cribriform
DCIS location: Both associated and separate from invasive tumor mass
Nuclear grade: High
Necrosis: Present
Location of CA++: DCIS
Benign epithelium

ER/PR/HER2 Results
Performed on Case: (mastectomy)
ER: Positive
PR: Positive
HER2: Negative by IHC

Pathological staging (pTN): pT 2 N 1mi

SYNOPTIC REPORT - BREAST, ER/PR RESULTS
Specimen: Surgical Excision
Block Number: B1

ER: Positive Allred Score: 8 = Proportion score: 5 + Intensity Score 3
PR: Positive Allred Score: 8 = Proportion Score 5 + Intensity Score 3

COMMENT:
The Allred score for estrogen and progesterone receptors is calculated by adding the sum of the proportion score (0 = no staining, 1 = <1% of cells staining, 2 = 1 - 10% of cells staining, 3 = 11-30% of cells staining, 4 = 31-60% of

cells staining, 5 = >60% of cells staining) to the intensity score (1 = weak intensity of staining, 2 = intermediate intensity of staining, 3 = strong intensity of staining), with a scoring range from 0 to 8.
ER/PR positive is defined as an Allred score of >2 and ER/PR negative is defined as an Allred score of less than or equal to 2.
Methodology: Fixation Type and Length: Tissue was fixed in 10% neutral buffered formalin (
for no less than 8 and no longer than 24 hours. Antibody and Assay Methodology: Mouse anti-human ER and PR, (
Comment: This assay can be used to select invasive breast cancer patients for hormone therapy (1).
ER and PR analysis was performed on this case by immunohistochemistry utilizing the ER (ER 1D5, 1:100) and PR (PGR 136, 1:100) antibody provided by Dako, following the manufacturer's instructions listed in the package insert. This assay was not modified, and adherence to all instruction and guidelines were strictly followed. Interpretation of the ER/PR immunohistochemical staining characteristics is guided by published results in the medical literature (1), information provided by the reagent manufacturer and by internal review of staining performance within the Pathology Department.
1. Harvey JM, et al. Estrogen receptor status by immunohistochemistry is superior to the ligand-binding assay for predicting response to adjuvant endocrine therapy in breast cancer. J Clin Oncol. 17:1474-1481, 1999

SYNOPTIC REPORT - BREAST HER-2 RESULTS
HER2 Status Results, Immunohistochemistry Evaluation
Specimen: Surgical Excision
Block Number: B1

Interpretation: NEGATIVE
Intensity: 1+
% Tumor Staining: 1%
Fish Ordered: No

METHODOLOGY
Methodology: Fixation Type and Length: Tissue was fixed in 10% neutral buffered formalin (
for no less than 8 and no longer than 24 hours. Antibody and Assay Methodology: Rabbit anti-human HER2, HerceptestTM (FDA-approved test kit), . Control Slides Examined: External kit-slides provided by manufacturer (cell lines with high, low and negative HER2 protein expression), and in-house known HER2 amplified control tissue were evaluated along with the test tissue. These control slides run along side of this patient's sample showed appropriate staining. Adequacy of Specimen: Adequate, well preserved, clear-cut invasive carcinoma identified for HER2 evaluation.
Scoring Criterion and Scoring System:
IHC Level of Expression(Score) /Tumor Cell Membrane Staining Pattern
Negative (0)/Absence of Staining
Negative (1+)/Faint Incomplete membrane Staining, >10% of Cells
Equivocal (2+)/Weak complete membrane Staining, >10% of Cells
Positive (3+)/Strong complete membrane Staining, >10% of Cells
Equivocal Category for HER2 IHC results: A HER2, 2+ staining result that is interpreted as equivocal may not indicate gene amplification. A FISH test for HER2 gene amplification will be ordered for all HER2 IHC 2+ results.
COMMENT
This assay can be used to select invasive breast cancer patients for Trastuzumab (Hereptin) therapy (1,2). Clinical Trials have shown that Trastuzumab substantially increases the likelihood for an objective response and overall survival for patients with metastatic HER2-positive breast cancer, regardless of whether HER2 tumor status was determined as IHC 3+ or FISH positive. Trastuzumab added to adjuvant chemotherapy substantially increase disease-free survival and decreases the risk of disease recurrence by about 50% for patients with early-stage HER2 protein over-expressed or gene amplified invasive breast cancer (3).
HER2 analysis was performed on this case by immunohistochemistry utilizing the FDA approved Dako HercepTest (TM) test kit following the manufacturer's instructions listed in the package insert. This assay was not modified, and adherence to all instruction and guidelines were strictly followed. Interpretation of the HER2 immunohistochemical staining characteristics is guided by published results in the medical literature (4), information provided by the reagent manufacturer and by internal review of staining performance within the Pathology Department.
HER2 TEST VALIDATION
This HER2 immunohistochemical assay has been validated according to the recently revised recommendations and guidelines from the NCCN HER2 testing in Breast Cancer Task Force, and the jointly issued recommendations and guidelines from ASCO and the CAP (5). 80 randomly selected breast cancer samples were tested for HER2 by IHC as outline above and interpreted as, negative (score 0/1+) equivocal (score 2+) and positive (score 3+) without knowledge of the previous reported results.

These cases were also blindly read using two different FISH assay as amplified or non-amplified and the HER2/CEP17 ratios were recorded. After analyzing these results, there was 100% concordance between the IHC and FISH results for cases that were interpreted as either positive or negative by IHC. 9 of the 80 cases were interpreted as equivocal by IHC and of these 3/9 (33%) were non-amplified by FISH and 6/9 (66%) were found to be amplified.

The Pathology Department Immunohistochemistry laboratory takes full responsibility for this tests performance and has programs in place to regularly monitor the proficiency and the interpretation of HER2 assays. The

laboratory also participates in external quality assurance HER2 programs including the CAP proficiency testing program.

REFERENCE
1. Carlson RW, Anderson BO, Burstein HJ, et al., NCCN breast cancer clinical practice guidelines in oncology. J Natl Compr Canc Netw. 2005;3:238-289.
2. Carlson RW, Brown E, Burstein HJ, et al., NCCN Task Force Report: adjuvant therapy for breast cancer. J Natl Compr Canc Netw. 2006;4:S1-S26.
3. Romond EH, Perez EA, Bryant J, et al. Trastuzumab plus adjuvant chemotherapy for operable HER2-positive breast cancer. N Eng J Med 2005;353(16):1673-84
4. Leong ASY, Formby M, Haffajee Z, et al. Refinement of immunohistologic parameters for Her2/neu scoring validation by FISH and CISH. Appl Immunohistochem Mol Morphol. 2006;14:384-389.
5. Wolff AC, Hammond EH, Schwartz JN, et al., American Society of Clinical Oncology/College of American Pathologists Guideline Recommendations for Human Epidermal Growth Factor Recepto 2 Testing in Breast Cancer. Arch of Path and Lab Med 2007; 131:18-43.

PRE-OPERATIVE DIAGNOSIS:
Left Breast Cancer, Right Atypical Hyperplasia

ADDENDUM:
NOTE: Addition to gross description for specimen B – a representative section of skin is submitted in cassette B20 and microscopically, shows no evidence of carcinoma.
ONCOTYPE DX BR' GT CANCER ASSAY
RESULTS: Recurr e Score =: 9
CLINICAL EXPF .NCE: Patients with a recurrence score of: 9 in the clinical validation study had an average rate of Distant urrence at 10 years of 7%

ER Score: Positive 10.8
PR Score: Positive 8.5
Interpretation: Positive ER Score is >= 6.5 Positive PR Score is >= 5.5

See separate report for further information.
Test performed at:

Gross Dictation: Pathologist,
Microscopic/Diagnostic Dictation: Patholog
Microscopic/Diagnostic Dictation: Pathologist
Final Review: Pathologist,
Final Review: Pathologist,
Final: Pathologist,
Addendum: Pathologist
Addendum Final: Pathologist,
Addendum: Pathologist,
Addendum Final: Pathologist

Criteria	Yes	No
Diagnosis Discrepancy		
Primary Tumor Site Discrepancy		
HIPAA Discrepancy		
Prior Malignancy History		
Dual/Synchronous Primary Noted		

Case is (circle): QUALIFIED / UNQUALIFIED
Reviewer Initials: Date Reviewed: