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

TSS.....

Path Site Code: breast, upper outer quadrant (lw) C50.4
CQCF Site: breast, NOS C50.9

SPECIMENS:
A. SENTINEL LYMPH NODE #1 LEFT AXILLA
B. LEFT BREAST
C. UPPER OUTER QUADRANT LEFT BREAST
D. LEFT AXILLARY CONTENTS

UUID:42E9A561-B052-412E-B0FD-563DC097C3C5
TCGA-E2-A140-01A-PR Redacted

SPECIMEN(S):
A. SENTINEL LYMPH NODE #1 LEFT AXILLA
B. LEFT BREAST
C. UPPER OUTER QUADRANT LEFT BREAST
D. LEFT AXILLARY CONTENTS

**********AMENDMENT**********

This case has been amended to change ER/PR results from pending to final results in the breast synoptic report and add ER/PR and Her2/neu synoptic reports.

INTRAOPERATIVE CONSULTATION DIAGNOSIS:
TPA: Sentinel lymph node #1, biopsy: Positive for carcinoma
Gross exam B: Left breast, mastectomy: Multiple tumors identified; closest is 1.5 cm from inferior/anterior aspect
By Dr called to Dr at

GROSS DESCRIPTION:
A. SENTINEL LYMPH NODE #1 LEFT AXILLA
Received fresh is a tan-pink fragment of fibrofatty tissue (4.0 x 2.0 x 1.0 cm). Dissection reveals a firm presumptive lymph node (1.4 x 1.0 x 0.8 cm). The specimen is serially sectioned and touch preps are taken. Submitted in toto in A1.
B. LEFT BREAST
Received fresh labeled "left breast" is a 1,184-gram simple mastectomy specimen (27.0 x 25.0 x 6.5 cm) with a stitch on the axillary tail. The specimen is partially surfaced with a tan-pink ellipse of skin (15.0 x 10.5 cm) with a 1 cm centrally located, partially flattened nipple and 3.5 cm areola rim. The skin surface is remarkable for a grey-white, well-healed scar in the upper outer quadrant measuring 1 cm that is 8.0 cm from the nipple. The specimen is inked and serially sectioned from medial to lateral into 14 slices; slice 1 being most medial, slice 14 being most lateral. The nipple is located in slice 8. The cut surface reveals a grey-white, firm, stellate mass (6.0 x 5.5 x 4.0 cm) located in the upper central and upper outer quadrants and present in slices 7, 8, 9, 10, and 11. This mass measures 1.5 cm from all margins. A second lesion is located in the 7 o'clock position (0.8 x 0.6 x 0.5 cm) in slice 6. Lesion #2 is located 0.6 cm from lesion #1, and measures 1.5 cm from the closest inferior margin. An ill-defined nodular area (lesion 3) is located 4.5 cm superior to lesion #2 in slice 6 and more than 2.0 cm from the deep margin. A portion of the specimen is submitted for tissue procurement. Gross examination did not reveal distinct 12:00 and 10:00 lesions as designated on the request form. Lesions 2 and 3 may correspond to the 10:00 lesions as they did appear grossly separate from the main tumor mass, although very close. The main mass appeared confluent grossly and may encompass the 12:00 lesion. The remaining cut surfaces reveal predominantly yellow lobulated adipose tissue interspersed with grey-white fibrous tissue. Inked code: Superior anterior – blue, orange – inferior anterior, black – posterior. Section code:
B1: Nipple serially sectioned, slice 8
B2: Base of nipple, slice 8
B3: Nodular area above lesion #2, slice 6
B4: Lesion #2, slice 6
B5: Inferior margin, slice 6
B6: Deep margin, slice 6
B7: Superior margin, slice 7
B8-B11: Lesion #1 submitted from superior to inferior, slice 7
B12: Inferior margin, slice 7
B13: Deep margin, slice 7
B14-B16: Lesion #1 submitted from superior to inferior, slice 8
B17: Inferior margin, slice 8
B18: Deep margin, slice 8
B19-B21: Lesion #1 from superior to inferior, slice 9
B22: Deep margin, slice 9
B23: Deep margin, slice 10
B24: Skin with underlining scar, slice 11
B25-B26: Lesion #1 from superior to inferior, slice 11
B27: Deep margin, slice 11
B28: Area immediately adjacent to lesion #1, slice 12
C. UPPER OUTER QUADRANT LEFT BREAST
Received is an unoriented tan-pink fragment of fibrofatty tissue weighing 37 grams and measuring (7.0 x 6.0 x 2.0 cm). The specimen is serially sectioned to reveal predominantly yellow lobulated adipose tissue interspersed with grey-white fibrous tissue. No lesion is grossly identified. Representative sections are submitted in cassettes C1-C4.

D. LEFT AXILLARY CONTENTS
Received labeled "left axillary contents" are multiple tan-pink fragments of fibrofatty tissue aggregating to (10.0 x 9.0 x 3.0 cm). Dissection reveals 17 possible lymph nodes ranging from (0.5 x 0.5 x 0.5 cm to 2.5 x 1.5 x 1.0 cm).
Section code:
D1: Four possible lymph nodes
D2: Four possible lymph nodes
D3: Four possible lymph nodes
D4-D5: One lymph node serially sectioned
D6: One lymph node serially sectioned
D7: One lymph node bisected
D8: One lymph node trisected
D9: One lymph node serially sectioned

DIAGNOSIS:

A. SENTINEL LYMPH NODE #1, LEFT AXILLA, BIOPSY:
- METASTATIC CARCINOMA TO ONE LYMPH NODE (1/1).

B. LEFT BREAST, MASTECTOMY:
- MULTIFOCAL INVASIVE DUCTAL CARCINOMA, POORLY DIFFERENTIATED (SBR GRADE 3), WITH MICROPAPILLARY FEATURES.
- TUMOR SPANS AT LEAST 6 CM AND IS PRESENT IN CENTRAL AREA AND UPPER OUTER QUADRANT.
- DUCTAL CARCINOMA IN SITU, CRIBRIFORM TYPE, NUCLEAR GRADE 2, MINOR COMPONENT.
- MARGINS, NEGATIVE FOR CARCINOMA.
- EXTENSIVE LYMPHOVASCULAR INVASION.
- SKIN AND NIPPLE, NEGATIVE FOR CARCINOMA.
- SKELETAL MUSCLE, NEGATIVE FOR CARCINOMA.

C. LEFT BREAST, UPPER OUTER QUADRANT, EXCISION:
- FIBROADIPOSE TISSUE, NEGATIVE FOR CARCINOMA.

D. LEFT AXILLARY CONTENTS, DISSECTION:
- 1/17 LYMPH NODES WITH METASTATIC CARCINOMA WITH EXTRANODAL EXTENSION (1/17).

SYNOPTIC REPORT - BREAST
Specimen Type: Mastectomy
Needle Localization: No
Laterality: Left
Invasive tumor: Present
Multifocality: Yes
WHO CLASSIFICATION
Invasive ductal carcinoma, NOS 8500/3
Tumor size: Size of Invasive focus: 6cm
Tumor site: Upper outer quadrant
Central
Margins: Negative
Distance from closest margin: 1.5cm
deep
Tubular score: 3 (<10% tubule)
Nuclear grade: 3
Mitotic score: 2
Modified Scarff Bloom Richardson Grade: 3 (8-9 points)
Necrosis: Absent
Vascular/Lymphatic Invasion: Present
Extent: extensive
Lobular neoplasia: None
Lymph nodes: Sentinel lymph node and axillary dissection
Lymph node status: Positive 2 / 18 Extranodal extension

DCIS present
Margins uninvolved by DCIS
DCIS Quantity: Estimate 2%
DCIS type: Cribriform
DCIS location: Associated with invasive tumor
Nuclear grade: Intermediate
Necrosis: Absent

ER/PR/HER2 Results
ER: Positive
PR: Positive
HER2: Pending
Pathological staging (pTN): pT 3 N 1a

SYNOPTIC REPORT - BREAST, ER/PR RESULTS
Specimen: Surgical Excision
Block Number: B20

ER: Positive Allred Score: 8 = Proportion score: 5 + Intensity Score 3
PR: Positive Allred Score: 7 = Proportion Score 5 + Intensity Score 2

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: Breast Core Needle Biopsy
Block Number: B20

Interpretation: EQUIVOCAL
Intensity: 2+
% Tumor Staining: 50%
Fish Ordered: Yes , on Date

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) (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.

CLINICAL HISTORY:

A year-old female with left multicentric disease, large 4.5 cm mass in upper outer quadrant 10 o'clock + IDC with 3 small masses; 12 o'clock + IDC 5 mm mass

PRE-OPERATIVE DIAGNOSIS:

None given

ADDENDUM:

PathVysion HER-2 DNA Probe Kit

Case No

Analytical Interpretation of Results: HER-2 NOT AMPLIFIED

Clinical Interpretation of results

Amplification of the HER-2 gene was evaluated with interphase fluorescence in-situ hybridization (FISH) on formalin-fixed paraffin embedded tissue sections using a chromosome 17 centromeric probe and a HER-2 probe that spans the entire HER-2 gene in the : by Dr. A majority of tumors cells displayed mild polysomy 17 with 2 to 3 chromosome 17 signals and 2 to 5 HER-2 signals, with a HER-2/CEP 17 Ratio </=2.0, consistent with no amplification of the HER2/neu gene.

Block used B20 Source of case:

Tissue fixation formalin-fixed tissue Outside Case No: NA

Tissue source breast Results interpreted: yes

HER2/CEP17 ratio: 1.65

This ratio is derived by dividing the total number of LSI HER-2/neu signals by the total number of CEP17 signals in at least 20 interphase nuclei with nonoverlapping nuclei in the neoplastic mammary epithelial cells. Cells with no signals or with signals of only one color are disregarded.

Method of ratio enumeration: manual count

Limitations

The Vysis PathVysion Kit is not intended for use to screen for or diagnose breast cancer. It is intended to be used as an adjunct to other prognostic factors currently used to predict disease-free and overall survival in stage II, node-positive breast cancer patients. In making decisions regarding adjuvant CAF treatment, all other available clinical information should also be taken into consideration, such as tumor size, number of involved lymph nodes, and steroid receptor status. No treatment decision for stage II, node-positive breast cancer patients should be based on HER-2/neu gene amplification status alone.

Overview of this test

FDA APPROVED REAGENT

PathVysion HER-2 DNA Probe Kit is FDA approved for selection of patients for whom Herceptin® therapy is being considered. These tests were performed in the /, under the direction

of Dr. The results of these studies should always be interpreted in the context of the clinical, morphological, and immunophenotypic diagnosis.

Gross Dictation: (
Final Review: Pathologist,
Final: Pathologist, (
Amendment: Pathologist,
Amendment Review: Pathologist,
Amendment Final: Pathologis
Addendum: Pathologist,
Addendum Final: Patholo

Criteria	Yes	No
Diagnosis Discrepancy		✓
Primary Tumor Site Discrepancy		✓
HIPAA Discrepancy		✓
Prior Malignancy History		✓
Dual/Synchronous Primary Noted		
Case is (circle):	QUALIFIED / DISQUALIFIED	
Reviewer Initials	Date Reviewed:	