Invasive Ductal Carcinoma: Case Report

Abstract
A case of invasive ductal carcinoma in a female breast is described. The pathological diagnosis was stage III invasive mammary carcinoma, ductal type. ER/PR testing was negative and HER2/neu was overexpressed with IHC. HER2/neu was also performed with FISH and was positive.

Introduction
Invasive ductal carcinoma (IDC), sometimes called infiltrating ductal carcinoma, is cancer that originates in the milk duct of the breast and has invaded the surrounding adipose tissue. Overtime, invasive ductal carcinoma can spread to lymph nodes and other tissues. IDC is the most common form of breast cancer and constitutes 80% of breast cancer diagnoses.\(^1\) According to the American Cancer Society in 2013, an estimated 232,340 new cases of invasive breast carcinoma will be diagnosed in women in the United States. They also estimate that 39,620 women in the United States will die from breast cancer in 2013.\(^2\) Thus breast cancer is the second most common cause of cancer death in women following lung cancer and accounting for 29% of newly diagnosed cancers.\(^2\)

The incidence rates of breast cancer are highest in non-Hispanic white women, followed by African American women, and the lowest rate is among Asian/Pacific Islander women. However, breast cancer death rates are highest in African American women.\(^2\) Breast cancer incidence and death rates generally increase with age, with 88% of women being 50 years old or older when diagnosed.\(^2\) Important risk factors of breast cancer are family history of breast cancer, previous history of breast cancer, the degree of estrogen stimulation, and fibrocystic disease with proliferation of an epithelial component.\(^2,3\)

Index case
Patient History
A 63-year-old postmenopausal woman who had four children initially felt a palpable lump in the lateral aspect of her right breast. Patient had no history of hormone replacement therapy, was a non-smoker, previously used oral contraceptives, and her menarche was at 13 years old. Patient also had a family history of breast cancer (maternal aunt). Previous surgical histories include an appendectomy, tonsillectomy and adenoidectomy, and diverticulitis (2003). In 2008, a needle localization was performed and a biopsy was obtained on the right breast lump which revealed microcalcifications that represented benign fibrocystic changes.

On 03/11/2013 a bilateral mammogram screening was performed and was unremarkable.

On 09/3/2013 a diagnostic mammogram and right breast ultrasound identified a few calcifications in the right breast at the 9 o’clock position.

On 09/11/2013 a fine needle aspiration (FNA) procedure was performed on a right axillary lymph node, and it was positive for malignant cells (see Image 1). In addition, a right breast biopsy of the lesion was obtained, and diagnosed as invasive mammary ductal carcinoma, and in-situ mammary carcinoma (see Image 2). Estrogen receptor (ER) and progesterone receptor (PR) were performed using immunohistochemistry (IHC) and were negative. Human epidermal growth factor receptor (HER2/neu) was performed using fluorescent in situ hybridization (FISH) and was positive.
Image 1: FNA of right axillary lymph node stained with papanicolaou from 09/11/2013

Image 2: H&E stain of right breast mass biopsy from 09/11/2013
On 09/30/2013 a bone scan was performed and no evidence of metastatic disease was identified. In addition, a computed tomography (CT) was taken of the chest, abdomen, and pelvis, and revealed the following: a 1.5 cm enlarged right axillary lymph node, multiple pulmonary nodules ranging from 4 to 5 mm, osteopenia with degenerative changes in the spine, and evidence of post-operative changes in the rectosigmoid junction from previous diverticulitis surgery. Patient was advised by a medical oncologist to start treatment with a neoadjuvant trastuzumab and pertuzumab, but the patient declined. She decided to consult with a naturopathic physician and decided against traditional therapy. The patient elected to pursue a Gerson diet.

On 01/09/14 the patient sought another opinion at the Cancer Treatment Centers of America (CTCA) and agreed to integrate traditional therapies to her treatment regimen. The patient was then referred to medical, surgical, and radiation oncologists.

On 01/20/14 a right modified radical mastectomy was performed and submitted to pathology in two parts. Part A was received in formalin labeled “node right above axillary vein” and consisted of four lymph nodes ranging from 0.3 to 1.6 cm. Lymph nodes were representatively submitted in four cassettes. Part B was received in formalin labeled “right breast and axillary contents” and consisted of an 18.5 x 21.1 x 3.1 cm and 640 gram oriented, modified radical mastectomy. The axillary tail measured 11 x 8.5 x 3 cm. The specimen was serially sectioned and revealed a 9.1 x 6.6 x 4.1 cm white, firm, and gritty mass in the lower inner and outer quadrants (see Image 3). A lymph node dissection was performed on the axillary tail and revealed multiple nodes ranging from 0.3 to 5.4 cm. Representative sections were submitted in 57 cassettes.

Image 3: Gross image of mass in right modified radical mastectomy from 01/20/14
Pathology Diagnosis
Part A was diagnosed as metastatic mammary carcinoma from the four lymph nodes above the axillary vein.

Part B was diagnosed as stage III invasive ductal mammary carcinoma of the right breast. The carcinoma directly invaded into the dermis and epidermis and was without skin ulceration. The carcinoma also invaded the skeletal muscle. The margins were uninvolved by invasive carcinoma. Thirty-four lymph nodes were evaluated and twenty-four contained macrometases (<2mm).

Pathologic staging was assessed as follows:
Primary tumor (invasive carcinoma) pT3: tumor >50mm in greatest dimension.
Regional lymph nodes pN3a: metastases in 10 or more axillary lymph nodes.
Distant metastasis pMX: not applicable.

A breast invasive prognostic panel was performed using IHC and the following markers and results were obtained: ER = negative, PR = negative, HER2/neu = overexpressed, proliferation marker Ki-67 = high, tumor protein p53 = negative, and BCL2 = negative.

Pathology Diagnostic Laboratory (PDL) breast recurrence score was additionally assessed and obtained a 68.92 with ≥ 18 indicating an intermediate to high risk distant recurrence probability. The PDL breast recurrence score had not been validated and was used in conjunction with patient history, tumor characteristics, and clinical judgment to help predict the patient’s outcome. The PDL breast recurrence score equation was developed by linear regression using 105 primary breast carcinoma cases with corresponding Oncotype DX score. The parameters used in the equation were Nottingham Histologic Grade, ER percent positive, PR percent positive, HER2/neu overexpression, Ki-67 percent positive, and p53 percent positive.

Discussion
The American Cancer Society recommends that women at 40 years old start receiving annual mammograms to help detect breast cancer. Mammography is a low dose x-ray procedure that visualizes internal structures of the breast to help identify malignancy. Screening mammograms are used for women that have no signs or symptoms of disease. Diagnostic mammograms are used to check for breast cancer after a lump or other sign or symptom has been identified. In addition to mammography, breast ultrasound may be used to image the breast and it utilizes sonography instead of x-rays. The benefit to using ultrasound is that it can help the radiologist differentiate a solid mass from a liquid cystic mass. Another screening method to help detect breast cancer is a clinical breast examination (CBE) since a small percentage of cancers may be missed on mammography, especially in women in their 40s. It is recommended that a breast exam be part of a regular health exam and is done at least every 3 years starting in women in their 20s.

The prognosis of invasive breast carcinoma is strongly influenced by the stage of the disease when the carcinoma is first diagnosed. There are two main staging systems for cancer and they are the TNM classification and the Surveillance, Epidemiology, and End Results (SEER) Summary Stage system. The TNM classification assesses the size of the tumor, and how far it has spread (T), involvement of nearby nodes (N), and presence of distant metastases (M). Then a stage is assigned ranging from 0 to IV. A stage 0 would indicate in situ, stage I indicates early invasive cancer, and stage IV constitutes advanced carcinoma. The TNM is commonly used in the clinical setting and was used in this case. The SEER is used in reporting cancer registry data and public health research and planning.
According to the American Cancer Society, the most recent data of relative survival rates for women diagnosed with breast cancer are: 89% at 5 years after diagnosis, 83% after 10 years, and 78% after 15 years.² Treatment options are considered after many factors are considered such as stage and biological characteristics of the cancer, patient’s age and preferences, and after weighing the risks and benefits of each. Surgery is the first step in treatment and is usually combined with other treatments such as radiation therapy, chemotherapy, hormone therapy, and/or targeted therapies.²

Hormone receptors are routinely performed on all invasive breast carcinomas and ductal carcinoma in situ (DCIS) using IHC. ER and PR testing is done to help predict the effectiveness of using hormonal therapies. Since normal breast tissue has estrogen receptors, but not all breast carcinomas do, if a breast carcinoma expresses one of these receptors, then hormonal therapy may be used to help treat the patient. Breast tumors that are ER/PR positive may respond to treatment with anti-estrogen drugs such as Tamoxifen or Aromatase Inhibitors (AIs).³, ⁶ The patient in this case was ER/PR negative so she most likely would not have benefited from anti-estrogen drugs.

HER2/neu status can be measured using either IHC or FISH. With IHC, the amount of HER2/neu protein that is present on the surface of cancer cells is measured, so if too many HER2/neu receptors are present, then the cells will receive too many signals telling them to keep growing and dividing. With FISH, the number of copies of the HER2 gene present are measured using gene amplification. This method looks to see if cancer cells have extra copies of the HER2 gene. The more copies of the HER2 gene that are present, the more HER2 receptors that the cells have. These receptors receive signals that stimulate the breast cancer cells to grow, so if a patient is HER2/neu positive, then the patient would most likely benefit from anti-HER2/neu drugs such as Herceptin (trastuzumab), Tykerb (lapatinib), and/or Perjeta (pertuzumab).², ⁷ Researchers are now studying how molecular subtypes of breast cancer may be useful in planning the treatment of patients and developing new therapies. Most studies divide breast cancer into four major molecular subtypes: Luminal A, Luminal B, Triple Negative/Basal-like, and HER2 type. Some characteristics that are used to group individuals into one of these four subtypes are hormone receptor status (ER/PR), HER2/neu status, and Ki-67 proliferation rate.² The patient in this case falls under the HER2 enriched type which constitutes 10% of breast cancers that produce excess HER2, and would most likely benefit from anti-HER2/neu drugs. This type of cancer is typically more aggressive and commonly associated with a poorer short-term prognosis.² At this time molecular subtypes are mostly used in research setting and prognosis and treatment decisions are still guided by tumor stage, hormone receptor status, and HER2/neu status.

References


