Bilateral inflammatory breast cancer in a pre-menopausal patient: A diagnostic dilemma

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Case Report

Abstract

We present the case of a premenopausal patient with inflammatory breast cancer that was originally misdiagnosed as mastitis. This case emphasizes the importance of close follow up for patients presenting to the acute care setting with symptoms of mastitis and reinforces recommendations regarding the imaging work up of these patients.

Keywords: Inflammatory breast cancer; bilateral; imaging; mastitis

Introduction

Inflammatory breast cancer (IBC) is a relatively rare disease that accounts for only 2-5% of breast cancers.1 To our knowledge, there are only four cases of bilateral IBC reported in the literature, with none of these cases occurring in a patient less than 50 years old.2-5 IBC presents a diagnostic dilemma in many acute care settings due to its clinical similarities to mastitis. IBC presents clinically as erythema, skin thickening, peau d’orange, and breast pruritus and/or tenderness. Adding to the diagnostic challenge, there is often no palpable breast mass or axillary adenopathy. Prompt diagnosis of IBC is dependent upon the clinical recognition of the presenting signs and symptoms and imaging plays a critical role.

Case presentation

A 38-year-old Hispanic female originally presented to an outside emergency room with complaint of worsening swelling and redness of the left breast over the previous four to six months. Shortly before presenting to the emergency room, the redness progressed and she developed nipple ulceration with nipple discharge. Unfortunately, she was diagnosed with mastitis, received oral antibiotics, and was discharged home.

Over the course of the following month, the redness and swelling worsened in the left breast and extended to the right breast. She presented to the emergency room at our hospital and the patient was admitted to the hospitalist service. On physical exam, the patient was found to be afebrile. There was induration and edema predominantly involving the left breast, with nipple retraction and discharge. There was no palpable mass in either breast. Her white blood cell count at that time was 7,000/mm3. An infectious disease consult was placed and the initial impression was severe bilateral mastitis. She was subsequently started on intravenous antibiotics. Additionally, there was also a recommendation for imaging evaluation of the breasts.

The day following admission, the patient underwent left breast MRI, which revealed an enhancing, spiculated, retroareolar mass with extension towards the nipple (Figure 1).

FIG. 1: T1 weighted post-contrast sagittal image of the left breast shows a spiculated, enhancing mass in the retroareolar area (arrow). There is diffuse skin thickening throughout the breast.

There were other, smaller patchy areas of enhancement as well. Additionally, there was skin thickening with diffuse enhancement. The right breast was partially included in the field-of-view and demonstrated a large enhancing mass with extension towards the nipple (Figure 2). There was also marked skin thickening and enhancement.

The patient also underwent bilateral mammogram and breast ultrasound. The mammogram revealed ill-defined areas of increased density in the supero-lateral aspect of both breasts. There was significant skin thickening. No focal mass was identified. There were diffuse microcalcifications in the left breast. The breast ultrasound demonstrated marked skin thickening with subcutaneous edema and edema tracking through the fibroglandular elements. No focal breast mass was identified.

In the field of breast imaging, the imaging modality for biopsy guidance is determined by the modality with which the lesion is best visualized. Without identification of a focal cluster of microcalcifications or a discreet mass on the mammogram or ultrasound, respectively, the patient underwent MRI guided vacuum assisted biopsy of both breasts. The pathology report demonstrated bilateral invasive ductal carcinoma, Nottingham grade 2 of 3 (Figure 3a). Both specimens demonstrated lymphovascular invasion, which was consistent with the clinical presentation of IBC (Figure 3b). Hormone receptor testing revealed the specimens to be estrogen and progesterone receptor negative and HER-2 Neu positive.

The hematology-oncology service was consulted and the patient was started on neoadjuvant chemotherapy, initially with four cycles of Adriamycin and Cytoxan, with partial response. Later, she was started on Taxotere, Carboplatin, and Herceptin, which demonstrated a much better response. She tolerated treatment well. Unfortunately, on a subsequent hospital admission for influenza approximately five months following diagnosis, the patient was found to have metastatic disease to the cervical and thoracic spine. Palliative chemotherapy was begun and a bilateral mastectomy was performed. At approximately one year following diagnosis, the patient presented with seizures and was found to have brain metastases. She underwent palliative whole brain radiation but was non-compliant with her radiation and chemotherapy appointments. The patient is now eighteen months out from initial diagnosis and is currently under the care of community hospice services.

Discussion

IBC is a rare and very aggressive form of breast cancer associated with a 25-50% 5 year survival.1 IBC tends to be diagnosed in younger women compared to non-inflammatory breast cancer, with the median age of diagnosis 57 and 62 years, respectively.1 Risk factors include obesity, first degree family history of breast cancer, and increased breast density.6 As many as 40% of patients present with distant metastases at the time of diagnosis.3

A key clinical feature that distinguishes IBC from non-inflammatory breast cancers is the rapidity of onset. Patients with IBC typically develop symptoms in less than a 3 month time frame, whereas, non-inflammatory breast carcinomas tend to take a prolonged time to develop, are frequently asymptomatic, and therefore often detected on screening mammography.6

Pathologically, IBC’s are also distinct from other invasive breast cancers. Approximately 40% of tumors are HER-2
A primary breast lesion is detected in.

As the tumor cells spread, there is obstruction and destruction of the lymphatics, resulting in lymphedema. The hair follicle dimple becomes accentuated and there is tethering of the Cooper’s ligaments, resulting in the dimpled appearance of orange peel, the so called “peau d’orange.”

The clinical presentation of IBC often presents a diagnostic dilemma. Most patients present with unilateral skin thickening, erythema, and nipple retraction. The differential also includes acute mastitis, prior radiation, trauma, CHF, and cirrhosis. It is most frequently misdiagnosed as mastitis. Up to 10% of lactating patients will develop mastitis and symptoms typically begin to resolve within 24-48 hours of initiating antibiotics. Any case of suspected mastitis that has not resolved within two weeks of initiating therapy should be viewed with high suspicion for underlying malignancy. At this point, imaging plays a critical role in early diagnosis and staging.

The first imaging test is typically a bilateral mammogram. Often, the findings are nonspecific and include skin thickening, foci of increased parenchymal density, and axillary adenopathy. Occasionally, there is no discrete mass in the breast. Like the clinical presentation and physical exam findings, the mammographic findings are often indistinguishable from mastitis. Less typical mammographic manifestations of IBC include pleomorphic calcifications, architectural distortion, and multiple masses.

Ultrasound evaluation is also frequently utilized in the initial diagnosis of IBC. Ultrasound is most useful in determining if there is a mass to be biopsied and in defining the margins and quantifying size. As in the case of our patient, ultrasound evaluation of IBC occasionally does not reveal a focal mass but rather diffuse skin edema, which can also be seen in the case of mastitis. If a mass lesion is seen on ultrasound, ultrasound-guided biopsy is the preferred method of obtaining pathological specimen.

The patient was atypical in that the first diagnostic exam was an MRI rather than ultrasound or mammogram. MRI plays a critical role in evaluation of IBC, specifically in patients with no definitive mass seen on mammography or ultrasound. A primary breast lesion is detected in 98-100% cases with MR imaging, compared to 68-80% of cases with mammography, and 94-95% of cases with ultrasound. The findings of IBC on contrast-enhanced MRI include enhancing skin thickening, segmental non-masslike enhancement, and type II or type III (washout) kinetics. In breast MRI, enhancement kinetics are used to further characterize any lesion that is suspicious. Washout kinetics (type III) are most predictive for malignancy and demonstrate a pattern of initial enhancement peaking at approximately two minutes followed by subsequent rapid washout of contrast enhancement. This pattern is in contrast to enhancement plateau, referred to as Type II, and persistent/increasing enhancement, or Type I (most benign pattern). Diffuse subcutaneous and pre-pectoral edema are also seen in IBC. Non-masslike enhancement, skin thickening, and edema can also be seen with acute mastitis. The two MRI findings that are most specific for IBC are the rapid washout kinetics and pre-pectoral edema.

Curiously, the screening MRI that was ordered for our patient was for a unilateral left breast MRI only. Fortunately for our patient, the malignant findings in the right breast were visible on the axial subtraction views. Performing a unilateral breast MRI should be strongly discouraged, as the presence of disease in the contralateral breast would most likely go undetected. The presence of contralateral disease changes not only the staging of the disease, but surgical and oncological treatment planning. In all cases where MRI is used for evaluation of breast malignancy, a bilateral exam should be performed. This not only helps to exclude disease in the contralateral breast, but gives a basis of comparison for normal enhancement patterns for that particular patient.

**Conclusion**

In summary, IBC is the most aggressive of all malignancies of the breast. Differentiating the clinical signs and symptoms from mastitis can be very challenging and often leads to a delay in diagnosis. It is imperative that the clinician maintain a high level of suspicion in patients that present with symptoms of mastitis, and that they educate the patient on the importance of follow up. If symptoms do not resolve within two weeks, further work up with diagnostic imaging should be pursued to exclude inflammatory breast cancer. MRI is recommended mainly in patients with an inconclusive mammogram or ultrasound and should always be ordered as a bilateral exam.

**Conflict of interest**

The authors declare that they have no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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**References**


