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CASE REPORT

Skin Nodules as a First Presentation of Synchronous Bilateral Invasive Lobular Breast Carcinoma: A Case Report

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Abstract

The most common cause of skin metastases in adult women is primary breast carcinoma, which comprises about 70% of cases [1]. Skin metastases have non-specific clinical appearances, making it challenging to differentiate them from other benign conditions [1]. We present a case of a 52-year-old female with type II diabetes and a three-month history of refractory skin lesions who did not respond to anti-inflammatory treatment. The patient subsequently complained of a right breast lump, evaluation of which led to the diagnosis of bilateral synchronous invasive lobular carcinoma.

Introduction

Breast cancer is the most common cancer in women worldwide. Invasive lobular carcinoma (ILC) is the second most common histological type of breast cancer. It comprises 5 – 15 % of all invasive breast carcinomas [2]. ILC is notoriously diagnosed at later stages due to its frequently subtle or occult radiological presentation. It is a challenge to identify on all breast imaging modalities. While breast cancer has an inclination to spread to skin, this is an unusual primary presentation [3]. More commonly, skin involvement is seen later in the course of metastatic disease. It appears less commonly as a first sign of extranodal disease [4], and rarely as the first sign of malignancy. We present an unusual case of a woman seeking medical consultation for multiple progressive erythematous skin lesions that were unresponsive to anti-inflammatory treatment over several months that then developed bilateral breast lumps. Subsequent multi-modality breast imaging and biopsy led to the diagnosis of bilateral invasive lobular carcinoma with metastatic cutaneous spread.

Case Report

A 52-year-old female who has had adult-onset type II diabetes, controlled on oral treatment, for the last five years, was referred to our breast imaging clinic for a self-palpated, firm, mobile right breast lump. She had a family history of breast cancer in a maternal aunt diagnosed at age 70 (type unspecified) and no personal history of breast cancer or any other malignancy. She had never undergone radiologic breast cancer screening. She reported a three-month history of multiple, progressive, painless skin lesions on the back of her neck [Figure 1]. Clinical inspection showed multiple, raised, oval and round erythematous papulonodular skin lesions of varying size scattered on the back of her neck and upper back. These lesions had not responded to initial anti-inflammatory medications given by her dermatologist over the two months prior to her breast imaging. In addition to the right breast lump felt by the patient and clinician, a left breast lump was also detected upon clinical breast examination.

Initial assessment by bilateral diagnostic 2D full field digital mammography and digital breast tomosynthesis (DBT) was performed. Bilateral symmetric areas of architectural distortion and bilateral high density oval masses with partially obscured margins involving the upper outer quadrants (UOQ) were best appreciated on tomosynthesis views [Figure 2]. There were no associated microcalcifications.

Targeted hand-held ultrasound showed hypoechoic oval masses with indistinct margins in the UOQs in both breasts measuring up to 1.6 cm on the right and 1.2 cm on the left [Figure 3], corresponding to the mammographic masses. Color Doppler ultrasound directed to the masses showed peripheral vascularity. Additional multiple hypoechoic regions with posterior acoustic shadowing corresponded to the mammographic areas of architectural distortion in the lower outer quadrant (LOQ) and lower mid regions of both breasts. They measured up to at least 3.8 cm in the right breast [Figure 2]. Both axillae showed morphologically normal lymph nodes with normal overall size, thin cortices and preserved fatty hila. This initial imaging was given a final BI-RADS category 4B for each breast. Recommendations were to biopsy the most suspicious lesions in each breast and obtain dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) of the breasts.

Bilateral DCE-MRI of the breasts was performed. After injection of contrast, discrete irregular masses with irregular margins showing intense heterogeneous enhancement were present in the UOQ from anterior to posterior depth bilaterally [Figure 4]. Two masses identified in the right breast measured 1.5 and 4.5 cm respectively at their maximum dimensions. Three connected masses identified in the left breast measured 1.5-2.5 cm at maximum dimension. Contiguous bilateral, multiple regions of heterogeneous clumped non-mass enhancement (NME) were present in the UOQ, LOQ, lower inner quadrant (LIQ), and retro-areolar regions. Kinetic curve analyses of all masses and non-mass enhancement showed type 3 washout kinetics.

Figure 1. Clinical photographs (a, b, c) show the patient's metastatic cutaneous papulonodules on the neck and upper back; and the site of skin punch biopsy (d, arrow).

Figure 2. Digital breast tomosynthesis images in right CC (a), right MLO (b), left CC (c, d) and left MLO (e) show bilateral symmetrical areas of architectural distortion (thin arrows in a, b, c, e) and bilateral high density oval masses with partially obscured margins (arrows in a, b, d, e).

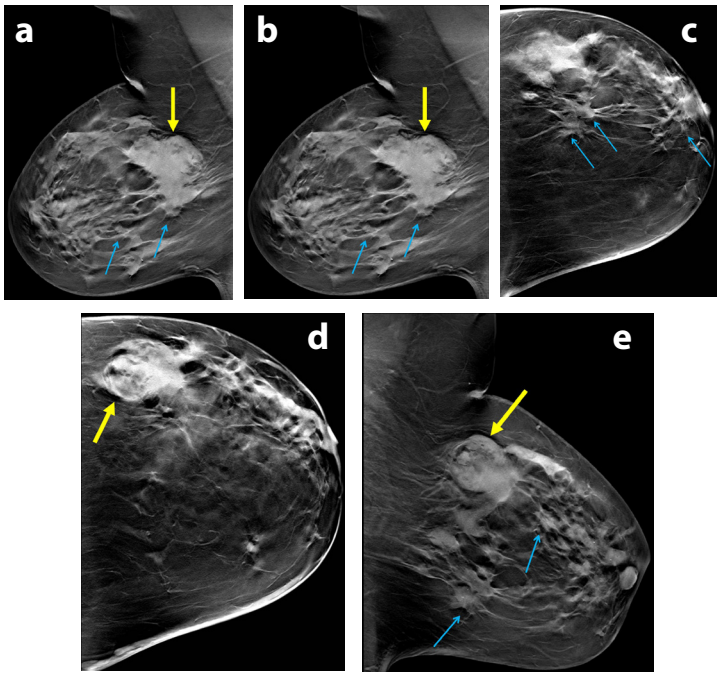
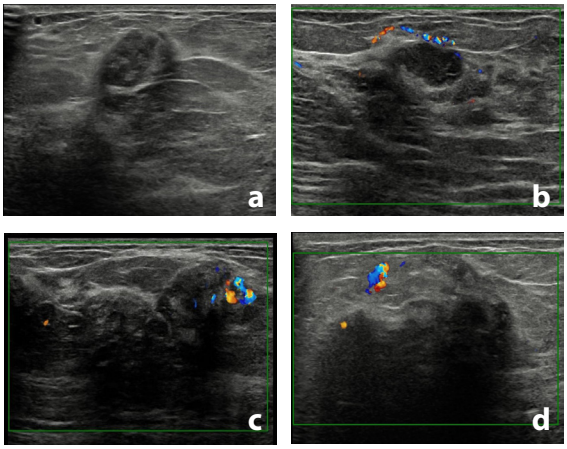


Figure 3. Images from targeted bilateral breast ultrasound show a 1.6 cm oval mass in the right UOQ (a) and a 1.2 cm oval mass in the left UOQ (b). Hypoechoic regions with shadowing in the right LOQ (c) and left LOQ (d) correspond to mammographic architectural distortion. All sites were biopsied and proven to be invasive lobular carcinoma.



Bilateral ultrasound-guided core needle biopsies were performed targeting two sites in each breast: the UOQ masses and the LOQ hypoechoic regions with shadowing. A synchronous skin punch biopsy was performed by the dermatologist on the same day to evaluate the upper back skin lesions.

PET/CT scan was requested by the oncologist as part of the staging workup [Figure 5]. The bilateral breast masses and NME previously reported on the breast MRI showed pathologic FDG uptake with maximum standardized uptake value (SUVmax) of ~2.9 on the right and an SUVmax of ~3.2 on the left. Multiple FDG-avid cutaneous nodules were identified in the upper back and in the lower abdomen that also showed mild FDG uptake with an SUVmax of ~3.4. The patient was unaware of the abdominal wall nodule until she was informed about it after the PET/CT. No other FDG-avid lesion was identified in other body organs, bones, or lymphatics.

Pathologic Findings

All four breast biopsies showed luminal A invasive lobular carcinoma, grade II. Immunohistochemistry showed positive estrogen and progesterone receptors and negative HER2/neu receptors for all four biopsy sites. The skin punch biopsy showed a single-file pattern of malignant cells, a pattern considered one of the characteristic features of invasive lobular carcinoma.

Figure 4. Post-contrast T1 breast MRI subtraction images show dominant, large irregular masses (arrows) in the right axial (a) and left axial (b) views, and multiple masses (arrows) in the left sagittal (c) sequence. An axial reconstructed MIP image (d) demonstrates bilateral, symmetric, heterogenous enhancement of irregular masses and non-mass enhancement (arrows). Bilateral segmental clumped non-mass enhancement (arrows) involves the bilateral lower outer quadrants (e).

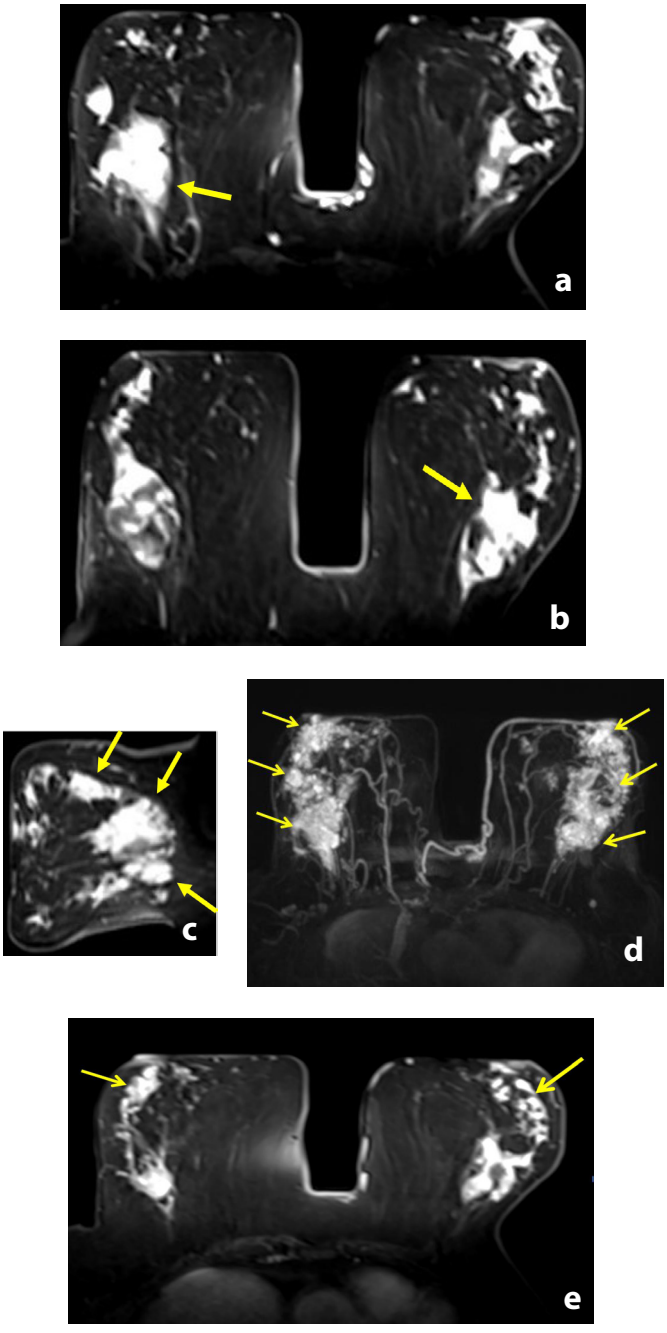
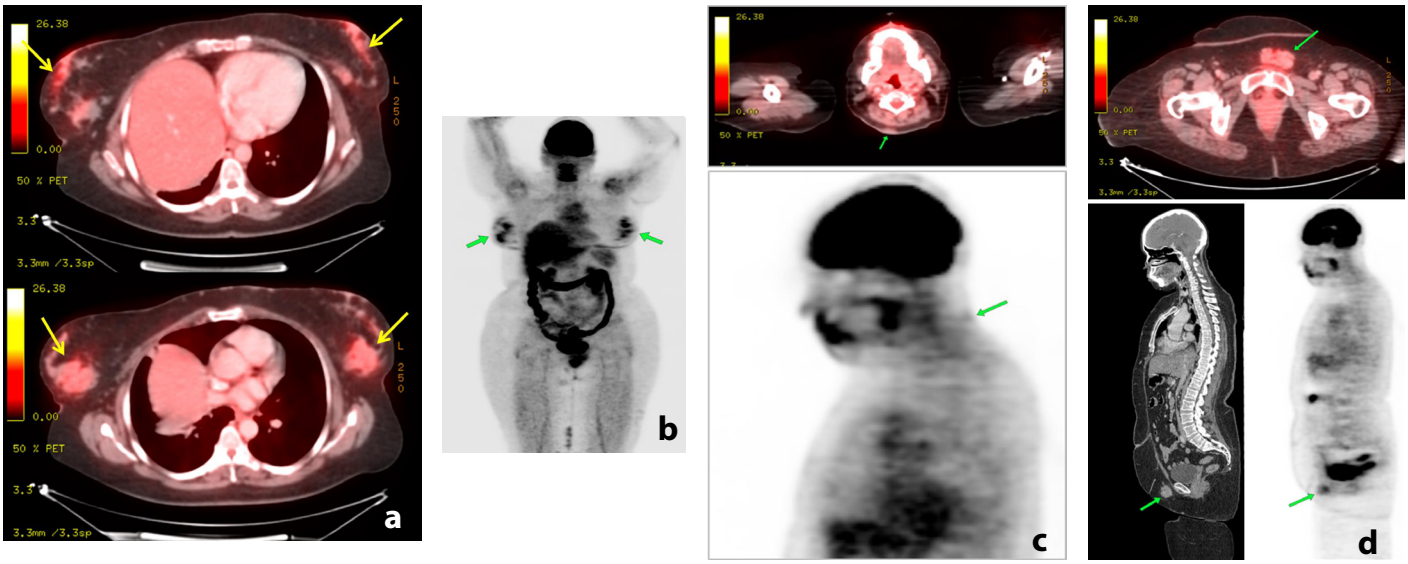


Figure 5. PET/CT shows bilateral breast primary carcinomas and metastatic disease. Fused axial PET/CT (a) and coronal MIP images (b) show bilateral ill-defined FDG-avid lesions in both breasts (arrows), which are associated with mild FDG activity. Fused axial PET/CT and sagittal MIP images show a clinically-identified FDG-avid metastatic skin nodule on the neck/upper back (c, arrows). Fused axial PET/CT, sagittal reconstructed CT, and sagittal MIP images show a lower anterior abdominal wall subcutaneous metastatic nodule (d, arrows) with mild FDG uptake.



Discussion

Cancer metastasis remains incurable and a major cause of death. In their work, Birkbak and McGranahan describe the genomic evolution of metastases [5]. Studies of breast cancer metastases in particular have shown that metastases arise from both single and monoclonal or multiple and polyclonal cell lines, leading to increased tumor heterogeneity [5]. In addition, single disseminated tumor cells have been detected in bone marrow, blood, or lymph nodes of patients with no signs of disease after surgical resection [6]. The single disseminated tumor cell eventually becomes metastases, which suggests that metastatic dissemination could occur early in the disease, not just at late-stage disease [6]. In our case, metastatic disease in the form of skin lesions was the first clinically detectable sign of this patient's breast cancer, three months prior to presenting with a palpable breast lump. This raises the possibility of early dissemination, especially given that workup demonstrated no clinical or imaging evidence of any other metastatic disease.

The overall incidence of skin metastases is relatively low at 5.3% [3]. Breast cancer is the most common cancer to spread to the skin, seen in about 8.9 – 26.5% of metastatic breast cancer patients [3]. Skin metastases are usually encountered months to years after initial breast cancer diagnosis and frequently at the same time as visceral metastases [4, 6]. The most common sites of cutaneous metastases are the chest, ipsilateral to the primary tumor; head and neck, and abdominal wall [1, 3, 7]. Based on a retrospective review of 164 cases, skin metastases present as papules and/or nodules 80% of the time [7]. It is noteworthy that acute-onset, persistent, firm papulonodular skin lesions, especially located on the chest, should alert the clinician to consider breast cancer metastases [3]. Breast cancer cutaneous metastases are more commonly disseminated through the lymphatics and carry a better prognosis than metastases to internal organs or the skeleton [8]. Surgical excision, if feasible, may improve quality of life.

Our patient initially presented with papulonodular skin lesions on the back of the neck and upper back. The papulonodular appearance is consistent with the literature, but their location is not the most common. A few case reports of skin metastases from breast cancer are reported in the literature [9, 10], but none have been described in association with bilateral invasive lobular cancers. Additional unique features of this case were the multiplicity and symmetry of bilateral palpable breast lumps and bilateral imaging findings, absence of local breast skin changes, and absence of axillary lymph node involvement.

Mammography performed at our facility showed bilateral oval masses and multiple bilateral areas of architectural distortion. Proposed differential diagnosis based on clinical history and imaging was primary or secondary malignancy, or other systemic disease. While it was considered, metastases to the breast was confounded by the lack of an obvious alternate primary and absence of regional or distant lymphadenopathy. In this patient with diabetes, the proposed possibility of bilateral diabetic mastopathy was unlikely. She was not on insulin therapy and had no reported renal insufficiency. Features that supported the diagnosis of diabetic mastopathy were the firmness and bilaterality of the breast lumps, asymmetries on mammogram, irregular masses on ultrasound, and absence of regional adenopathy

[11]. The presence of multiple skin lesions raised the remote possibility of systemic late-onset sarcoidosis. Primary breast sarcoid, however, is very rare, comprising less than 1% of cases [11] and usually presented with self-detected breast masses. Breast sarcoid is also more likely to be unilateral and associated with skin changes as well as ipsilateral axillary lymphadenopathy [12, 13].

Primary breast carcinoma, therefore, was the most likely diagnosis for our patient based on the architectural distortion and masses seen on mammography and US, as well as the non-mass enhancement and masses noted on MRI. Invasive lobular carcinoma often presents as architectural distortion, as shown in 10-34% of cases [14]. However, due to its pattern of growth, the imaging findings are often subtle. Detection is challenging and therefore it is more likely to present at a later disease stage, to be multifocal and bilateral, and to have metastases when diagnosed [15]. DBT improves perceptibility of architectural distortion. Such DBT detected lesions are more likely to be malignant when a corresponding lesion with indeterminate or suspicious features is also seen on ultrasound [16]. However, any areas of focal distortion on mammography without history of previous surgery or intervention should be considered a suspicious finding that warrants biopsy, even with negative ultrasound and MRI examinations, as it has >20% yield of breast cancer [17, 18].

The metastatic work up by PET-CT was essential for clinical staging of the disease. In general, breast cancer lesions tend to show mild to moderate FDG uptake in PET-CT examinations [19]. The mild FDG uptake (SUVmax ~2.9-3.2) reported in the PET-CT examination of this case is consistent with the histological type of the tumor and receptor status. Lobular carcinoma and tumors with positive estrogen and progesterone receptors tend to show lower FDG uptake in comparison to invasive ductal carcinoma and triple negative tumors [19]. In addition to the FDG avidity of bilateral breast tumors, the PET/CT also uncovered a lower abdominal wall metastasis. Even though in our case no intra-abdominal lesions were found on PET/CT, in a retrospective review evaluating intra-abdominal metastases of invasive lobular carcinomas, the peritoneum was the most common site of involvement. This is true in 47% of metastatic breast cancer cases, which negatively affects overall survival [20].

Synchronous bilateral breast cancers are rare. Their incidence is reported in the range of 0.3-12% of cases [21]. Synchronicity is defined as two separate primary breast cancers, one in each breast, diagnosed within one year of one another, or more conservatively, within three months [21, 22]. Researchers usually find that each breast cancer is independent rather than metastatic from one to the other, even with the same pathology and immunoreceptor status [21, 22]. It is also often clinically apparent in one breast and incidentally discovered in the other [22, 23]. In our case, the patient presented with bilateral disease although only the right was self-palpated. Also, which was true in our case, bilateral breast cancers are more commonly ILC and often strongly positive for estrogen and progesterone receptors [21, 23].

The multidisciplinary recommendations for this patient were neoadjuvant anti-hormonal treatment followed by bilateral mastectomy. At the most recent clinical follow-up, six months after initiation of therapy, partial response was noted in both the breast disease and cutaneous nodules.

Conclusion

Skin metastases from breast cancer are rarely a primary presentation, as they typically result from lymphatic spread. They carry a better prognosis than metastases to internal organs or the skeleton. This case report suggests that metastatic dissemination from breast cancer may occur before the primary tumor is clinically detected, and illustrates the role of multi-modality imaging in reaching the diagnosis, staging the disease, and offering treatment recommendations in concordance with the histopathological nature of the tumor.

Teaching Points

1. Metastatic dissemination from cancer may occur before the primary tumor is clinically detectable.

2. Persistent nodular and/or papular skin lesions which do not resolve with usual treatments may require biopsy to exclude malignancy.

3. Cutaneous metastases of an unknown primary require clinical inspection and examination of possible breast malignancy.

4. Screening mammography may have detected this patient's malignancies at an earlier stage with better treatment options.

5. Bilaterality is considered in evaluation of breast cancer patients at any stage, and multi-modality imaging is required for confirmation.

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Conflicts of interest

The authors report no conflicts of interest.

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