CASE REPORT

CE 1.0 Contact Hour

Paget's Disease of the Breast Presenting as Nipple Ulceration With Normal Mammogram

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ABSTRACT: Paget's disease of the breast (PDB) is a rare disorder of the nipple–areola complex that may present clinically as a unilateral, eczematous, or ulcerated papule or plaque. This case highlights the importance of either punch or incisional wedge biopsy to establish a diagnosis of PDB for patients who present with chronic cutaneous changes of the nipple, areola, or skin of the breast, regardless of any previous normal mammogram or breast ultrasound. Mammography alone cannot rule out a diagnosis of PDB in a patient with cutaneous changes of the breast.

Key words: Breast, Cancer, Dermatology, Mammogram, Paget

CASE PRESENTATION

In December 2017, a 56-year-old morbidly obese woman presented to her primary care provider with an ulcer obliterating her right nipple. Her past medical history was significant for poorly controlled Type II diabetes, morbid obesity, and depression. The patient also reported a vague history of multiple "friction ulcers" in the folds of her abdomen, which healed within a few weeks of initiating topical treatments. She had no personal or family history of breast cancer or ovarian cancer. She promptly underwent a mammogram and a breast ultrasound that were reported as normal. She was diagnosed with a "friction ulcer" of the right nipple that was attributed to her obese habitus and referred to a wound care clinic for treatment. After 3 months of diligent wound care with topical treatments, the ulcer did not heal. In March 2018, she was referred to dermatology for further evaluation.

The patient initially presented to the outpatient dermatology clinic in March 2018 with a shallow, well-defined pink ulcer obliterating her right nipple that had been present for about a year. She denied itching, bleeding, and pain associated with the ulcer. She reported worsening fatigue and denied any other skin lesions or concerns (Figure 1).

CLINICAL EVALUATION

A 4-mm punch biopsy was recommended from the right nipple. The differential diagnosis at the time of biopsy included amelanotic melanoma, squamous cell carcinoma, and Paget's disease of the breast (PDB). There was no supraclavicular, cervical, or axillary lymphadenopathy. A thorough breast examination did not reveal a palpable mass. A total body skin examination was otherwise unremarkable.

The pathology revealed:

Skin, breast, right, biopsy:

-Invasive ductal carcinoma, Nuclear Grade 2, arising in association with PDB
-Estrogen receptor: positive
-Progesterone receptor: positive
-HER2: negative

Comment: immunohistochemistry for GATA-3, Melan-A, HER-2, Cytokeratin 7, and Cytokeratin 5, support the diagnosis.

MANAGEMENT AND OUTCOME

Upon receipt of the biopsy results, the patient was promptly referred to oncology and subsequently diagnosed with Stage II invasive ductal carcinoma (IDC) associated with PDB. She underwent a right lumpectomy and had a positive sentinel lymph node biopsy of the right axilla. A computed tomography scan was ordered by oncology, and she was not found to have metastasis past the sentinel lymph node.

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FIGURE 1. Right nipple obliterated by ulcer. A 4-mm punch biopsy was obtained that included the center and lateral border of the ulcer.

The patient then received systemic adjuvant chemotherapy managed by oncology. She continues to follow closely with oncology and has not had disease recurrence.

BACKGROUND AND CLINICAL PRESENTATION OVERVIEW

PDB is a rare disease that presents most commonly in postmenopausal women between 50 and 60 years old, with a median age of 56–57 years (Karakas, 2011; Wong et al., 2019). Only 1%–4% of patients with breast cancer also present with PDB (Challa & Deshmane, 2015; Karakas, 2011; Wong et al., 2019). However, 92%–100% of PDB cases are associated with ductal carcinoma in situ and/or IDC (Ackerman et al., 2018; Karakas, 2011; Wong et al., 2019). PDB involving the nipple has been commonly associated with IDC and is thought to be because of epidermal extension of an underlying ductal breast carcinoma (Ackerman et al., 2018; Bolognia, Schaffer, & Cerroni, 2018; Wong et al., 2019). The patient's clinical presentation in the case study described above is classical for PDB associated with IDC.

Cutaneous involvement is a primary feature of PDB, which makes it distinct from more common types of breast cancer (Wong et al., 2019). The classic clinical presentation of PDB is a chronic, eczematous, scaly papule or plaque of the nipple–areola complex or surrounding skin. Progression may lead to obliteration of the nipple–areola complex (Ackerman et al., 2018; Broecker et al., 2017). PDB may simulate an eczematous dermatitis, which commonly leads to a delayed diagnosis (Karakas, 2011). PDB should be suspected in any patient with chronic, cutaneous changes of the breast that do not respond promptly to topical treatments (Aguayo-Carreras, Bonilla-Garcia, Perez-Lopez, Cuenca-Barrales, & Tercedor-Sánchez, 2017). Patients may also complain of itching, pain, or discomfort.

PDB is characterized histologically by Paget cells in the nipple epidermis, which are thought to migrate there from breast carcinoma present in deeper ductal structures (Ackerman et al., 2018; Bolognia et al., 2018). Immunohistochemical stains are sometimes needed to differentiate PDB from histologically similar entities such as malignant melanoma and squamous cell carcinoma in situ. Cytokeratin 7, Cytokeratin 5, HER-2, and Melan-A stains are often used (Ackerman et al., 2018).

Treatment and prognosis of PDB depend on the type of underlying associated breast carcinoma and presence or absence of axillary lymph node involvement (Ackerman et al., 2018). Treatment of PDB is typically composed of surgery, chemotherapy, or radiation therapy, either alone or in combination (Aguayo-Carreras et al., 2017). Patients with PDB should be promptly referred to oncology for staging and treatment. Breast conserving surgery and appropriate adjuvant treatment may be carefully considered for a select group of patients (Helme, Harvey, & Agrawal, 2015; Wong et al., 2019). Our patient wished to avoid a mastectomy, which impacted the treatment modalities chosen.

DISCUSSION

This case study highlights the importance of histologic examination via incisional or deep punch biopsy to confirm a diagnosis of PDB, regardless of prior normal mammogram or breast ultrasound. As seen in our patient, most patients with cutaneous changes limited to only the nipple and without a palpable mass will have a normal mammogram (Aguayo-Carreras et al., 2017; Helme et al.,2015; Wong et al., 2019). Despite high prevalence of underlying breast cancer among patients with PDB, only approximately 35%–65% of patients with biopsy-proven PDB exhibit findings on mammography that are concerning for underlying breast carcinoma (Kang et al., 2019; Karakas, 2011). Mammography is still required in all biopsy-confirmed cases of PDB because of a high association between PDB and underlying breast carcinoma (Aguayo-Carreras et al., 2017; Kang et al., 2019). Our patient also had a breast ultrasound before histologic confirmation of the diagnosis. Breast ultrasonography is typically used in conjunction with mammography but has not been shown to improve the sensitivity of mammography to detect PDB (Helme et al., 2015).

Presence of a palpable breast lump has been correlated with increased sensitivity of mammography to detect

underlying carcinoma associated with PDB (Helme et al., 2015; Karakas, 2011). Magnetic resonance imaging (MRI) is highly sensitive for detection of breast cancer, especially in patients with a normal mammogram (Karakas, 2011). However, negative or normal imaging studies alone cannot rule out PDB in a patient presenting with cutaneous changes of the breast and should be correlated with biopsy and clinical findings to establish a diagnosis of PDB.

A complete breast examination should be performed in all patients with suspected or confirmed PDB. The presence of a palpable breast mass has been found to correlate with whether an underlying breast cancer associated with PDB is likely to be invasive or in situ and has been associated with a 48%–69% incidence of lymph node involvement, compared with a 21%–25% incidence of lymph node involvement with no palpable breast mass (Helme et al., 2015).

A punch, wedge, or shave biopsy of the involved tissue can be performed; it is important to obtain a full-thickness biopsy of the nipple and areola to establish the diagnosis (Karakas, 2011). It is important to consider that a shave biopsy of the nipple will often not include the entire epidermis and may yield an inadequate sample. If the first biopsy does not contain adequate tissue, a repeat wedge biopsy or excision of the nipple may be necessary (Karakas, 2011).

This case illustrates a delayed diagnosis of PDB associated with IDC because a negative mammogram was interpreted as absence of breast cancer despite presence of suspicious cutaneous changes of the breast. It is important for all individuals who provide healthcare to women to be aware of all of the cutaneous signs of breast cancer. A full-thickness surgical punch or wedge biopsy is the gold standard to confirm or exclude a diagnosis of PDB (Karakas, 2011). It is especially important to remember that patients who present with PDB isolated to the nipple and without a palpable breast mass may present with a normal mammogram despite presence of underlying IDC or ductal carcinoma in situ. Mammography has low sensitivity to detect PDB and should be used as a complimentary diagnostic tool to surgical wedge or punch biopsy when PDB is suspected.

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