

Case Report

Metaplastic Breast Carcinoma with Secondary Paget Disease Occurring after Prophylactic Mastectomy: Diagnostic Considerations

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Keywords

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- Secondary squamous Paget disease
- Prophylactic mastectomy

Abstract

Invasive mammary carcinoma occurring after prophylactic mastectomy is rare. We report a case of a 42-year-old female diagnosed with metaplastic breast carcinoma after prophylactic mastectomy. Previously, the patient underwent bilateral mastectomy followed by reconstruction for unilateral invasive mammary carcinoma. One decade later, she presented with a 10 cm mass in the contralateral chest wall. On subsequent wide local excision and axillary lymph node dissection, an invasive carcinoma with squamous differentiation was identified. Examination of the skin epidermis revealed Paget cells with squamous differentiation. Given that this malignancy was arising after prophylactic mastectomy, the differential diagnosis included primary breast carcinoma, contralateral metastatic breast carcinoma and squamous cell carcinoma. The final diagnosis was primary invasive ductal carcinoma with squamous differentiation (metaplastic carcinoma) involving the epidermis of the skin as secondary Paget disease.

To our knowledge, this is the first report to describe a primary metaplastic carcinoma of the breast occurring after prophylactic mastectomy. With the recent trend of women with breast cancer choosing bilateral mastectomy over unilateral lumpectomy at increasing rates, our report provides a relevant discussion detailing the pathology work up and diagnostic considerations that apply to cases of invasive carcinoma after prophylactic mastectomy.

ABBREVIATIONS

CPM: Contralateral Prophylactic Mastectomy; MBC: Metaplastic Breast Carcinoma; NST: No Special Type; ER: Estrogen Receptor; PR: Progesterone Receptor

INTRODUCTION

Primary breast carcinoma occurring after prophylactic mastectomy is uncommon. A single retrospective study of 1500 patients found that approximately 0.6% of patients developed invasive cancer after prophylactic mastectomy [1]. When considering only high risk patients, the incidence increased to 1.18% [2]. Individual case reports of primary breast carcinoma occurring after prophylactic mastectomy have been reported in the literature [2,3], but none thus far have described a primary metaplastic carcinoma of the breast.

CASE PRESENTATION

A 32-year-old female presented with a right breast mass diagnosed on core biopsy as invasive mammary carcinoma (Figure 1A). The patient underwent a right skin-sparing total mastectomy with sentinel lymph node biopsy and contralateral prophylactic skin-sparing total mastectomy followed by reconstructive surgery. The right breast mastectomy demonstrated invasive ductal carcinoma, grade 2, measuring 4.8 cm that was estrogen receptor (ER) negative, progesterone receptor (PR) negative and Her2 negative. All lymph nodes were negative. The left prophylactic mastectomy was benign. The patient received adjuvant chemotherapy, and although genetic testing was recommended, the patient declined and was lost to follow-up. Ten years later, the patient presented with a 10 cm fungating left chest wall mass that ulcerated through the skin. A core biopsy of the mass performed at an outside hospital was diagnosed as

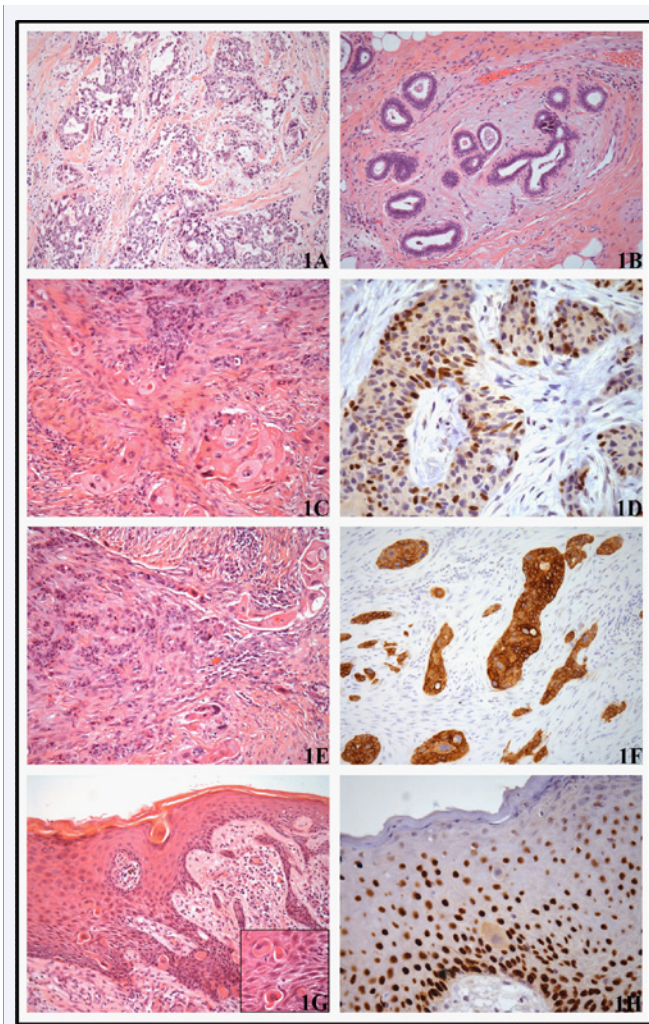


Figure 1 (A) Right breast invasive ductal carcinoma (H&E, 200X). (B) Normal breast epithelium status post left CPM (H&E, 200X). (C) Left breast invasive carcinoma with squamous differentiation status post left CPM (H&E, 200X). (D) Left breast invasive carcinoma with positive staining for p63 (p63, 400X). (E) Left breast invasive carcinoma with squamous differentiation status post left CPM (H&E, 200X). (F) Left breast invasive carcinoma with positive staining for Cytokeratin 7 (CK7, 200X). (G) Left breast skin with secondary Paget disease status post left CPM (H&E, 200X). Inset: Paget cells (H&E, 400X). (H) Left breast skin with Paget cells staining negative for p63 (p63, 400X).

metaplastic carcinoma with squamous differentiation that was ER negative, PR positive (staining 20% of tumor nuclei) and Her2 negative. The patient underwent 3 cycles of neoadjuvant chemotherapy followed by wide local excision of the left chest wall and left axillary lymph node dissection performed at our institution. The wide local excision specimen demonstrated a 3 x 2.5 cm tumor bed with residual invasive carcinoma with squamous differentiation that ulcerated through the skin with intraepidermal spread of malignant cells. Four of 21 lymph nodes were positive for metastatic carcinoma. Given that this carcinoma occurred after prophylactic mastectomy, a differential diagnosis including primary invasive mammary carcinoma, contralateral breast metastasis, and squamous cell carcinoma was considered. Histologic slides of the 2002 right breast carcinoma were

reviewed and showed no similarity to the current carcinoma. Although the wide local excision of the left chest wall did not show ductal carcinoma *in situ*, normal breast tissue was identified (Figure 1B), supporting the likelihood of a primary mammary carcinoma. The invasive carcinoma demonstrated nests of high grade polygonal tumor cells with abundant eosinophilic cytoplasm consistent with squamous differentiation (Figures 1C and 1E). These same malignant cells were present in the epidermis suggestive of squamous cell carcinoma *in situ* (Figure 1G). However, immunohistochemistry showed that the invasive carcinoma was diffusely positive for CK7 (Figure 1F), with 50% of tumor cells staining strongly with p63 (Figure 1D). In addition, the majority of the tumor cells present in the epidermis were p63 negative (Figure 1H). Finally, focal areas of the invasive carcinoma were consistent with invasive ductal carcinoma, no special type (NST). These histologic features and immunoprofile supported the final diagnosis of invasive ductal carcinoma with squamous differentiation (metaplastic carcinoma) with involvement of the epidermis as secondary Paget disease.

DISCUSSION

The risk of contralateral breast cancer can be five-fold greater in a breast cancer patient when compared to a female without a history of breast cancer [4]. Contralateral prophylactic mastectomies (CPM) have been shown to yield a 90% reduction in breast cancer risk [5], and therefore breast cancer patients may opt to undergo CPM. In fact, the current national trend shows an increasing number of women with unilateral breast cancer choosing CPM [6]. Although prophylactic mastectomies offer a great reduction in risk of development of carcinoma, it is not 100% effective in preventing a new primary breast carcinoma [2,5,7,8]. Multiple case studies have reported occurrence of primary breast carcinoma after prophylactic mastectomy and most cases have occurred with skin-sparing mastectomies [8,9]. Some authors attribute this to breast tissue left behind despite meticulous surgical efforts [2]. In our case example, the patient had a history of left prophylactic skin-sparing total mastectomy, and we were able to demonstrate the presence of normal breast epithelium in the left chest wall wide local excision specimen.

For carcinomas occurring in the chest wall after CPM, multiple etiologies should be considered for prognosis and appropriate management of the patient. In a patient with a history of breast cancer, the histomorphology and breast receptor profile should be compared to the remote primary breast carcinoma to differentiate between a contralateral metastasis versus a new primary, as the former would be considered worse prognosis. Another etiology would include a carcinoma that is not of breast origin, such as primary carcinomas of the breast skin or metastatic spread from a primary carcinoma arising at a distant site. Therefore, adequate patient history is important when considering metastasis in the differential diagnosis. In our case example, primary metaplastic breast carcinoma (MBC) with squamous differentiation occurred after CPM. MBC accounts for less than five percent of all breast cancers [10], and to our knowledge, this is the first reported case of MBC occurring after prophylactic mastectomy. As defined in the World Health Organization Classification of Tumours of the Breast, metaplastic carcinomas encompass a group of neoplasms characterized by differentiation of the neoplastic epithelium into

squamous cells and /or mesenchymal-looking elements [11]. Metaplastic squamous cell carcinomas of the breast may be purely squamous cell or mixed with invasive ductal carcinoma NST, as is seen in our case example. Squamous cell differentiation in MBC is malignant and should not be mistaken for squamous metaplasia which is a benign change of ductal epithelium that can occur after biopsy or surgical excision [12], or can be found in benign papillomas and fibroadenomas of the breast [13]. MBCs that are high grade tend to be larger tumors with less involvement of regional lymph nodes and have worse 5-year survival rates when compared to invasive ductal carcinoma NST [14]. As a group, metaplastic carcinomas are typically triple negative, lacking ER, PR and HER2 expression. Immunohistochemical analysis and genomic profiling support that MBCs are part of the spectrum of basal-like breast cancers with myoepithelial phenotype [15]. MBCs, with or without squamous differentiation are often positive for p63, a myoepithelial marker [16], as well as a marker of squamous differentiation. Our case is also unique, since it is the first description of Paget cells with squamous differentiation. By definition, Paget disease of the breast is an *in situ* adenocarcinoma of the nipple epidermis where individual carcinomatous cells originating from ductal carcinoma *in situ* of the lactiferous ducts of the nipple, travel up the duct and sinus into the nipple epidermis of the skin without crossing the basement membrane [17]. Although histologically identical, secondary Paget disease of the breast results from epidermotropism of an invasive breast carcinoma that invades the breast skin. In our case example, the patient did not have a true nipple as a result of prophylactic total mastectomy and therefore, by definition, the chest wall skin was involved by secondary Paget disease. The presence of secondary Paget disease in our case was a confounding feature highlighting the alternative diagnoses to consider in the differential for carcinomas that arise in the chest wall after prophylactic mastectomy.

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