Case Report

Occult Breast Carcinoma Presenting as Scalp Metastasis

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Abstract
Breast cancer is the most common tumor among women, and approximately 6% of the patients have de novo metastatic breast cancer. Occult breast cancer accounts for only 0.1–0.8% of the cases and most commonly presents with axillary lymphadenopathy. Scalp metastases are rare and have been described as a sign of progression or widespread metastatic disease. Here, we describe a rare case of de novo metastatic breast cancer to the scalp as the single site of spread and without an identifiable primary breast tumor.

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Introduction

Breast cancer is the most common malignant neoplasm in women and the second leading cause of cancer death in women in the USA. It is estimated that approximately 252,710 individuals will be diagnosed in 2017, and only 6% will present with de novo metastatic disease [1]. Occult breast cancer accounts for 0.1–0.8% of the cases and most commonly presents with axillary lymphadenopathy. Despite improvements in breast imaging, the fre-

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quency of detection of a primary tumor in that particular context has not substantially improved over time [2].

Cutaneous metastases were first reported more than 50 years ago. They have been associated with lung, gastric, and breast cancers in the late stages [3]. Scalp metastases are uncommon. In most series, they represent a sign of progression after treatment or one of the sites of widespread disease in the natural history of metastatic breast cancer [4, 5]. Lemieux et al. [4] recently reported 2 cases of scalp metastases after scalp cooling and adjuvant therapy for breast cancer as the only site of progression. In another report [5], the same group reported 7 cases of scalp metastases along with other organ involvement after adjuvant chemotherapy for breast cancer. A recent systematic review and meta-analysis estimated an incidence of scalp metastases as the first site of recurrence to be around 0.025% and unlikely to be related to scalp cooling for adjuvant chemotherapy [6].

Herein, we present the rare case of a single metastasis to the scalp with an undetectable primary breast carcinoma.

Case Report

The patient is a 66-year-old female with a history of diabetes mellitus type 2, essential hypertension, and benign thyroid nodules who presented to her dermatologist with a left parietal scalp lesion. The patient had first noticed the lesion 5 months prior, which had been gradually growing in size. She denied any history of cancer, including breast or skin malignancies, and was up to date with her screening mammography. A scoop excision was performed. Surgical pathology results showed a malignant dermal neoplasm involving the skin dermis and extending the surgical resection margins (Fig. 1). Immunohistochemical (IHC) stains revealed that the tumor cells were strongly positive for estrogen receptor, progesterone receptor, and E-cadherin (Fig. 2). Cytokeratin (CK) 20 was focally weakly positive and CK7 staining was negative. A diagnosis of adenocarcinoma consistent with a breast primary was made. The patient sought a second opinion at our institution and her pathology slides were reviewed. Additional immunostains were performed. The tumor was strongly positive for GATA-3 and was confirmed negative for CK7. CK20, p63, and TTF-1 were also negative (Fig. 3). There was no evidence of Her2/neu amplification by IHC staining and dual in situ hybridization.

Clinically, the breast examination was unremarkable. A 3D mammography taken 4 weeks after the initial biopsy showed no mammographic evidence of malignancy. A positron emission tomography (PET)/computerized tomography (CT) 6 days later showed a mild left scalp defect thought to be postoperative in nature. No definite evidence of adenopathy or metastatic disease was identified. Four months after the scoop biopsy, bilateral breast magnetic resonance imaging (MRI), performed at our institution, showed no identifiable breast lesion. The pathology specimen was sent for Biotheranostics CancerTYPE ID® classifier analysis, which uses real-time RT-PCR to measure the expression of 92 genes in a patient's tumor and classifies the tumor by matching the gene expression pattern of the patient's tumor to a reference database that includes 50 known tumor types. The test results showed a 96% probability of the breast being the primary site.

She was referred to breast surgical oncology and plastic surgery for re-excision of margins followed by antiestrogen therapy with anastrozole.

Discussion

Scalp metastases in breast cancer usually present in conjunction with other sites of disease and after detection of a primary rumor. The axilla is the most common site of metastasis of an unidentified breast tumor [2]. The diagnosis of cutaneous metastasis of a breast carcinoma in the absence of a known primary requires a careful pathological and radiological workup to rule out other possible primary sites.

From the pathology's point of view, the main differential diagnosis of a subcutaneous adenocarcinoma of unknown etiology is a primary skin adnexal (sweat gland) adenocarcinoma. Because the treatment and prognosis in these two scenarios differ greatly, a definitive diagnosis is of the utmost importance [7]. Morphologically, both adenocarcinomas display similar features and IHC staining is necessary to make a definitive diagnosis. Most of the popular breast carcinoma IHC markers, i.e., mammaglobin and gross cystic disease fluid protein (GCDFP), can be positive in skin adnexal adenocarcinoma. Furthermore, these stains are not very sensitive, with a positivity of approximately half of primary breast carcinomas for mammaglobin and approximately 30% for GCDFP-15 [8]. In addition, staining with these markers may be patchy and therefore not useful in small biopsies. Estrogen receptor can also be expressed by primary sweat gland adenocarcinomas, limiting its use in this setting [8]. The majority of breast carcinomas are positive for CK7 and negative for CK20 [9]; however, in our practice we have found rare cases of CK7-negative breast carcinomas. GATA-3 has become popular in the breast cancer literature as a sensitive marker for breast carcinoma; however, it lacks specificity and should be used in conjunction with other markers [10]. p63, a homologue of p53, can be useful in this setting, since breast carcinomas are generally negative for p63 or only focally positive, whereas adnexal carcinomas are usually strong and diffusely positive for this marker [7]. Since a single specific marker in the differentiation between breast carcinoma and skin adnexal tumors has not been identified thus far, a panel of IHC stains should always be performed.

In addition to skin adnexal adenocarcinoma, other primary sites should also be considered in the differential diagnosis. Besides breast carcinoma, other malignant neoplasms that metastasize to the skin include lung, ovarian, and colon cancer, as well as melanoma and sarcoma [11]. A limited panel of IHC stains should be performed to rule out other sites, taking into consideration the patient's clinical history and tumor morphology. Our patient underwent exhaustive evaluation including PET/CT, mammography, and breast MRI, and no other areas of concern were found. Considering the low false negative rate of breast MRI in detecting a breast primary in cases of metastatic axillary lymphadenopathy when there is suspicion of a primary breast tumor [12], close observation instead of breast surgery was recommended in this patient.

The CancerTYPE ID test, used in our case, profiles 92 genes obtained by extracting RNA from tumor-enriched, formalin-fixed, paraffin-embedded tissue sections and performing real-time quantitative PCR. Tumors can be ruled out with 95% confidence. The test has a sensitivity of 87% at the main cancer site level and 82% at the subtype level, and a false rule-out rate of 5% [13–15]. In addition to the pathological evaluation, this test also provided us with further reassurance regarding the primary site of origin.

In sum, this case illustrates a very rare presentation of a de novo occult primary breast cancer with only one site of metastasis to the scalp. Meticulous pathological and radiological analyses are necessary in order to establish a conclusive diagnosis. Physicians should perform thorough dermatologic examinations routinely, as skin lesions could represent a manifestation of metastatic breast cancer.

Statement of Ethics

The authors have no ethical conflicts to declare.

Disclosure Statement

The authors declare that there is no conflict of interest regarding the publication of this paper.

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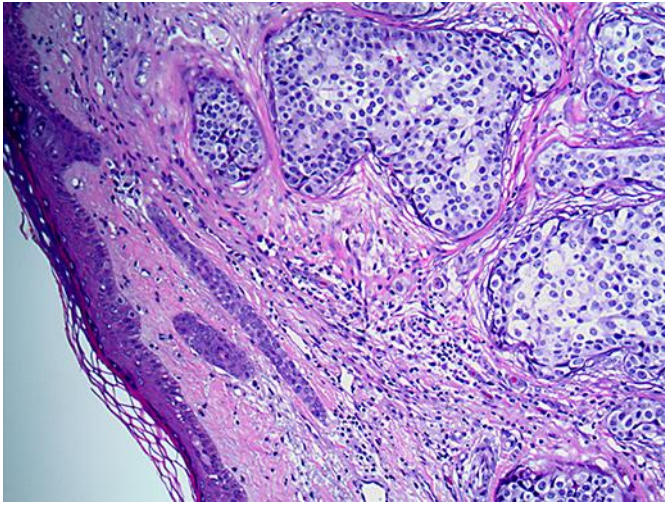
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Fig. 1. Adenocarcinoma involving the dermis (upper right). The surface epidermis is intact. A small hair follicle is seen just underneath the epidermis. HE. ×100.
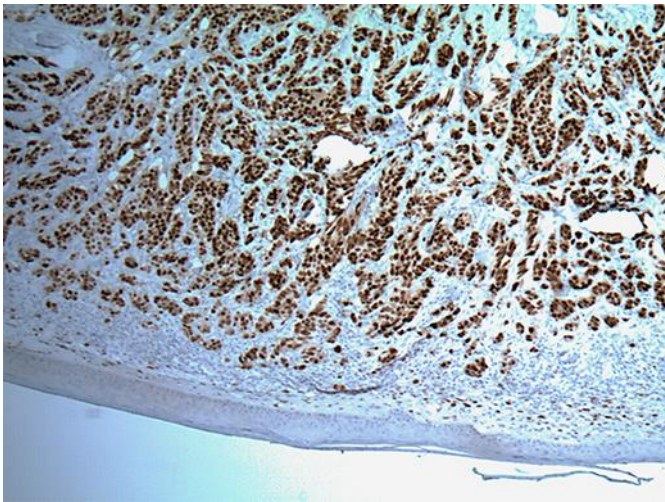

Fig. 2. Immunohistochemical staining for estrogen receptor is strongly positive in the tumor cells. ×50.

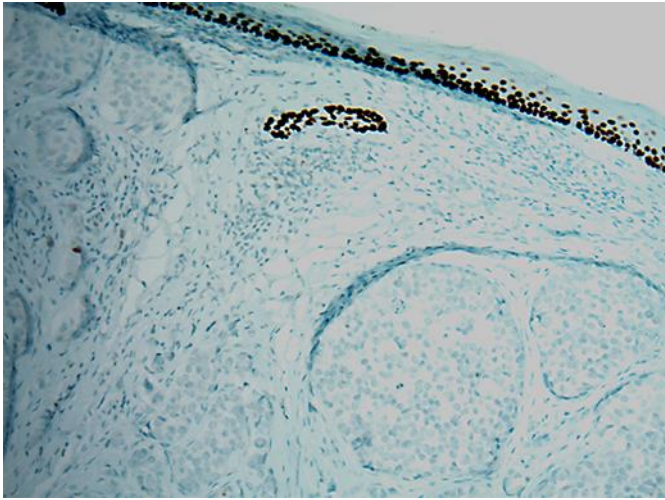Costa et al.: Occult Breast Carcinoma Presenting as Scalp Metastasis

Fig. 3. Immunohistochemical staining for p63 is negative in the tumor and positive in the benign skin elements and epidermis. ×100.