



Scalp metastasis from occult primary breast carcinoma: A case report and review of the literature☆☆☆



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ABSTRACT

Background: Isolated distant cutaneous metastasis of breast carcinoma is uncommon. Furthermore, isolated metastasis of the scalp seems to be very rare in breast cancer.

Case presentation: A 44-year-old woman was referred to our dermatology department with concerns of a firm, painless, immobile, hardened, skin-colored mass fixed to the underlying tissues. The lesion measured 2 to 3 cm on the scalp frontalis without regional or distant lymphadenopathy. The patient had a history of benign right breast biopsy test results.

Immunohistochemistry test results were positive for cytokeratin (AE1/AE3), cytokeratin 7, chromogranin, estrogen receptor, and gross cystic disease fluid protein-15; group PR/HER2 were both weakly positive. Cytokeratin 20, thyroid-lung transcription factor, S100 protein, vimentin and thyroglobulin were all negative. Pathology test results showed adenocarcinoma that was consistent with breast primary.

Conclusion: Although cutaneous metastasis of the chest wall due to breast carcinoma is a common condition, scalp metastasis as the first sign of occult breast cancer is an extremely rare condition. We describe an isolated scalp metastasis as the initial presentation of breast cancer in a young woman in this report, which highlights that health care providers should be alert to the possibility that atypical soft tissue masses may represent a neoplasm. Further consideration of the scalp lesions among healthy looking patients is recommended.

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Introduction

Herein, we review the literature on cutaneous scalp metastasis from occult primary breast carcinoma. We illustrate the issue with the example of a 44-year-old female patient who presented with a frontal scalp cutaneous mass, but imaging modalities such as mammography and ultrasound found no primary breast cancer, and positron emission tomography revealed no particular metastases in her breast or other organs. Histopathology test results showed adenocarcinoma with neuroendocrine features and positive estrogen receptors. Although the primary cancer site was not determined, pathologists and oncologists suspected that it arose from indolent breast adenocarcinoma.

Isolated distant cutaneous metastasis of breast carcinoma is uncommon. Scalp involvement is very rare in breast cancer (Prabhu et

al., 2009). Cutaneous metastasis usually presents with direct invasion or local infiltration, which indicates advanced disease (Prabhu et al., 2009; Shafiuddin et al., 2014). The expected survival rate at the time of diagnosis with cutaneous metastasis from breast cancer is estimated at < 1 year. The survival benefit of chemotherapy in the management of patients with occult primary breast carcinoma is not definitive. Our patient responded well to the treatment without recurrence after 3 years of follow up.

Case history

A 44-year-old female patient presented to our practice with a painless left frontal scalp mass of 1-year duration. She had a history of a benign breast cyst with a right breast cystectomy secondary to fibroblastic changes 3 years ago, but was otherwise healthy with no history of weight loss.

The frontal scalp mass was skin-colored, nontender, hard, immobile, and measured 2.5 cm. (Fig. 1). There was no regional or distant lymphadenopathy. Clinically, the breast examination was unremarkable.

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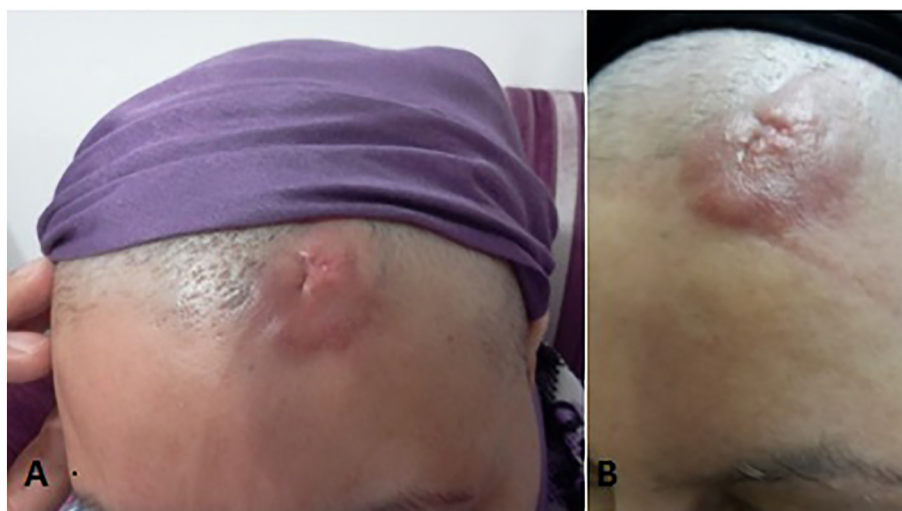


Fig. 1. Metastatic cutaneous mass over the frontal scalp of a 44-year-old female patient.

Blood test results showed elevated tumor markers, carcinoembryonic antigen (CEA) (37 ng/ml [normal up to 3.5 ng/ml]), elevated CA125 (34.7 U/ml [normal <35 U/ml]), and normal CA19.9 (<0.3 U/ml [normal <37 U/ml]).

A punch biopsy was performed. Histology test results showed a deposition of somehow differentiated adenocarcinoma with neuroendocrine features (Fig. 2) Immunohistochemistry results (Table 1) showed a pattern that was more favorable of metastatic carcinoma of a primary breast neoplasm (Figs. 2–4).

The patient underwent several imaging tests (whole body bone scintigraphy, brain magnetic resonance imaging [MRI], abdominal U/S, breast and lymph nodes U/S, chest computed tomography with and without contrast, and breast MRI), and all imaging results were essentially normal. The detailed results are as follows:

- Whole body bone scintigraphy demonstrated abnormal increased uptake in the right femoral head without considerable abnormal uptake through the rest of skeleton.
- Brain MRI revealed plate-like, well-defined signal abnormality (low on T1, intermediate on T2W, FLAIR) in the subcutaneous adipose tissue of left superior frontal region with remarkable enhancement. The mass had no intracranial extension.
- Abdominal ultrasound was unaltered.
- Ultrasonography of the breast and lymph nodes showed normal echo without cystic or solid lesions and no pathological lymph nodes.
- CT of the chest with and without contrast showed wedge-shaped consolidation in right middle lobe with air bronchospasm. Areas of ground glass opacity in right and left upper lobes. Findings were compatible with pneumonia and resolved with antibiotic therapy. No definite evidence of mediastinal lymphadenopathy or pleural effusion was observed.
- Breast MRI showed no obvious mass or abnormal enhancing area in either breast; however, reactive-appearing lymph nodes in the axillary regions were observed and presented generally benign findings.

We referred the patient to an oncologist for further evaluation and treatment. She was initiated on systemic chemotherapy, consisting of four cycles of adriamycin and cyclophosphamide, followed by four cycles of docetaxel. Subsequently, the patient had a surgical removal and graft of the scalp mass (Fig. 5). After a period of radiation therapy, the patient continued on tamoxifen 20 mg/day. Our patient had a good response to treatment without recurrence with 3 years of follow

up. Close observation rather than breast surgery was recommended for this patient.

Discussion

Isolated distant cutaneous metastasis of breast carcinoma is uncommon, and scalp involvement is very rare in breast cancer (Prabhu et al., 2009). Cutaneous metastases comprise 0.7% to 9% of all metastases and may be the first manifestation of internal malignancy or a sign of recurrence and poor prognosis (Prabhu et al., 2009). Scalp tumors account for 2% of all skin tumors and may originate from the epithelium, pilosebaceous unit, eccrine, and apocrine or present as metastases (Prabhu et al., 2009).

Lookingbill et al. (1990) conducted a systematic review of 7316 patients with cancer and found 367 cases (5.0%) with cutaneous involvement. Among these cases, cutaneous involvement was present in 92 at the time of presentation (1.3%); skin involvement was the first manifestation of cancer in 59 patients (0.8%); 22 cases had direct expansion of the tumor into the skin, with 20 and 17 with local and distal metastases, respectively. Chuang et al. (2007) found metastatic tumors in 12.8% of cases with malignant scalp lesions. Lung cancer was the most common primary tumor, followed by cancers of the colon (11.76%), liver (7.84%), and breast (7.84%). Of note, metastatic tumors of undetermined origin accounted for 29.41% of all metastatic scalp tumors.

Breast cancer is the most common malignant neoplasm in women. Approximately 6% of patients have de novo metastatic breast cancer. Occult breast cancer accounts for only 0.1% to 0.8% of cases and most commonly presents with axillary lymphadenopathy. Cutaneous metastases of breast carcinoma usually arise in the overlying skin or proximal to the primary tumor. There are different morphological types of cutaneous metastasis of breast carcinoma, including solitary to multiple erythematous infiltrating nodules or masses, carcinoma erysipeloids, carcinoma en cuirasse, carcinoma telangiectaticum, alopecia neoplastica, and zosteriform pattern (Rolz-Cruz and Kim, 2008; Santos-Juanes et al., 2007).

In 2011, Kuwayama et al. reported on a woman with a hard, alopecic mass on her scalp. Skin biopsy and histopathological assay test results revealed adenocarcinoma. Scalp metastases in breast cancer usually present in conjunction with other sites of disease and after detection of a primary tumor. Scalp metastases are rare and have been described as a sign of progression or widespread metastatic disease (Prabhu et al., 2009).

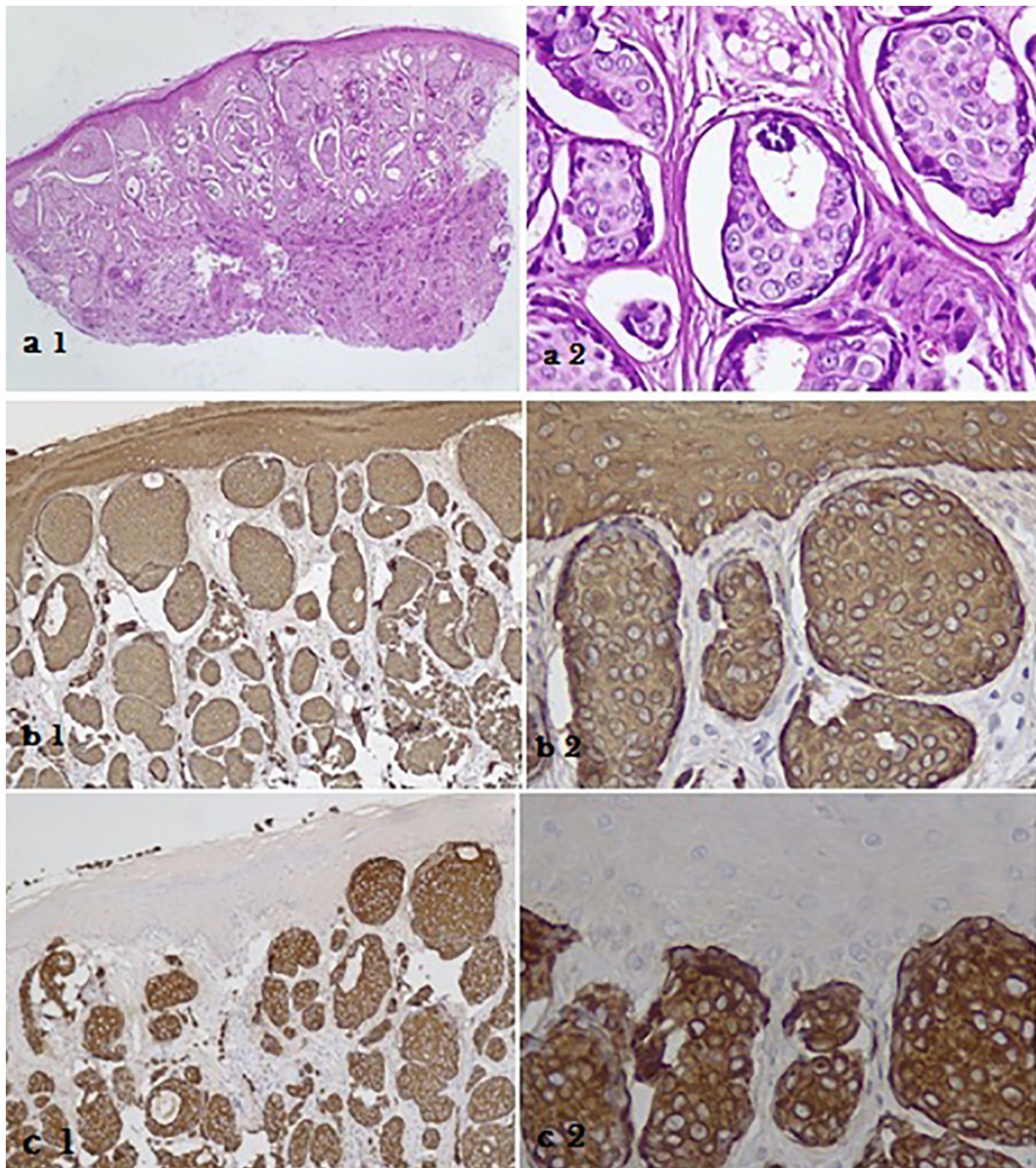


Fig. 2. Histopathologic study of frontal mass biopsy, stained by hematoxylin and eosin and immunohistochemistry. (A) 1 and 2 low and high magnification respectively, hematoxylin and eosin, deposits of malignant epithelial neoplasm with minute foci of calcification and necrosis (adenocarcinoma with neuroendocrine feature); (B) 1 and 2 low and high magnification respectively, immunohistochemistry with cytokeratins strongly positive for the tumor cells; (C) 1 and 2 low and high magnification respectively, positivity for CK7 within the tumor cells.

Table 1
Summary of immunohistochemical stain findings

Antibody	Result
Cytokeratin (AE1/AE3)	+
Cytokeratin7	+
Chromogranin	+
Estrogen receptor	+
Gross cystic disease fluid protein-15	+
GATA3	+
Mammaglobin	+
Progesterone receptor	+/-
Her2neu	+/-
Cytokeratin 20	-
Thyroid-lung transcription factor (TTF-1)	-
P63	-
Vimentin	-
Thyroglobulin	-
CK5/6	-

Shelke et al. (2012) reported on multiple cutaneous metastases from ductal carcinoma of the breast in a male patient. The researchers showed multiple nonulcerated, firm-to-hard papulonodular lesions on the chest, abdomen, extremities, and scalp.

In our case, the female patient presented with a scalp tumor from indolent breast adenocarcinoma before revealing the breast imaging modalities. The diagnosis of cutaneous metastasis in the absence of a known primary requires a careful pathologic and radiologic workup to rule out other possible primary sites. Treatment and prognosis in each primary differ; thus, a definitive diagnosis is of the utmost importance.

Apocrine carcinomas characteristics from the scalp or elsewhere are similar to those of cutaneous metastases of breast adenocarcinoma (female breast can be thought of as a modified apocrine gland). 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 a

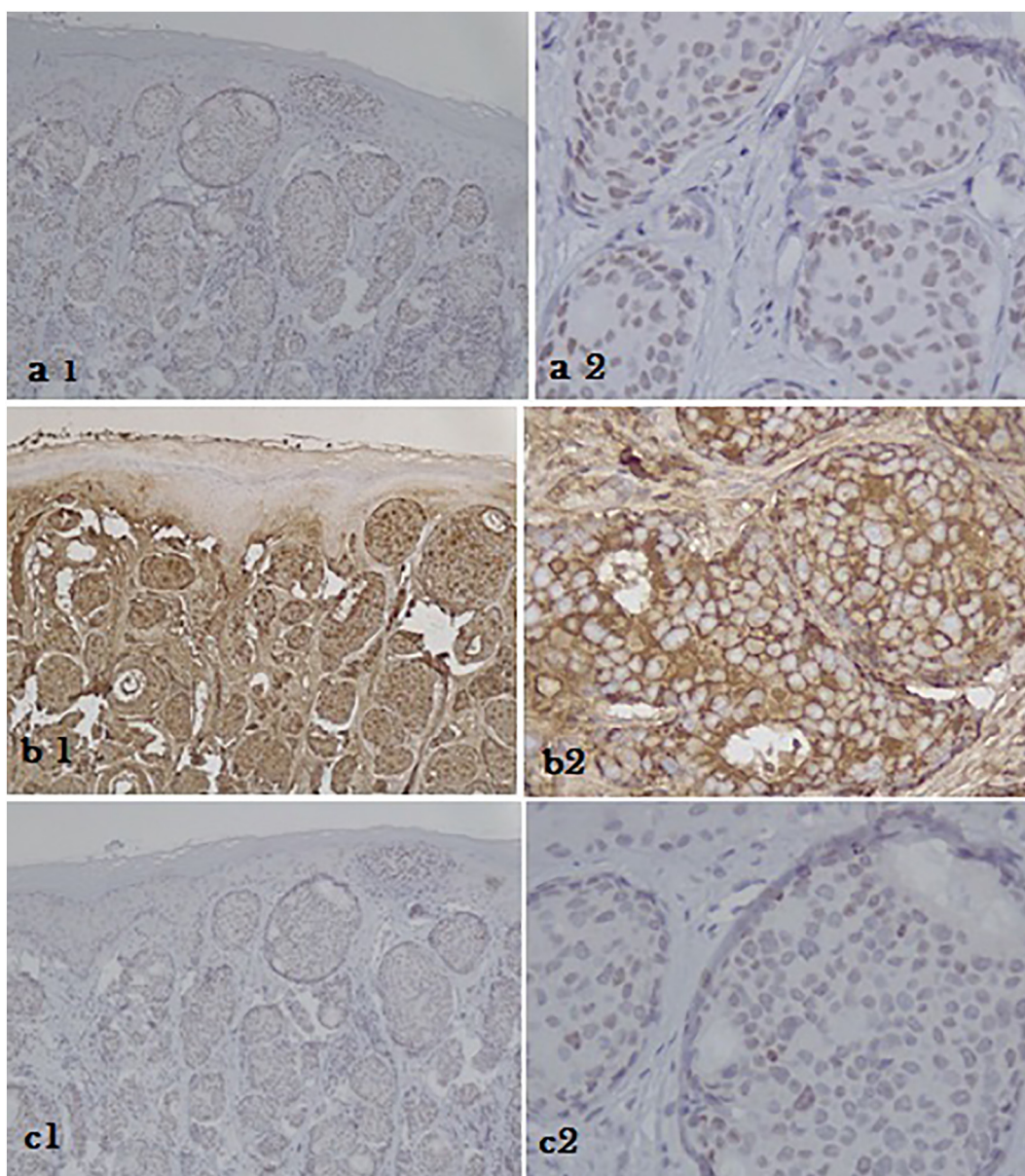


Fig. 3. Immunohistochemistry study of frontal mass biopsy. (A) 1 and 2 low and high magnification respectively, immunohistochemistry showing estrogen receptor positivity for metastatic cells; (B) 1 and 2 low and high magnification respectively, immunohistochemistry shows GCDFP15 strongly positive for the tumor cells; (C) 1 and 2 low and high magnification respectively, positivity for progesterone receptor within the tumor cells.

single specific marker in the differentiation between breast carcinoma and skin adnexal tumors has not been identified thus far, a panel of immunohistochemical stains should always be performed. Also, in a skin adnexal adenocarcinoma, primary sites of malignant neoplasms other than breast carcinoma should always be excluded, such as lung, ovarian, and colon cancer, as well as melanoma and sarcoma (Alcaraz et al., 2012; Krathen et al., 2003; Lookingbill et al., 1990; Obaidat et al., 2007; Tlemcani et al., 2010).

An example is the case report of a 60-year-old woman who had primary scalp cutaneous apocrine carcinoma that was first misdiagnosed as cutaneous metastasis from breast adenocarcinoma (Kim et al., 2012). Another example is a case report of the axillary cutaneous apocrine carcinoma mimicking the metastatic lobular breast carcinoma. Immunohistochemistry demonstrated solid apocrine carcinoma of the skin (Zelger et al., 2008).

Taking into consideration the patient's clinical history and tumor morphology, metastatic carcinomas usually can be distinguished

from primary cutaneous cancers by typical histopathological patterns, such as the epidermal connection, intraepidermal, or intraadnexal (in situ component) tumor, or the presence of a benign counterpart in primary cutaneous cancers (Nibhoria et al., 2014). Immunohistochemical staining, particularly with cathepsin D, which is an aspartic protease and predominantly seen in breast carcinoma metastases, is of diagnostic value (Borkar and Pandit-Taskar, 2008; Manohar et al., 2012). P63 is a useful marker to distinguish between metastatic tumors and primary cutaneous adnexal tumors (Rollins-Raval et al., 2011).

Sihto et al. (2011), in a nationwide cohort study, found that tumors with early skin metastases expressed infrequently E-cadherin as a predictor of the preferential distant metastasis site. Additionally, pan-cytokeratins, epithelial membrane antigen, and carcinoembryonic antigen also stain positive in the majority cases, and reactivity of the metastatic tumor to androgen receptor is a key point toward the primary origin of breast carcinoma (Prabhu et al., 2009). Imaging that

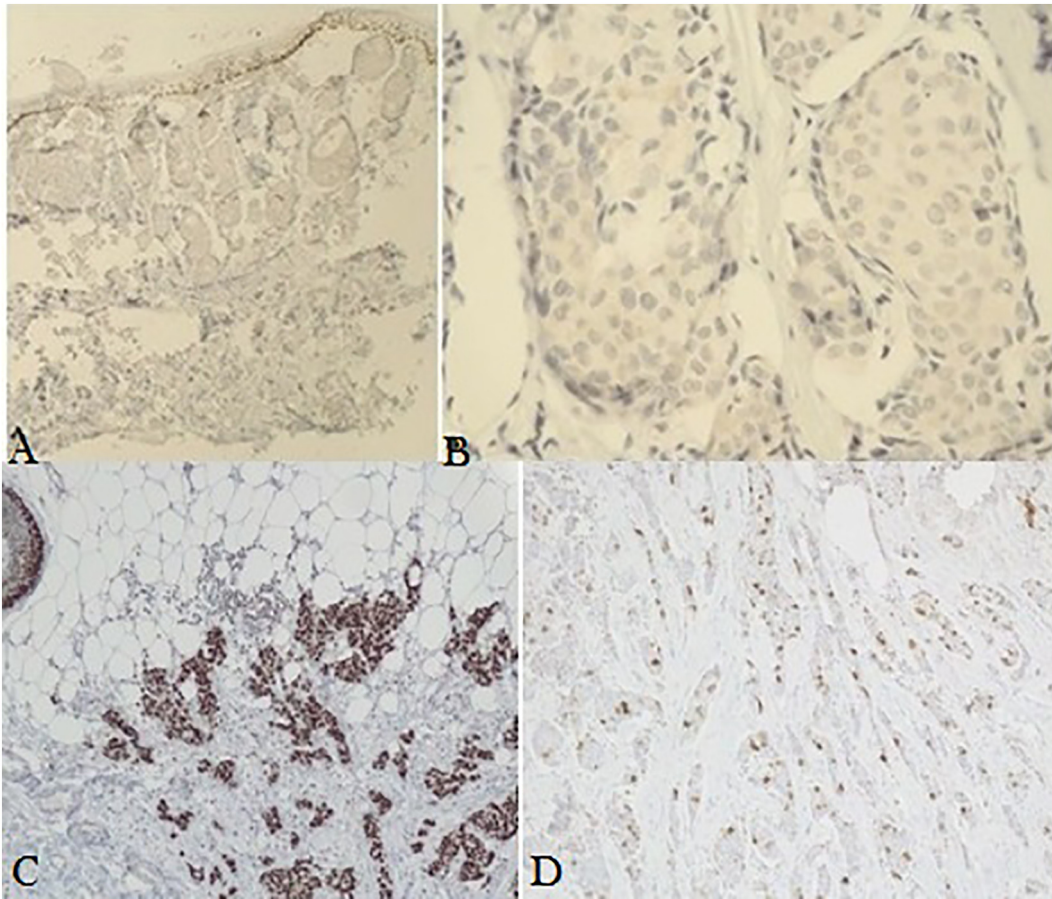


Fig. 4. Immunohistochemistry study of frontal mass biopsy. (A and B) low and high magnification respectively, immunohistochemistry showing P63 negativity for metastatic cells; (A) shows normal epidermis is positive for P63; (C) immunohistochemistry shows GATA 3 positivity for metastatic cells; and (D) immunohistochemistry shows mammaglobin positivity for metastatic cells.

uses positron emission/computed tomography scans is advised to stage breast cancer and revealed to be better than conventional imaging (Manohar et al., 2012; Borkar and Pandit-Taskar, 2008). Two known cases of breast carcinoma were reported with distant asymptomatic skin metastases (scalp and eyelid), which were incidentally detected with a positron emission tomography scan (Schwartz, 1995).

However, despite improvements in breast imaging, the frequency of detection of a primary tumor in that particular context has not substantially improved over time. Furthermore, immunohistochemical stains are not very sensitive, with a positive result for approximately half of the primary breast carcinomas for mammaglobin and

approximately 30% for GCDFP-15. Estrogen receptor can also be expressed by primary sweat gland adenocarcinomas. The majority of breast carcinomas are positive for CK7 and negative for CK20. However, rare cases of CK7-negative breast carcinomas exist. GATA-3 has become popular in the breast cancer literature as a sensitive marker for breast carcinoma but lacks specificity and thus should always be used in conjunction with other markers (Bhargava et al., 2007; Cohen et al., 2009; Huo et al., 2013; Kaufman et al., 2003; Klein et al., 2005; Mentrikoski and Wick, 2015; Sellheyer and Krahl, 2010).

Conclusion

This report illustrates a very rare case of scalp metastasis as the first sign of occult breast cancer and shows that the diagnosis of a cutaneous mass in the absence of a known primary lesion requires a careful pathologic and radiologic workup to rule out other possible primary sites.

The close resemblance of immunohistochemistry in cutaneous adnexal carcinomas versus metastatic adenocarcinomas requires meticulous pathologic and radiologic analyses to establish a conclusive diagnosis.

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Fig. 5. Surgical removal and graft of scalp mass.

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