Primary cutaneous apocrine carcinoma: 2 cases and review of the pertinent histologic findings

Jessica Schweitzer, DO, PGY-2,[a] Jennifer Vermeesch, DO, PGY-3,[a] Theresa Zaleski, DO,[a] Megan Iacco, MD,[b] Kent Krach, MD,[a] Jessica Ghaferi, MD,[c] and Jenny Cotton, MD, PhD[c]
Ann Arbor, Michigan

Key words: adenocarcinoma; adnexal carcinoma; cutaneous apocrine carcinoma; signet-ring cells.

INTRODUCTION

Primary cutaneous apocrine carcinoma (PCAC) is a rare cutaneous adnexal tumor that presents a diagnostic challenge, with histology and staining mirroring those seen in mammary ductal carcinoma and other adnexal neoplasms. We report the first case, to our knowledge, of PCAC with in-transit metastasis responding to primary radiotherapy as a treatment. We also describe a case of PCAC treated with axillary lymph node dissection, wide local excision, and adjuvant radiotherapy. We hope this review provides greater awareness of this neoplasm in the differential diagnoses of metastatic breast carcinoma, as the prognostic implications may differ significantly.

Abbreviations used:

ER:	estrogen receptor
IMDC:	intramammary ductal carcinoma
PCAC:	primary cutaneous apocrine carcinoma
PR:	progesterone receptor

CASE 1

A 73-year-old white man with a medical history of chronic lymphocytic leukemia presented with a 3-year history of a slow-growing, painless mass in his left axilla with occasional serosanguinous drainage. Courses of topical antibiotics, antifungals, and topical steroids were ineffective. Physical examination found numerous, indurated brightly erythematous plaques and nodules in the axilla and lateral left breast with nipple inversion (Fig 1).

Punch biopsy found dermal aggregates of large, pleomorphic epithelioid cells with abundant cytoplasm (Fig 2). Some cells displayed a signet-ring appearance (Fig 3). Immunohistochemical staining showed pancytokeratin, cytokeratin 7, gross cystic disease fluid protein, and GATA3 positivity. Stains for cytokeratin 20, S-100, thyroid transcription factor, CDX2, and prostate-specific antigen were negative. Estrogen receptor (ER), progesterone receptor (PR), and HER2/neu were negative. Given the concern for metastasis from a primary breast or solid organ malignancy, the patient underwent an extensive workup including a full body positron emission tomography scan, computed tomography scans, serum tumor markers, and mammography, with no other malignant foci identified. With the patient's comorbidities and extensive involvement, he was treated with radiation therapy and showed a clinical response (Fig 4). Unfortunately, the patient died of a myocardial infarction 2 weeks after completion of radiation therapy.

CASE 2

A 56-year-old white man presented with an enlarging lesion in his left axilla that had been present for 5 years. He was treated previously for a presumed abscess with antibiotics for several weeks with no resolution. On physical examination, a 3- × 3-cm, erythematous-to-brown, firm plaque with central nodularity was present. Punch biopsy found similar findings to those in case 1 including a diffuse infiltrate extending from the papillary dermis to the subcutis, composed of cells with indistinct borders

From Departments of Dermatology[a] and Dermatopathology,[c] Saint Joseph Mercy Hospital, and IHA Dermatology.[b]
Funding sources: None.
Conflicts of interest: None declared.
Correspondence to: Jessica Schweitzer, DO, PGY-2, Dermatologic Residency Clinic Reichert Health Center, 5333 McAuley Drive Room 5003, Ypsilanti, MI 48197. E-mail: Jschweitzer09@gmail.com.

JAAD Case Reports 2016;2:411-4.
2352-5126

http://dx.doi.org/10.1016/j.jdcr.2016.08.003

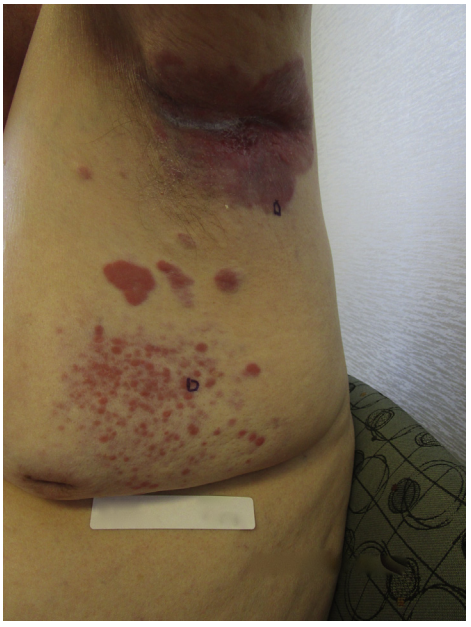

Fig 1. Primary cutaneous apocrine carcinoma. Case 1: multiple, indurated brightly erythematous plaques and nodules in the axilla and lateral left breast with nipple inversion.

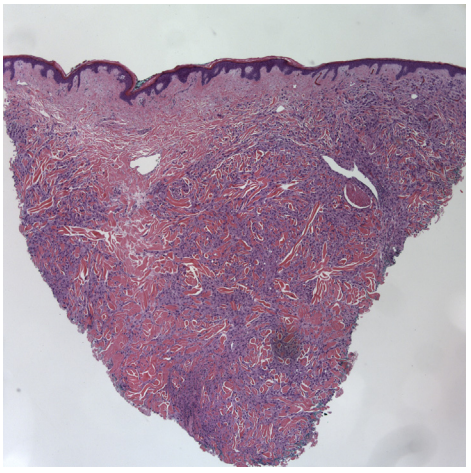

Fig 2. Dermal aggregates of large, pleomorphic epithelioid cells with abundant cytoplasm. (Hematoxylin-eosin stain; original magnification: ×4.)

and abundant eosinophilic granular cytoplasm. Single-cell infiltration was noted in some areas. Staining was positive for pancytokeratin, p63, epithelial membrane antigen, and GATA3. Stains for CD68, S-100, ER, and PR were negative. The patient underwent a positron emission tomography—computed tomography scan, which showed axillary lymph node involvement and was managed with wide local excision and axillary lymph node dissection. At the time of publication, he was receiving ongoing adjuvant radiotherapy.

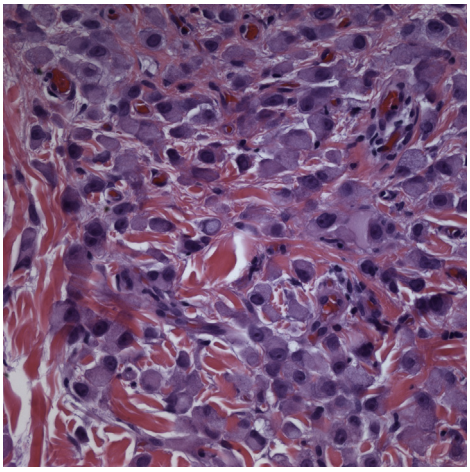

Fig 3. Some cells displayed a signet-ring appearance. (Hematoxylin-eosin stain; original magnification: ×20.)

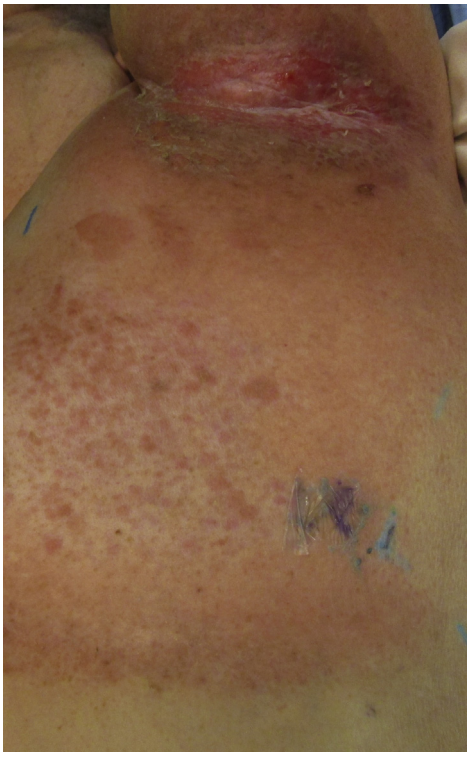

Fig 4. Case 1: after radiation therapy.

DISCUSSION

PCAC is an extremely rare adnexal carcinoma that occurs in middle-aged adults with approximately 50 cases reported in the literature. It arises in areas of high apocrine gland density, including the axilla and the anogenital region but has also been described on the eyelid, ear, chest, and extremities. The clinical findings vary, but PCAC typically presents with erythematous, slow-growing, firm or cystic nodules.

Table I. Staining patterns for IMDC versus PCAC

Stain	IMDC	PCAC
Cytokeratin 5,6	+/−	+ strong and diffuse
p63	−	−/+
GATA3	+	+
Mammaglobin	Strongly +	Weakly +
Adipophilin	+ strong and diffuse	−
ER	+	+
PR	−/+	+/−
AR	+	+
CEA	−	+
HER2/neu	+	−
GCDFP-15	+	+

AR, Androgen receptor; *CEA,* carcinoembryonic antigen; *IMDC,* intramammary ductal carcinoma; *PCAC,* primary cutaneous apocrine carcinoma.
Data from refs.[3-6,9,10]

PCAC can share many features with intramammary ductal carcinoma (IMDC), which is not surprising, as mammary ducts are modified apocrine sweat glands.[1] Given the rarity of the tumor and lack of studies, differentiating PCAC from cutaneous breast metastasis is difficult to make on histologic grounds and requires an in-depth knowledge of the spectrum of various stains (Table I). One of the most useful markers distinguishing primary cutaneous adnexal tumors from breast metastasis is p63. Unfortunately, p63 is not usually expressed in PCAC but is helpful if present.[2] Mammaglobin, a well-known marker for IMDC that has stained with strong positivity in prior studies, was also recently observed to have weak positivity in PCAC and IMDC.[2]

In addition to ruling out IMDC, a signet-ring cell morphology was seen in case 1, raising concern for metastatic stomach or colon carcinoma. This variant has been reported in 6 other cases of PCAC[3,4] and shows very similar staining characteristics including positivity for epithelial membrane antigen, carcinoembryonic antigen, gross cystic disease fluid protein-15, and cytokeratins.

Aside from IMDC, the clinical and histopathologic differential diagnoses include melanoma, lymphoma, mycosis fungoides, extramammary Paget disease, microcystic adnexal carcinoma, and apocrine hidradenocarcinoma. Given this broad differential diagnosis, a thorough workup and history should be performed to exclude these etiologies.

Although no standard of care exists due to its rarity, most cases are managed with wide local excision with suggested surgical margins of 1 to 2 cm.[5] Fifty percent of patients have lymph node metastasis at the time of diagnosis, but the decision to perform sentinel lymph node biopsy is controversial.[5-7] It has been proposed that lesions greater than 5 cm in diameter, those that are moderately or poorly differentiated, or those that have clinically involved lymph nodes should undergo lymph node dissection.

Other options for treatment include Mohs micrographic surgery in cosmetically sensitive areas, adjuvant radiotherapy, and hormonal therapy. PCAC responds poorly to conventional chemotherapy; however, 1 case of adjuvant radiotherapy with wide resection and tamoxifen therapy succeeded in achieving remission.[5] ER^+ tumors have also responded to tamoxifen, and $HER2/neu^+$ tumors have responded to combination therapy with trastuzumab and lapatinib. A recent report of lapatinib and capecitabine led to complete remission in a patient with metastatic disease. The patient in case 1 showed a clinical response to primary radiation therapy, but complete histopathologic response and sustained remission could not be determined, as the patient died of unrelated causes. Case 1 is the first reported case of primary radiation therapy used to treat PCAC, and the second reported case of PCAC showing response to radiation therapy.[5] Case 2 is continuing with ongoing adjuvant radiotherapy after wide local excision and axillary lymph node dissection.

Those with well-differentiated tumors tend to do well and have a long-term remission (88%) if surgery can be performed.[8] Those with poorly differentiated tumors have a worse prognosis. There is a 28% 5-year local recurrence rate, with the time of recurrence ranging from 5 months to 10 years. Despite the rarity of this tumor, we present 2 cases of PCAC highlighting their clinical, histologic, and immunohistochemical profile. We hope that this review provides greater awareness of this neoplasm in the differential diagnoses of a metastatic breast carcinoma, as the prognostic implications may differ significantly.[3]

REFERENCES

1. Zeiger B, Steizmueller I, Dunst K, et al. Solid apocrine carcinoma of the skin: report of a rare adnexal neoplasm mimicking lobular breast carcinoma. *J Cutan Pathol*. 2007; 35(3):332-336.
2. Fernandez-Flores A. Primary Cutaneous Apocrine Carcinoma Versus Metastasis, A Plea to the Dermatopathology Community. *Am J Dermatopathol*. 2010;32(8):853-854.
3. Droubi D, Zeitouni NC, Skitzki J, et al. Primary signet-ring cell carcinoma of the axilla. *J Cutan Pathol*. 2013;40(2): 269-273.
4. Chamberlain R, Huber K, White J, et al. Apocrine gland carcinoma of the axilla: review of the literature and recommendations for treatment. *Am J Clin Onc*. 1999;22: 131-135.

5. Seong M, Kim E-K, Han K, et al. Primary apocrine sweat gland carcinomas of the axilla: a report of two cases and a review of the literature. *World J Surg Oncol*. 2015;13:59.
6. Hollowell K, Agle S, Zervos E, et al. Cutaneous apocrine adenocarcinoma: defining epidemiology, outcomes, and optimal therapy for a rare neoplasm. *J Surg Onc*. 2012;105:415-419.
7. Warkel RL, Helwig EB. Apocrine gland adenoma and adenocarcinoma of the axilla. *Arch Dermatol*. 1978;114:198-203.
8. Cardoso JC, Calonje E. Malgnant sweat gland tumors: an update. *Histopathology*. 2015;67:589-606.
9. Piris A, Peng Y, Boussahmain C, et al. Cutaneous and mammary apocrine carcinomas have different immunoprofiles. *Hum Pathol*. 2014;45(2):320-326.
10. Robson A, Lazar A, Nagi JB, et al. Primary cutaneous apocrine carcinoma: a clinico-pathologic analysis of 24 cases. *Am J Surg Pathol*. 2008;32:682-690.