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CASE REPORT

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Cutaneous basal cell carcinoma mimicking small cell carcinoma

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Key Clinical Message

Neuroendocrine differentiation seen in basal cell carcinomas (BCC) is not generally appreciated by oncologists and can introduce a component of confusion when diagnosing a tumor and developing a management plan. Understanding that BCC commonly have this feature can assist the treating oncologist.

KEYWORDS

basal cell carcinoma, cutaneous small cell carcinoma, management, mimicry

1 | INTRODUCTION

Primary cutaneous small cell carcinoma is a rare entity; a case report and review of the literature reported in 2013 commented on only two previous cases in the literature.[1] Although small cell carcinoma arises primarily from lung parenchyma, it is also and less commonly seen arising in extrapulmonary sites including those of the genitourinary, gastrointestinal, and head and neck structures.[2-4] Architectural and immunohistochemical features of small cell carcinomas universally reveal neuroendocrine differentiation, and this molecular trait has been theorized to underlie the platinum-sensitive nature of the disease.[5] Neuroendocrine differentiation of solid tumors is not unique to small cell carcinomas and historic[6,7] as well as contemporary series[8] have documented this feature in cutaneous basal cell carcinomas. Given the different management of small cell carcinoma and basal cell carcinoma, accurate diagnostics remain critical to ensure optimal tumor control while limiting treatment toxicities. This case report and review of the literature illustrates the importance of clinical and pathological distinction between these tumors.

2 | CASE PRESENTATION

DG is a 78-year-old woman with a recent history of a favorable breast cancer who, after completing breast-conserving surgery and breast radiotherapy, developed a left neck nodule described as subdermal in location. The patient was on an aromatase inhibitor as systemic anti-endocrine therapy for her breast cancer, and the nodule was located along the medial crest of the left trapezius muscle. There was no overlying skin ulceration or pigmentation, and the patient was referred to her breast surgeon who suspected a regionally involved lymph node. The patient underwent a 20 gauge core biopsy revealing small cell carcinoma. The limited material revealed an epithelial neoplasm with features suggestive of a small cell carcinoma.

In addition to routine hematoxylin and eosin stain (Figure 1), immunohistochemical stains were performed with appropriate controls. Tumor cells stained positive for CD 56 and chromogranin (Figures 2 and 3) leading two pathologists to render the diagnosis of small cell carcinoma.

The patient was seen by a medical oncologist who performed a physical examination and noted a never-smoking history. A staging CT-PET fusion study was performed which revealed a moderately glucose avid focus involving the superior posterior left neck with an SUV of 3.6. A small focus of uptake was also seen involving a right-sided retroperitoneal lymph node with an SUV of 4.1 considered suspicious for neoplasm. The radiologist indicated this latter lesion was not amenable to biopsy given its size and location. No visceral disease or clear primary site was otherwise identified.

Given her excellent performance status and diagnosis of an aggressive small cell carcinoma, the patient went onto uneventfully complete four cycles of platinum-based doublet chemotherapy. Following the four cycles, she underwent a restaging CT-PET fusion which showed complete physiologic resolution of the neck and retroperitoneal disease.

The patient was then referred for consideration of consolidative involved field radiotherapy to the neck, and she completed 4300 cGy in 20 fraction without event. Noted at her radiation oncology intake examination was the presence of a large scar extending several centimeters beyond her initial neck core biopsy site. The patient admitted to having had surgery 2 years previously at that site for a skin cancer. Slides and tissue blocks were requested from the outside provider who excised her cutaneous malignancy 2 years prior and were compared ultimately to the current core biopsy (Figures 4, 5 and 6). The original tissue from two years earlier, and resected from the same site, revealed a deeply infiltrative basal cell carcinoma requiring three surgeries to clear the margins. Specifically, an initial shave biopsy was followed by two excisions. No prior mention was made of neuroendocrine differentiation. The older material was recut and was found to stain strongly for CD 56 and chromogranin. Comparisons

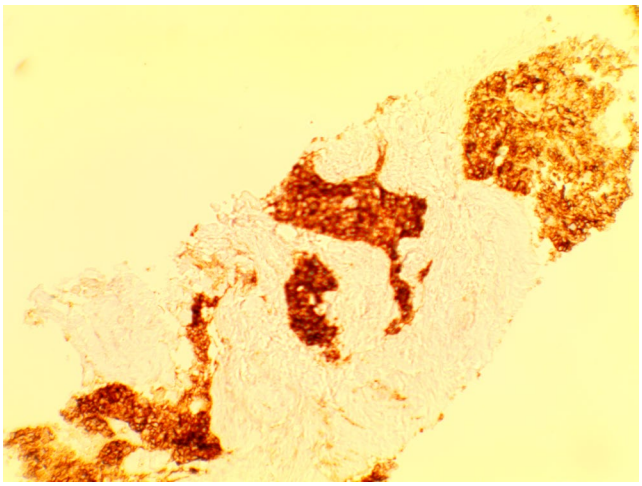

FIGURE 2 2018 Basal cell carcinoma CD56

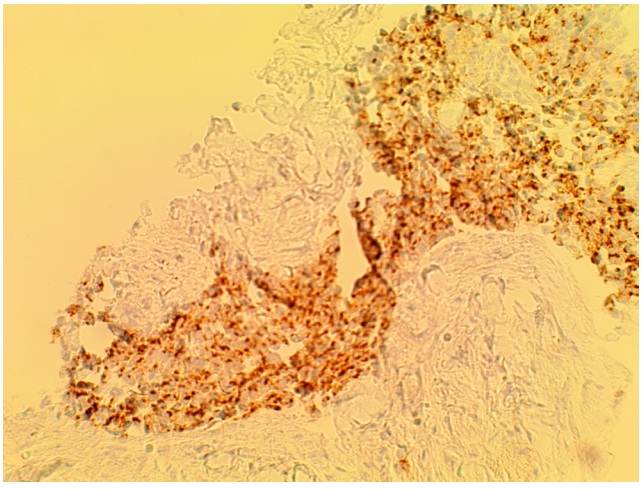

FIGURE 3 2018 Basal cell carcinoma chromogranin

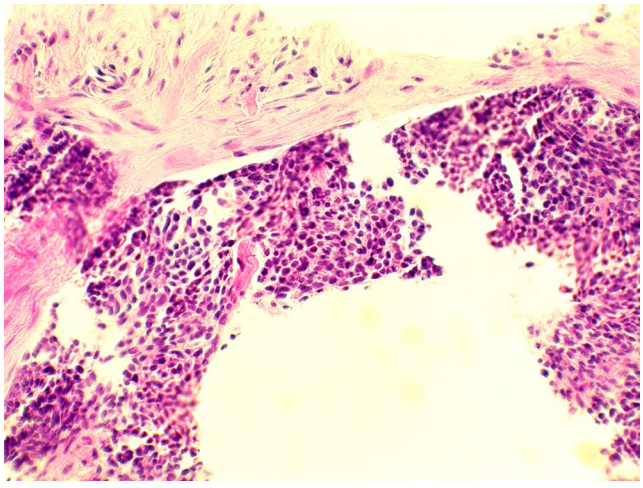

FIGURE 1 2018 Basal cell carcinoma H&E

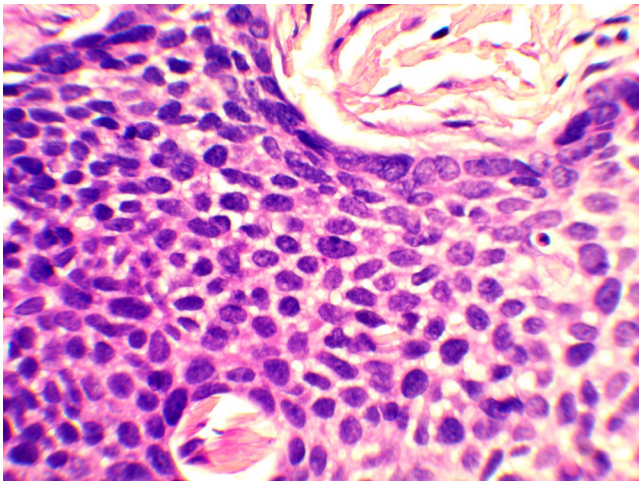

FIGURE 4 2016 Basal cell carcinoma H&E

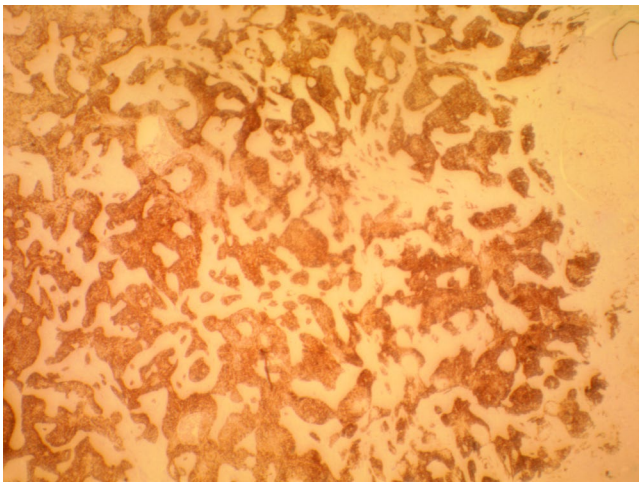

FIGURE 5 2016 Basal cell carcinoma CD56

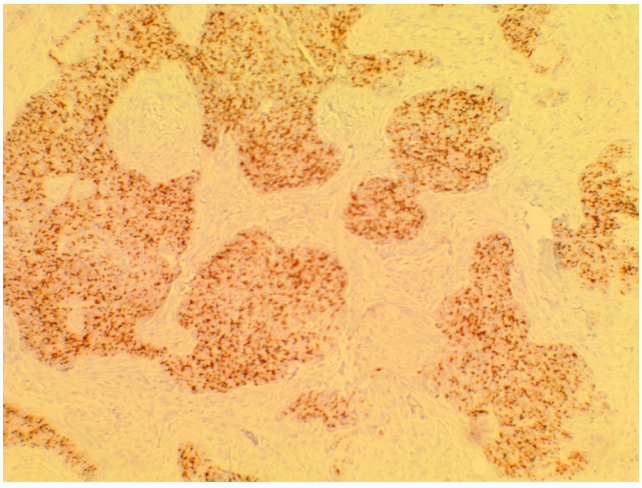

FIGURE 6 2016 Basal cell carcinoma chromogranin

were made between the new small cell and older basal cell carcinoma by two experienced community pathologists and a third from a tertiary care facility, and all agreed the two tumors were basal cell carcinoma.

3 | DISCUSSION

Basal cell carcinoma is the most commonly seen human malignancy with estimates of two million cases annually in the US.[9] Alternatively, primary cutaneous small cell carcinoma is an exceedingly rare tumor with as few as two cases ever reported.[1] Given the need to utilize clinicopathological criteria to evaluate, manage, and prognosticate on outcome for solid tumors, oncologists rely on clinical judgment and pathologic review of submitted material to best inform patients. How then can a basal cell carcinoma be mistaken for a small cell carcinoma? Data from epidemiology, pathological review of submitted material, and clinical presentation and response to therapy remains paramount to guide the treating clinician.

This patient was a never smoker. From an epidemiologic perspective, small cell carcinomas of the lung are almost invariably found in smokers, while extrapulmonary small cell carcinomas are not.[10] Although the majority of small cell carcinomas are pulmonary in origin, 20% are found in extrapulmonary sites, and in one series, 9% were described as unknown in initial location.[11]

The 20 gauge core biopsy was chosen in lieu of a gross total resection because the oncologist suspected a metastatic lymph node. The material was routinely processed and, given its hematoxylin and eosin stained morphology, was then immunostained to confirm the diagnosis of a small cell carcinoma. Our institution's practice to confirm the diagnosis with staining for chromogranin and CD56 is supported in the literature.[12] Ultimate comparison of the two specimens, representing a two-year interval, confirmed both to be basal cell carcinoma by hematoxylin and eosin and immunostaining characteristics. The neuroendocrine features of basal cell carcinoma have been historically[6,7] and more recently described.[8]

This patient presented with a subdermal nodule which led the surgical oncologist to suspect a regionally metastatic lymph node in a woman with a recent diagnosis of invasive breast cancer. No superficial lesion, pigmentation, or skin ulceration was noted to cue the clinician to a primary cutaneous malignancy. The staging CT-PET fusion revealed a glucose avid lesion in the neck as well as in the retroperitoneum. This is consistent with an extensive stage small cell carcinoma of unknown primary site. Although not commonly used or studied, there are data suggesting that basal cell carcinoma can show glucose avidity on a PET scan particularly when the lesion is aggressive.[13] Finally, there are data suggesting that aggressive basal cell carcinomas are responsive to platinum-based chemotherapy.[14] The patient's presentation, results of a staging CT-PET study, and normalization of the PET scan postchemotherapy is consistent with a small cell carcinoma or an aggressive basal cell carcinoma.

4 | CONCLUSION

This case presentation describes a patient who presented with a subdermal nodule thought to represent a primary cutaneous small cell carcinoma but was ultimately confirmed to be a recurrent focus of deeply infiltrative basal cell carcinoma. The epidemiology, initial pathological review, clinical presentation of this tumor, and response to therapy supported a diagnosis of cutaneous small cell carcinoma. Missing, however, was the history of a deeply infiltrative cutaneous basal cell carcinoma in the same location. The pathological features of cutaneous small cell carcinoma by core biopsy and basal

cell carcinoma can be similar enough to either require more tissue be removed or further defining staining be performed. Ultimately, a careful history and physical examination with attention to a past surgical history relative to the current site of interest would have resulted in the need to review prior pathology before moving forward.

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTION

SEP: was responsible for study design, patient vignette, reading of the appropriate literature, composition of the manuscript and, answering editorial comments. MY: was responsible for pathology review, reading of the appropriate literature, manuscript composition and, answering editorial comments. RP: was responsible for patient management, reading of the appropriate literature, composition of the manuscript and, answering editorial comments. JP: was responsible for study design, patient vignette, patient management, reading of the literature, composition of the manuscript and, answering editorial comments.

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