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Case presentation

Cutaneous metastasis of Papillary thyroid carcinoma to the neck: a case report and review of the literature

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Abstract

Papillary thyroid carcinoma, the most common subtype of thyroid malignancy, rarely presents with cutaneous metastasis. Despite metastatic cutaneous lesions presenting as slow and indolent growing nodules of the head and neck, such lesions most frequently appear in the setting of diffuse and dramatic metastatic disease and portend a bleak prognosis. Given the rarity of these metastases, the diagnosis may be delayed and often the initial diagnosis is incorrect. Several case reports have been published in the literature noting unusual or interesting presentations of thyroid carcinoma with cutaneous metastasis. Herein we present a patient with a prior diagnosis of thyroid carcinoma presenting with a slowly growing ulcerated nodule on the neck nine years after partial thyroidectomy. Characteristic histopathology was found on microscopic examination. In addition, we review the literature regarding papillary thyroid carcinoma with cutaneous metastasis and the diagnostic challenge these lesions present to practitioners.

Keywords: cutaneous metastasis, papillary thyroid carcinoma, neck metastasis

Introduction

Cutaneous metastases from visceral malignancies are uncommon; even rarer are those that arise from thyroid carcinoma. Thyroid carcinoma with cutaneous metastasis usually occurs in the setting of diffuse disease and typically is associated with a dismal prognosis. Medullary, papillary, follicular, and anaplastic thyroid carcinomas with skin metastasis have been infrequently reported in the literature and remain a diagnostic challenge for practitioners. We report a patient with papillary thyroid carcinoma who developed cutaneous metastasis on the neck nine years after initial malignancy diagnosis. We summarize the features of patients with cutaneous metastasis from thyroid carcinoma and discuss the obstacles practitioners face in the identification of uncommon neoplasms.

Case synopsis

A 95 year old man with a past medical history of prostate and thyroid cancer presented with a 3 year history of an enlarging bleeding cutaneous ulcer on the right neck. Nine years earlier, the patient had been diagnosed with thyroid cancer (unknown type), which was treated by partial thyroidectomy. The patient had recurrence of his cancer five years later, but owing to multiple comorbidities repeat surgery was deferred. After one year of regular follow-up visits with a primary care physician for cancer surveillance, the patient was lost to follow-up.

The patient then presented to us with an enlarging neck mass, occasional dysphagia with solids and no respiratory symptoms. Cutaneous exam disclosed a 1.3 cm x 0.9 cm erythematous pearly nodule on the right anterior neck with a small area of ulceration. A firm fixed subcutaneous nodule was discovered on the right lateral neck, approximately 10 centimeters posterior to the erythematous nodule, likely representing lymphadenopathy.

Biopsy of the nodule was performed and sent for staining with Hematoxylin & Eosin (H&E) (Figure 1). It showed cuboidal cells in a complex and branching papillary pattern with fibrovascular cores and rare psammoma bodies. The nuclei of the cells showed the characteristic chromatin clearing seen in papillary thyroid carcinoma. There were no intranuclear inclusions. Immunohistochemical (IHC) stains revealed a strong nuclear staining with thyroid transcription factor-1 (TTF-1) and Cytokeratin 7 (CK7) (Figure 2a and b). Given the patient's positive past medical history of prostate cancer, IHC staining of prostate specific antigen (PSA) was performed and was negative in the specimen (Figure 2c). Correlation of the clinical presentation and the pathology findings was diagnostic for cutaneous metastasis of papillary thyroid carcinoma.

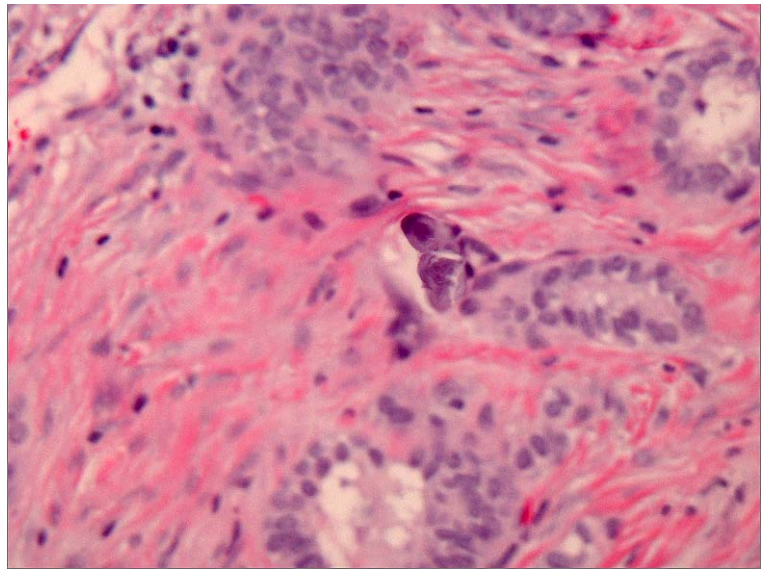
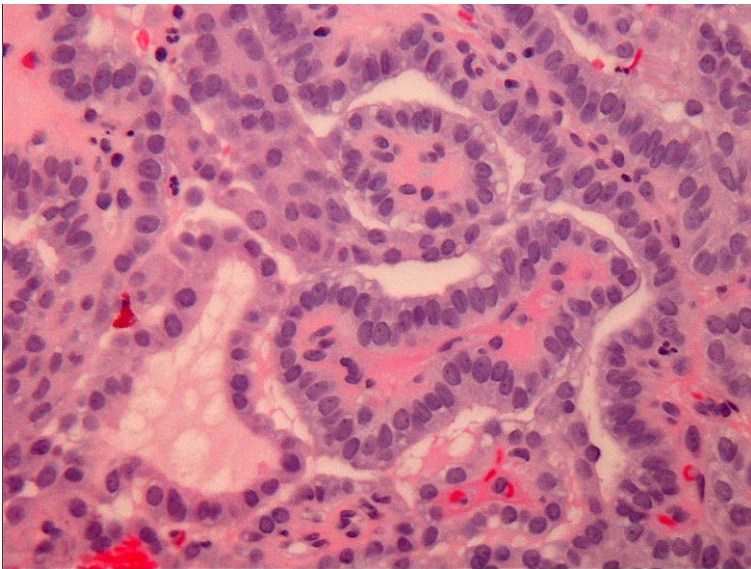
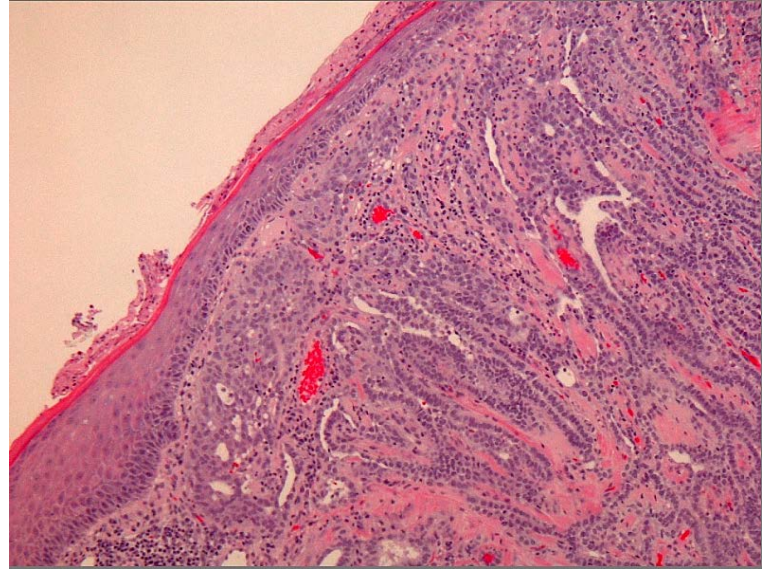
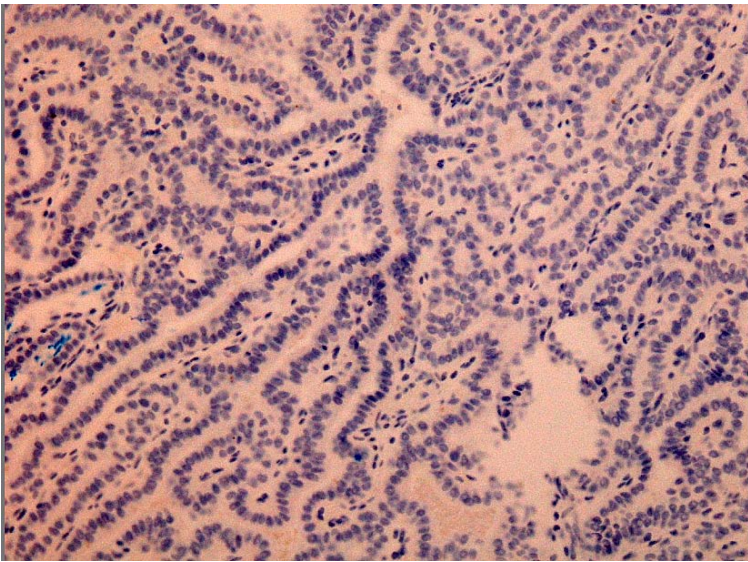
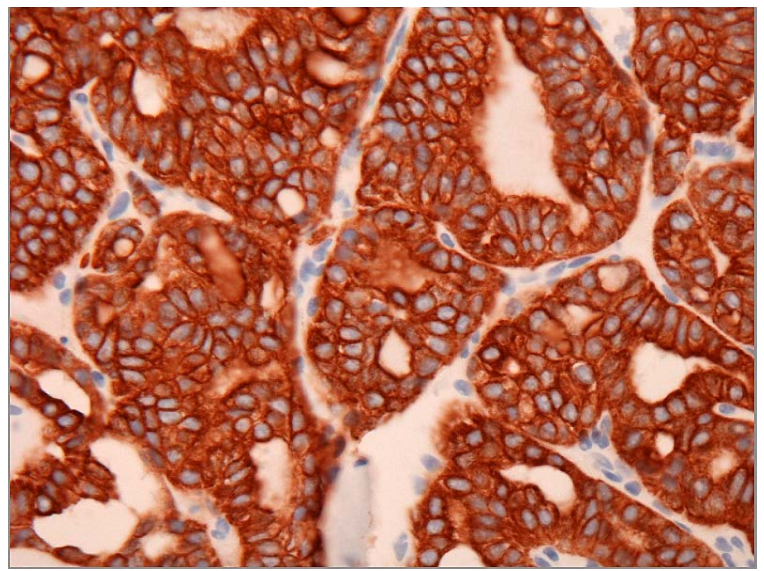
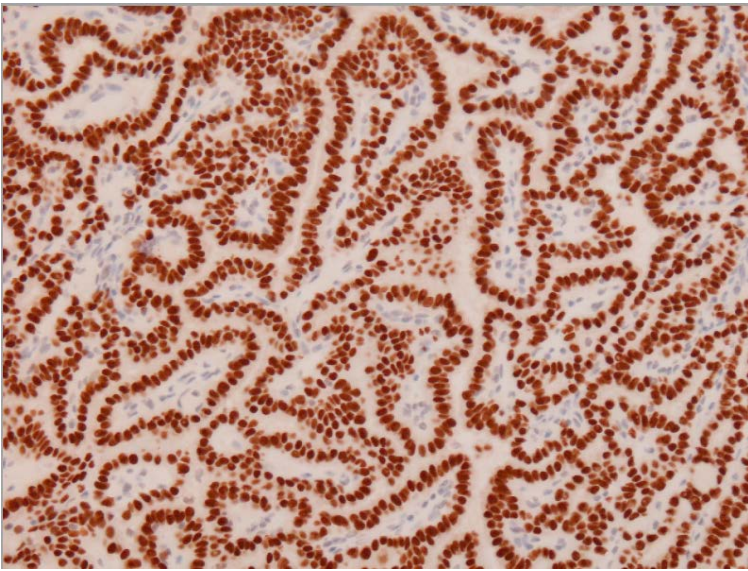


Figure 1 (a, b, and c). Low (a) and high (b and c) magnification views of metastatic papillary thyroid carcinoma: Low magnification (a) shows tumoral involvement of the dermis composed of numerous follicles lined by cuboidal epithelial cells in a papillary pattern. High magnification (b) shows the tumor cells in the dermis with papillary architecture. The cuboidal cells with round nuclei show chromatin clearing, scant granular cytoplasm and eosinophilic colloid material within some follicles. High magnification (c) shows psammoma bodies, (round collections of calcium), in the center of the field, typically also seen in papillary thyroid carcinoma.

Figure 2 (a, b, and c). Medium (a and c) and high (b) magnification views of metastatic papillary thyroid carcinoma after immunohistochemical (IHC) staining. Medium magnification (a) depicts strong nuclear positivity of the tumor cells with thyroid transcription factor-1 (TTF-1) indicative of thyroid or pulmonary neoplastic origin. Higher magnification (b) depicts strong positive staining with cytokeratin 7 (CK7), in the cytoplasm. Medium magnification (c) depicts negative staining with prostate specific antigen (PSA) indicating the tumor is not of prostatic origin.



Discussion

Cutaneous metastases are uncommon, with an overall total incidence of 5.3% for all visceral malignancies [1]. These lesions are usually not morphologically distinctive and may mimic many common dermatologic disorders. The most common primary tumor is breast adenocarcinoma and the most common site of cutaneous involvement is the chest [1]. Skin metastases are a rare phenomenon of thyroid carcinoma; several studies examined large groups of patients with papillary thyroid carcinoma (PTC) and the reported prevalence of cutaneous metastases were 0.06-0.82% [2, 3]. Other studies have looked at the different subtypes of thyroid carcinoma with skin metastasis and reported contradicting trends. One study of 50 patients reported follicular thyroid carcinoma as the most prevalent subtype with cutaneous metastasis. Another study of 43 patients described PTC as the most common subtype with cutaneous metastasis [5]. Of the cases reported in the latter study, 41% had PTC, 28% had follicular thyroid carcinoma, 15% had anaplastic thyroid carcinoma, and 15% had medullary thyroid carcinoma [5].

Several mechanisms for the occurrence of cutaneous metastasis from internal malignancies have been proposed, including direct extension, hematogenous spread, lymphatic spread, and the implantation of exfoliated tumor cells during biopsy or surgery [6]. PTC with cutaneous metastasis has been reported involving the thyroidectomy scar [7], as well as fine needle aspiration tract of previous thyroid nodule biopsy [8]. The majority of metastatic skin lesions from PTC involve the scalp (approximately 2/3 of cases) and the remainder generally involve the head and neck regions [5]. It has been suggested that the scalp may be the most common site for cutaneous metastasis owing to local vascular factors essential for the highly complex nature of tumor formation. The scalp, along with the face and chest, has a rich dermal capillary network that may initially trap tumor cell emboli from the systemic circulation; this prolific vascular network can also provide the appropriate environment for successful formation of metastatic foci [9].

PTC comprises 50-89% of all thyroid cancers, and - when metastatic - involves the regional cervical lymph nodes in 40% of all cases, but only rarely involves distant sites (10% of all metastases). Distant sites of metastasis include the lung (49% of distant metastases) and bone (25% of distant metastases). Unusual sites of distant spread include the liver, kidneys, adrenal glands, ovaries and skull [10]. Cutaneous metastasis of thyroid carcinoma usually present as slow growing erythematous or violaceous dermal nodules or plaques on the scalp, face or neck that may be tender or pruritic, and can ulcerate [11]. These lesions can easily be mistaken for a primary adnexal skin tumor, which has a nonspecific clinical presentation and similar histopathology on biopsy [12]. In fact, several of the case reports of thyroid carcinoma with cutaneous metastasis had initial diagnoses of primary adnexal tumor [10, 13, and 14].

Immunohistochemical (IHC) stains can be used to help differentiate between primary adnexal skin tumors and cutaneous metastasis from an internal malignancy. For thyroid carcinoma in particular, thyroid transcription factor-1 (TTF-1), thyroglobulin, and cytokeratin 7 (CK7) have all been used. Thyroid transcription factor-1 is a nuclear protein expressed predominantly in

thyroidal follicular cells (as well as thyroidal C cells, lung cells, and brain cells), and is used as a marker of thyroid differentiation. The use of this molecular marker detects thyroid metastases with a sensitivity of 92.9% when used alone [13]. Additionally the IHC marker for TTF-1 has provided a useful screening tool, to distinguish pulmonary and thyroid carcinomas from other primary carcinomas or mesothelioma [15-17]. Cytokeratin 7 is a type II keratin of simple non-keratinizing epithelia found in follicular cells of the thyroid gland, and can also be found in breast, lung, and ovarian and urothelial tissue [18].

Dermoscopy is used by some practitioners to allow better visualization of cutaneous lesions via magnification and/or a non-polarized light source. A study of dermoscopy in 20 patients with cutaneous metastatic lesions (including 2 thyroid cases) reported the most common finding under dermoscopy to be a vascular pattern. The most frequent subtype of vascular pattern noted was serpentine (or linear irregular vessels) in 77% of non-pigmented lesions [19]. This finding for cutaneous metastases from thyroid carcinoma has been supported by a case report of poorly differentiated thyroid carcinoma. Examiners described the lesion under dermoscopy as the presence of an “atypical” polymorphous vascular pattern consisting of linear irregular and dotted vessels [20]. Although this particular observation is not specific to thyroid carcinoma, it may serve as a possible general indicator for cutaneous metastasis.

Unusual variants of thyroid carcinoma with cutaneous metastases have been reported, including a patient with poorly differentiated thyroid carcinoma [13], a patient with a skin lesion as the initial presenting symptom without any extensive metastatic disease [21], a patient with skin lesions lacking the classic cytological and architectural features of follicular variant PTC [10], and a patient with a novel chromosomal translocation t(3;5)(q12;p15.3) as compared to the classic genetic rearrangements involving RET- or TRK proto-oncogenes seen in PTC [22]. One study probing into the genetics of PTC with cutaneous metastasis reported a mutation in BRAF^{V600E} in 5 out of 11 lesional biopsies. This mutation, while previously reported as the most common genetic abnormality in PTC, had not been observed in the cutaneous metastatic lesions. Although this study included a relatively small subset of patients, the BRAF^{V600E} mutation did not appear to have a strong association with a poor prognosis [23].

Conclusion

Cutaneous metastases pose a diagnostic challenge to practitioners through nonspecific clinical presentations and the requirement of special histopathological or immunohistochemical characteristics for proper identification. In consideration of papillary thyroid carcinoma with metastasis to the skin, lesional biopsy and immunohistochemical staining with thyroid transcription factor-1 and cytokeratin 7 are useful for a timely diagnosis. Although several unusual manifestations of this rare entity have been reported, classically these lesions present as slowly growing erythematous nodules in the setting of diffuse metastatic disease. We describe the common presentation of cutaneous metastasis of papillary thyroid carcinoma with distinguishing microscopic images, and provide a literature review to aid the clinical practitioner in the appropriate diagnosis of this unusual cutaneous manifestation.

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