Papillary Thyroid Cancer Cutaneous Metastasis: A Case Report and Literature Review

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Abstract

Background: It is known that neoplastic cutaneous metastasis is a rare occurrence, especially in setting of thyroid cancer. Multiple literature searches have been performed, namely those done by Dahl, et al. and Koller, et al., which documented very limited number of cases. We present a report of an 85-year old man with a history of papillary thyroid carcinoma (PTC) who was treated by total thyroidectomy and post-operative radioactive iodine (I-131) ablation seven years prior who presented with concerning anterior neck skin lesions.

Summary: Excisional biopsy results were consistent with PTC metastatic lesions. Further imaging revealed additional superficial subcutaneous nodules as well as cervical and mediastinal hypermetabolic lymph nodes. Pathology results after initial excisional biopsy reveal strong positive reactivity to TTF-1 and thyroglobulin along with architecture consistent with malignant cells of thyroid papillary carcinoma, similar to his primary treatment seven years ago. Additional anterior neck nodules were debulked, though he was left with focally positive margins secondary to tracheal adhesions. A decision to abstain from surgical intervention for the concomitant mediastinal lymphadenopathy was made due to the highly associated morbidity with minimal overall benefit. A literature search was performed using pertinent and significant terms regarding thyroid and skin neoplasms.

Conclusions: Cutaneous lesions as metastatic disease processes should be considered in the differential diagnosis as they may mimic a myriad of diagnoses, prompting appropriate additional workup including patients with a history of thyroid carcinoma.

Keywords: Thyroid carcinoma, Papillary thyroid carcinoma, Cutaneous metastasis

Abbreviations: PTC: Papillary Thyroid Carcinoma; TTF-1: Thyroid Transcription Factor 1; H&E: Hematoxylin and Eosin; EBRT: External Beam Radiation Therapy.

Introduction

Thyroid cancer represents 3.4% of all cancers diagnosed per year [1]. It exists in multiple forms with differentiated thyroid carcinomas (papillary and follicular variants), medullary, and anaplastic variants. PTC is the most common type, encompassing 80% of all cases [2]. Papillary and follicular variants arise from thyroid follicular cells, in contrast to medullary thyroid cancer which arises from parafollicular C cells.

The spread of medullary and papillary disease is usually via the lymphatic system while follicular carcinoma commonly spreads hematologically. Though the incidence of malignant cutaneous metastasis is known, it is a rarely reported entity with an overall poor prognosis [3]. In addition, these metastatic foci may be difficult to distinguish from more commonly encountered cutaneous lesions [4]. It is imperative, therefore, that clinicians maintain a heightened awareness of such, especially in a patient with a history of thyroid malignancy.

Methods

A comprehensive literature search was performed using the terms ‘thyroid neoplasms’ and ‘skin neoplasms’ as a secondary search term in Medline as well as using the both keywords on PubMed.

Case Description

An 85-year-old male presented with a chief concern of two skin lesions on his anterior neck that have been present for two years. The lesions had been growing in size over this period and as he reported, had begun to bleed with shaving. He had a similar lesion removed from his arm previously, but the patient was not aware of the diagnosis of that lesion. His past medical history was significant for dementia and papillary thyroid carcinoma (PTC) that was diagnosed and treated by two successive hemi-thyroidectomies with reoperative radioactive iodine ablation seven years prior, although an official record of the radioactive therapy was unable to be confirmed. He also had a history of excision of a squamous cell carcinoma along the skin of the mandible. Family history was significant for a father who passed away from prostate carcinoma and a brother who died of lung carcinoma. The patient was a previous smoker with a 30-pack year history but had been abstinent for 40 years.

Physical exam revealed two pink/red cutaneous lesions 0.5 cm and 1 cm in diameter on the anterior neck beneath his left mandible without surrounding erythema, ulceration or drainage. At the time of evaluation the lesions were concerning for basal cell carcinoma. Of note, these lesions were located well cephalad to his previous thyroidectomy scar.

Given the evolving nature of the lesions, the decision to perform an excisional biopsy was made. At the time of excisional biopsy no concerning features or invasion of the subcutaneous tissue or muscle were noted. Histologic evaluation with thyroid transcription factor 1 (TTF-1) showed strong positive reactivity (Figure 1A–C). A combined TTF-1 and thyroglobulin stain performed at an outside institution was also positive. Hematoxylin and Eosin (H&E) staining revealed architecture consistent with malignant cells of thyroid carcinoma.
follicular cell origin (Figure 1D). A subsequent I-131 uptake scan showed no functional thyroid tissue elsewhere. Further workup included a neck ultrasound that revealed no residual thyroid tissue in the left and right thyroid beds but was significant for four enlarging lesions in the inferior neck just left of midline, the largest of which measuring 1.7 cm. Additionally, hypoechoic subcutaneous nodules measuring 0.8 cm and 0.5 cm were noted, suspicious for recurrent disease. PET scan revealed three hypermetabolic nodules in the subdermal adipose tissue anterior to the left thyroidectomy bed with a combined area measuring 3.6 x 2.1 x 1.8 cm, as well as low grade activity in the right level 5 cervical lymph nodes and stations 5 and 7 mediastinal lymph nodes. At the time of the diagnosis of the cutaneous thyroid metastatic deposits, the thyroglobulin level was 0.4 ng/mL and TSH 2.11.

Post-operatively, he was evaluated by radiation oncology. Although radiotherapy has been used for the treatment of metastatic thyroid cancer, it is infrequently used for gross disease. Therefore, a discussion was held between the patient, family and multidisciplinary teams and a decision was made to excise the anterior neck lesions given their superficial nature. Surgical treatment was deferred for the mediastinal lymphadenopathy due to the higher associated morbidity with minimal overall benefit. Histologic evaluation of the excisional biopsy of these lesions with H&E revealed papillary architecture with orphan annie nuclei and nuclear envelope grooves (Figures 2A-B). The lesions again stained positively for TTF-1 (Figure 2C) confirming our presumption of metastatic disease. An R1 resection was achieved for the cervical neck masses due to significant adherence to the anterior trachea. An R0 resection was not pursued as the operating surgeon felt the risks of tracheal injury outweighed the benefit given the patient’s overall clinical presentation. He was therefore followed up in clinic for wound checks and recovered well.
with a more limited number of reports of cutaneous metastasis we encountered a greater number of reports of scalp metastasis along the head and neck regions [8]. During our literature review, follicular carcinoma compared to papillary carcinoma manifesting Dhal, et al. [7]. Whereas in the literature review by Koller, et al they anaplastic (15%), and medullary carcinomas (15%) as reported by carcinoma was the most common (41%), followed by follicular (28%), the highest propensity to metastasize to the skin [6]. Papillary carcinoma (H&E, 100X).

Discussion

It is documented that skin lesions from metastatic thyroid cancer may appear as solitary or multiple, asymptomatic plaques or nodules, of different color variations, similar to either benign or malignant dermal lesions. As Alwaheeb, et al notes, while the scalp represents the most common site of thyroid carcinoma skin metastasis, there is no consensus on which thyroid carcinoma variant has the highest propensity to metastasize to the skin [6]. Papillary carcinoma was the most common (41%), followed by follicular (28%), anaplastic (15%), and medullary carcinomas (15%) as reported by Dahl, et al. [7]. Whereas in the literature review by Koller, et al. they concluded that the greater propensity for cutaneous metastasis was follicular carcinoma compared to papillary carcinoma manifesting along the head and neck regions [8]. During our literature review, we encountered a greater number of reports of scalp metastasis with a more limited number of reports of cutaneous metastasis specifically to the neck (approximately 16 reported patients in literature) [3–10]. Of note, the recurrence of cancer at the thyroidec- tomy scar is reportedly rare [12].

Additionally, cutaneous metastases may mimic the appearance of more commonly encountered cutaneous lesions, as in the patient we present in this report. Cutaneous metastasis, albeit rare, is a known manifestation of thyroid carcinoma and is associated with advanced disease and a poor prognosis. It is inferred that biopsy proven cutaneous manifestations may be correlated with associat- ed visceral metastasis as well. The skin lesions can manifest as a multitude of appearances with a broad differential making initial diagnosis difficult. In our patient, the diagnosis was not suspected clinically upon initial presentation and appeared similar to basal cell carcinoma on physical exam.

Mortality associated with initial diagnosis of PTC over 5 and 10 years is quite low at 1.9% and 3%, respectively [13]. The high sur- vivability leads to a large population of patients requiring monitor- ing for recurrence, which carries a poor prognosis. Risk factors for recurrence include male sex, such as in our patient, advanced initial stage at diagnosis, and evidence of extrathyroidal spread within the primary tumor [14].

A majority of follicular and papillary carcinomas stain positive for thyroglobulin [7]. A distinguishing histological factor for PTC is its characteristic orphan annie nuclear inclusion morphology as well as nuclear envelope groove formation, also present within its cutaneous manifestations. Moreover, staining with TTF-1 is another adjunct marker to confirm PTC, signifying thyroid differentiation [15], as was apparent in our patient.

The mainstay of management of primary diagnosed PTC is total thyroidectomy with adjuvant radioactive iodine therapy. Most re- currences are reported within the first 10 to as many as 20 years post-operatively [16]. Our patient presented with recurrence seven years after initial diagnosis and treatment. In local disease recur- rence, surgery remains the therapy of choice [17], in conjunction with radioactive iodine, radiofrequency ablation, or observation in the appropriate populations [18]. While there is no consensus on external beam radiation therapy (EBRT), there has been some data suggesting benefit in those with residual disease and prominent lymphadenopathy > 2 cm [5]. However, given our patients overall clinical presentation, the decision to defer radiotherapy was made.

As the incidence of thyroid cancer increases [19,20] providers must remain vigilant in the detection of associated manifestations of widespread disease or recurrence. Initial diagnosis is typically made with excisional biopsy and subsequent immunohistochemistry staining. Subsequent follow up studies include thyroid function tests and imaging studies using ultrasound, I-131 uptake and/or PET scans. Due to its deceiving appearance, cutaneous metastasis of PTC can easily be overlooked. A thorough history and physical exam, including an extensive skin evaluation is prudent in patients with a history of thyroid cancer and reported new skin growths.

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