Case Report

Thinking outside the box: An unusual presentation of papillary thyroid carcinoma

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ABSTRACT

Thyroid malignancies are the most commonly encountered endocrine tumours, for which there is a wide spectrum of disease with varying potential for aggressiveness. Papillary thyroid cancer is the most common occurrence of this malignancy and is typically indolent in nature, rarely progressing to metastatic disease. Our case represents an atypical presentation of metastatic papillary thyroid cancer that was initially believed to be an aggressive digital papillary adenocarcinoma and provides interesting consideration when composing differential diagnoses.

INTRODUCTION

Thyroid cancer represents the most common endocrine malignancy and is often subdivided into differentiated or medullary thyroid cancer, with the former accounting for greater than 80% of these occurrences.[1] Clinical behavior is highly variable as tumours may be indolent, slowly progressing neoplasms or rather aggressive malignancies with significant patient mortality.[2,3] Thyroid carcinomas typically present with an asymptomatic mass or swelling of the neck; however, instances of incidental discovery have been reported.[3] Here we describe an unusual presentation of metastatic thyroid carcinoma initially believed to be an aggressive digital papillary adenocarcinoma (ADPA).

CASE REPORT

An 85-year-old man sought medical attention because of a non-healing finger lesion. Approximately one year earlier a metal sliver slipped under the nail bed of his left fourth digit while moving an old bed. Initially, he unsuccessfully attempted to remove the sliver using a needle. Curiously, the lesion increased in size over the following year, becoming painful and prone to bleeding. After presenting to his family physician, he was referred for surgical excision. A partial transverse excision of the nail was performed in order to facilitate removal of the granulating lesion and the tissue was sent for routine histopathological examination. There, microscopic investigation of the excised tissue (Figure 1A-B) revealed a papillary glandular lesion composed of cells with mild to moderate nuclear pleomorphism and relatively easily found mitoses. Glands and papillary structures lined by one or occasionally two layers of epithelial cells were seen. Collectively, these features are consistent with aggressive tumors with a high propensity for local recurrence designated as ADPA, which possess a range of documented morphologies. Histopathological assessment of the excised tissue showed involvement of the painted margin (Figure 1C). An amputation was recommended given the high rate of recurrence and metastases seen with ADPA's, however, the patient refused digital amputation and was referred to Radiation Oncology for consideration of post-operative radiation instead.

When initially seen by Radiation Oncology the patient was clinically well and had no other associated lesions or additional symptoms. Past medical history was significant for a remote left-sided renal cell carcinoma treated with radical nephrectomy 25 years earlier. He was also followed for goiter and treated for hypothyroidism. His medications included Eltroxin, Metformin, Aspirin and Crestor. Family history was non-contributory. The patient had no allergies and did not smoke or consume alcohol. Review of systems was unremarkable, and he denied the presence of any constitutional symptoms. On physical examination, the patient appeared to be in good general condition without evident lymphadenopathy and an unremarkable abdominal exam. Clinical examination of the left fourth digit showed a well-healed surgical scar with no evidence of macroscopic disease.

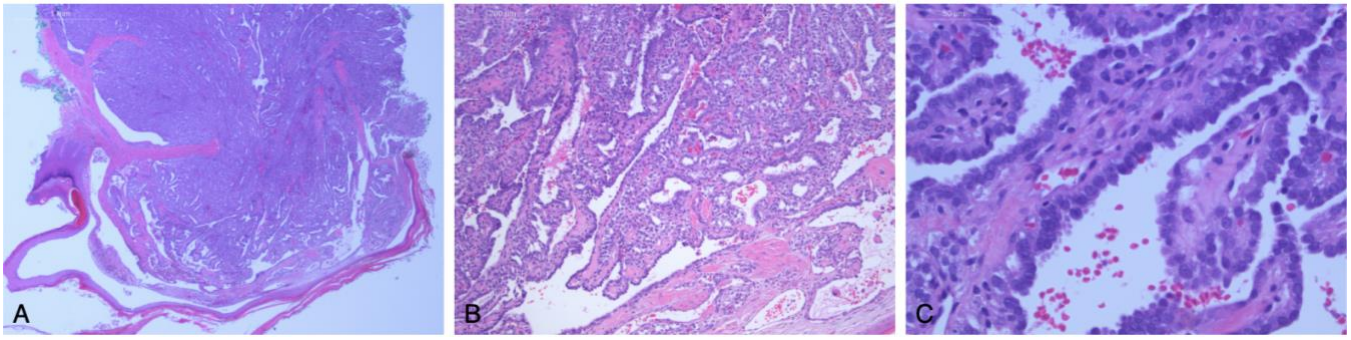

Figure 1. Histopathologic examination of excised tissue at increasing magnification demonstrating a papillary glandular lesion with mild to moderate nuclear pleomorphism and involvement of the excision margin.

Given the clinical presentation, the surgeon felt that soft tissue sarcoma was the most likely diagnosis, however, the patient's history of goiter paired with the papillary histologic appearance on biopsy lead to consideration of metastatic papillary thyroid carcinoma (PTC) as a possible alternative. Whatever the diagnosis, the best initial management to guide treatment and prognosis is to determine the stage of the disease. Moreover, the possibility that this represented a metastatic lesion from another primary site existed and warranted further investigations. Therefore, thyroglobulin levels were measured and found to be elevated at 8200 µg/L, with a TSH of 0.10 mU/L and Free T4 of 15 pmol/L. Ultrasound imaging of the thyroid demonstrated an enlarged right lobe with two solid nodules - the largest measuring 82x64x94mm with a partially necrotic center - and an associated enlarged right cervical lymph node.

A computed tomography (CT) scan showed a large thyroid mass measuring 8.1 cm in its largest diameter along with pre-tracheal, anterior mediastinal and subcarinal lymphadenopathy. There were innumerable pulmonary lesions and a lobulated paraspinal mass in the lower right thorax. Subsequent whole-body bone scan with technetium labeled methylene diphosphonate (MDP) was negative for active metastatic disease. These laboratory and radiologic findings were strongly suggestive of metastatic Differentiated Thyroid Cancer (papillary type).

The patient underwent a total thyroidectomy with a level VI neck dissection in accordance with the revised American Thyroid Association guidelines for large (>4cm) papillary tumors.[4] Immunohistochemical staining of the sample was positive for thyroglobulin (Figure 2A) and thyroid transcription factor 1 (TTF1) (Figure 2B). Examination of the biopsy sample under high power field (Figure 2C) showed characteristic intranuclear inclusions as well as some empty appearing nuclei; eponymously called "Orphan Annie eyes." These findings confirmed the diagnosis of PTC with metastatic thyroid carcinoma also present in resected level VI lymph nodes. Such findings are representative of T3, N1B, M1 (stage 4C) disease. Therefore, 5250 MBq of intravenous iodine-131 was administered in an effort to reduce tumor burden and ablate thyroid tissue. Seven days after ablative therapy, an iodine-131 scan showed extensive metastatic disease involving lymph nodes, bones, lungs, and skull. The scan was repeated six months later (Figure 3) and showed persistent metastatic disease in all sites. Whole body iodine-131 planar images (Figure 3A) and SPECT-CT imaging (Figure 3B) demonstrated multiple foci of increased uptake in the neck, lungs, mediastinum, pelvis and right femur.

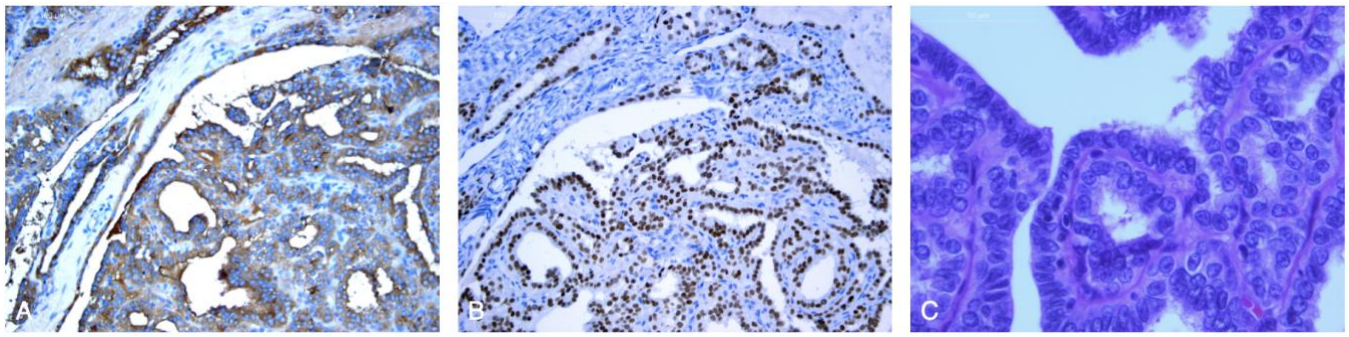

Figure 2. Immunohistochemical staining displaying: A) Positivity for thyroglobulin. B) Positivity for TTF1. C) Intranuclear inclusions as well as some empty appearing nuclei ("Orphan Annie eyes").

In further effort to suppress the excretion of TSH and inhibit tumor growth, this gentleman was prescribed a regular dose of Synthroid at 125 ug/day. He was scheduled to have regular follow-ups at three-month intervals with repeat blood work and magnetic resonance imaging (MRI) of the axial skeleton. Despite this management, this gentleman's disease continued to progress, and he died four years after initial presentation. During this time, he was also treated with whole brain and mediastinal irradiation for brain metastases and for palliative treatment of dysphagia, respectively. The patient was planned for a second course of iodine ablation but did not receive the treatment.

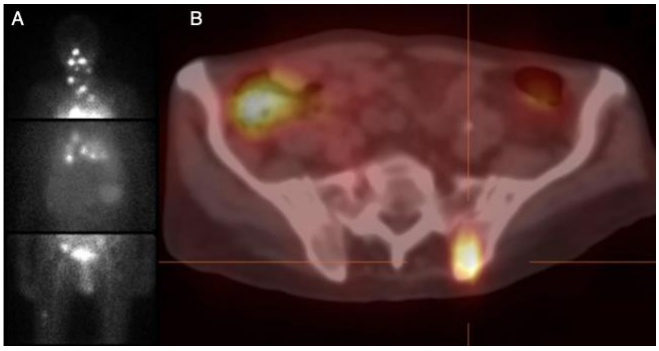

Figure 3. A) Whole body iodine 131-planar image displaying multiple foci of increased uptake in the neck, lungs, mediastinum, pelvis, and right femur. B) Whole Body iodine-131 SPECT-CT reconstructed images demonstrating increased uptake within the left iliac crest.

DISCUSSION

ADPA's are rare eccrine sweat gland neoplasms originally described in 1979 with further characterization of these neoplasm as aggressive digital papillary adenoma (ADPA) and aggressive digital papillary adenocarcinoma (ADPAca) in 1984.[5,6] Since the original description, relatively few instances have been reported in a series of three retrospective studies and case reports.[2,7-11] The most common tumour sites are the volar surfaces of the hands and feet. The rate of local recurrence is 5% and the rate of metastasis is 12 to 14%.[8,9]

Conversely, thyroid carcinoma is the most common endocrine malignancy with approximately 25,000 new cases diagnosed annually in North America. The most common class includes differentiated thyroid cancers, arising from the follicular epithelium and further classified into the two sub-types of papillary thyroid carcinoma (PTC) and follicular thyroid carcinomas. PTC is the most common histological subtype of thyroid carcinoma, comprising about 80% to 85% of all thyroid malignancies in developed countries.[1] They exhibit a relatively indolent course and have the most favourable prognosis of all thyroid malignancies with long-term disease-free survival of approximately 90-95%. Most cases are sporadic in nature, although prior exposure to radiation therapy (RT) is a well-established risk factor.[12]

Unlike follicular carcinomas, loco-regional lymph node involvement is common at presentation of PTCs and may be observed in approximately 33% to 61% of cases.[2] In contrast, distant metastases are far less prevalent, occurring in only 4-15% of cases. The lung is the most frequent site of spread, followed by bone and brain.[3] Soft tissue metastases are very rare and typically occur on the scalp face or neck.[4,13] In PTC, the presence of distant metastases is the most significant poor prognostic factor, however 10-year survival is still around 50%.[12,14] The worst prognosis, a 5-year survival as low as 8%, has been observed in patients with distant metastases in more than one organ.[15] Radioactive ablation is recommended in all patients with PTC and known distant metastases as such treatments are shown to improve overall survival in these patients.[4,14]

The present case depicts a very unusual presentation of a typically indolent and highly treatable disease. Unusual metastatic presentations and patterns of PTC generally herald a much worse prognosis as was seen in the present case. The BRAF(V600E) gene mutation is a common genetic anomaly in PTC that has been shown to be an independent predictor of aggressive disease.[16,17] Vemurafenib is a BRAF kinase inhibitor that is currently FDA approved for the treatment of BRAF(V600E) positive melanoma. In one non-randomized open label phase II trial, Vemurafenib showed anti-tumor activity in patients with progressive BRAF(V600E) papillary thyroid carcinoma refractory to radioactive iodine.[18] It is unknown whether Vemurafenib would have been beneficial in this patient as the testing was not available, however, it is possible there may have been some impact on longevity.

CONCLUSION

PTC is the most common histological subtype of thyroid carcinoma and generally carries an indolent course with infrequent reports of distant metastatic spread. We have reported a case of a metastatic PTC initially mistaken for an ADPA, further denoting the importance of thorough clinical work-up.

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