De-differentiation of Conventional Papillary Thyroid Carcinoma into Squamous Cell Carcinoma

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Introduction

Primary squamous cell carcinoma (SCC) of the thyroid is an extremely rare entity comprising less than 1% of thyroid malignancies [1]. It has been associated with the tall-cell variant of papillary thyroid carcinoma (PTC) [2-5]. It is theorized that SCC of the thyroid may arise from de-differentiation of more common thyroid carcinomas. Here, we present a unique case of SCC of the thyroid gland arising in the background of classic PTC with primary site and regional nodal disease demonstrating both histologies. Similar transformations involving the tall cell variant of PTC and spindle cell carcinoma were noted to be particularly aggressive [2-4]. However, little is known about its pathogenesis and disease prognosis. This study was exempt by the University of Wisconsin, Madison Institutional Review Board.

Case Report

An 81-year-old man with a 15 pack-year smoking history was referred to the otolaryngology clinic with suspicion of locoregionally advanced anaplastic thyroid carcinoma. He presented with hoarseness and globus sensation of two months duration along with mild fatigue, decreased appetite, central neck fullness and mild left-sided otalgia. On exam, he had an immobile 5 cm mass in his left central neck and palpable lymphadenopathy in level III. Flexible fiber-optic examination of the larynx demonstrated immobility of the left true vocal cord. Further work-up by ultrasound demonstrated small nodular disease within the right thyroid lobe and a large heterogeneous mass with significant calcification in the left lobe. Fine-needle aspiration of the left level III lymph node was consistent with PTC. Computed tomography demonstrated invasion of the left cricoid cartilage, and a positron emission tomography scan showed a hypermetabolic thyroid mass that extended into the larynx and a hypermetabolic left level III lymph node (Figure 1). There was no evidence of distant metastases and there were no other obvious lymph node metastases in the neck.

The patient underwent a direct laryngoscopy, total laryngectomy, total thyroidectomy and a left selective neck dissection (Levels II through VI). Intraoperative frozen section analysis of the thyroid mass revealed SCC and the level III lymph node revealed both SCC and PTC.

Histopathology identified a moderately to poorly differentiated SCC of both thyroid lobes, the thyroid cartilage, and the laryngeal soft tissues, but there was no mucosal abnormality. The right lobe also demonstrated both conventional and follicular variant PTC. Seven out of 33 lymph nodes were positive for carcinoma (5 nodes positive for PTC and 2 nodes positive for both PTC and SCC). There was no extranodal extension. Immunohistochemical staining for p63 and thyroglobulin highlighted different populations with thyroid follicular and squamous differentiation within the same tumor (Figure 2).

The patient's post-operative course was unremarkable and he was treated with a course of external beam radiation (60 Gy in 2 Gy fractions) and radioactive iodine (157 mCi of I-131). Surveillance imaging done at 6 months revealed no evidence of disease in the neck, but numerous pulmonary nodules were apparent. A radioactive iodine scan revealed no uptake in the pulmonary nodules. The patient ultimately died of metastatic disease 3 months later.

Discussion

This unique case demonstrates an aggressive SCC of the thyroid gland in the background of PTC. Given the clinical presentation, the differential for this lesion included anaplastic thyroid carcinoma versus poorly differentiated variants of more common thyroid carcinomas.
such papillary carcinoma. The pathologic finding of SCC and PTC suggested the possible presence of a secondary malignancy such as laryngeal or hypopharyngeal carcinoma co-occurring as a collision tumor. However, the absence of a primary upper aerodigestive tract SCC, the pattern of spread, and the close histological association between the two cell types leads us to believe that the SCC de-differentiated from a conventional papillary carcinoma. This rare occurrence has only been documented often in association with the tall cell variant of PTC [2-5]. These prior studies reported a close histological association between papillary and squamous cells where islands of SCC were observed to merge with tall cell variant cells. There are several theories to account for the etiology of primary SCC of the thyroid. The embryonic nest theory suggests that squamous cells are derived from embryonic remnants such as the thyroglossal duct and the metaplasia theory posits that environmental stimuli such as inflammation (Hashimoto’s thyroiditis) can lead to squamous metaplasia [1]. In our patient, however, there were no histologic findings suggestive of an embryonic remnant or squamous metaplasia. There was a clear transition between the PTC and the SCC which may be consistent with de-differentiation. The transformation of PTC (typically tall-cell) to SCC represents a rare and aggressive tumor with a clinical presentation similar to anaplastic thyroid cancer. Further work is needed to understand the mechanism of transformation in this unique presentation.

Figure 2: (A) Lymph node metastasis revealing two different histological patterns, 20X; (B) A high-power view of the contrasting tumor morphologies with cells towards the top exhibiting classic nuclear features and architectural characteristics of PTC and cells in the bottom view revealing infiltrative groups with keratin, 400X; (C) Immunohistochemical staining for p63 is diffusely positive in the tumor cells with squamous carcinoma morphology, 400X; (D) Immunohistochemical staining for thyroglobulin has patchy positivity in the tumor cells with papillary carcinoma morphology, 400X.

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