Papillary Thyroid Carcinoma Recurring as Squamous Cell Carcinoma 10 years after Total Thyroidectomy: Lessons from Rapidly Progressive Papillary Thyroid Carcinoma

Ji In Lee¹, Yun Jae Chung¹ and Sei Young Lee²

Abstract

Primary squamous cell carcinoma (SCC) of the thyroid is very rare. There are no reports of metastatic papillary thyroid carcinoma (PTC) converting to SCC in cervical lymph nodes following total thyroidectomy due to conventional PTC. An 86-year-old woman with a remote history of total thyroidectomy due to PTC underwent palliative neck surgery to treat recurrent bleeding originating from a metastatic tumor of the cervical lymph nodes. The resected mass was composed of mixed SCC and PTC. Although primary SCC rarely occurs in the thyroid, conversion of PTC to SCC should be suspected if preexisting PTC exhibits highly aggressive behavior.

Key words: papillary thyroid carcinoma, squamous cell carcinoma, lymph node, metastasis, recurrence


Introduction

Primary squamous cell carcinoma (SCC) of the thyroid is very rare, accounting for less than 1% of all primary thyroid carcinomas (1). Since it was first described by von Karst, approximately 150 cases have been reported in the literature (1-5). However, a review of the relevant literature revealed that there have been no reports of metastatic papillary thyroid carcinoma (PTC) converting to SCC in cervical lymph nodes following total thyroidectomy due to conventional PTC.

Primary SCC of the thyroid has a remarkably aggressive clinical course similar to that of anaplastic thyroid carcinoma (ATC), with a median survival time of less than one year (1, 6).

We herein report a case of primary thyroid SCC with a subsequent rapidly progressive course presenting as cervical lymphadenopathy in a patient with a remote history of total thyroidectomy due to conventional PTC.

Case Report

An 86-year-old woman presented to our clinic with a two-month history of an enlarging right-sided neck mass. She had undergone total thyroidectomy 10 years earlier at an outside hospital. According to the patient’s medical records, the pathology of that tumor was consistent with conventional PTC and she did not receive radioactive iodine therapy. Since the total thyroidectomy, the patient had been taking levothyroxine (150 μg daily).

On admission, she had no obstructive symptoms, such as dysphagia or shortness of breath. A physical examination disclosed a hard, nontender lymphadenopathy of the right cervical area with a maximum transverse diameter of 2 cm. The laboratory results revealed a serum thyroid-stimulating hormone (TSH) level of <0.01 mIU/L (0.30-5.00), a free T4 level of 1.77 ng/dL (0.89-1.76), a thyroglobulin level of 0.15 ng/mL and an anti-thyroglobulin antibody level of 2,000 U/mL (0-100). The laryngoscopic findings were unremarkable. Neck ultrasonography (US) revealed multiple enlarged lymph nodes, ranging from 1.0 cm to 1.5 cm in size,
PET/CT scan revealed hypermetabolic masses (SUV max = 24.8) at right levels III and IV, whereas there were no significant interval changes in the metastatic lung lesions (Fig. 1D). Hemostasis could not be achieved with a compression dressing. Accordingly, palliative neck surgery was performed with the goal of controlling the cancer-related bleeding (Fig. 2B). Microscopically, the tumor was composed of conventional PTC along with sheets of squamous cells exhibiting prominent cytologic atypia (Fig. 3A, B). Ancillary tests with immunohistochemistry showed strong immunoreactivity to thyroid transcription factor-1 (TTF-1) in each region of the PTC and SCC (Fig. 3C, D). All immunohistochemical staining analyses for cytokeratin 5, p53 and p63 were positive in the tumor regions, thus demonstrating atypical squamous differentiation. The BRAFV600E mutation was identified in the DNA extracted from each region of the conventional PTC and SCC using real-time PCR amplification with the Multiplex BRAF ACE detection system (Seegene, Inc., Seoul, South Korea). BRAFV600E amplification was detected in the region of conventional PTC and SCC in cycles 24 and 23, respectively (Fig. 4A, B). Following debulking surgery of the tumor mass and removal of the involved skin, the wound was closed using a pectoralis major myocutaneous flap and skin graft (Fig. 2C). One month after the flap operation, the patient underwent treatment with 6,000 cGy (30 fractions of 200 cGy for seven weeks) of external beam radiotherapy (EBRT) on the right side of the neck. However, another local recurrence of the tumor immediately developed below the operative site two months after EBRT (Fig. 2D). At that time, the patient declined further treatment and was discharged. She died three months later due to cancer progression and related complications.

Primary SCC of the thyroid is an extremely rare neoplasm, representing less than 1% of all primary thyroid cancers (1). Classically, the tumors present as suddenly enlarging neck masses with associated pressure symptoms. At the time of diagnosis, the tumors have usually invaded adjacent tissues and lymph nodes or even metastasized more widely. Therefore, the median survival time is usually less than one year (1), making this entity similar to ATC (6).

As the thyroid gland does not typically contain squamous epithelium, several theories exist regarding the mechanisms underlying the development of primary SCC. One theory is that the involved squamous cells are derived from various embryonic remnants, including thyroglossal duct structures, tumors, and she was discharged on levothyroxine medication.

Ten months later, the patient was readmitted due to a markedly enlarged right-sided neck mass (up to 10 cm) associated with recurrent bleeding. The metastatic lymph node was found to have penetrated the overlying skin (Fig. 2A). Both neck CT and 18F-FDG PET/CT scans were performed to evaluate the cancer progression. Markedly enlarged multiple lymph nodes at right levels III and IV as well as tracheal deviation to the left were found on a follow-up neck CT image (Fig. 1C). A follow-up 18F-FDG PET/CT scan also revealed rapidly enlarged hypermetabolic masses (SUV max = 24.8) at right levels III and IV, whereas there were no significant interval changes in the metastatic lung lesions (Fig. 1D).

Both neck CT and 18F-FDG PET/CT scans were compatible with a diagnosis of metastatic PTC. Computed tomography (CT) of the neck also showed multiple metastatic lymph nodes at right levels III and IV (Fig. 1A) and tracheal deviation to the left. (D) 18F-FDG PET/CT scan showing rapidly enlarged hypermetabolic masses (SUV max = 24.8) at right levels III and IV (black arrow). In contrast, there were no significant interval changes in the metastatic lung lesions. (E) Coronal fusion 18F-FDG PET/CT image showing lung metastasis.

At right levels III and IV.

US-guided fine needle aspiration (FNA) cytology of the right level III lymph nodes was performed to assess the presence of metastatic thyroid cancer. The FNA results were compatible with a diagnosis of metastatic PTC. Computed tomography (CT) of the neck also showed multiple metastatic lymph nodes at right levels III and IV (Fig. 1A). To evaluate the presence of metastatic tumors in other sites, a fluorine-18 fluorodeoxyglucose positron emission tomography (18F-FDG PET/CT) scan was performed. The 18F-FDG PET/CT scan revealed hypermetabolic masses (SUV max = 21.7) at right levels III and IV in addition to bilateral lesions in the lung fields, suggesting thyroid cancer metastasis (Fig. 1B). Due to the patient’s advanced age, both she and her family declined any further treatment for the metastatic
Figure 2. Gross findings of the metastatic neck lesions before, during and after surgery. (A) An 8x10-cm easy bleeding mass involving the skin. (B) Surgical findings following removal of the mass. (C) Reconstruction of the surgical defects using a pectoralis major myocutaneous flap. (D) Multiple fungating cutaneous recurrence on the supraclavicular area.

Figure 3. Histopathological and immunohistochemical findings. (A, B) Microscopic findings revealed that the tumor is composed of mixed (A) conventional PTC and (B) SCC (Hematoxylin and Eosin staining, 400x magnification). (C, D) Immunohistochemical staining for TTF-1 demonstrated strong reactivity in each region of the (C) conventional PTC and (D) SCC (TTF-1, 400x magnification). PTC: papillary thyroid carcinoma, SCC: squamous cell carcinoma, TTF-1: thyroid transcription factor-1

However, a more commonly accepted alternative theory is that squamous metaplasia facilitates the development of SCC in the affected epithelium. Occasionally, primary SCC of the thymic epithelium and ultimobranchial remnants (7).
thyroid occurs in association with other thyroid pathologies, including adenomatous goiters, Hashimoto’s thyroiditis, PTC and ATC (3, 5, 8). Recently, Ko et al. reported a case of primary SCC with a BRAF<sup>V600E</sup> mutation in exon 15 (3). The BRAF<sup>V600E</sup> mutation is the most common and is restricted to PTC and ATC arising in the setting of PTC (9). In the case described here, the resected tumor exhibited features of PTC as well as SCC, with additional testing showing BRAF<sup>V600E</sup> positivity in both regions. Furthermore, immunohistochemical staining for TTF-1 revealed strong immunoreactivity in both regions of the tumor, suggesting that the SCC was derived from the preexisting PTC. Therefore, this case further supports the theory that squamous metaplasia and malignant transformation to SCC develop from preexisting thyroid carcinomas. The resulting rapid progression of the transformed SCC, which follows a similar clinical course to that of other head and neck SCCs, resulted in mortality in the case described here.

**Discussion**

In a previous report, Kunisue et al. described a case of metastatic PTC of the thyroid with extensive squamous metaplasia in the submandibular lymph node (2). More recently, Kitahara et al. reported a case of local recurrence with extensive squamous conversion of the remnant thyroid four years after subtotal thyroidectomy due to PTC (4). However, to the best of our knowledge, no previous reports exist regarding SCC recurrence in a local cervical lymph node with rapid progression mimicking ATC in a patient with a history of total thyroidectomy due to PTC.

Metastatic SCC to the thyroid usually occurs as a result of direct invasion by laryngeal, tracheal or esophageal carcinomas or is secondary to metastasis from breast, lung or gastrointestinal tract carcinoma. Therefore, these diagnoses must be excluded prior to making a diagnosis of primary SCC of the thyroid (10). In order to exclude metastatic SCC from other sites, we performed the necessary evaluations, including laryngoscopy, esophagoscopy, neck and chest CT scans and <sup>18</sup>F-FDG PET/CT scans. No evidence was found to suggest any other origin for the resulting SCC, except the preexisting PTC.

When this patient first presented with an enlarging neck mass, palliative neck dissection and high-dose radioactive iodine therapy were recommended in order to prevent locoregional progression, resulting in aerodigestive tract obstruction, and treat the lung metastases. In spite of her advanced age, the patient exhibited good physical performance and did not have any medical diseases prohibiting palliative treatment, including surgery and radioactive iodine therapy. Nonetheless, the patient refused any such treatments. When the patient presented 10 months after discharge, the tumor was noted to have rapidly progressed. Given these findings in the context of the patient’s advanced age, anaplastic changes resulting from the preexisting PTC were suspected. However, the pathology of the tumor surprisingly revealed SCC. Therefore, we encourage clinicians to consider both SCC conversion and ATC as underlying etiologies in the setting of preexisting PTC with clinical features of rapid and unexpected progression. Although PTC has an excellent
prognosis, if not adequately treated, it can transform into SCC or ATC, both of which are associated with dismal outcomes, especially in old age. Therefore, we recommend that, if no contraindications to surgery exist, elderly patients with PTC be treated adequately to prevent the possibility of conversion to more aggressive malignancies. In conclusion, we herein reported an extremely unusual case of malignant cervical lymphadenopathy following total thyroidectomy due to PTC, with a pathology consistent with primary SCC. Although primary SCC rarely occurs in the thyroid, conversion from PTC to SCC should be suspected if preexisting PTC exhibits uncharacteristically aggressive behavior.

The authors state that they have no Conflict of Interest (COI).

References