Acta Scientific Otolaryngology (ISSN: 2582-5550)

Volume 3 Issue 8 August 2021

Case Report

Small Cell Neuroendocrine Carcinoma of the Palatine Tonsil After Concurrent Chemoradiotherapy for Laryngeal Cancer: A Rare Case Report

Bo-Nien Chen[1,3]*, Chih-Yung Yang[1] and Shiuan-Li Wey[2]

[1]Department of Otolaryngology-Head and Neck Surgery, Hsinchu MacKay Memorial Hospital, Hsinchu, Taiwan

[2]Department of Pathology, Hsinchu MacKay Memorial Hospital, Hsinchu, Taiwan

[3]Mackay Medical College, New Taipei, Taiwan

***Corresponding Author:** Bo-Nien Chen, Department of Otolaryngology-Head and Neck Surgery, Hsinchu MacKay Memorial Hospital, Hsinchu, Taiwan.

Received: July 01, 2021;

Published: July 22, 2021

Abstract

Objectives: Small cell neuroendocrine carcinoma (SCNEC) of the palatine tonsil is extremely rare, highly invasive, and associated with poor prognosis. Herein, we present an extremely rare case of SCNEC of the palatine tonsil after concurrent chemoradiotherapy (CCRT) for laryngeal cancer. We also provide a brief review of its clinicopathological characteristics and treatment modalities.

Methods: A 66-year-old Taiwanese woman visited our hospital with a 2-week history of left-sided sore throat. She had a history of laryngeal cancer treated with CCRT 5 years ago. Asymmetric enlargement of the left palatine tonsil with extensive ulceration was noted. Biopsy of the left palatine tonsil was performed and SCNEC was diagnosed. The patient subsequently underwent surgical intervention (wide excision of the left palatine tonsil and left supraomohyoid neck dissection) and adjuvant chemotherapy.

Results: The patient tolerated the treatment well and symptoms resolved. Tumor recurrence was not observed in follow-up magnetic resonance imaging after therapy at the 12-month follow-up time point, and the patient has resumed a normal life.

Conclusion: This report highlights the importance of considering the effect of CCRT on SCNEC occurrence and expands the spectrum of reported radiation-induced neoplasms in the head and neck region. It is critical for clinicians to be aware of this extremely rare and highly invasive malignancy.

Keywords: Small Cell Neuroendocrine Carcinoma; Concurrent Chemoradiotherapy; Postradiation Neoplasia; Tonsillar Malignancy

Abbreviations

SCNEC: Small Cell Neuroendocrine Carcinoma; CCRT: Concurrent Chemoradiotherapy; MRI: Magnetic Resonance Imaging; CT: Computed Tomography; PET: Positron Emission Tomography; NEC: Neuroendocrine Carcinoma

Introduction

The palatine tonsil is one of the most common sites of primary oropharyngeal malignancies. The predominant malignancy in the palatine tonsil is squamous cell carcinoma, but minor salivary gland tumors, lymphomas, melanomas and sarcomas can also occur [1]. Small cell neuroendocrine carcinoma (SCNEC) originating from the palatine tonsil is extremely rare, highly invasive, and associated with poor prognosis [1-3]. Herein, we present an extremely rare case of SCNEC of the palatine tonsil after concurrent chemoradiotherapy (CCRT) for laryngeal cancer. We also provide a brief review of its clinicopathological characteristics and treatment modalities.

Case Report

A 66-year-old Taiwanese woman visited our hospital with a 2-week history of left-sided sore throat. She had a history of laryngeal squamous cell carcinoma (T4aN0M0, stage IVA) treated with CCRT 5 years ago. She had neither local recurrence nor distant metastasis of the laryngeal cancer in routine follow-up.

In the clinic, her physical examination revealed asymmetric enlargement of the left palatine tonsil with extensive ulceration (Figure 1). Magnetic resonance imaging (MRI) revealed a 1.7 cm × 2.9 cm soft tissue mass with moderate enhancement over the left palatine tonsil (Figure 2A). A biopsy of the left palatine tonsil was performed. Histopathological sections revealed mucosal tissue largely infiltrated with anastomosing broad bands and large sheets of hyperchromatic round to oval neoplastic cells (Figure 3). The tumor cells were positive for cytokeratin, thyroid transcription factor-1, cluster of differentiation 56 (CD56), synaptophysin, and p16 (Figure 4) and some were positive for CD99 but negative for p40 immunohistochemical staining. Combined with the histopathological features and the results of immunohistochemical staining, the lesion was consistent with SCNEC. Moreover, the findings of a bone scan, computed tomography (CT) of the chest and abdomen, and positron emission tomography (PET) were negative for metastatic disease. The patient was given a diagnosis of SCNEC (T2N0Mb, stage II). She subsequently underwent surgical intervention (wide excision of the left palatine tonsil and left supraomohyoid neck dissection) and adjuvant chemotherapy (cisplatin combined with etoposide, 6 cycles in total). The patient tolerated the treatment well, and symptoms resolved. Tumor recurrence was not observed in follow-up MRI (Figure 2B) after therapy at the 12-month follow-up time point, and the patient has resumed a normal life. However, longer-term follow-up is required to assess for late recurrence.

Figure 1: Physical examination revealed asymmetric swelling and ulcerating mucosa of the left palatine tonsil (star; square, uvula; triangle, tongue).

Figure 2: (A) Magnetic resonance imaging (MRI) revealed a 1.7 cm × 2.9 cm soft tissue mass (yellow star) with moderate enhancement over the left palatine tonsil. (B) Tumor recurrence was not observed in follow-up MRI 12 months after therapy.

Figure 3A

Figure 3B

Figure 3: Histopathological sections revealing mucosal tissue largely infiltrated by anastomosing broad bands and large sheets of hyperchromatic round to oval neoplastic cells. (A) Hematoxylin and eosin (H&E) stain, 20× magnification. (B) H&E stain, 400× magnification.

Figure 4A

Figure 4B

Figure 4: Immunohistochemical staining of the lesion. The tumor cells were positive for synaptophysin (A, 200× magnification) and p16 (B, 100× magnification).

Discussion

Neuroendocrine tumors are composed of heterogeneous neoplasms. They can be divided into 2 types on the basis of neural or epithelial origin. Neuroendocrine carcinoma (NEC) is a malignant epithelial neoplasm with neuroendocrine differentiation that has been reported in many organs throughout the body [4]. Scholars have hypothesized that NEC arises from cells that are involved in the diffuse endocrine system [5]. According to the World Health Organization classification of 2017, NEC is divided into well-differentiated, moderately differentiated, and poorly differentiated forms. The latter is additionally divided into SCNEC and large cell NEC [3]. Many terms have been used to refer to SCNEC, including small cell carcinoma, oat cell carcinoma, anaplastic small cell carcinoma, and poorly differentiated (grade III) NEC [1].

SCNEC usually originates from pulmonary tissue, and extrapulmonary SCNEC accounts for only 2.5% to 5% of cases. Although extrapulmonary SCNEC is rare, gastrointestinal, genitourinary, breast, head and neck and unknown primary SCNEC have been reported [1,2]. In the head and neck region, the larynx is the most commonly involved site of SCNEC, followed by the salivary glands, the nasal cavity, and the paranasal sinuses. SCNEC originating from the palatine tonsil is extremely rare; only 14 cases have been reported since the first report by Koss., *et al*. in 1972 [1].

Palatine tonsillar SCNEC occurs most often in the sixth to seventh decades of life and is more common in men than in women (1.75:1 ratio) [1,2]. Clinically, the tumor usually manifests as a painless neck mass. A rapid clinical course (from 2 weeks to 3 months) and progressive enlargement of the neck mass may indicate tumor malignancy [1]. Other symptoms include sore throat and odynophagia, dysphagia, and obstructive sleep apnea syndrome [2]. Although paraneoplastic syndromes, including syndrome of inappropriate antidiuretic hormone secretion, Cushing syndrome, and Lambert-Eaton myasthenic syndrome, have been associated with head and neck SCNEC, there are no reports of these syndromes being associated with palatine tonsillar SCNEC [1].

The diagnosis of SCNEC depends mainly on histologic and immunohistochemical examination [2]. In light microscopy, hallmarks of SCNEC include small round to oval cells packed in sheets, cords, or ribbons with hyperchromatic nuclei, sparse cytoplasm, a high nuclear to cytoplasmic ratio, and frequent necrosis and mitosis. Immunohistochemistry reveals that cytokeratins and epithelial membrane antigen are immunoreactive, and positive staining of general neuroendocrine markers, including synaptophysin, chromogranin, neuron-specific enolase, and CD56, can provide evidence of neuroendocrine differentiation of tumor cells [1,2,4,5]. The differential diagnosis includes paraganglioma (which shows positive staining for S-100 but negative staining for cytokeratin) and malignant lymphoma (which is immunoreactive for leukocyte common antigen but negative for neuroendocrine markers) [1]. Fine-cut imaging with CT or MRI can assess the tumor size and its invasion depth. In addition, it is necessary to confirm that the tumor is not a metastasis of another distant primary tumor, especially from the lung [4,6].

SCNEC of the palatine tonsil exhibits aggressive biologic behavior and is prone to develop early regional or distant metastasis. In addition to locoregional spread to the cervical lymph nodes, the tumor metastasizes to the liver, lung, bone, and an unusual location, the adrenal gland [4]. Some smaller series have reported that 14.5% to 25% of patients present with distant metastatic disease. PET-CT is highly valuable for diagnosis and treatment planning because it can confirm the presence of both the primary tumor and metastatic lesions on the basis of tracer uptake [2].

The poor prognosis of patients can be explained by the aggressiveness of SCNEC, and the standard treatment protocol remains uncertain [1]. In terms of local control, current opinion favors the use of radiotherapy directed at the primary tumor site and neck rather than surgery or their combination [1]. In the present case, because the patient had received radiotherapy for laryngeal cancer before, to reduce the side effects of radiotherapy, we replaced radiotherapy with surgery (wide excision of the left palatine tonsil and left supraomohyoid neck dissection). In follow-up 12 months after therapy, we found that surgery had been effective in achieving local control.

Despite some controversy, many investigators have suggested that chemotherapy should be considered in all patients with SCNEC of the head and neck because of its propensity for early metastasis. Among all the chemotherapeutic agents, platinum-based regimens such as cisplatin and etoposide have been the most commonly used in recent years [1,2,5]. The use of new chemotherapeutic agents such as irinotecan, which has shown encouraging effects against small cell lung cancer, has also been reported in 1 case of SCNEC arising from the tonsil. Despite multimodality treatment, recurrence or distant metastasis was found in 66.7% of palatine tonsillar SCNEC cases, and these patients ultimately died of their disease in 2.5 years with a median overall survival time of 18.0 months [1].

Radiotherapy could potentially lead to unrecognized mutations, predisposing a patient to a second malignancy. In the present case, SCNEC was suspected as a second head and neck malignancy induced by radiotherapy previously used to treat the patient's laryngeal cancer. Thus, this represents a rare late-onset complication of radiotherapy. Although CCRT is currently the most common treatment for laryngeal cancer, such "cured" patients are at risk of a second malignancy. The risk of radiation treatment should be clearly communicated to patients before initiation.

Conclusion

Here we present an extremely rare case of the development of SCNEC of the palatine tonsil after CCRT for laryngeal cancer. This report highlights the importance of considering the effect of CCRT on SCNEC occurrence and expands the spectrum of reported radiation-induced neoplasms in the head and neck region. The risk of radiation treatment should be clearly communicated to patients before initiation. SCNEC of the palatine tonsil is extremely rare and highly aggressive, with a poor prognosis. Therefore, it is critical for clinicians to be aware of the uncommon occurrence of this disease and its management.

Disclosure of Conflict of Interest

None.

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Volume 3 Issue 8 August 2021