A case report of thyroid metastasis from p16-positive oropharyngeal squamous cell carcinoma

Masao Takenobu1), Sueyoshi Moritani1), Kana Yoshioka1), Tsuyoshi Morisaki2) and Hiroya Kitano1)

1) Kusatsu General Hospital, Otolaryngology Head and Neck Thyroid Surgery, Shiga, Japan
2) Tottori University Faculty of Medicine, Department of Otolaryngology, Head and Neck Surgery, Tottori, Japan

Abstract. Thyroid metastasis from head and neck squamous cell carcinoma (SCC) is a very rare form of rarely observed metastatic thyroid tumor. We herein report a case of thyroid metastasis from oropharyngeal SCC (OSCC). The patient was a 68-year-old male diagnosed with p16-positive tonsillar OSCC on the right side with multiple lymph node metastases and a thyroid mass, which was determined as metastatic p16-positive OSCC by immunohistochemistry of specimens collected by fine-needle aspiration cytology (FNAC). He received one cycle of induction chemotherapy followed by concurrent chemoradiotherapy. No visible primary lesions were observed after treatment. The disappearance of the tonsillar lesion was considered to be a complete response by the magnetic resonance imaging (MRI) and positron emission tomography-computed tomography (PET-CT). The thyroid lesion was also decreased, but a solid lesion with unclear boundaries in the right thyroid lobe remained. Therefore, the patient underwent total thyroidectomy to remove any residual tumor. Postoperative pathological evaluation revealed no residual viable carcinoma cells in the resected specimen. As illustrated in this case, immunohistochemistry of the FNAC specimen for p16 was successful in determining the thyroid tumor as a metastatic lesion from the oropharynx. Although radical radiotherapy might be sufficient to control thyroid gland metastasis of OSCC, in this case, early-stage remedial surgery was thought to be necessary for a secure radical cure.

Key words: Thyroid metastasis, Oropharyngeal squamous cell carcinoma, Head and neck cancer, P16 positive, Fine needle aspiration cytology

OROPHARYNGEAL SQUAMOUS CELL CARCINOMA (OSCC) is a common head and neck carcinoma, accounting for more than 10% of all head and neck squamous cell carcinoma (HNSCC) cases [1]. OSCC frequently metastasizes to lymph nodes, and distant metastases are rare at first medical examination [2, 3]. Intrathyroid metastasis of HNSCC including OSCC is extremely rare with only a few cases reported thus far [4, 5]. Certain OSCC cases that have been recently recognized to be associated with human papillomavirus (HPV) infection are associated with a favorable sensitivity to radiotherapy and better prognosis [6-9]. However, the treatment outcomes of HPV-associated OSCC with thyroid metastasis remain unclear. In this report, we present the case of a patient with HPV-associated OSCC and thyroid metastasis who received multimodal therapy.

Case Report

A 68-year-old male presented with a right tonsillar tumor and several masses in bilateral neck. Histopathology of tonsil biopsy specimen revealed squamous cell carcinoma (SCC), and immunohistochemistry revealed positivity for p16, a surrogate marker for HPV infection (Fig. 1a). Immunohistochemistry was performed using labeled streptavidin biotin method in E6H4 clone (Roche Diagnostics K. K., Tokyo, Japan). Magnetic resonance imaging (MRI) revealed the tumor mass in the right tonsil, bilateral neck, and upper mediastinal metastatic lymph nodes, and a mass in bilateral thyroid lobes (Fig. 2a, b), which measured as a 3.8 × 3.0-cm solid lesion in the right lobe and a 3.4 × 2.4-cm cystic lesion in the left lobe. Both lesions were discontinuous lesions to the primary tumor site and the lymph
nodes. Furthermore, the primary site of the tumor in the right tonsil spread to the right base of the tongue and arytenoid mucosa. The laboratory data were as follows: TSH 0.63 μU/mL, free T3 3.03 pg/mL, free T4 1.13 ng/dL, Thyroglobulin antibody 12 IU/mL.

Positron emission tomography-computed tomography (PET-CT) scan showed 18F-fluorodeoxyglucose accumulation in the right thyroid mass as well as the primary lesion and the cervical lymph nodes, whereas no accumulation was detected in the left thyroid mass (Fig. 2c, d).

Specimens obtained from both thyroid lobes by fine-needle aspiration cytology (FNAC) under ultrasonography revealed that, whereas the left thyroid mass was an adenomatous nodule, the right thyroid mass was SCC (Fig. 1b). Immunohistochemical analysis of the specimen from the right thyroid lobe was also p16-positive, revealing that the right thyroid mass was metastatic OSCC, and not a primary thyroid SCC. Therefore, the patient received a diagnosis of T4aN2cM1 OSCC.

The patient received one cycle of induction chemotherapy which included docetaxel (60 mg/m² body surface area), cisplatin (60 mg/m² body surface area), and fluorouracil (500 mg/m² body surface area), which was followed by concurrent chemoradiotherapy. Specifically, radiotherapy to the primary tumor site and the whole neck region included a dose of 60 Gy in 30 fractions, with three cycles of concurrent cisplatin (80 mg/m² body surface area). No visible primary lesions were observed after treatment. The follow-up MRI at two months post-treatment showed that the right thyroid mass and the metastatic lymph nodes including the upper mediastinum were significantly reduced in size, whereas no remarkable change was observed in the nodule of the left lobe (Fig. 2e). Disappearance of the tonsillar lesion was considered as complete response (CR). The PET-CT scan at three months post-treatment showed no remarkable accumulations in any of the metastatic lesions including both thyroid lobes and the primary lesion (Fig. 2f). Ultrasonography showed a 1.5 × 1.5-cm solid lesion with unclear boundaries in the right thyroid lobe. Therefore, total thyroidectomy was performed to avoid the possibility of a viable residual tumor (Fig. 3). The right recurrent laryngeal nerve was preserved, and there were no signs of invasion to the trachea. The section of the right thyroid lobe showed the presence of a solid lesion containing the granuloma and necrotic tissue (Fig. 4).

Postoperative pathological findings showed multiple foreign body granulomas, probably due to cancer chemotherapy, without viral SCC cells in the right lobe and follicular adenoma in the left lobe. The patient’s clinical course was favorable, and MRI at six months after surgery showed no recurrence.

**Discussion**

Metastatic thyroid tumor is rare, with a previously reported rate of 0.1% of all the thyroidectomies [10, 11]. Primary tumors that metastasize to the thyroid are often found in the lungs or kidneys [12]. Since distant metastases of head and neck cancers are commonly found in the lungs, bone, liver, and skin, in decreasing order of frequency, metastasis to the thyroid gland is extremely rare [13]. Among the head and neck cancers, nasopharyngeal carcinoma is the most commonly reported primary lesion that metastasizes to the thyroid gland [4, 14, 15]. Reports of thyroid metastasis of OSCC are extremely rare, with many of them being recurrent cases [4, 5].

The onset of OSCC is associated with drinking, smoking, and HPV infection that is associated with OSCC independently of smoking and drinking [6]. HPV-positive OSCC has a generally good prognosis, with 5-year survival rates of 53.5%–77.4%, whereas the 5-year survival of HPV-negative OSCC ranges from 31.5% to 56.6% [7, 8]. Similarly, the 3-year survival rates were reported as 82.4% and 57.1% in HPV-positive and HPV-negative cases, respectively [9].

p16 is a marker of HPV-associated OSCC [16, 17].
The patient reported here was diagnosed with SCC that was determined to be p16-positive by pharyngeal biopsy. The suspected malignant tumor lesion in the right thyroid lobe was also confirmed as p16-positive SCC by FNAC. These findings conclusively ruled out the possibility of concurrent primary tumors, with SCC of the oropharynx and the thyroid gland, and confirmed the diagnosis of OSCC metastasis to the thyroid gland. Our extensive literature review indicated this to be the first case of its kind.

OSCC metastasis to the thyroid gland is a distant metastasis, and the current case was stage IVb T4aN2cM1, according to the tumor-node-metastasis classification. The prognosis of HNSCC with distant metastasis is generally poor [13]; however, compared with HPV-negative OSCC, control of the distant metastatic lesions is reportedly better in HPV-positive OSCC cases [13, 18]. Nonetheless, whether the prognosis of HPV-positive OSCC with thyroid gland metastasis is good remains unknown.

In the present case, the thyroid glands were included in the radiotherapy field. The National Comprehensive Cancer Network Guidelines also recommend treatment of OSCC with distant metastasis that conform to the treatment algorithm of the primary site depending on the conditions. Therefore, the current case underwent radical treatment which resulted in CR to radiotherapy to both the primary lesion and the metastatic sites, including the thyroid glands. CR was confirmed by imaging, and disappearance of the 18F-fluorodeoxyglucose accumulation was observed by PET-CT as well.

The utility of PET-CT after radiotherapy for head and neck cancers as well as for OSCC metastasis to thyroid glands has been previously reported [5, 19-21]. However, the number of reported cases are few, and its utility for post-treatment evaluation remains unknown. There-
fore, based on the possibility that residual tumors might not be entirely ruled out, the patient underwent early-stage remedial surgery. Total thyroidectomy, and not hemithyroidectomy, was performed because of two reasons. First, the possibility of malignant lesions within the adenomatous goiter of the contralateral lobe could not be ruled out. Second, there was a high chance that the patient would require levothyroxine treatment either way as a consequence of post-radiotherapy hypothyroidism [22, 23]. The surgery revealed no residual viable tumors in the thyroid gland. In addition, there were no signs of suspected residual tumors in the cervical lymph nodes. Therefore, neck dissection was not performed. All together, these results might suggest that radical radiotherapy was sufficient to control thyroid gland metastasis of OSCC. However, just a total thyroidectomy will not extremely worsen the quality of life except the every-day medicine. Therefore, in this case, early-stage remedial surgery was thought to be appropriate to achieve a secure radical cure. Moreover, given that the present case was p16-positive, data from additional patients with similar findings are necessary. In conclusion, we described a case of thyroid metastasis from p16-positive OSCC controlled by multidisciplinary treatment.

References


