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Primary combined small cell carcinoma and squamous cell carcinoma of the oropharynx with special reference to EGFR status of small cell carcinoma component: Case report and review of the literature

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ABSTRACT

Combined small cell carcinoma (SCC) and squamous cell carcinoma (SqCC) of the oropharynx is extremely rare and shows an aggressive clinical course. There are only 5 reported cases of combined SCC and SqCC in the English language literature. Here, we report a 59-year-old male presenting with a right tonsillar mass. The mass was biopsied, and the histological findings showed a proliferation of small-sized tumor cells with scant cytoplasm. Immunohistochemically, the tumor cells were positive for neuroendocrine markers (synaptophysin, chromogranin A, and CD56). Our first diagnosis was tonsillar small cell carcinoma. We treated the patient with concurrent chemoradiotherapy together with cisplatin followed by surgery. The resected tonsillar specimen showed a residual tumor composed of SCC and SqCC, and lymph nodes showed metastatic tumor cells of the SCC component. Immunohistochemically, the SCC component was positive for all neuroendocrine markers and p16; on the other hand, the SqCC component was positive for p40, p63, p16, and EGFR. Fluorescence *in situ* hybridization revealed that neither component showed any *EGFR* gene copy number gain. The patient was treated with adjuvant chemotherapy consisting of irinotecan and cisplatin. Liver and bone metastases developed, resulting in the death of the patient. We discuss the present case and review similar cases. Most cases of combined SCC and SqCC occur regardless of p16 status, and a therapeutic strategy has yet to be determined. Further examination of this kind of combined tumor is necessary.

1. Introduction

Small cell carcinoma (SCC) is known as a malignant epithelial tumor that shows neuroendocrine differentiation; it originates mainly in the lung and occurs rarely in the head and neck region [1]. In this region, SCC of the larynx is the most common site, while SCC of the oropharynx is extremely rare [1]. Because of this low incidence, a therapeutic strategy for

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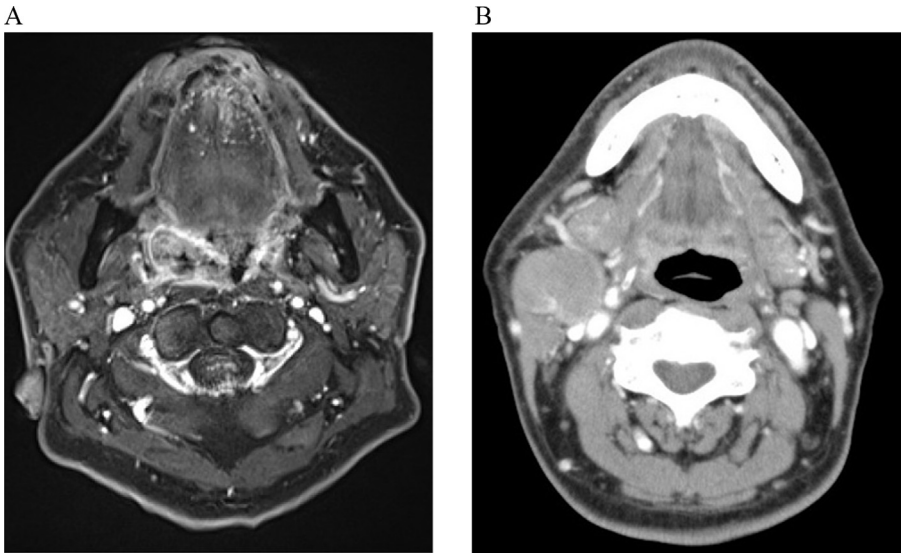

Fig. 1. (A) A post-contrast T1-weighted magnetic resonance imaging scan showing a right tonsillar mass measuring 4.2 cm in its largest diameter. (B) Contrast-enhanced computed tomography scan showing cervical lymphadenopathy.

SCC of the oropharynx has not been established. On the other hand, almost all oropharyngeal malignant tumors show squamous cell carcinoma (SqCC). In SqCC of the oropharynx, human papilloma virus (HPV) infection is one of the most common etiological factors and is known to be associated with a better prognosis [2]. Additionally, epidermal growth factor receptor (EGFR) protein overexpression and gene copy number gain (high polysomy and gene amplification) have been reported in 70–100% and 17–58%, respectively, of SqCC of the head and neck, and are reported to be associated with a worse prognosis [2]. Recently, monoclonal antibody against EGFR (e.g., cetuximab) has been used clinically to treat head and neck cancers. However, EGFR status in SCC is still controversial. Here, we report a rare case of combined SCC with SqCC of the oropharynx with special reference to the pathological features of each component.

2. Case presentation

A 59-year-old male was introduced to our hospital complaining of a sore throat and a right neck mass he had first noticed 4 weeks earlier. He smoked (20 cigarettes per day for 37 years) and drank alcohol (20 g per day). A physical examination revealed an ulcerated mass in the right palatine tonsil and multiple lymphadenopathy at level II on the affected side.

Contrast-enhanced computed tomography (CT) and magnetic resonance imaging (MRI) scans of the head and neck showed a 4.2 cm well-defined, enhancing tumor in the right palatine tonsil with multiple right lymph node involvement (Fig. 1A and B). A thoracicoabdominal CT scan indicated no other lesions. The whole body positron emission tomography–computed tomography (PET–CT) showed prominent fluorodeoxyglucose uptake within the right palatine tonsil and right level II lymph nodes without distant metastasis.

A right palatine tonsil biopsy was taken. Histopathologically, a hematoxylin and eosin-stained section showed a proliferation of small round cells with scant cytoplasm (Fig. 2A). Immunohistochemically, these tumor cells were positive for chromogranin A, synaptophysin (Fig. 2B), neural cell adhesion molecule (CD56), low molecular weight cytokeratin, and

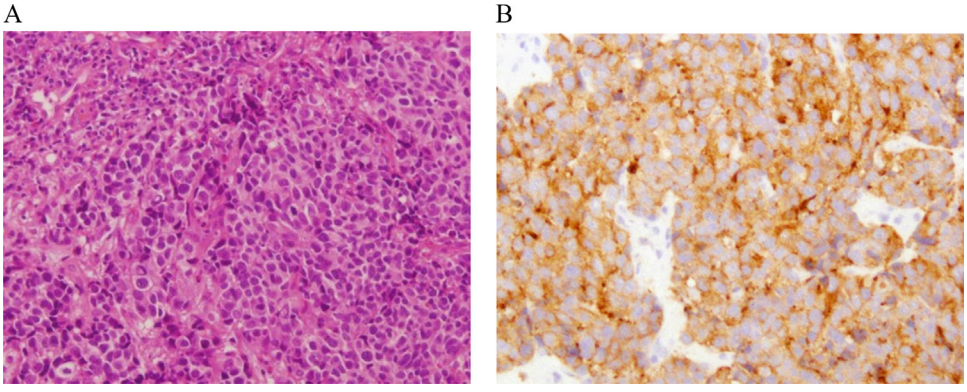

Fig. 2. The biopsy specimen showed a proliferation of small round to ovoid tumor cells with scant cytoplasm (A). The tumor cells showed immunoreactivity for synaptophysin (B).

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