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Combined small cell carcinoma of the hypopharynx

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ABSTRACT

We report an extremely rare case of combined small cell carcinoma (combined SmCC) of the hypopharynx. A 73-year-old male presented with multiple left neck swellings for 1 month. A tumorous lesion was found in the left pyriform sinus, and biopsy revealed that the lesion was squamous cell carcinoma (SqCC). Surgery was performed and pathological examination led to a diagnosis as combined SmCC, composed of SqCC and small cell carcinoma (SmCC). One month after surgery, a contrast-CT indicated metastases to the cervical lymph node (LN), mediastinum and liver. We performed 5 courses of chemotherapy with the use of cisplatin (CDDP) and irinotecan (CPT-11). The patient temporarily showed a favorable response to the chemotherapy; however, eventually he died of regrowth of the tumor. Combined SmCC is a disease with a poor prognosis. Although biopsy sometimes fails to detect the SmCC component, intensive diagnosis and treatment are necessary.

1. Introduction

SmCC, a type of neuroendocrine tumor, often occurs in the lung, and rarely in the head and neck region. Furthermore, combined SmCC, which consists of SmCC combined with SqCC or other histological types of carcinoma, is extremely rare. Even though the larynx is most common site of occurrence in the region, there have been only 17 cases of combined SmCC of the larynx reported to date [1–11]. Combined SmCC of the hypopharynx is even rarer, and only 2 cases have been reported [1,2]. In this report, we present an additional case of primary combined SmCC of the hypopharynx.

2. Case report

The patient was a 73-year-old male, with a history of excessive alcohol consumption and smoking for about 50 years. He presented with a one-month history of progressive left-neck swelling and hoarseness. There was no history of weight loss, dysphagia, or dyspnea. A tumorous lesion was found in the left pyriform sinus on laryngeal fiberscopy, and diagnosed by biopsy as SqCC at another hospital. The patient was referred to our hospital for further treatment. A pathologist at our hospital checked the biopsy sample and also diagnosed SqCC, although no SmCC component was observed in the biopsy specimen. Laryngeal fiberscopy revealed an ulcerated hemorrhagic tumor in the left pyriform sinus (Fig. 1). The left vocal cord was fixed. A contrast-computed tomography (CT) scan of the neck also detected a 49 mm × 41-mm inhomogeneously enhancing tumor extending through the left pyriform sinus to the thyroid membrane, as well as multiple LN metastases with central necrosis in the left neck (Fig. 2). Moreover, fluorodeoxyglucose – positron emission tomography (FDG-PET) showed high-level accumulation in the primary tumor, with a standardized uptake value (SUV) max of 14.6. Although marked FDG accumulation with an SUV max of 8.9 was observed in multiple lesions of the left cervical LN, there was no evidence of right cervical LN or distant metastasis. The patient was diagnosed with hypopharyngeal cancer and classified as T4aN2bM0 according to the staging system in 2009 established by UICC [12]. We conducted tracheostomy, total pharyngolaryngectomy in conjunction with left hemithyroidectomy, left posterolateral neck dissection (level II–V), right lateral neck dissection (level II–IV), bilateral paratracheal dissection, bilateral retropharyngeal neck dissection, and free jejunal transfer. We present a macroscopic photo of the surgical specimen in Fig. 3. A 60 mm × 30-mm deeply ulcerated tumor was found in the left pyriform sinus. Microscopically, we observed two components in the lesion: well-differentiated SqCC, and a small-sized SmCC containing chromatin-rich nuclei with scanty cytoplasm (Fig. 4 A). The SqCC component was mainly distributed near the mucosal side, whereas most of the cancer cells found at the depth were identified as SmCC. Immunohistochemically, neuroendocrine markers, including CD56, synaptophysin, and chromogranin A, were positive for a SmCC component, but negative for a SqCC component (Fig. 4B–D). Taken together, the patient was diagnosed with combined SmCC.

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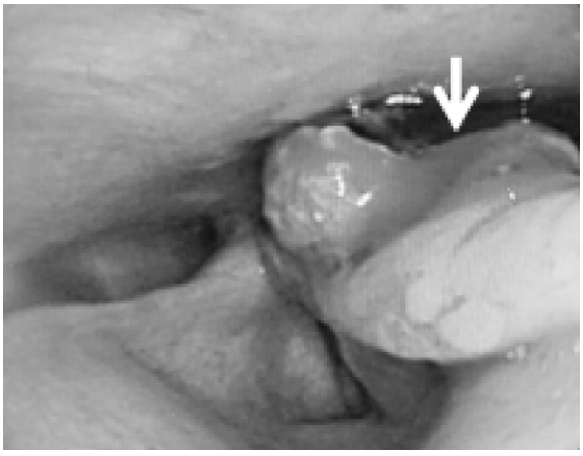

Fig. 1. Laryngeal fiberscopic image. An ulcerated hemorrhagic tumor was observed in the left pyriform sinus (arrow).

We could not detect invasion to the cervical esophagus. The surgical margin was negative. Pathologically, multiple metastatic cervical LNs were noted in the left level II, III, and V areas.

A contrast-CT scan was performed 1 month after the surgery, which detected a 14-mm LN metastasis in the left level II, a 16-mm LN metastasis in the upper mediastinum, and a 25-mm metastasis in the liver. In addition, fine needle aspiration performed on the left at the level II cervical LN revealed metastasis of SmCC, but not metastasis of the SqCC component.

The patient was assigned to chemotherapy with a regimen of CPT-11 at 60 mg per square meter of body surface on days 1, 8 and 15, and CDDP at 60 mg per square meter of body surface on day 1. A contrast-CT scan obtained after the second course of treatment showed that the patient had achieved a favorable response to chemotherapy, with successful regression of the left cervical LN metastasis from 14 to 10 mm, that of the mediastinal LN metastasis from 16 to 12 mm, and that of the liver metastasis from 25 to 15 mm. However, after the fourth course, no improvement was noted in the mediastinum and liver, whereas the left level II LN metastasis was found to have grown. Moreover, a

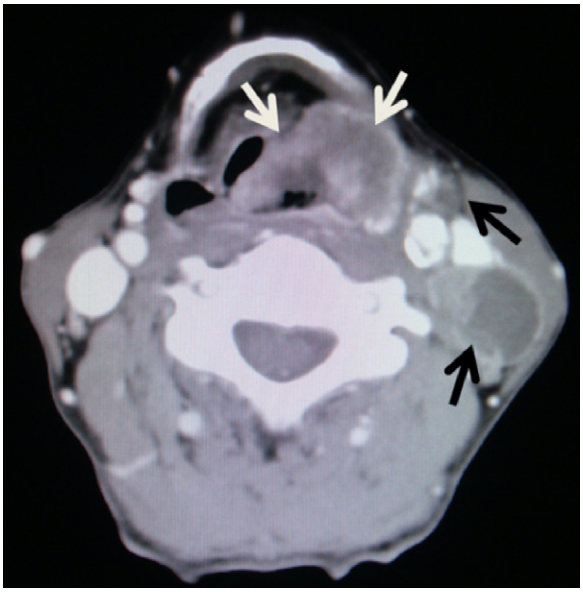

Fig. 2. Contrast-CT scan of the neck before treatment. An enhanced tumor (49 mm × 41 mm) was observed in the left pyriform sinus (white arrows). Multiple LN metastases were observed in the left neck (black arrows).

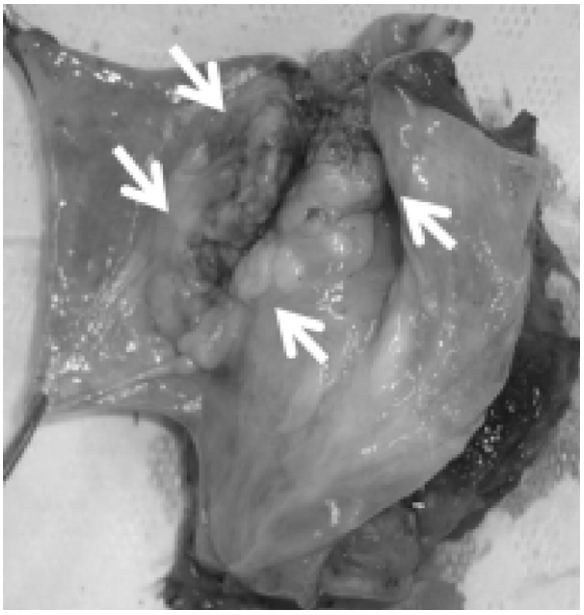

Fig. 3. Macroscopic photo of the surgical specimen. A deeply ulcered tumor was observed in the left pyriform sinus (white arrows).

12-mm lung metastasis was newly found in the left lung apex. Although an additional course was given in accordance with the patient's request, a contrast-CT scan after the completion of the fifth course showed enlargement of the left level II LN and lung metastases. The condition of the patient started to deteriorate, and he died of the disease 9 months after the initial treatment.

3. Discussion

Here, we reported the rare case of combined SmCC of the hypopharynx. There are only 2 reports of hypopharyngeal combined SmCC [1,2]. Table 1 shows a summary of these and our case. We experienced difficulty in the diagnosis and treatment of the current case.

Pathogenically, combined SmCC is considered to develop by the transformation of SqCC into SmCC. Here, we detected a sarcoma-like anaplastic cells among SqCC in the primary lesion. This area would be corresponding to the transformation of SqCC. In addition, we observed the anaplastic cells at the submucosal area in the surgical specimen, though that we could not fail to detect such transforming cells into SmCC at the initial biopsy, as is the case of other combined SmCC of the larynx [5,10,11]. This transformation from SqCC to SmCC in the submucosal area might be associated with the hypothesis that neuroendocrine tumors arise from endocrine cells and mainly grow in the submucosal area [13]. Biopsy from the superficial zone of the tumor would not be able to detect the SmCC component. To avoid misrecognition of the SmCC component, a large volume of specimen containing deep tissues is required.

Combined SmCC of the hypopharynx is so rare that its treatment is not established. In the larynx, SmCC has a poorer prognosis compared to SqCC, partially owing to its more frequent metastasis [14]. Seven of 17 reported cases of laryngeal combined SmCC were pathologically confirmed to show the presence of metastasis to LNs and/or distant organs [1,2,4–8]. Metastatic lesions of all 7 cases included SmCC. Of the 7 cases, one case showed the metastasis including both combined SmCC and SCC, another case showed the metastasis of SqCC. All reported hypopharyngeal combined SmCC showed the presence of metastasis included SmCC. (Table 1). This clearly shows that the metastasis of a SmCC component is more likely to occur than that