Clinical Case Report

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Small cell carcinoma of the pyriform sinus successfully treated with concurrent chemo-radiotherapy

A case report

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Abstract

Background: Primary small cell carcinomas (SCCs) are uncommon in extrapulmonary sites and account for only 2.5% to 5.0% of all SCCs. SCCs in the pyriform sinus are rare and there is little information regarding this disease, especially on therapeutics. Herein, we present a case of successfully treated SCC in the right pyriform sinus that occurred in a patient with small cell lung carcinoma (SCLC) that completely resolved 4 years prior.

Methods: A 1.5 × 1.5-cm mass in the right pyriform sinus was detected on imaging studies in a 71-year-old male at a regular check-up visit after being in remission from SCLC.

Results: Based on histologic examination and immunohistochemistry, the tumor in the right pyriform sinus was diagnosed as an extrapulmonary SCC. Chemo-radiotherapy was applied to the SCC of the pyriform sinus with a regimen of etoposide and cisplatin. The patient exhibited complete response to treatment and has been disease free for 11 months.

Conclusion: This interesting case shows that chemotherapy with concurrent radiation may be an effective therapeutic modality for localized extrapulmonary SCC similar to localized SCLC, which is treated with concurrent chemo-radiotherapy as the standard therapeutic option.

Abbreviations: CT = computed tomography, PET = positron emission tomography, SCC = small cell carcinoma, SCLC = small cell lung carcinoma.

Keywords: pyriform sinus, small cell carcinoma

1. Introduction

Small cell carcinomas (SCCs) are aggressive neuroendocrine tumors that are most commonly found in the lung. SCC is well-known for poor prognosis as the reported median survival is 2 to 4 months without treatment in the most common form, the small cell lung carcinoma (SCLC).[1] Primary SCCs found in extrapulmonary sites are uncommon and account for only 2.5% to 5.0% of all SCCs.[2,3] The frequently reported extrapulmonary sites are esophagus, larynx, and bladder.[4] In the head and neck region, the larynx is the most common extrapulmonary site for SCC, but accounts for <0.5% of all primary laryngeal carcinomas.[5] Despite the anatomical proximity to the larynx, SCC in the pyriform sinus is very rare and approximately 5 cases have been reported in the English literature in the past 10 years. Previous reports have introduced various therapeutic modalities such as chemotherapy and radiation for SCC of the pyriform sinus, but information regarding optimal treatment remains elusive.[6–10]

In this current case, SCC in the pyriform sinus was incidentally detected in a 71-year-old male with a history of SCLC in remission for 4 years after undergoing treatment. Interestingly, the patient also exhibited a complete response in SCC of the pyriform sinus through conventional cisplatin-based chemotherapy with concurrent radiation.

2. Case report

A 71-year-old man was admitted to our hospital for evaluation of an incidental mass in the right pyriform sinus detected on regular

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JHL, JSJ, and SRK have contributed equally to this work.

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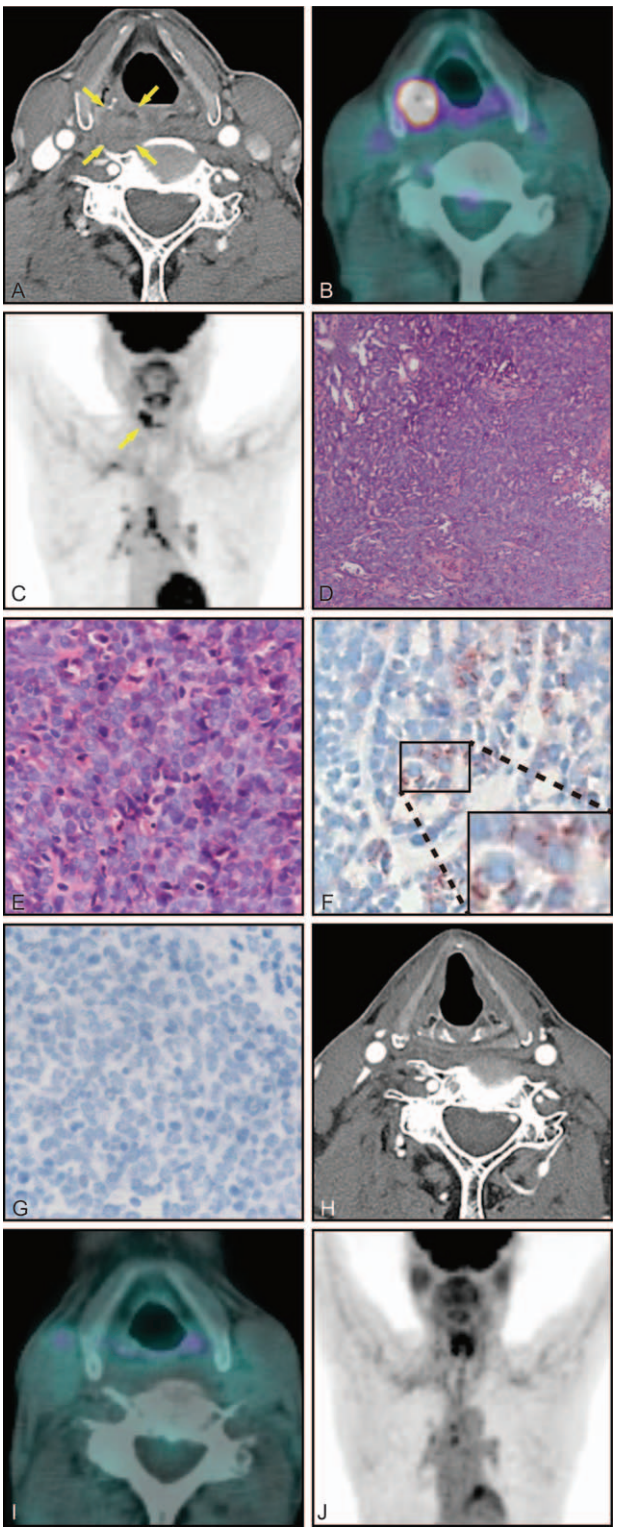

Figure 1. (A) Postenhancement axial CT scan of the head and neck reveals a heterogeneously enhancing 1.5 × 1.5-cm-sized mass (arrows) in the right pyriform sinus of the hypopharynx. (B) FDG PET-CT scan displays elevated glucose metabolism (maximum standardized uptake value = 29.28). (C) Arterial phase coronal image of whole body FDG-PET scan highlights elevated glucose metabolism (arrow) in the neck and no evident SCLC. (D) H&E staining (×100) shows the highly cellular component of the pyriform sinus mass. (E) High-power field examination (×400) of the specimen demonstrates dense sheets of small cells with a high nuclear-to-cytoplasm ratio, hyperchromasia, nuclear molding, and high mitotic count. (F) Immunohistochemistry (×400) was positive for CD56. Brown-stained cells were considered to express CD56 as shown in inset image. (G) Immunohistochemistry (×400) was negative for thyroid transcription factor-1. (H) Postenhancement axial CT scan of the head and neck shows no evidence of tumor after chemoradiotherapy. (I) FDG PET-CT scan displays absence of increased metabolism after treatment. (J) Arterial phase coronal image of whole body FDG-PET scan exhibits no hypermetabolic lesions in the neck or chest on follow-up scan. CT = computed tomography, FDG = 2-deoxy-2-[18F]-fluoro-D-glucose, H&E = hematoxylin and eosin, PET = positron emission tomography, SCLC = small cell lung carcinoma.

follow-up examinations for surveillance of SCLC after being disease free for 4 years. The patient was successfully treated with a chemotherapy regimen consisting of etoposide and cisplatin with concurrent radiation therapy. The patient was a farmer and an ex-smoker with a 50 pack-year smoking history, and had a history of excessive alcohol use.

The mass in the right pyriform sinus of the hypopharynx was a heterogeneously enhancing 1.5 × 1.5-cm mass (Fig. 1A) and had a high glucose metabolism (maximum standardized uptake value = 29.28) (Fig. 1B) on positron emission tomography (PET)-computed tomography (CT) scan. The tumor invaded the lateral and posterior wall of the aryepiglottic fold. Superiorly, the tumor adhered to the inner cortex of the thyroid cartilage. No evidence of cervical lymph node enlargement and recurrence of previous SCLC in the lung were present, but several hypermetabolic mediastinal lymph nodes were present on PET-CT scan images (Fig. 1C). Bronchoscopy revealed no endobronchial lesions such as masses, infiltration, or obstruction. Hematoxylin and eosin staining of the excisional biopsy sample of the mass in the pyriform sinus showed dense sheets of small cells with a high nuclear-to-cytoplasm ratio, hyperchromasia, nuclear molding, and a high mitotic count, indicating SCC (Fig. 1D and E). Immunohistochemistry was positive for neuroendocrine marker CD56 (123C3, Zymed Laboratories, Inc., South San Francisco, CA) and negative for thyroid transcription factor-1 (SPT24, Leica Biosystems, Newcastle, UK) (Fig. 1F and G). To confirm whether mediastinal lymph nodes showing hypermetabolic signs on PET-CT represented metastatic lesions, we performed surgical biopsy and pathological examination, which indicated that the PET-CT results were false-positive.

Collectively, the patient was diagnosed with localized SCC in the right pyriform sinus and treated with 6 cycles of chemotherapy composed of cisplatin 90.6 mg (75 mg/m^2) on day 1 and etoposide (VP-16) 120.7 mg (100 mg/m^2) on days 1 to 3 and a total radiation dose of 70 Gray in 35 fractions given over 7 weeks. The patient had exhibited complete response to treatment based on head and neck CT and PET-CT 6 months after initial discovery (Fig. 1H–J). The patient recovered without complications, and there has been no evidence of recurrence over 11 months of follow-up.

3. Discussion

The clinical experience of SCC of the pyriform sinus is limited because of its extremely low incidence. According to previous reports, the average patient age was 64.8 years, ranging from 50 to 78 years (Table 1).[6–10] In the previous cases shown in Table 1, 4 patients were male and 1 patient was female. Four patients had a history of smoking, but no patients had a history of malignancies. In all cases, the therapeutic approach was chemotherapy with or without radiation therapy to the primary site of the tumor. Only 3 patients who received platinum-based chemotherapy remained disease free.

Table 1

Review of case reports on small cell carcinoma of the pyriform sinus.

Authors	Age/sex	Smoking	Symptoms	History of malignancy	Metastasis at diagnosis	Pathologic description	Treatment	Follow-up
Gaba et al[6]	65/M	Yes (NS)	Dysphagia, odynophagia	None	None	NS	Chemotherapy (platinum-based, NS), radiation	Disease free, 2 y
Sano et al[7]	67/F	Yes (80 PY)	Swelling	None	None	Hyperchromatic nucleus	Chemotherapy (etoposide, carboplatin), radiation	Deceased, 13 mo
Yoshida et al[8]	78/M	Yes (50 PY)	Sore throat	None	None	Dense nuclei, granular chromatin, scant cytoplasm	Chemotherapy (docetaxel, cisplatin, 5-fluorouracil)	Disease free, 3 y
Treglia et al[9]	64/M	NS	Dysphonia, dysphagia	None	Regional LNs	Hyperchromatic nucleus, scant cytoplasm	Chemotherapy (NS)	Deceased, 8 mo
Bayram et al[10]	50/M	Yes (60 PY)	Sore throat, swelling	None	Both lungs	Absent nucleoli, crush artifact, scanty cytoplasm, hyperchromatic nucleus, necrosis, nuclear molding, scant granular chromatin	Chemotherapy (etoposide, cisplatin), radiation	Disease free, 15 mo

F = female, LN = lymph node, M = male, NS = not specified, PY = pack-year.

Interestingly, unlike the previous cases, our patient had a history of SCLC and was disease free for a total of 4 years. Second primary malignancies can be defined based on previous reports as a diagnosis of cancer that occurs 2 years after the resolution of primary cancer.[11] Thus, this case could be diagnosed initially as a second primary malignancy presenting as extrapulmonary SCC. However, since extrapulmonary SCCs are pathologically indistinguishable from metastatic SCLCs, to confirm the diagnosis we needed to verify that there was no evidence of SCLC on further work-up including chest imaging, bronchoscopy, and pathology.[12] In our current case, chest CT scanning and bronchoscopic examination showed no evidence of SCLC recurrence. Additionally, bronchial washing cytology revealed that there were no malignant cells in the specimen. These laboratory data supported the diagnosis of a second primary extrapulmonary SCC rather a metastatic lesion.

Clinical features of SCC found in extrapulmonary sites are similar to SCLC in many ways. However, therapeutic approaches to SCC in various sites have been reported to be modified by anatomical location and disease extent. Additionally, despite the rarity of SCC in extrapulmonary sites, surgery, chemotherapy, radiation, and combined therapy have been applied to achieve local and systemic disease control. For example, surgery is suggested for early-stage SCCs of the uterine cervix, bladder, and salivary gland.[4,13–17] Chemotherapy with concurrent radiation was efficacious in control of the primary SCC of the larynx.[17–20] Adjuvant chemotherapy, preferably with a platinum-based regimen following local control, was effective in SCCs of the esophagus, larynx, uterine cervix, and advanced-stage SCCs of the bladder. However, no superior method for local control has been documented for SCCs of the esophagus, colon, stomach, gallbladder, and prostate.[4,21–24]

The pyriform sinus is a complex anatomical structure of the hypopharynx that adjoins the larynx and trachea. It is bounded laterally by the ala of the thyroid cartilage and thyrohyoid membrane and medially by the aryepiglottic fold and cricoid cartilage.[25] Therefore, surgical resection of pyriform sinus tumors through laryngopharyngectomy is followed by the loss of deglutition and speech, and requires extensive postsurgical rehabilitation. Considering patient quality of life, chemotherapy may be a more desirable initial choice for localized tumors in this anatomical region. A promising chemotherapy regimen for SCC of the pyriform sinus is the standard treatment for SCLC, cisplatin-based chemotherapy with concurrent radiation. Review of 4 previous reports with specified chemotherapeutic agents revealed that cisplatin-based regimens in combination with etoposide, docetaxel, or 5-fluorouracil have been successful in achieving complete response of primary SCC of the pyriform sinus.[6–9] Except for a single case of metastatic recurrence, all patients achieved disease free status during the follow-up period. In particular, 3 patients had radiation therapy in adjunction to cisplatin-based chemotherapy.[6,7,10] Review of these 3 cases showed that 2 patients were male and that all patients had history of heavy smoking. In 2 cases, the primary tumor was found in the right pyriform sinus. At the time of initial presentation, the patients had locally advanced tumor manifesting symptoms associated with mass effect in the hypopharynx and clinically evident adjacent lymph node invasion. In our patient, chemotherapy with cisplatin and etoposide with concurrent radiation was also successful in treating SCC of the pyriform sinus. Similar to majority of the cases, in our case, SCC in the right pyriform sinus was found in a 71-year-old male with a 50 pack-year history of smoking. Unlike other cases, the tumor was discovered at an early stage confined to the pyriform sinus. In the retrospective view, early detection and successful management of aggressive SCC of the pyriform sinus might have been possible as our patient was on a regular follow-up on a resolved SCLC.

In summary, we report our experience with an extremely rare case of SCC occurring in the right pyriform sinus of the hypopharynx in a patient with a history of SCLC. Complete response of SCC was achieved after etoposide/cisplatin chemotherapy and concurrent radiation, which is the regimen recommended as the standard first-line therapeutic modality for SCLC. This report suggests that platinum-based chemotherapy with concurrent radiation may be preferable over surgical resection for localized extrapulmonary SCC, especially when found in the pyriform sinus.

4. Ethical review and patient consent

The Institutional Review Board of Chonbuk National University Hospital waived the need for IRB approval for this case report, but patient consent was required as the study dealt with retrospective use of the patient's medical record and related images. Written informed consent was obtained from the patient prior to the publication of this case report and accompanying images.

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