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*Case Report*

# Primary small cell neuroendocrine carcinoma of the nasopharyngeal cavity: a case report

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**Abstract:** Primary small cell neuroendocrine carcinoma (SNEC) of the nasopharyngeal cavity is extremely rare. We report of a 43-year-old male with a history of hearing loss of the right ear and swelling on the left side of his neck for one month. Magnetic resonance imaging (MRI) scan of the head and neck revealed a thickened roof and posterior wall of the nasopharynx, and a mass in the nasopharyngeal cavity with invasion of the staphylinus externus and levator veli palatine. Histopathological diagnosis revealed SNEC. He was successfully treated with concurrent chemoradiotherapy. No local recurrence or distant metastasis was identified after 10 months of follow-up.

**Keywords:** Nasopharyngeal carcinoma, small cell neuroendocrine carcinoma, chemoradiotherapy

## Introduction

SNEC mainly occurs in the lung, and extra-pulmonary SNEC accounts for 4% of all cases [1]. Primary SNEC of the nasopharyngeal cavity is extremely rare and only a few cases of nasopharyngeal SNEC have been reported in the English literature. We report a patient with nasopharyngeal SNEC who was successfully treated with concurrent chemoradiotherapy. The clinical and pathologic features of the cancer and the optimal treatment of this patient are discussed.

## Case report

A 43-year-old male with a history of hearing loss of the right ear and swelling on the left side of his neck was examined in December 2016. Before that, he had two months history of spontaneous epistaxis accompanied with slight headache. MRI scan of the head and neck demonstrated various degrees incrassation of soft tissue of the nasopharyngeal posterior wall, a mass in the nasopharyngeal cavity with invasion of the staphylinus externus and levator veli palatine, the size was about 3 cm × 2 cm. Multiple lymphadenopathies were identified, especially there was an enlarged lymph node measuring approximately 4 cm × 4 cm on the left side of the neck (**Figure 1**). Two biopsies were taken from different areas of the mass with nasopharyngoscopy. Histologic examination found that dysplastic cells presented widespread. Immunohistochemical staining was positive for cytokeratin (CK), CK8/18, CD56, synaptophysin, and negative for CK5/6, CD20, Neuron Specific Enolase (NSE), Thyroid Transcription Factor-1 (TTF1). Histologic and immunophenotypic features were characteristic for SNEC (**Figure 2**). Contrast-enhanced CT to the chest and abdomen were performed, but no definitive lesions were found. Moreover, a bone scan also excluded the possibility of bone metastasis.

This patient was treated with 4 courses of combination chemotherapy (cisplatin 80 mg/m$^2$, day1, etoposide 100 mg/m$^2$, day1-3, 3 weeks per cycle). Concomitant radiation therapy was given with 95% gross tumor volume (GTV) 56 Gy (2.24 Gy/fx × 25 fractions), 95% GTVnd 56 Gy (2.24 Gy/fx × 25 fractions), 95% planning target volume (PTV) 50 Gy (2 Gy/fx × 25 fractions)

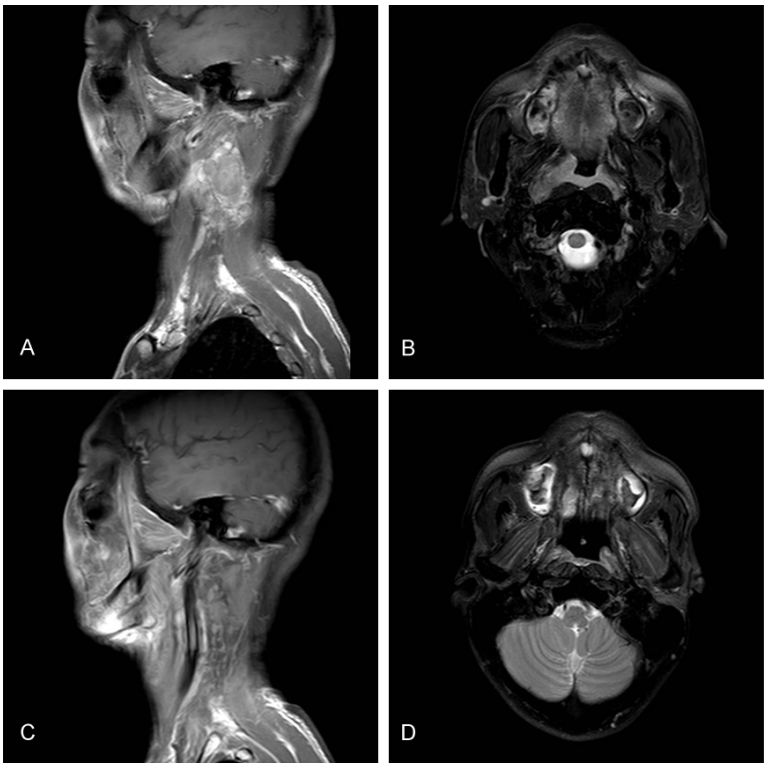


**Figure 1.** MRI scan of head and neck. A, B. Magnetic resonance imaging scan of the head and neck revealed the thickened roof and posterior wall of the nasopharynx, and a mass in the nasopharyngeal cavity, there was an enlarged lymph node measuring approximately 4 cm × 4 cm on the left side of the neck. C, D. The primary tumor had almost disappeared, the enlarged lymph nodes had significantly shrunk or disappeared.

using intensity-modulated radiotherapy. Following completion of chemoradiotherapy, visual observation showed that the primary tumor had almost disappeared, the enlarged lymph nodes had significantly shrank or disappeared which was determined by CT scan of the head and neck. Neither local recurrence nor distant metastasis was found during the 10 months of follow-up after treatment.

## Discussion

Most prevailing carcinoma of head and neck is squamous cell carcinoma, followed by adenocarcinoma [2]. SNEC occurs mainly in lungs, and primary SNEC of the nasopharyngeal cavity is extremely rare and a few number of cases have been previously reported. Because of the aggressive nature, SNEC of the nasopharyngeal cavity has been demonstrated to be characterized by fast tumor expansion, early local recurrence, and widespread metastasis, which lead to a poor prognosis. Distant metastases frequently occur in lungs, liver, and bone [3, 4].

Occasionally, the presenting symptoms of patients with SNEC of the nasopharyngeal cavity is nasal obstruction, rhinorrhea, and recurrent epstaxis, moreover, some patients have facial pain, swelling, and headache, which was also seen in our case. The association between paraneoplastic endocrine syndromes and SNEC is well demonstrated, but they were not present in this case.

Endoscopic findings, imaging studies, and pathologic evaluation of immunohistochemical characteristics play an important role in the diagnosis of SNECs of the nasopharyngeal cavity. The histopathologic features, which are similar in SNEC of all anatomic sites, reveal small round cells with hyperchromatic nuclei and sparse cytoplasm with a high nucleo-cytoplasmic ratio. Immunohistochemically, the tumor is usually strongly positive for synaptophysin, CD56, and CK, but negative for S-100 and neurofilaments. In the present patient, the tumor cells were immunohistochemically positive for (CK), CK8/18, CD56, synaptophysin, and negative for CK5/6, CD20, NSE, and TTF1. Imaging studies, such as CT or MRI can provide information about the extent of local tumor invasion and distant metastasis, which is helpful for primary tumor staging, also can be used for monitor the effects of treatment [5].

Unfortunately, because of the rarity of this tumor, there are no agreements or guidelines for adequate management. Treatment recommendations are generally extrapolated from similar cancers such as SNEC of pulmonary origin. Three mainly therapeutic methods including surgery, radiotherapy and chemotherapy either alone or in combinations are currently used for SNEC of the nasopharyngeal cavity [6]. Since these tumors are considered chemosensitive and radiosensitive, and most of patients

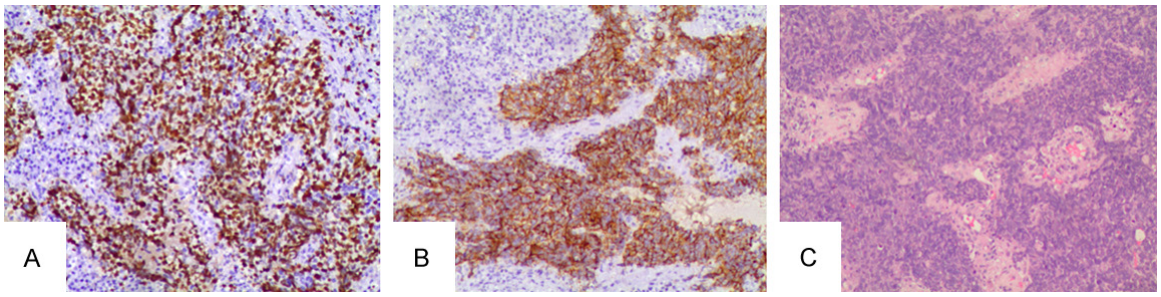


**Figure 2.** Immunohistochemical staining. A. Proliferation index of Ki67 (HE × 100). B. Cell membrane staining of CD56 (HE × 100). C. The neoplastic cells with hyperchromatic nuclei and scanty cytoplasm distribute enlarge expanse (HE × 100).

have no opportunity for surgery because of late discovery, the combination of chemotherapy and radiation therapy is most likely to achieve the most favorable outcome and is thus recommended as the first options for those patients present in an advanced stage. Platinum-based combination chemotherapy was the first-line treatment of choice, and frequently used agents include cyclophosphamide, cisplatin, doxorubicin, vincristine, carboplatin, etoposide, and methotrexate [7, 8].

Because of the characteristics of biological behavior of these tumor, there are high potential risks for local recurrence and distant metastasis to the patients with SNEC of the nasopharyngeal cavity. In a review of literature [9], overall local recurrence rate was 33% and metastasis 31%. The 1- and 5-year survival rate was about 57% and 10%, respectively.

Research on targeted therapy in small cell lung cancer (SCLC) has made progress, and new targeted agents are developing, but currently, there are no targeted agents specific to SNEC.

## Conclusion

Diagnosis and treatment of SNEC of the nasopharyngeal cavity remain a challenge. Further intensive studies are required to develop more personalized treatments in order to improve survival and quality of life of SNEC patients.

## Disclosure of conflict of interest

None.

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