



Autopsy and Case Reports

ISSN: 2236-1960

Hospital Universitário da Universidade de São Paulo

Azevedo, Daniela; Rios, Elisabete; Vendeira, Lurdes; Sarmiento, Cristina
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Autopsy and Case Reports, vol. 7, no. 1, 2017, January-March, pp. 31-35
Hospital Universitário da Universidade de São Paulo

DOI: <https://doi.org/10.4322/acr.2017.002>

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Small cell neuroendocrine carcinoma of the nasopharynx: a rare case report

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Azevedo D, Rios E, Vendeira L, Sarmento C. Small cell neuroendocrine carcinoma of the nasopharynx: a rare case report. *Autopsy Case Rep* [Internet]. 2017;7(1):31-35. <http://dx.doi.org/10.4322/acr.2017.002>

ABSTRACT

Small cell neuroendocrine carcinoma rarely appears primarily in the head and neck and exhibits aggressive behavior with a poor prognosis. The pathologist has a significant role in the diagnosis, and a consensual treatment still does not exist. The authors report the case of a middle-aged male patient who presented repeated episodes of massive epistaxis. The diagnostic work-up disclosed the diagnosis of small cell neuroendocrine carcinoma of the nasopharynx. The patient was treated with chemotherapy followed by radiotherapy. Imaging examinations performed after the end of treatment showed apparent complete remission of the disease. The patient was kept under active surveillance with no signs of local relapse or distant metastasis after 4 years of follow-up.

Keywords

Carcinoma, Small Cell; Neuroendocrine, Carcinoma; Nasopharynx

INTRODUCTION

Small cell neuroendocrine carcinoma is a high-grade tumor that usually presents aggressive behavior. The lungs represent the most common primary site, and extra pulmonary cases comprise only 2.5–5% of the cases,^{1,2} mainly involving the esophagus,³ colon,⁴ urinary bladder,⁵ and cervix.⁶ The involvement of the head and neck structures is even rarer, and in these cases, the larynx is the most frequently involved organ.⁷ Due to its rarity, the diagnosis and treatment are challenging. We present the case of a nasopharyngeal small cell neuroendocrine carcinoma, which, as far as we know, is the ninth case reported in the literature.⁸⁻¹⁵

CASE REPORT

A 54-year-old Caucasian male patient sought medical care complaining of recurrent epistaxis and dysphonia for 2 weeks. He had a history of heavy smoking. Physical examination and laboratory tests were normal. The computed tomography (CT) of the paranasal sinuses revealed the presence of an extensive nasopharyngeal lesion measuring 5 × 6 cm predominantly involving the left side, extending to the nasal fossae, parapharyngeal space, and pterygoid muscles. There was neither intracranial extension nor bone involvement.

A nasofibroscope was performed showing a reddish lesion of the left nasal fossae, which was biopsied.

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The result was inconclusive (esthesioneuroblastoma vs. small cell carcinoma), but another biopsy favored the diagnosis of small cell neuroendocrine carcinoma, confirmed by the immunohistochemical study, which presented diffuse expression of CAM 5.2 and synaptophysin in rare neoplastic cells, in the absence of neuron-specific enolase, chromogranin, and neurofilaments (Figure 1).

The magnetic resonance imaging (MRI) detected the infiltration of the soft palate and confirmed the presence of a tumor in the nasopharynx measuring 6.5 cm at its longest axis; presenting a similar extension observed with the CT.

Clinical staging was II: cT2N0M0 according to the proposal for the 8th edition of the American Joint Committee on Cancer (AJCC)/Union for International Cancer Control (UICC).¹⁶

The patient was treated with primary chemotherapy with carboplatin AUC5 (day 1) and etoposide 100 mg/m² (days 1, 2, and 3) every 21 days. After the end of the fourth cycle of chemotherapy, the patient underwent a planning CT scan (Figure 2) and started radiotherapy receiving a total dose of 70 Gy to the nasopharynx and 60 Gy to the cervical region.

On the second month of follow-up, another pharyngeal MRI was performed, which demonstrated that the pharynx was free of neoplastic lesions and no cervical lymph nodes were enlarged.

A CT scan of the thorax and abdomen was conducted on the sixth month of follow-up, which showed a spiculated pulmonary nodule measuring 16 mm and another nodular lesion in the pancreatic tail, which were tackled by aspiration biopsy. The cytology was inconclusive for the pulmonary nodule, and negative

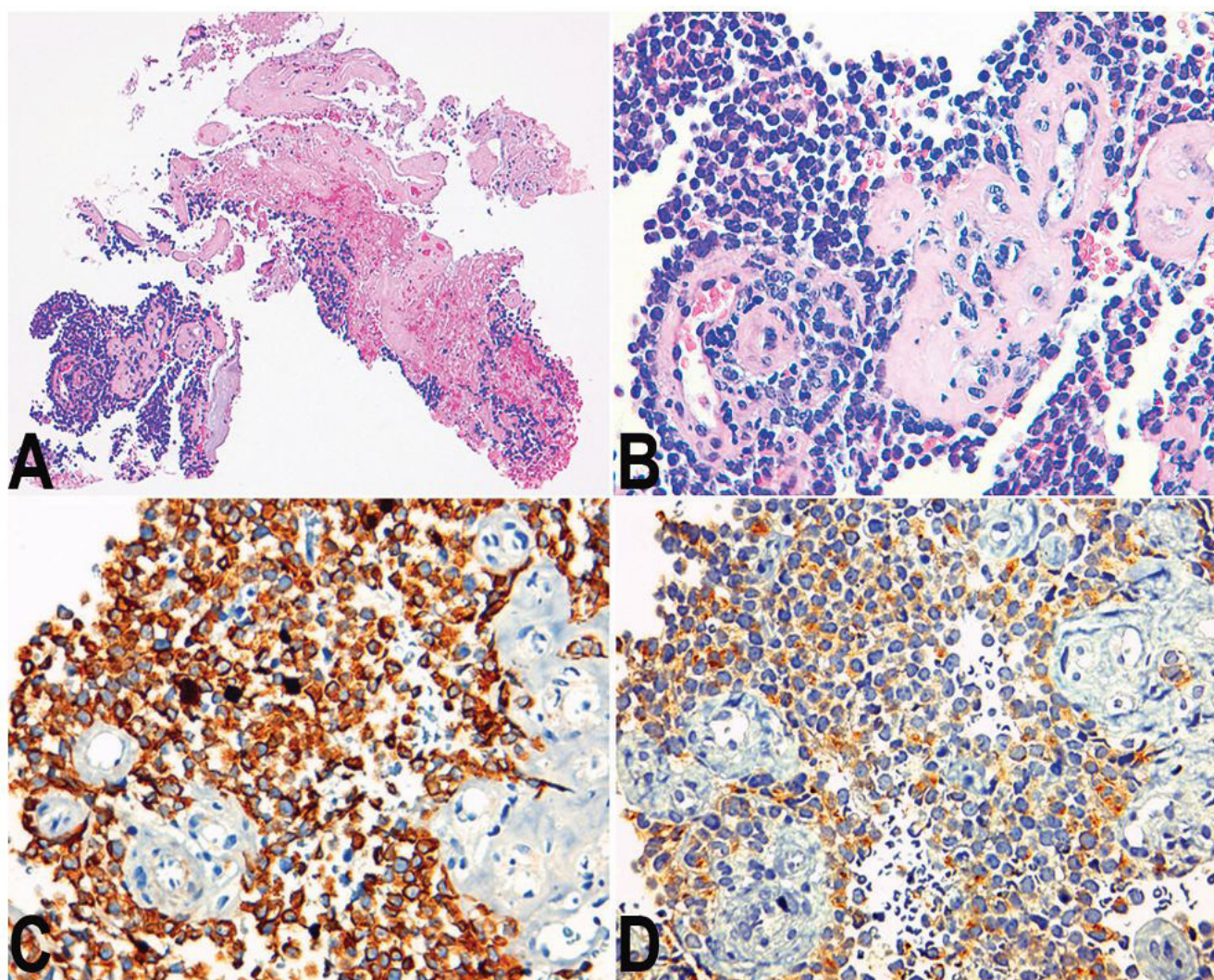


Figure 1. Photomicrography of the biopsy specimen. **A** - Extensive areas of necrosis (H&E, 100X); **B** - Sheets of small cells with high nuclear-cytoplasmic ratio surrounding the vessels (H&E, 400X); **C** - Positivity immunostaining for CAM 5.2 (400X); **D** - Focal positivity for synaptophysin (400X).

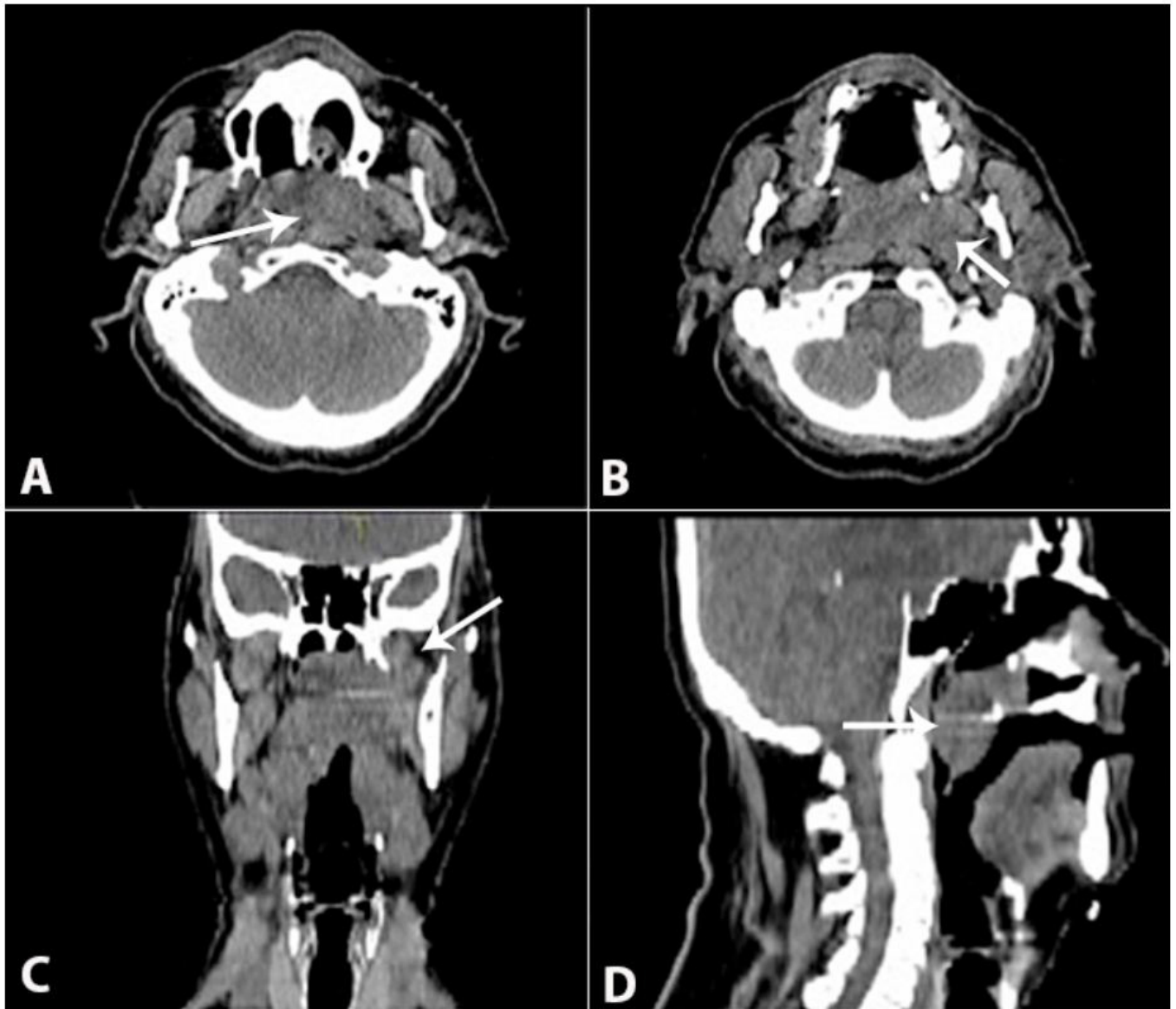


Figure 2. Planning CT scan showing the extensive nasopharyngeal lesion extending to the nasal fossae, parapharyngeal space, and pterygoid muscles, with soft palate invasion. **A and B** - Axial sections; **C** - Coronal section; **D** - Sagittal section.

for malignancy for the pancreatic lesion. The positron emission tomography using ^{18}F -fluorodeoxyglucose (PET- ^{18}F -FDG) revealed the radiotracer uptake (SUV max = 6.96) in two lymph nodes of the pulmonary hilum and another in the subcarinal topography, besides a mild enhancement of the radiotracer uptake (SUV max = 2.33) in the middle pulmonary lobe, both suspected of metastasis. No other sites, namely the pancreas and the nasopharynx, showed abnormal radiotracer concentration consistent with a malignant disease. A transbronchial fine-needle aspiration of the hilar lymph nodes was performed by endobronchial ultrasound, and the cytological examination was

negative for malignancy. Oncologic surveillance was maintained afterward.

DISCUSSION

The neoplasms with neuroendocrine differentiation involving the head and neck structures, including the nasopharynx, are exceedingly rare. The diagnosis of such an entity is challenging because of the morphological characteristics as well as the biopsy sample size, which does not always allow the distinction among other types of neoplasms. The immunohistochemical study has an indispensable central role to confirm the epithelial and

Table 1. Cases of small cell neuroendocrine carcinoma of the nasopharynx by age at diagnosis, gender, treatment and outcome

Case/Reference	Age at diagnosis (years)	Gender	Treatment	Outcome
Lin et al. ⁸	43	M	Induction ChT followed by RT	Died 38 months after diagnosis
Deviprasad et al. ⁹	40	M	Surgery	Died 11 months after surgery
Subha ¹⁰	51	M	Radiotherapy	Relapse after the first month of the end of treatment and died
Lee et al. ¹¹	41	M	Induction ChT followed by CCRT	Remission 9 months after completion of therapy
Shunyu et al. ¹²	52	M	CCRT	—
Takahashi et al. ¹³	54	M	CCRT	Died 32 months after diagnosis
Aguar et al. ¹⁴	43	F	Induction ChT followed by CCRT	Persistence of disease after ending treatment
Bellahammou et al. ¹⁵	46	F	ChT	Died 4 months after diagnosis

CCRT = concomitant chemoradiotherapy; ChT = chemoradiotherapy; F = female; M = male.

neuroendocrine nature of this kind of tumor, which expresses variably cytokeratins (such as CAM 5.2) and neuroendocrine markers like synaptophysin, neuron-specific enolase, chromogranin and CD56.¹⁷ According to the WHO classification, neuroendocrine tumors of the nasal cavity and paranasal sinuses may be divided into typical carcinoid tumors, atypical carcinoid tumors, and small cell neuroendocrine carcinoma.¹⁸ Recently, a new classification for neuroendocrine tumors of the head and neck was proposed and is similar to that of the lung and gastrointestinal tract. This classification divides these tumors into neuroendocrine carcinoma grade 1, grade 2, and large or small cell neuroendocrine carcinoma grade 3, which are based on the morphology, the mitotic index, and the presence or absence of necrosis. According to this classification, small cell neuroendocrine carcinomas present tumor cells with small size, scant cytoplasm, nuclei with finely granular chromatin, inconspicuous or absent nucleoli, a high mitotic rate, and frequent necrosis,¹⁹ which is in line with the case presented herein. The additional expression of CAM 5.2 and synaptophysin, confirmed by immunohistochemistry, endorsed the diagnosis of small cell neuroendocrine carcinoma. As mentioned above, the expression of cytokeratins and neuroendocrine markers may vary among tumors. In the majority of cases, the analysis of the other eight cases reported in the literature showed the expression of chromogranin,^{8,11,14,15} synaptophysin,^{8,11,14} and CD56,^{11,14,15} with only one expressing neuron-specific enolase.⁸

To summarize, small cell neuroendocrine carcinomas of the nasopharynx are high-grade tumors, and therefore convey a poor prognosis.

The therapeutic options for these tumors are varied. However, the treatment of choice is still undefined because only eight cases have been reported in the literature to date (Table 1).

CONCLUSION

Despite the lack of a consensual therapeutic modality, the multimodality approach (chemo and radiotherapy) showed evidence of increment in the survival rate of patients with the diagnosis of sinonasal small cell neuroendocrine carcinoma.^{20,21} In our case, the option of sequential treatment (chemo followed by radiotherapy) was based on the histology type and the tumor size. Despite the poor prognosis of this entity, we verified no evidence of locoregional relapse or distant metastasis at the end of a 4-year period of follow-up.

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Conflict of interest: None

Financial support: None

Submitted on: November 24th, 2016

Accepted on: February 23rd, 2017

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