

# SMALL-CELL NEUROENDOCRINE CARCINOMA OF NASOPHARYNX: A CASE REPORT

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## ABSTRACT

Extrapulmonary small cell carcinomas are extremely rare, accounting for 0.1-0.4% of all malignancies and 2.5-4% of small cell carcinomas. In the head and neck region, the most common primary sites are the larynx, salivary gland, nasal cavity, paranasal sinus, tonsil, and oral cavity. Small cell carcinomas occurring in nasopharynx are exceedingly rare, to our best knowledge, only four cases of primary nasopharyngeal small cell carcinoma have been described in English literature. We report another case of nasopharyngeal small cell carcinoma arising in a 46-year-old woman. She accused, for five months, nasal blockage, right hypacusia, exophthalmos and reduced visual acuity. Cerebral and facial magnetic resonance imaging showed an extensive mass of the nasopharynx with the invasion of the sphenoidal body, the diagnosis of disseminated small cell carcinoma of nasopharynx was established. The patient received three courses of systemic chemotherapy; unfortunately, she died after the third course. The prognosis of such entity is poor and is similar to that for patients with extensive small cell lung cancer.

**KEYWORDS:** nasopharynx, small-cell carcinoma, prognosis

## Introduction

Small cell carcinoma is a distinct clinicopathologic entity that usually arises in the lung, but can also originate from a wide range of extrapulmonary sites. Extrapulmonary small cell carcinomas are extremely rare, accounting for 0.1-0.4% of all malignancies and 2.5-4% of small cell carcinomas [1], these tumors have been described most frequently in the urinary bladder,

prostate, esophagus, stomach, colon and rectum, gallbladder, head and neck, cervix, and skin.

In the head and neck region, the most common primary sites are the larynx, salivary gland, nasal cavity, paranasal sinus, tonsil, and oral cavity [2,3], small cell carcinomas occurring in nasopharynx are extremely rare, to our best knowledge, only four cases have been described in English literature.

Despite a good response to chemotherapy initially, most patients with both pulmonary and extrapulmonary small cell carcinoma develop metastatic disease, and the prognosis is poor. In this article, we report another case of nasopharyngeal small cell carcinoma arising in a 46-year-old woman.

## Case report

A 46-year-old woman accused, for five months, nasal blockage, right hypacusia, exophthalmos and reduced visual acuity, nasal endoscopy cerebral and facial magnetic resonance imaging showed an extensive contrast-enhancing mass involving the nasopharynx and the sphenoidal body with a partial filling of pits choanal (Figure 1).

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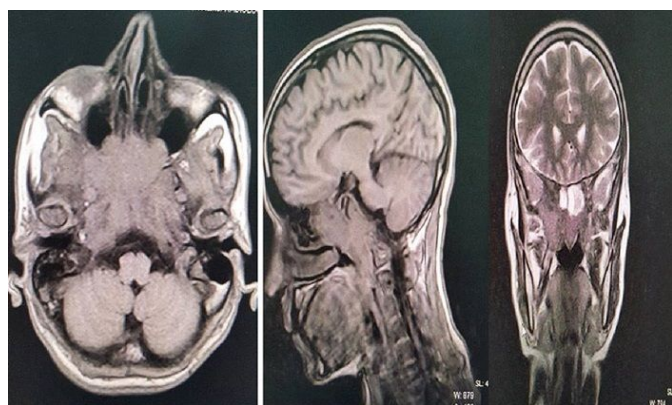
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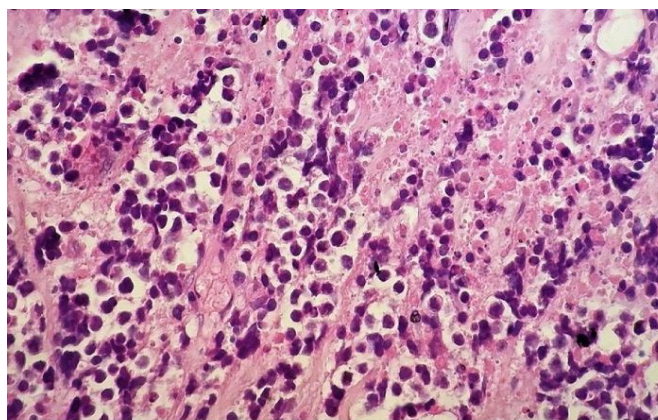
**Table 1** Clinical presentations, treatment, and outcomes of small cell carcinoma of the nasopharynx.

Case/reference	Age /sex	Clinical presentation	Clinical appearance of the tumor	Treatment	Outcomes
Lin et al. [5]	43/M	Pulsating otalgia and odynophagia for 10 months	A soft bulging mass nasopharynx with downward invasion of the soft palate	CCRT	Died 38 months after diagnosis
Li-yu,et al. [6]	41/M	Blood tinged sputum and left hearing loss with tinnitus for 3 months	An irregular left nasopharyngeal mass	CCRT	Remission 9 months after completion of therapy
Deviprasad et al. [7]	40/M	Right-sided nasal obstruction and epistaxis for 18 months	Pinkish globular mass in the nasopharynx	Surgery	Local recurrence and died 11 months after surgery
Shunyu et al. [8]	52/M	Nasal blockage, epistaxis and right-sided aural fullness for 6 months	A nasopharyngeal mass	CCRT	
Our case	46/F	Nasal blockage, hypoacusia, exophthalmos and reduced visual acuity for 5 months	Nasopharyngeal mass with involvement of spheroidal body	CMT	Died 4 months after diagnosis

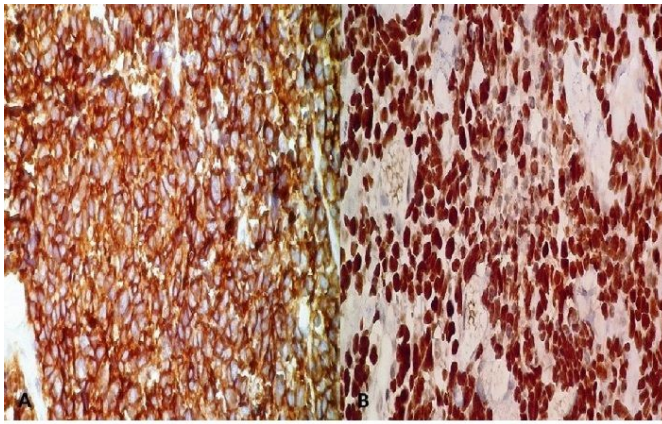
M: Male, F: Female, CCRT: concomitant chemoradiotherapy; CMT: chemotherapy



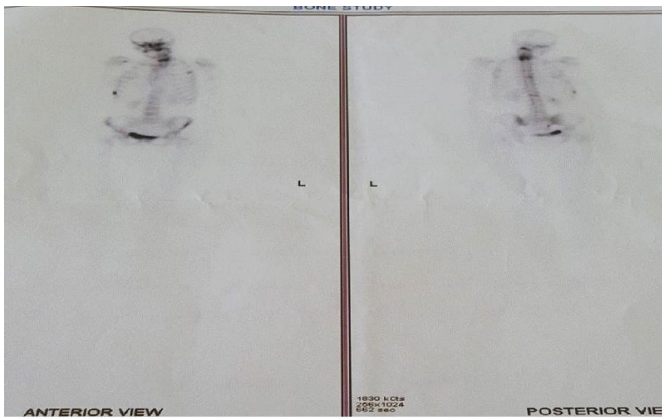
**Fig. 1.** Post gadolinium coronal, sagittal, frontal magnetic resonance images of the face, revealing an extensive mass of nasopharynx invading the sphenoidal body and partial filling of pits channel.



**Fig. 2.** Histologic section is demonstrating small- to medium-sized cells with scanty cytoplasm, nuclear molding, necrosis, and brisk mitosis.



**Fig. 3.** A: Positive immunostaining for CD56. B: The Ki-67 labeling index was 70%.



**Fig. 4.** Scintigraphic images are showing bone metastases in cervical, dorsal (D10), lumbar (L1) vertebrae, 8th right and 4th left ribs.

A biopsy performed, the histological examination with immunocytochemistry analysis revealed a small-cell neuroendocrine carcinoma of the nasopharynx (Chromogranin +, CD 56 +, high Ki67 =70%) (Figure 2, 3A, 3B).

A Thoraco-abdominal, pelvic computed tomography for clinical staging showed bone metastases (cervical, dorsal (D10) and lumbar (L1) vertebrae, 8th right and 4th left ribs) confirmed by bone scintigraphy (Figure 4).

The diagnosis of stage IV small cell carcinoma of nasopharynx established, the patient received systemic chemotherapy based on etoposide (120 mg/m<sup>2</sup> Day 1, 2, 3 plus cisplatin (100 mg/m<sup>2</sup> Day 1) combination every three weeks associated with bisphosphonates, the patient reported a very small clinical benefit after two courses of chemotherapy and a decrease in pain intensity, unfortunately, she died after the third course at her domicile and we couldn't assess the cause of her death.

## Discussion

The current World Health Organization classification of tumors of the head and neck describes three categories of nasopharyngeal carcinoma "non-keratinizing" carcinoma, keratinizing squamous carcinoma, and basaloid squamous carcinoma. The "non-keratinizing" group is divided into differentiated and undifferentiated subtypes [4]. Due to their rarity, neuroendocrine carcinomas of the nasopharynx are not included in this classifica-

tion. In the sinonasal tract (where neuroendocrine carcinoma is also uncommon), these neoplasms can be divided into carcinoid tumor, atypical carcinoid tumor, small cell carcinoma neuroendocrine type, and neuroendocrine carcinoma "not otherwise specified", small cell carcinoma neuroendocrine type is also referred to as small cell carcinoma, oat cell carcinoma, and poorly differentiated neuroendocrine carcinoma. Only four cases of small cell carcinoma occurring in the nasopharynx have been reported in English literature, their clinical features and outcomes including our case are described in Table 1.

The initial clinical features of nasopharyngeal small cell carcinoma, in this case, and the four cases previously described are similar to those of other nasopharyngeal tumors and are due to locoregional disease, also it can present with symptoms from distant metastases or with paraneoplastic syndromes, as occurs with small cell carcinoma in the head and neck region, common sites of metastases include cervical lymph nodes, lung, liver, bone marrow, and vertebrae [9].

Because of its nonspecific clinical and radiological manifestations, small cell carcinoma of the nasopharynx is indistinguishable from other tumors, and the diagnosis is essentially based on the light of microscopic examination aided by immunohistochemical staining, its histopathologic appearance is the same as that of small cell lung carcinoma, generally, it is a high-grade carcinoma composed of small to intermediate sized cells. Necrosis, large numbers of apoptotic cells, high mitotic rate, and lack of neurofibrillary stroma are microscopic hallmarks of these tumors, the most useful neuroendocrine markers include CD56, Chromogranin, and synaptophysin [10]. Because of the rarity of small cell carcinoma of the head and neck region, the initial management of patients with the locoregional disease is patterned after that for other tumor types arising in the same extrapulmonary site. In general, this includes surgery and combined radiotherapy and chemotherapy [11]. Although all data are derived from case reports and no randomized clinical trials, have been conducted. As reported in small cell carcinoma of the larynx, Treatment with surgery may control the primary tumor, but does not offer any chance for cure, radiation therapy was also reported to be equally successful in achieving local control compared to surgery. However, the greatest impact on survival was achieved by systemic chemotherapy. [12-13]

The management of systemic disease with chemotherapy is patterned after the approach used in small cell lung cancer; Various chemotherapeutic combination regimens have been explored in the first-line treatment including cisplatin and etoposide; cyclophosphamide, Adriamycin, and vincristine; adriamycin, cyclophosphamide and etoposide and ifosfamide, carboplatin and etoposide [14].

The prognosis for patients with the disseminated disease is poor despite chemotherapy and is similar to that for patients with extensive small cell lung cancer. In a study of extrapulmonary small cell carcinomas [15], which included seven cases involving the paranasal sinuses, the median survival of 14 patients with primary head and neck small cell carcinomas was only 14.5 months. Follow-up data have shown a local recurrence rate of 45% and a distant metastasis rate of 35%. In another study of small cell carcinoma in head and neck region conducted by YASUMATSU and al. [16] nine patients were included, the median overall survival was 14.5 months, with a three-year survival rate of 23.7%.

## Conclusion

Primary nasopharyngeal small cell carcinoma is a very rare entity, more cases are needed for understanding the clinical behavior of this rare group of tumors, no specific treatment guidelines exist at present, chemotherapy of systemic disease is patterned after the approach used in small cell lung cancer.

## Authors' Statements

### Competing Interests

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

There were no financial support or relationships between the authors and any organization or professional bodies that could pose any conflict of interests.

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