INTRODUCTION

Small cell neuroendocrine carcinoma of the paranasal sinuses was first described by Raychowdhuri in 1965 [10], drawing attention to the resemblance between the lesion and pulmonary small cell carcinoma. We report a case of small cell neuroendocrine carcinoma of ethmoid sinus with invasion of the upper medial aspect of right maxillary sinus and medial aspect of right orbit. The optimal treatment and the immuno-histo-chemical characteristics are discussed.

CASE REPORT

A case of 40-year-old, previously healthy man who smoked a pack of cigarettes daily and drank alcohol on social occasion for 20 years, presented with a two-week history of diplopia, frequent epistaxis and nasal obstruction. Physical examination showed limited movement of right eye to medial aspect but the absence of neck lymphadenopathy. Local examination by an otolaryngologist showed a fleshy mass in the right nostril which was biopsied. Histological examination revealed a tumor co...
sisting of small-sized round to elongated cells with scanty cytoplasm and dark clumped chromatin (Fig. 1). Immuno-histo-chemical characteristics were demonstrated, including the presence of AE1/AE3, CD56, synaptophysin and NSE (neuron specific enolase) (Fig. 2), but the absence of chromogranin. Computed tomography revealed a mass in the ethmoid sinus with extension into the upper medial aspect of right maxillary sinus and medial aspect of right orbit (Fig. 3) but no enlarged lymph node over neck. The patient underwent partial maxillectomy and ethmoidectomy via Weber-Fuggerson approach and adjuvant radiotherapy with 50 Gy in 25 fractions to tumor bed via 3-fields technique, followed by systemic chemotherapy of cyclophosphamide, vincristine and pharmorubicin. Neither local recurrence nor distant metastasis was noted during follow-up of 6 months.

**DISCUSSION**

Malignant tumors arising in the paranasal sinuses account for 0.2 to 0.8% of all cancers. Squamous cell carcinoma is by far the most common malignant tumor, followed by adenocarcinoma, lymphoma, plasma cell tumor, malignant melanoma, esthesioneuroblastoma and sarcoma [9]. Primary small cell neuroendocrine carcinoma of ethmoid sinus is an uncommon and distinctive tumor with an aggressive clinical behavior. There appeared to be a sex predilection based on the primary site: most of the small cell neuroendocrine carcinoma of head and neck region were found in male subjects. A history of tobacco use was common, particularly in tumors that occurred in the head and neck region, but there was not as strong an association with smoking as there was with pulmonary small cell carcinoma [8].

Small cell neuroendocrine carcinoma is similar to those tumors in lung, composed of
small to intermediate-sized cells with a high nucleo/cytoplasmic ratio. Nuclei are round to oval and hyperchromatic, and contain dense or finely granular chromatin. The cytoplasm is scanty to moderate, has a pale eosinophilic or amphophilic quality and possesses poorly defined cell borders. The immuno-histochemical features of these tumors were investigated in some studies. In the report by Bayardo et al, the expression of neuroendocrine markers such as neuron specific enolase (NSE), synaptophysin and chromogranin, although positive in all cases, was variable and might be focally weak with individual markers. All of the cases showed strong diffuse staining for Cam 5.2 or AE1/AE3. S-100 and neurofilaments were negative in all cases [1].

The clinical features of small cell neuroendocrine carcinoma are nonspecific and similar to those of other sinonasal tumors [3]. Tumor may appear initially as a subcutaneous nodule in the inner canthus. The other common symptoms are epistaxis, diplopia, proptosis, pain and nasal obstruction. Paraneoplastic syndromes due to the ectopic production of adrenocorticotrophic hormone (ACTH) and antidiuretic hormone also occur. Kameya et al. reported increased levels of adrenocorticotrophic hormone (ACTH) and calcitonin in two of their patients [6] but the clinical evidence of endocrine overactivity was rarely detected. Extrapulmonary small cell neuroendocrine carcinomas can disseminate widely. Limited disease is defined as tumor confined to the organ of origin and the local regional nodes that are encompassable within a radiation portal. Tumors that have spread beyond one radiation portal are defined as extensive. In contrast to small cell lung cancer, most patients in whom an extrapulmonary primary site is identified have limited disease at the time of diagnosis. In a series of 71 patients from the Mayo Clinic, 76% of the tumors were localized at diagnosis [4]. However, invasion of adjacent structures is common and has been found in most cases because the bony partitions between the nasal cavity, sinuses, orbit and cranial vault are quite thin and offer little resistance to cancer spread.

Extrapulmonary small cell neuroendocrine carcinoma is usually a fatal disease with a 13% 5-year survival rate [4]. In the study of extrapulmonary small cell carcinoma from Mayo Clinic, the median survival of fourteen patients with head and neck tumors was around 14 months [4]. The need for a multi-disciplinary treatment approach is indicated in treating these aggressive tumors. For most ethmoid sinus tumors, if they are resectable, surgery is usually performed first; post-operative irradiation is advised, even if resection margins are negative [5]. But for patients with locoregional small cell neuroendocrine carcinoma, the combination of chemotherapy and radiotherapy is a reasonable alternative to surgery [8]. Chemotherapy may well have a more prominent role in the management of the small cell neuroendocrine carcinoma whose morphological and immuno-histochemical features are similar to those of pulmonary small cell carcinoma. Despite the small numbers of cases reported and the various treatment modalities used, some suggestions regarding treatment options were made. Surgery or radiotherapy and adjuvant chemotherapy with a platinum-based regimen may be used with curative intent in patients with limited local disease. It is mandatory to use a platinum-based chemotherapeutic regimen for the control of systemic relapses. Twenty seven percent of the patients in the combined experience of Koss et al, Weiss et al and Bayardo et al. developed distant metastasis [7,11,1]. Galanis et al reported an 80% incidence of distant failure and a median time of relapse of 10 months for those patients with para-nasal tumors treated with surgery alone [4]. In the report of Bhattacharyya et al, the use of combined cisplatin and etoposide chemotherapy with proton radiation demonstrated initial success in treatment of these tumors [2]. This protocol had an accept-
able complication rate and conveyed less morbidity than craniofacial resection and conventional radiotherapy and further follow-up is required to determine the long-term success rate of this therapeutic protocol.

**CONCLUSION**

Small cell neuroendocrine carcinoma of ethmoid sinus is rare. Few studies have reported some experience with malignant tumors in this location or other para-nasal sinuses. The best outcome was achieved by early diagnosis and by aggressive multi-disciplinary approach.

**REFERENCES**

小细胞神经内分泌癌：病例报告及文献回顾

林逢嘉  林立青  蘇正川  林奎利  郭珍妮

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副鼻窦恶性肿瘤占人类所有恶性肿瘤的0.2到0.8%。鳞状细胞癌是最常见的组织型态，原发小细胞神经内分泌癌是一罕见且恶性之肿瘤，其组织型态及免疫化学染色特征与肺小细胞癌相似；临床上需并用手术或放射治疗及化学治疗等方式处理。

我们报告一位原发小细胞神经内分泌癌的病例，肿瘤侵犯至右眼窝内侧及上颌鼻窦腔；于肿瘤摘除手术后辅以放射治疗及化学治疗。追踪至今约六个月，无局部复发或远处转移情况发生。文中另探讨小细胞神经内分泌癌之最佳处理模式及其免疫化学染色特征。

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关键词：小细胞神经内分泌癌，筛骨腔，放射治疗