Small cell neuroendocrine carcinoma of nose and paranasal sinuses: a study of three cases with short review of the literature

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Abstract Primary small cell neuroendocrine carcinoma (SNEC) of nose and paranasal sinuses is an extremely rare malignant tumour known for its aggressive clinical course, high rate of recurrence and poor prognosis. Only 69 cases have been reported in world literature till March, 2006. This tumour usually occurs in elderly persons with main complaints being nasal obstruction, epistaxis, loss of visual acuity, exophthalmos, local pain and rarely tender swelling over the sinuses. Computerized tomography scan (CT) is essential to assess the size, extent of the tumour, evidence of bone destruction and infiltration to orbit and brain. Due to its rarity, the understanding of pathogenesis of the disease, diagnosis and ideal treatment have been difficult. The origin of the tumour is believed from basal cells of the olfactory mucosa. The present study deals with three cases of SNECs of nose and paranasal sinuses in elderly males, their clinical presentations, CT scan findings, histopathological diagnosis with short review of literature.

Keywords Small cell neuroendocrine carcinoma · Nose · Paranasal sinuses

Introduction

Small cell neuroendocrine carcinoma (SNEC) of head and neck is very rare and has been reported only since 1965 [1, 2]. Due to its rarity the understanding of pathology of the disease and planning for ideal treatment have been difficult. Review of literature shows that till March, 2006 less than 270 cases of head neck SNEC have been published including 69 cases of SNEC in the nasal and paranasal cavities [3] From January, 1995 till December 2007 three cases of SNEC of nose and paranasal sinuses were encountered. In the present study the clinical presentations, imaging studies, histopathological diagnosis, treatment protocol and short review of literature of this rare tumour is discussed.

Materials and methods

From January 1995 till December 2007 out of total number of 576 biopsies from nose and paranasal sinuses only three cases of SNEC were encountered. All the patients were elderly males of more than 62 years of age. The patients presented with nasal obstruction, epistaxis, pain over maxillary and frontal sinuses, headache and visual disturbances. One patient had a large tender swelling in frontonasal region. (Fig. 1). All the three patients had undergone computed tomography (CT) scanning but primary tumour localization was difficult because of considerable spread of disease at the time of diagnosis. In all the three patients extension of the tumour from nose and paranasal sinuses with infiltration to orbit and brain were evident in the CT scan (Fig. 2). The patient with frontonasal swelling showed extensive bone destruction with infiltration in the surrounding soft tissue and skin by the malignant tumour. None of the patients presented with paraneoplastic endocrine syndrome. X Ray chest did not show any evidence of metastasis. Multiple friable blackish white tumour tissues were obtained in all the cases. Hematoxylin and eosin (H&E) stained sections revealed sheets and cords of small cells (Fig. 3a). The cells

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have little cytoplasm having large, pleomorphic nuclei varying in appearances from densely hyperchromatic to that of a punctate chromatin distribution. Mitotic features

Fig. 1 Clinical photograph showing a large frontonasal mass in an elderly male

Fig. 2 CT Scan (coronal cut) showing a large tumour involving nasal cavity and paranasal sinuses with destruction of bones and infiltration to orbit and brain

and scattered areas of necrosis having the typical crush artefact of neoplastic cells were seen in the sections (Fig. 3B). As H&E staining was not sufficient to establish diagnosis of SNEC [4], help of immunohistochemistry was taken for confirmation. The malignant cells showed neuroendocrine differentiation as evidenced by strong positivity with chromogranin (Fig. 4) and synaptophysin. As the patients had advanced malignancies with infiltration to orbit and brain, radiotherapy and chemotherapy were advised in all the three patients. However the patients refused further treatment.

Discussion

Small cell neuroendocrine carcinomas are mainly located in the lungs. Extrapulmonary SNEC represents 4 percent of all SNECs [1]. Less than 270 cases of head and neck SNEC have been published till March, 2006 including 69 cases of SNEC in nasal and paranasal sinuses in world literature [3].

Fig. 3 (a) Photomicrograph of neuroendocrine carcinoma showing sheets of small cells. (Stain- Hematoxylin and Eosin; Magnification X400). (b) Photomicrograph of neuroendocrine carcinoma showing areas of necrosis and typical crush artifact of neoplastic cells. (Stain- Hematoxylin and Eosin; Magnification X100)

Fig. 4 Photomicrograph of immunohistochemical staining for neuroendocrine carcinoma showing strong immunoreactivity for chromogranin. (Magnification X400)

Neuroendocrine tumours are classified by several authors as follows [5]. Carcinoid tumours are commonly considered to be well differentiated neuroendocrine carcinomas whereas atypical carcinoid tumours are regarded as moderately differentiated neuroendocrine carcinomas and SNECs are classified as poorly differentiated neuroendocrine carcinomas. These cells contain membrane bound granules in the cytoplasm which can be demonstrated by Grimelius stain [4], electron microscopy [6] and their endocrine differentiation can be demonstrated by immunohistochemistry [4, 7]. The tumour cells originate from the basal cells in the olfactory mucosa [8].

No particular risk factor for this tumour occurring in elderly patients has been identified [9]. The clinical signs are non-specific. The most frequent are rhinological syndrome, ophthalmic signs and other signs suggesting loco-regional invasion [10]. Metastatic cervical lymph nodes have also been described [10]. The main rhinological symptoms are nasal obstruction, rhinorrhoea and epistaxis. The ophthalmic signs include exophthalmos, loss of visual acuity and limitation of eye mobility while the locoregional invasion can be suspected in presence of local pain, anosmia or any tender swelling over the nose or paranasal sinuses. CT scan can reveal signs of malignancy in presence of bone destruction, extensive spread of growth with erosion of meninges and infiltration in brain [11]. In spite of advanced imaging techniques the initial localization of the tumour is rarely precise, usually because of late discovery [11].

For staging of neuroendocrine tumours of sinonasal tract, the Kadish staging system is often used [8]. Accordingly the tumours are reported as stage-A (tumours limited to nasal cavity), stage-B (tumours localized in the nasal cavity and paranasal sinuses) and stage-C (tumours extending beyond nasal cavity and paranasal sinuses). In the present study all the three patients were in advanced stage-C. Recently new sinonasal staging system proposed by the sixth edition of

the American Joint Committee on Cancer (AJCC) staging manual had been published [12]. Whatever may be the staging system, the three patients in the present study had advanced malignancies due to infiltration in the orbit and brain with gross destruction of bones.

The association between the paraneoplastic endocrine syndrome and SNEC is well documented [4]. None of the three patients had any endocrine syndrome which is rare in SNECs of head and neck. Review of literature shows only in 5 cases of SNECs of nasal and paranasal sinuses endocrine syndromes have been described [4].

Three therapeutic methods are currently used to treat SNEC of nose and paranasal sinuses. Surgery, radiotherapy and chemotherapy either alone or in combinations are used by various ENT and head and neck oncologists [9]. The treatment of SNECs has varied considerably over time. A group of oncologists favoured surgery followed by radiotherapy [13]. However more recent studies have claimed that neoadjuvant chemotherapy with cisplatin and etoposide and high dose proton-photon radiotherapy is a successful treatment approach for patients with SNECs [14]. Review of literature shows that in spite of advances in therapy most of the patients had recurrences or metastases with median survival rate between two and three years [3]. The three patients in the present study had extremely poor prognosis due to orbit and brain involvement. Moreover they refused any treatment after the diagnosis.

In conclusion nasal and paranasal SNECs are very rare highly aggressive tumours with high incidence of recurrence, metastasis and poor prognosis. More extensive studies are required to assess their detail malignant potential including a more rational standard treatment protocol.

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