Small Cell Neuroendocrine Tumor of Base of Tongue - Treatment Strategies of A Rare Entity

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ABSTRACT
Neuroendocrine tumors are rare in head and neck region, while larynx is the most common site of presentation where they represent 0.5-1.0% of epithelial tumor, whereas only few cases of small cell neuroendocrine tumor of base of tongue has been reported so far. A 56-year old male presented with growth base of tongue. After thorough investigations the growth confirmed as a case of poorly differentiated high grade small cell neuroendocrine carcinoma and was clinically labeled as stage III (T3N0M0). The patient was treated with radiotherapy and combination chemotherapy. Presently the patient is having stable disease without any symptoms.

Keywords: Neuroendocrine Tumor, Radiotherapy, Chemotherapy, Head and neck Tumor, Base of tongue tumors.

INTRODUCTION
Neuroendocrine tumors are well known clinicopathological entities that mainly occur in lungs. Extra pulmonary small cell neuroendocrine tumors represent about 2.5% (1). The head and neck region is uncommon site for occurrence of NET. Larynx is the most common site of presentation where they represent 0.5-1.0% of epithelial tumor (2). The base of tongue neuroendocrine carcinoma is extremely rare. Only infinitesimal number of cases has been reported so far in base of tongue. The appropriate treatment protocols and therapeutic regimens are not defined due to rarity of these tumors.

CASE REPORT
A 56-year old smoker male presented with complaints of pain during swallowing. There were no complaints of fever, cough, weight loss and appetite loss. Past and personal histories were unremarkable. General and physical examination were within normal limits. No lymph nodes were palpable in cervical, axillary or other parts of body. On local examination there was a palpable growth over right side base of tongue of 3x3 cm size, not crossing midline. Tongue mobility was normal. Complete hemogram, serum biochemistry, chest skiagram and Ultrasound abdomen and pelvis were normal. Biopsy from the tumor site confirmed it to be a case of poorly differentiated high grade small cell neuroendocrine carcinoma.

Figure 1A: Photomicrograph showing sheets, Nests and groups of small cells revealing neuroendocrine differentiation. H&E 200X
Diagnosis confirmed by histopathological appearance and immunohistochemical profile (Figure 1A-B). CECT Chest and abdomen did not show any abnormality in lungs or any other site. Then the patient finally diagnosed to having Primary small cell high grade (Poorly differentiated) neuroendocrine tumor of base of tongue and was clinically labeled as stage III (T3N0M0).

**TREATMENT SUMMARY**

The patient was initially given three weekly intravenous chemotherapy with vincristine, doxorubicin and cyclophosphamide (VAC) and after 3 courses there was partial response but patient developed grade II neutropenia.

Then patient was given External Beam Radical Radiotherapy (66Gy/33 fraction/6.3 weeks). The patient was having no evidence of disease after four months of follow-up but subsequently he developed recurrence in form of growth over base of tongue, 2x3cm in size. CECT revealed enhancing soft tissue growth over right side base of tongue (Figure 2A & 2B)

In view of the poor response and hematological toxicity subsequent to VAC regimen, patient was switched over to three weekly intravenous chemotherapy with carboplatin and Etoposide. Patient again developed grade II neutropenia and in view of the same, injectable etoposide was replaced by oral etoposide. Even with oral etoposide, patient developed grade II neutropenia but local disease was non progressive during this phase except few small lymph nodes, which were seen in right cervical region on CECT.

Due to hematological toxicity and the appearance of lymph nodes, the patient was switched to single agent weekly Paclitaxel. Presently the patient is having non progression of disease till now.

**DISCUSSION**

Neuroendocrine tumors are heterogeneous family of neoplasms with differences in histomorphology, tissue origin, clinical behavior and therapeutics implications. They are known to be clinically aggressive with early dissemination to neighboring organs and lymph nodes, and largely resistant to therapy.

The diagnosis of NET has remained a histological one: therefore the detailed pathologic examination and immunohistochemistry is necessary for establishment of diagnosis.
The World Health Organization (WHO) classification classify neuroendocrine tumors into three main categories (3,4):  
- Well-differentiated neuroendocrine tumors, further subdivided into tumors with benign and those with uncertain behavior  
- Well-differentiated (low grade) neuroendocrine carcinomas with low-grade malignant behavior  
- Poorly differentiated (high grade) neuroendocrine carcinomas, which are the large cell neuroendocrine and small cell carcinomas.

The appropriate treatment protocols and therapeutic regimens are not defined due to rarity of these tumors. However, therapeutic modalities indicated for poorly differentiated NEC include surgery, combination chemotherapy and radiotherapy.

In present case the patient was first given Combination chemotherapy with VAC regimen and experienced partial response with grade II neutropenia. Patient remained disease free after radical radiotherapy for only four months.

However small cell NEC are considered relative chemo sensitive tumors but in present case with standard chemotherapy regimen (carboplatin and Etoposide) for small cell lung cancer patient disease remain stable. Moreover, patient developed grade II hematological toxicity with both regimens. After that patient switched over to weekly Paclitaxel keeping in view of symptoms, performance status and toxicity experienced with previous regimens.

Latif N et al reported a case of limited stage primary small cell carcinoma of the tongue and claimed it to be the first case in the literature. They treated the case with cisplatin and Etoposide chemotherapy concomitant with radiation and observed excellent response (5). But in present case the patient had stable disease with all regimens. This case highlights more aggressive and recurrent behavior and relative radioreistant nature of the tumor.

Key Message: In NET treatment protocols and therapeutic regimens are not defined due to rarity of these tumors. NECs are having aggressive behavior and carries poor prognosis. Chemo radiotherapy is indicated as the treatment of choice for poorly differentiated NET. It is important to report single institution experiences of rare cases such as NET of Base of Tongue, to predict behavior, forming a consensus on the treatment and its outcomes.

REFERENCES