

# Small cell neuroendocrine carcinoma of buccal mucosa: Innocuous but invasive

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## Abstract

Small cell neuroendocrine carcinoma (SNEC) was first described in the 19<sup>th</sup> century which is usually seen in association with lung cancer and is very rare in the oral cavity. Here, we report one such case in a 39-year-old male patient who presented with swelling on the left middle third of the face for 6 months. This is the 12<sup>th</sup> SNEC of oral cavity case so far reported in the English literature and the third case to be present on buccal mucosa. It presented as a nodular swelling over the buccal mucosa and was clinically diagnosed as a traumatic fibroma. The histopathological sections showed diffuse sheets of round cells with granular chromatin. Immunohistochemical findings helped us arrive at a final diagnosis. SNECs are highly proliferative tumors characterized by early and widespread metastases through the vascular channels. Hence, the diagnosis and appropriate management of these lesions is important to decrease the morbidity and mortality rate.

**Keywords:** Lung carcinoma, small cell neuroendocrine carcinoma, traumatic fibroma

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## INTRODUCTION

Small cell neuroendocrine carcinoma (SNEC) is a poorly differentiated and a high-grade tumor that occurs most commonly in lungs.<sup>[1]</sup> It is an aggressive malignant neoplasm with regional and distant metastasis. Extrapulmonary SNECs account for 2.5%–5% of all SNECs among which head-and-neck SNECs contribute to 10%–15% and they tend to arise in different structures of head-and-neck region.<sup>[2]</sup> Among these, larynx is the most common site, followed by the salivary glands and sinonasal region.<sup>[3]</sup>

To the best of our knowledge, 12 cases of primary SNECs occurring in the oral cavity have been reported in the

English literature.<sup>[1]</sup> They have predominantly occurred on the tongue, with two cases reporting on buccal mucosa. Here, we report a rare case of SNEC on the left buccal mucosa.

## CASE REPORT

A 39-year-old male came to the Outpatient Department of Government Dental College and Hospital, Hyderabad, with a chief complaint of swelling on the left middle third of the face for 6 months. The patient developed swelling on the left cheek region which was initially small in size with a gradual increase to the present size and was not associated with pain.

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On extraoral examination, a diffuse swelling was noticed on the left middle third of the face measuring approximately 5 cm × 4 cm in size leading to mild facial asymmetry. Superoinferiorly, the swelling extended from the infraorbital rim to the line joining ala of nose and ear lobule. Anteroposteriorly, it extended 2 cm from ala of the nose to the tragus of the ear. A single submandibular lymph node was palpable which was mobile, tender and soft to firm in consistency. The swelling was firm and nontender on palpation with no local rise in temperature.

Intraorally, a solitary swelling was seen on the left buccal mucosa measuring approximately 3 cm × 3 cm, slightly erythematous in color with white pebbled surface. Anteroposteriorly, it extended on the buccal mucosa from the distal aspect of 24–28 region [Figure 1]. On palpation, the swelling was nontender and firm in consistency. It was clinically diagnosed as traumatic fibroma, and thus, no imaging techniques were advised. An incisional biopsy was performed and sent for histological evaluation.

On macroscopic examination, a single soft-tissue bit was received, which was creamish brown in color measuring about 1.0 cm × 1.0 cm and firm in consistency [Figure 2]. The tissue was sent for routine histological processing.

Microscopically, the hematoxylin and eosin (H&E)-stained sections showed a highly cellular connective tissue stroma with nests and sheets of small round-to-ovoid cells with ill-defined borders, scanty cytoplasm and finely granular nuclear chromatin [Figure 3]. Surrounding these cells, numerous foci of spindle-shaped cells with pleomorphic, hyperchromatic nuclei and inconspicuous nucleoli were evident [Figures 4-6]. The tumor cells showed increased mitoses (2–3 per five high-power field) intermixed with



**Figure 1:** Intraoral picture showing swelling on the left buccal mucosa with white and pebbled surface

foci of necrosis and hemorrhage. The connective tissue surrounding the cells was dense with collagen fiber bundles.

With the above H&E findings, a diagnosis of poorly differentiated round cell tumor was made. The histological differential diagnoses included were lymphoma, neuroendocrine carcinoma (NEC), melanoma and Merkel cell carcinoma.

Immunohistochemical analyses were performed on a panel of markers to arrive at a final diagnosis which included CD45, CD56, CK20, CK8/18 and S-100. The analysis revealed strong and moderate positive expression to CK 8/18, CD56, respectively, and negative to CK20, CD45 and S-100 [Figures 7-10]. With these histopathological findings and immunohistochemical analyses, a definite and final diagnosis of SNEC of the buccal mucosa was made.

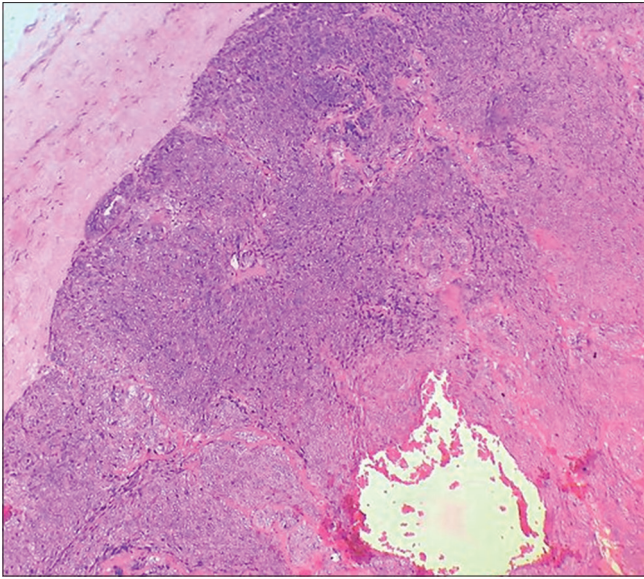
## DISCUSSION

NEC is a poorly differentiated and aggressive carcinoma commonly occurring in the lungs with rare occurrence in nonpulmonary (head and neck, mucosal and salivary gland) areas. It has well-defined clinicopathologic and immunohistochemical characteristics and are characterized by the presence of secretory granules and peptide substances.<sup>[4]</sup> The World Health Organization (2017) has classified NECs into three categories: well, moderate and poorly differentiated which, in turn, is divided into two subtypes - small cell and large cell types,<sup>[5]</sup> whereas the primary NEC occurring in the oral cavity has been classified into typical carcinoid, atypical carcinoid, large cell and small cell NEC. The SNEC is known by other terminologies such as “small-cell carcinoma,” “oat cell carcinoma” and “anaplastic small cell carcinoma.”<sup>[6]</sup>

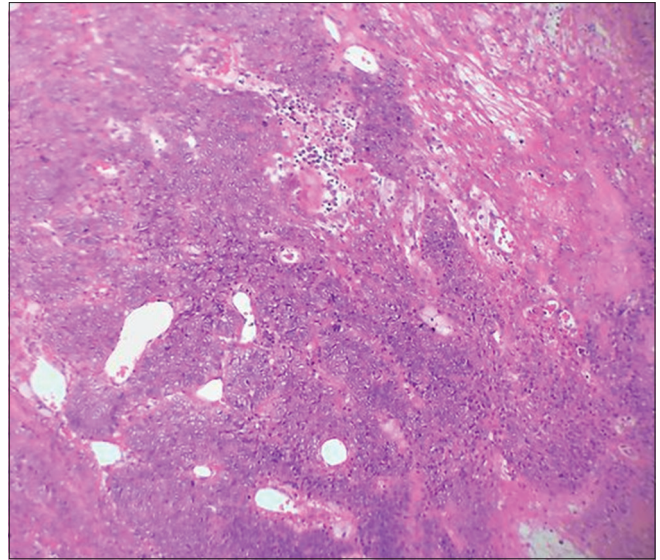
Oral SNECs occur in the age group of 40–83 years (average of 67.5 years). In the present



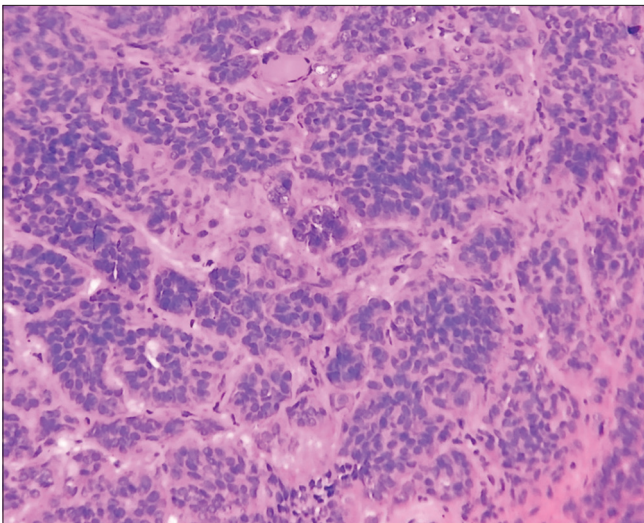
**Figure 2:** Macroscopic picture showing single creamish brown soft-tissue bit measuring about 1.0 cm × 1.0 cm



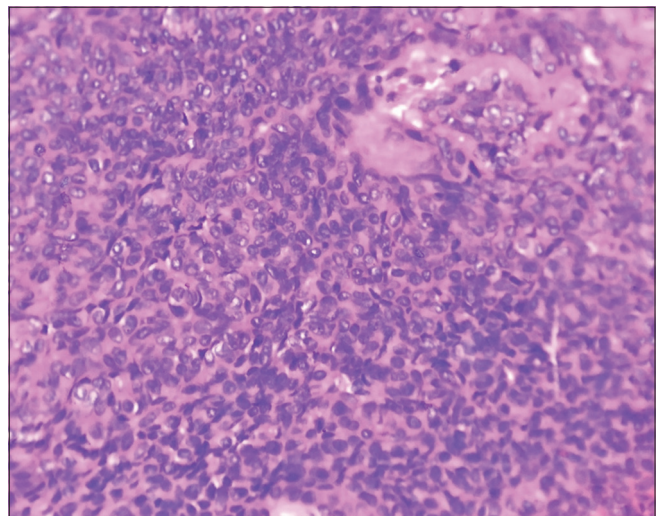
**Figure 3:** Photomicrograph showing sheets and nests of round cells with surrounding capsular tissue (H&E, x4)



**Figure 4:** Photomicrograph showing small cells with ill-defined borders surrounded by oval-to-spindle-shaped cells with pleomorphism (H&E, x10)



**Figure 5:** Photomicrograph showing nests of round-to-oval small cells with hyperchromatic nucleus and pleomorphism (H&E, x40)



**Figure 6:** Photomicrograph showing cells with ill-defined borders, scanty cytoplasm and finely granular nuclear chromatin (H&E, x40)

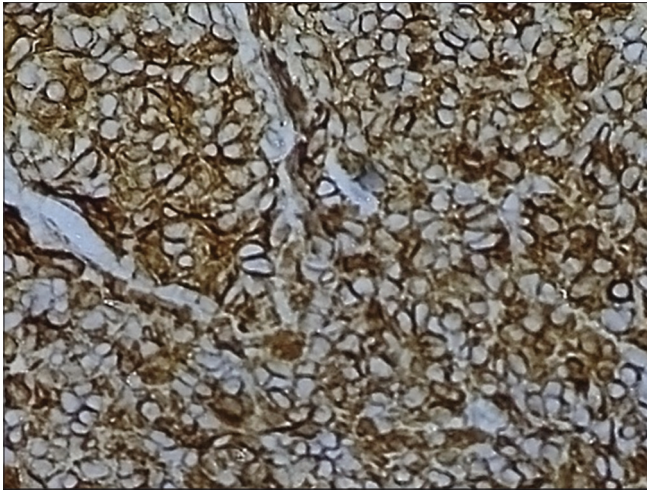
case, the patient was a 39-year-old which is similar to the case reported by Esmati *et al.*<sup>[4]</sup> Both pulmonary NECs and SNECs of oral cavity occur commonly in males (81.8%) than in females which is comparable to our current case.<sup>[1]</sup>

The most common risk factors for SNEC include smoking and alcohol consumption as per the cases reported till date.<sup>[7]</sup> On the contrary, the patient in the present case had no history of tobacco smoking but consume alcohol occasionally.

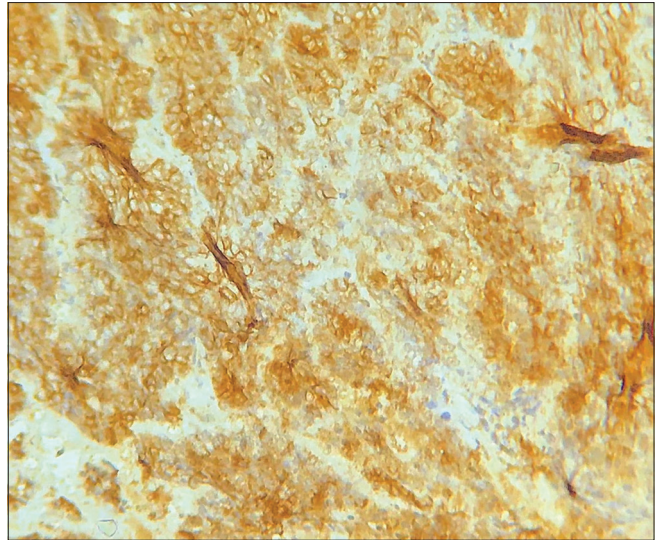
The sites commonly involved in the oral cavity are tongue (64%), gingiva (9%) and buccal mucosa (18%).<sup>[1]</sup> In

the present case, the lesion has occurred on the left buccal mucosa which is one of the rare sites of involvement reported so far.

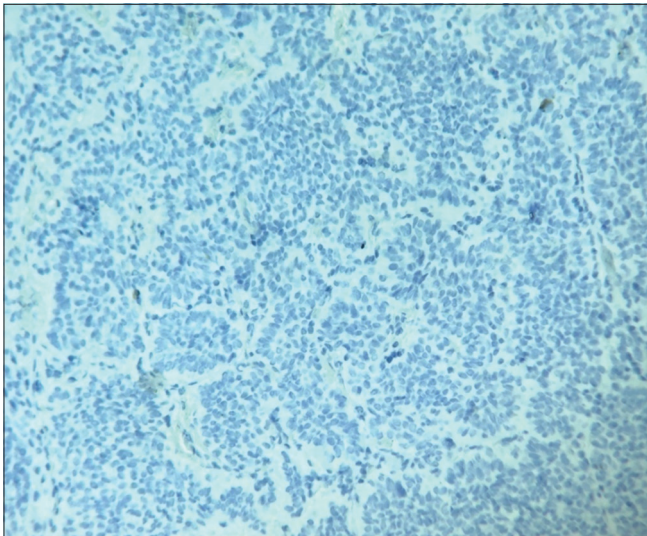
The histopathological features of our case are similar to those of classic small-cell carcinoma, consisting of tightly packed round-to-ovoid cells, small in size with scanty eosinophilic cytoplasm, hyperchromatic nuclei with fine granular chromatin and inconspicuous nucleoli.<sup>[8]</sup> The tumor cells were arranged in nests and sheets with frequently occurring mitotic figures and areas of necrosis. On considering these findings, a provisional histological diagnosis of poorly differentiated round cell tumor was given.



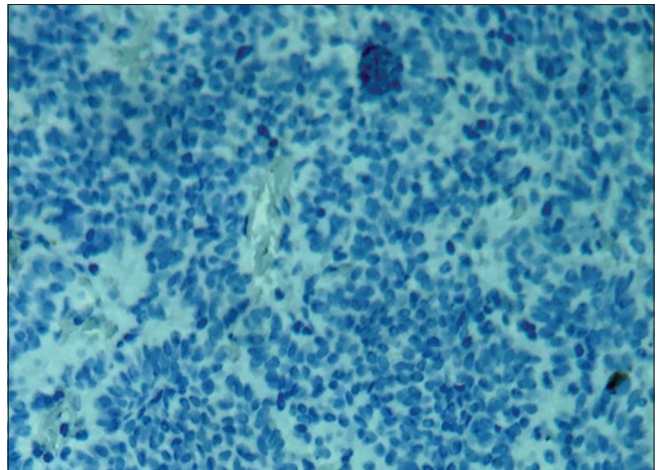
**Figure 7:** Photomicrograph showing tumor cells with uniform and strong membranous positivity to CK8/18 (immunohistochemistry x40)



**Figure 8:** Photomicrograph showing tumor cells with uniform and moderate positivity to CD56 ((immunohistochemistry x10)



**Figure 9:** Photomicrograph showing tumor cells with negative expression to CK20 ((immunohistochemistry x10)



**Figure 10:** Photomicrograph showing tumor cells with negative expression to CD45 ((immunohistochemistry x10)

Immunodiagnosis was done using a panel of markers where the tumor cells showed moderate positive expression to CD56 which is a neural cell adhesion molecule and an integral membrane glycoprotein indicating the neuroendocrine differentiation of tumor cells. Furthermore, the cells showed strong positive expression to CK8/18 which is a low molecular weight cytokeratin ascertaining the epithelial origin of the tumor cells.

As the lesion was negative for CD45 (common leukocyte antigen), the diagnosis of lymphoma was ruled out. Even S-100 immunomarker was negative excluding melanoma from the diagnosis. Negative expression of tumor cells to CK20 which is a major cellular protein and specific for Merkel cells helped us to rule out Merkel cell carcinoma.

Since SNECs are highly aggressive in nature with distant metastasis, they are more effectively treated by a multimodality approach.<sup>[9]</sup> In localized SNEC of the oral cavity, surgical excision with postoperative chemotherapy or radiation therapy is usually considered as an effective treatment, whereas chemotherapy is the mainstay of treatment for metastatic high-grade head-and-neck NECs as found by Barker *et al.*<sup>[10,11]</sup> In our case, the patient was referred to a cancer institute for further treatment which included surgery followed by chemotherapy and radiotherapy. The patient was under regular follow-up for 1 year every 2 months and no recurrences were observed. The prognosis of SNECs of head and neck is unpredictable. Majority of cases showed a very poor prognosis with high metastatic potential.<sup>[12]</sup> The study conducted by Baugh *et al.* has shown a median survival rate of 19 months in

patients who received chemotherapy whereas 11 months in those who did not receive any chemotherapy.<sup>[13]</sup> The site of primary tumor may also be prognostically important as reported by Hatoum *et al.* They found that SNECs arising from salivary glands have a better prognosis when compared to other areas in the head-and-neck region.<sup>[14]</sup>

## CONCLUSION

Primary SNEC of the oral cavity is very rare with only limited number of cases published so far. The present case reported on buccal mucosa is the third such case to be published in the English literature. The overall prognosis remains poor owing to rarity of these tumors in the head-and-neck region, with lower survival rates and no definite treatment approach till date. Hence, more such cases need to be reviewed for understanding the biologic behavior and also for proper treatment planning.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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