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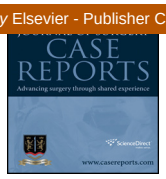

Small cell neuroendocrine tumour of the anterior tongue: A case report

James A. Cymerman[a,*], Raghav Kulkarni[a], David Gouldesbrough[b], James McCaul[c]

[a] Head & Neck Research, Bradford Institute for Health Research, Temple Bank House, Bradford Royal Infirmary, Duckworth Lane, Bradford BD9 6RJ, UK
[b] Department of Pathology, Bradford Royal infirmary, Duckworth Lane, Bradford BD9 6RJ, UK
[c] Lead for Research and Clinical Trials in Head & Neck Cancer, Bradford Institute for Health Research, Temple Bank House, Bradford Royal infirmary, Duckworth Lane, Bradford BD9 6RJ, UK

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ABSTRACT

INTRODUCTION: Neuroendocrine carcinomas (NECs) are rare in the oral cavity. There is ambiguity regarding the classification of these tumours, but their aggressive nature is recognised throughout the literature. Merkel cell carcinoma (MCC) is rare and more frequent in skin, though it has also been described intra-orally. High grade neuroendocrine tumours (HGNEC) and MCCs behave aggressively and aggressive treatment strategies have been advocated. We describe the first small cell HGNEC on the anterior tongue.
PRESENTATION OF CASE: We present the first report of a pT1pN1M0 small cell HGNEC in a 75 year old man on the left lateral anterior tongue. This was widely resected with 20 mm peripheral and deep margins to achieve disease clearance. Selective neck dissection of levels 1–4 was also carried out.
DISCUSSION: Histological analysis of the tumour confirmed a primary poorly differentiated neuroendocrine tumour of small cell type (small cell HGNEC). Resected node bearing tissue from levels 1–4 confirmed metastasis to a level III node with no extra capsular spread giving a pT1pN1M0 classification. Margins of 11.7 mm from the invasive tumour to mucosal margin medially and 7.0 mm for the deep margin despite surgical 20 mm margin resection. To the best of our knowledge small cell neuroendocrine carcinoma has not been described in the anterior tongue.
CONCLUSION: The aggressive nature of this tumour type mandates aggressive surgical resection with margins similar to those now recommended for skin Merkel cell carcinomas. We advocate a wide excision margin of 20 mm to give adequate clearance, with neck dissection in order to pathologically stage this cancer type.

1. Introduction

Neuroendocrine carcinomas (NECs) are rare in the oral cavity. There is ambiguity regarding the classification of these tumours, but their aggressive nature is recognised throughout the literature. Merkel cell carcinoma (MCC) is rare and more frequent in skin, though it has also been described intra-orally. High grade neuroendocrine tumours (HGNEC) and MCCs behave aggressively and aggressive treatment strategies have been advocated. We describe the first small cell HGNEC on the anterior tongue.

2. Presentation of case

A 75 year old gentleman presented to the Oral & Maxillofacial Surgery department with a three month history of a painful, non-healing ulcer on the left lateral border of his tongue. His medical history was unremarkable. Initial examination showed a 5 mm diameter ulcerated lesion on the left lateral border of his tongue (Fig. 1). There was no clinical evidence of cervical lymphadenopathy and the remainder of his oral cavity examination was normal.

A diagnostic biopsy revealed features of a poorly differentiated neuroendocrine carcinoma with a small cell component. Immunohistochemistry demonstrated the tumour cells to be strongly positive for neuroendocrine markers (CD56, chromogranin and synaptophysin) and epithelial markers (AE1/3, MNF116, CK7) and focally strong CK20 positivity in the glandular component. Cells were negative for melanoma and lymphoid markers.

Further investigations included MRI neck, CT thorax, liver and neck, blood profiling and an ECG. The primary lesion was not demonstrated on either of the scans.

Following discussion at the Head & Neck MDT meeting surgical resection was planned. The patient underwent temporary tracheostomy, selective neck dissection (levels 1–4), excision of primary lesion (Fig. 2) with a radial forearm free flap reconstruction and full thickness abdominal skin graft to arm donor site. Surgery proceeded without complication.

* Corresponding author. Tel.: +44 01274 383920.
E-mail addresses: james.cymerman@bthft.nhs.co.uk, jacymerman@me.com (J.A. Cymerman).

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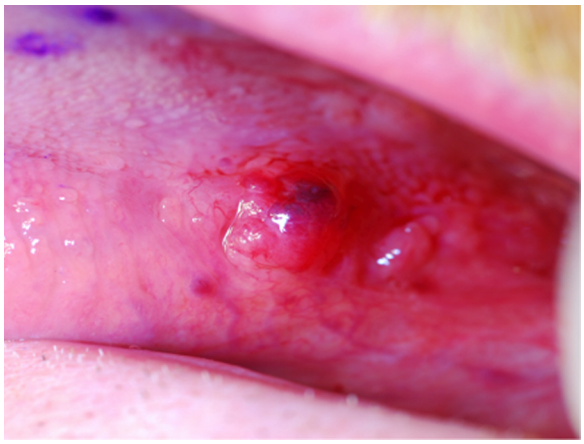

Fig. 1. Clinical photo showing tumour in-situ (centrally positioned).

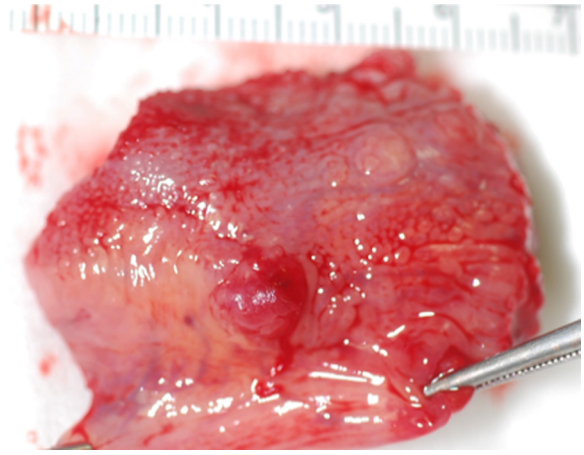

Fig. 2. Excised Tumour Specimen with 2 cm margins.

Histology macroscopically reported a nodular abnormality approximately 11 mm in maximum AP diameter. Microscopic examination of excised tissue (Figs. 3 and 4) showed tumour clearance of 11.7 mm from the invasive tumour to mucosal margin medially and 7.0 mm from deep margin. Analysis of 49 cervical lymph nodes from levels 1–4 showed a single 7 mm metastasis in level three in the left neck. There was no extracapsular spread.

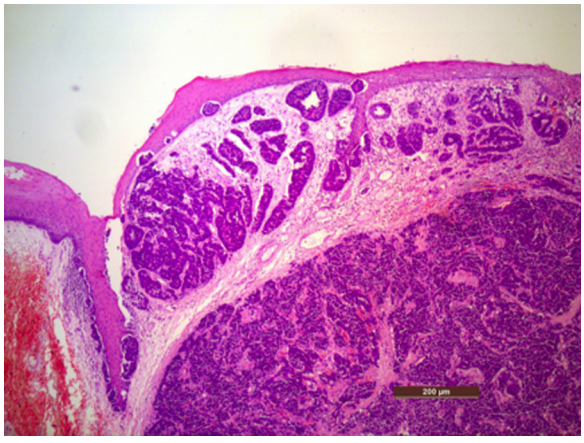

Fig. 3. Low-power view of poorly differentiated carcinoma with focal undifferentiated small cell like appearance (bottom right). H&E x 50.

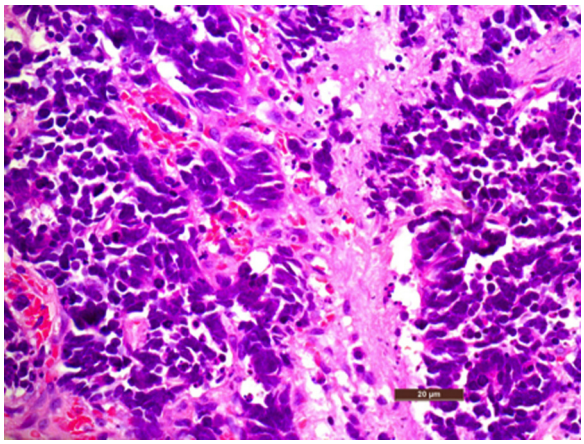

Fig. 4. High power view of undifferentiated small cell like morphology including nuclear debris. H&E X400.

Following head and neck cancer multidisciplinary MDT review adjuvant radiotherapy for the neck was planned.

3. Discussion

In the head and neck mucosa, the majority of neuroendocrine carcinomas (NECs) arise in the larynx, while the second most common site is the salivary glands.[1–3] NECs are rare in the oral cavity with some confusion and ambiguity regarding the classification of these tumours. Merkel cell carcinoma (MCC) is another distinct neuroendocrine carcinoma reported most frequently on skin and salivary glands, MCC has been reported in the oral cavity. The aggressive nature of these tumours is recognised throughout the literature.[3–5]

The distinction among these different tumours in the head and neck is important, and is usually accomplished using a combination of clinical status, anatomic site, histology and immunohistochemistry.[4] The WHO classification of laryngeal NECs is derived from that for lung NECs. This has been extrapolated to other head and neck site primary mucosal NECs and comprises tumour types listed in Table 1.

Surgery is the mainstay of treatment of NECs (including MCC) at all body sites and has been reported to significantly improve survival overall over other single modality treatments.[6–8] High grade or poorly differentiated neuroendocrine tumours are aggressive and to decrease local recurrence of these a wide excision margin has been advocated (up to 3 cm) though this can be difficult to accomplish in the head and neck.[6–8] In this case a

Table 1
Classification of neuroendocrine tumours (of the larynx) WHO 2005.

Terminology	Synonyms
A. Typical carcinoid	Carcinoid, well differentiated (Grade I) neuroendocrine carcinoma
B. Atypical carcinoid	Malignant carcinoid, moderately differentiated (Grade II) neuroendocrine carcinoma, large cell neuroendocrine carcinoma
C. Small cell carcinoma, neuroendocrine type	Small cell neuroendocrine carcinoma, poorly differentiated (Grade III) neuroendocrine carcinoma
D. Combined small cell carcinoma, neuroendocrine type, with non-small cell carcinoma (squamous cell carcinoma, adenocarcinoma, etc.)	Combined small cell carcinoma, composite small cell carcinoma
E. Paraganglioma	Non-chromaffin paraganglioma

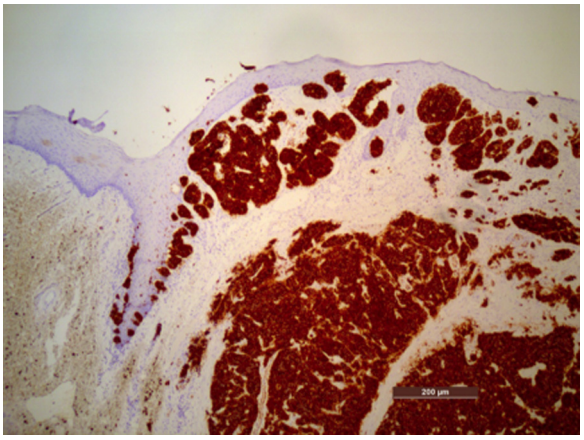

Fig. 5. Immunohistochemistry indicating strong diffuse staininf for the neuroendocrine marker CD 56 including in the undifferentiated small cell like area. CD56 X50.

surgical margin of 20 mm resulted in microscopic clearance of only 11.7 mm at mucosal margin and 7 mm deep margin, reflecting the infiltrative nature of this rare tumour type. Electrochemotherapy has also been described as effective therapy for Merkel cell carcinoma in the head and neck and therefore may have a role here.[9]

NECs demonstrate positive immunohistochemical staining for one or more neuroendocrine markers including: chromogranin A, synaptophysin, CD57, CD56, neuron-specific enolase, and neurofilament. Histological analysis of our tumour confirmed a primary poorly differentiated neuroendocrine tumour of small cell type (small cell HGNEC). This NEC was immunohistochemically positive for CD56 (Fig. 5), chromogranin and synaptophysin and epithelial markers (AE1/3, MNF116, CK7) and focally strong CK20.

4. Conclusion

NECs occurring within the oral cavity are an exceptionally rare entity. The aggressive nature of this tumour type at other sites requires an early and precise diagnosis and mandates aggressive surgical resection. We advocate a wide excision margin of 2 cm to give adequate clearance in those patients who are fit for such surgical procedures. Electrochemotherapy may have a role in patients not fit for major surgery.

Conflict of interest statement

None.

Funding

None.

Ethical approval

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contributions

Mr James Cymerman – main author & literature reviewer.
Mr Raghav Kulkarni – secondary author & literature reviewer.
Dr David Gouldesbrough – Head & Neck pathologist–diagnosed lesion, advised on pathology and supplied histology for report.
Professor James McCaul – secondary author, literature reviewer and overseer of report.

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