Neuroendocrine Carcinoma of the Oropharynx: A report of 2 cases and review of the literature

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Introduction

Neuroendocrine carcinoma (NEC) is a malignant epithelial neoplasm with neuroendocrine morphology. Sites of origin include the pulmonary tract, GI, genitourinary, breast, head and neck sites.¹ Incidence in the head and neck is low and mainly arises in the larynx followed by salivary glands, nose and paranasal sinuses.² NEC of the oropharynx is extremely rare. Only 42 cases have been reported since first identified by Koss *et al* in 1972.³ Misawa K *et al* summarised the first 40 cases and reported 2 further cases in 2016; giving a total of 42 cases.⁴ Standardised treatment guidelines have not yet been established. Here we report 2 further cases to add to the current body of literature with an emphasis on diagnosis and management.

Case 1

A 53 year old man presented with a sensation of a lump in his throat, odynophagia and a right neck lump. Clinical examination revealed an ulcerating mass in his left soft palate and right level II cervical lymphadenopathy. MRI and PET CT scans confirmed intense metabolic activity in the left soft palate, right level II neck region and in the left parapharyngeal lymph nodes. Final histology was confirmed to be T2 N2c M0 large cell neuroendocrine carcinoma of the left soft palate with high proliferation index (see Figures 1 and 2).

Figure 1

Poorly differentiated carcinoma undermining surface non-dysplastic stratified squamous epithelium (H&E x50). Case 1 above, Case 2 below

Figure 2

Poorly differentiated carcinoma showing increased nuclear/cytoplasmic ratio with enlarged nuclei with stippled chromatin. Mitotic activity present (H&E x 400). Case 1 on left, Case 2 on right

Characteristic immunohistochemical features were also seen (see figures 3, 4 and 5). After seeking advice from our neuroendocrine MDT Lead, the patient received induction chemotherapy with cisplatin and etoposide for three cycles followed by radical chemo-radiotherapy with 60 grays (Gy) in 30 fractions with concurrent cisplatin and etoposide at week one and four. A 3 month post-treatment PET CT scan showed an excellent anatomical and metabolic response to the administered therapy at the site of the primary tumour as well as previously involved lymphadenopathy.

Case 2

A 62 year old man presented with a two-month history of odynophagia, left-sided sore throat and left otalgia.

Clinical examination revealed asymmetry of the palatine tonsils with the left larger than the right with no other abnormal findings detected.

Baseline MR and PET CT imaging showed an intensely metabolically active left tonsil mass measuring 2.3 centimetres with central ulceration and a prominent left level II lymph node. There was no distant disease. Final histology was confirmed to be T2 N1 poorly differentiated NEC of the left palatine tonsil (see figures 1 and 2). The right tonsil showed reactive lymphoid hyperplasia only. As in case 1, characteristic immunohistochemical features were also seen (see figures 3, 4 and 5).

Figure 3

Positive immunohistochemical staining for broad-spectrum cytokeratins confirms poorly differentiated carcinoma (surface non-dysplastic epithelium also stains positively/internal positive control) (MCK x 100). Case 1 on left, Case 2 on right

Figure 4

Positive immunohistochemical staining for specific neuroendocrine marker synaptophysin (Synaptophysin x 400). Case 1 on left, Case 2 on right

As in case 1, the recommendation was for radical non-surgical treatment in the form of chemoradiation. Similarly, the patient received induction chemotherapy with cisplatin and etoposide for two cycles followed by radical chemo-radiotherapy with 70 grays (Gy) in 35 fractions with concurrent cisplatin at week one and five.

Despite some early toxicity, the patient has just completed treatment and is due his response assessment PET CT scan next month.

Figure 5

Positive immunohistochemical staining of the majority of the nuclei of the poorly differentiated neuroendocrine carcinoma with proliferation marker Ki67 (Ki67 x 400). Case 1 on left, Case 2 on right

Discussion

NEC of the oropharynx is rare. Typical histopathological appearances can be seen in Fig.s1 and 2. Immunohistochemical analysis usually demonstrates positive staining for general neuroendocrine markers including synaptophysin, CD56 and chromogranin.¹

Current evidence suggests that oropharyngeal NEC is more aggressive than the more commonly encountered SCC with a poorer prognosis.²

One review suggested a median survival of 18 months for small cell NEC of the tonsil.⁵

It has been proposed that systemic chemotherapy should be part of the treatment protocol for all cases of NEC, especially of the small cell variety.⁵ This certainly guided our choice of treatment.

Notably, a recent study which analysed the largest known series of small cell carcinoma of the head and neck, showed that in patients with locally advanced disease, there was no survival benefit with the addition of surgery to chemoradiation.⁶

Conclusion

- NEC of the oropharynx is rare and known to be aggressive with a poor prognosis.
- Diagnosis is based on characteristic histopathological and immunohistochemical features.
- With no prospective data, recommended treatment modalities are based on retrospective information.
- The optimal treatment protocol, whilst uncertain, appears to favour radiotherapy combined with chemotherapy.

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