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## Case Report

# <sup>18</sup>F-FDG PET/CT and PET/MRI fusion imaging for neuroendocrine carcinoma of the tongue: A case report

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## ARTICLE INFO

## Article history:

Received 27 September 2021

Revised 17 December 2021

Accepted 19 December 2021

## Keywords:

Neuroendocrine carcinoma

Tongue

Positron emission tomography

Computed tomography

Magnetic resonance imaging

## ABSTRACT

Neuroendocrine carcinoma (NEC) involving the tongue is a rare and aggressive disease that is more common in middle-aged and elderly males. We report a case of a 56-year-old male who presented to our hospital with sore throat and was found to have a mass in the left root of the tongue. <sup>18</sup>F-FDG PET/CT revealed intense FDG uptake in the mass of the tongue base, as well as different uptake of FDG in the mid-posterior mediastinal mass, right adrenal gland, and enlarged lymph nodes in the neck and mediastinum. Gadolinium-enhanced MRI clearly showed the extent of the tongue lesion, additionally suggesting the presence of brain metastases. <sup>18</sup>F-FDG PET/MRI fusion images of the neck were obtained on the workstation, which may have a higher diagnostic value for tongue NEC. The patient underwent a biopsy of the mass in the left root of the tongue and was pathologically diagnosed with NEC. Whole-body <sup>18</sup>F-FDG PET/CT and regional PET/MRI fusion images have complementary roles in the diagnosis of tongue NEC, and the former is mainly applied to determine the clinical stage of the disease and to guide treatment.

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## Introduction

Neuroendocrine carcinoma (NEC) can occur in any epithelial organ, including the lung, digestive system, breast, urogenital system, and head and neck. The larynx is the most common site of NEC in the head and neck, and it can also occur in the nasal cavity, nasopharynx, middle ear and salivary glands [1],

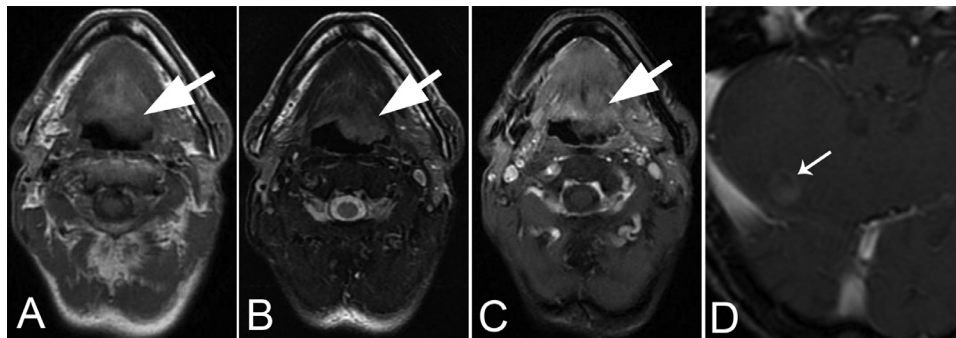
while it is very rare in the tongue and has only been reported in several case reports [2–8]. Few studies have sufficiently discussed the imaging performance of tongue NEC. Therefore, we report fluorine-18-fluorodeoxyglucose (<sup>18</sup>F-FDG) positron emission tomography/computed tomography (PET/CT) and positron emission tomography/magnetic resonance imaging (PET/MRI) fusion imaging of this disease to provide reference information for the diagnosis of similar diseases in the future.

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<https://doi.org/10.1016/j.radcr.2021.12.040>

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**Fig. 1 – MRI images.** MRI revealed an irregular approximately 3-cm tumor in the left root of the tongue (A–C, large arrows). The tumor of the tongue was isosignal on T1WI (A), slightly hypersignal on T2WI (B), with heterogeneous enhancement (C). In addition, a lesion with ring enhancement in the right cerebellum was found on a contrast-enhanced scan (D, small arrow).

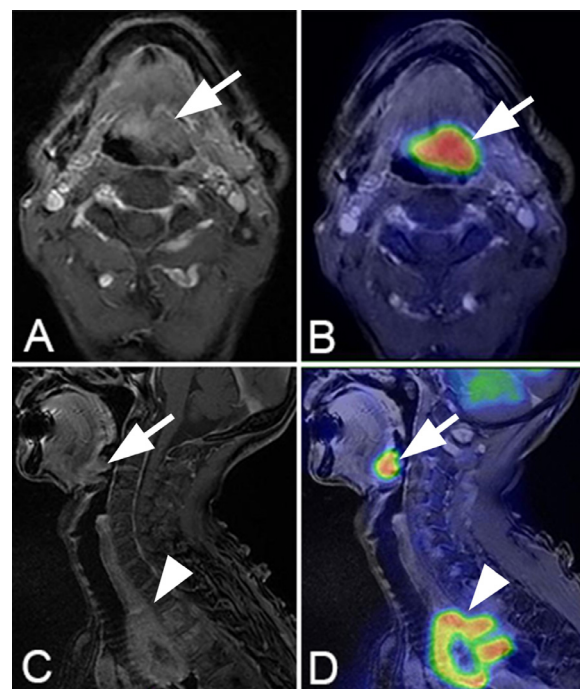
### Case report

A 56-year-old man presented with sore throat 6 months ago, which worsened when swallowing. His symptoms did not improve after treatment with oral medication in other hospitals, so he visited our hospital for further treatment. Physical examination showed a mass in the left root of the tongue with a hyperemic appearance and nonsmooth mucosa. Carbohydrate antigen 19-9 was 159.9 U/ml (normal range: 0–35 U/ml), and carcinoembryonic antigen was 111.39 ng/ml (normal range: 0–5 ng/ml).

His gadolinium-enhanced MRI of the neck revealed an irregular tumor of approximately 3 cm in the left root of the tongue, with significantly heterogeneous enhancement. The diagnosis of a malignant tumor originating from the mucosa of the tongue was considered. In addition, MRI showed lesions with ring enhancement in the right cerebellar and left occipital lobes, which were considered metastases (Fig. 1).  $^{18}\text{F}$ -FDG PET/MRI fusion images were obtained by fusing the gadolinium-enhanced MRI and  $^{18}\text{F}$ -FDG PET images on the workstation.  $^{18}\text{F}$ -FDG PET/MRI fusion imaging of the neck demonstrated intense FDG avidity in the tongue mass. It also revealed an irregular soft mass involving T2–T4 vertebrae with avidly heterogeneous enhancement in the middle and posterior mediastinum, showing a high uptake of FDG (Fig. 2).

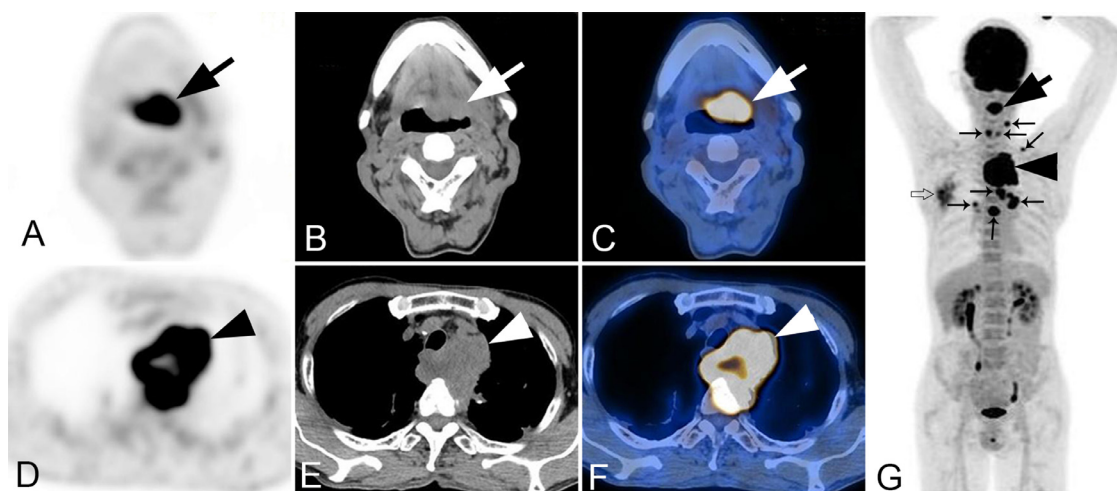
$^{18}\text{F}$ -FDG PET/CT was performed to further determine the clinical staging of the disease. The tumor on the left root of the tongue showed high uptake of FDG, with a maximum standard uptake value (SUVmax) of 15.2, which was considered the primary tumor. The following lesions with different FDG uptake were considered metastases. The soft mass in the middle and posterior mediastinum with an SUVmax of 16.1 was poorly circumscribed from the esophagus and aortic arch, involving the T2–T3 vertebrae and the left second posterior rib. There were multiple enlarged lymph nodes in the neck and mediastinum, with SUVmax values of 7.7 and 14.7, respectively. Furthermore, an ovoid nodule of the right adrenal gland showed moderate uptake of FDG, with an SUVmax of 4.7 (Fig. 3).

Due to the presence of multiple lesions, the patient could not be treated with surgery. Thus, a biopsy of the mass in the root of the tongue was performed, and the pathological di-

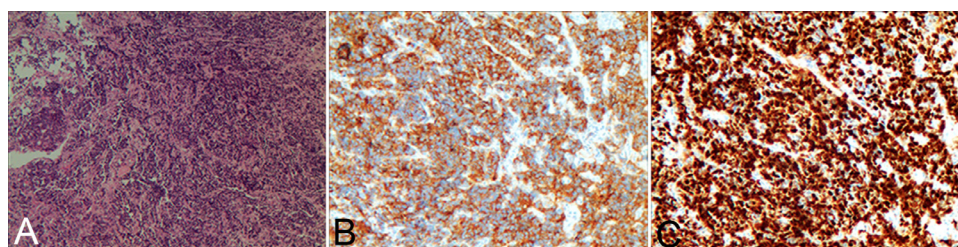


**Fig. 2 –  $^{18}\text{F}$ -FDG PET/MRI fusion images.** Axial contrast-enhanced MRI (A) and fused PET/MRI images (B) demonstrated intense FDG avidity in the tumor of the tongue base (arrows). Sagittal contrast-enhanced MRI (C) and fused PET/MRI images (D) also revealed an avidly enhancing mass in the middle and posterior mediastinum involving the T2–T4 vertebrae, showing a high uptake of FDG (arrowheads).

agnosis was NEC. Histologically, the tumor cells were small to medium in size, with little cytoplasm, a high nuclear-to-cytoplasm ratio, and moderate-to-severe cell atypia. Immunohistochemical staining revealed positivity for synaptophysin and CK7 and a Ki67 index of approximately 90% (Fig. 4). The patient was advised to undergo radiotherapy and chemotherapy, but he requested to be transferred to another hospital; therefore, prognostic information was not available.



**Fig. 3** –  $^{18}\text{F}$ -FDG PET/CT images. Axial PET (A, D), axial CT (B, E), fused axial PET/CT images (C, F) and frontal maximum intensity projection (MIP) PET images (G) revealed intense FDG uptake of the tumor in the left root of the tongue (A–C, G, large arrows) and mid-posterior mediastinum (D–F, G, arrowheads), with maximum standard uptake values (SUVmax) of 15.2 and 16.1, respectively. The frontal PET MIP image also revealed multiple enlarged lymph nodes in the neck and mediastinum with various uptake of FDG (small arrows). Moderate uptake of FDG was shown due to inflammation in the right lung (hollow arrow).



**Fig. 4** – Pathological features of tongue neuroendocrine carcinoma. H-E staining (A,  $\times 40$ ) showed that tumor cells were small to medium in size and arranged in cords and clusters. Immunohistochemical staining revealed positivity for synaptophysin (B,  $\times 100$ ) and CK7 (C,  $\times 100$ ).

## Discussion

High-grade neuroendocrine neoplasms are aggressive diseases that include poorly differentiated neuroendocrine neoplasms (namely, NECs) and well-differentiated neuroendocrine neoplasms with high proliferation [9]. NEC can occur in various organs of the body, of which the lung is the most common organ, while NEC occurring in the oral mucosa is very rare, such as the tongue [10]. Published case reports have suggested that NEC of the tongue mostly occurs in middle-aged and elderly patients (range 40–79 years), is more common in males and is relatively uncommon in females [2–8]. A case report mentioned the  $^{18}\text{F}$ -FDG PET/CT findings of tongue NEC but did not detail the uptake of FDG in the lesions [3]. In our case, FDG uptake varied in the tumor of the tongue, mediastinal mass, right adrenal gland, and enlarged lymph nodes of the neck and mediastinum. Due to the presence of multiple lesions throughout the body, the physician only performed a biopsy on the lesion of the tongue base. Therefore, it was im-

possible to obtain pathological results of each lesion, which made it difficult to identify the primary lesion. However, NEC of the tongue, either primary or secondary, is very rare [3,11].

Somatostatin receptor scintigraphy (SRS) is more widely used in the diagnosis of neuroendocrine tumors. SRS with  $^{111}\text{In}$ -diethylenetriaminepentaacetic acid-octreotide has a diagnostic sensitivity of 89% compared to 58% for  $^{18}\text{F}$ -FDG PET/CT, but the latter has a higher sensitivity for tumors with a high Ki67 index [12].  $^{68}\text{Ga}$  DOTA peptides and  $^{18}\text{F}$ -FDG PET/CT have complementary roles in the initial staging, restaging and clinical follow-up of neuroendocrine tumors, since the former can provide information on somatostatin receptor expression to guide targeted therapy, while the latter can assess tumor aggressiveness and provide risk stratification [13]. Additionally,  $^{18}\text{F}$ -FDG PET has high value in predicting the prognosis of neuroendocrine tumors, in which positive patients have shorter survival and worse prognosis [14]. In our case, the mass of the tongue base had a high Ki67 index and showed intense FDG uptake, which also suggested that the tumor was highly aggressive. However, we were unable to obtain prognostic infor-



mation of the patient for certain reasons. The main value of  $^{18}\text{F}$ -FDG PET/CT in multifocal NEC is to determine the clinical stage of the tumor and to guide the selection of an appropriate treatment plan. In this case, the  $^{18}\text{F}$ -FDG PET/CT examination suggested multiple metastases in the body, and the patient was recommended to undergo standardized radiotherapy and chemotherapy due to lack of surgical indications.

The MRI findings vary depending on the primary site of NEC. Small cell NEC occurring in the paranasal sinuses presents with hemorrhage, necrosis and cystic sites on MRI, showing significant heterogeneous enhancement, and half of them have a "geographic" or "cribriform-like" appearance [15]. The MRI findings of endometrial NEC show diffuse infiltration of the myometrium with high T2 signal intensity and loss of normal uterine architecture [16]. In our case, tongue NEC showed an irregular soft mass in the left root of the tongue with heterogeneous enhancement. The MRI features of tongue NEC may actually be nonspecific, but further confirmation with an expanded sample size is still needed due to the case report nature of this study. Gadolinium-enhanced MRI can clearly show the extent of tongue NEC invasion due to the higher resolution of soft tissues. In addition, MRI is more sensitive than  $^{18}\text{F}$ -FDG PET/CT for the detection of brain metastases, as normal brain tissue generally takes up FDG and is less likely to detect small metastases with slight FDG uptake, resulting in false-negative results. Regional  $^{18}\text{F}$ -FDG PET/MRI fusion images can clearly demonstrate the extent of the primary tumor and metastases and also show FDG uptake of the lesions, which may have a higher diagnostic value.

The pathological diagnosis of NEC mainly depends on the morphological features of cells and immunohistochemical markers. Our patient showed moderate-to-severe cellular atypia and positivity for the neuroendocrine marker synaptophysin and epithelial marker CK7, which was consistent with the diagnosis of high-grade NEC [6]. Surgery combined with chemoradiotherapy is the main treatment strategy for NEC in the head and neck, and the prognosis is associated with the pathological type and differentiation of the tumor [17]. Esmati et al. reported a patient with limited tongue NEC who underwent partial excision followed by chemoradiotherapy, without signs of recurrence at the approximately 5-year follow-up [5]. For multifocal NEC involving the tongue, chemotherapy with etoposide and carboplatin may prolong survival [3].

## Conclusion

To summarize, NEC involving the tongue is rare.  $^{18}\text{F}$ -FDG PET/CT has diagnostic advantages in highly proliferative NEC and plays an essential role in the clinical staging of the disease, which can guide the choice of treatment strategy. MRI is superior in showing the invasion extent of soft tissue lesions and has a higher detection rate for brain metastases. Whole-body  $^{18}\text{F}$ -FDG PET/CT and regional PET/MRI fusion images should be considered complementary in the diagnosis of NEC patients. Few studies have reported the treatment and prognosis of tongue NEC, and more studies are needed to elucidate these further.

## Declaration of competing interest

None.

## Acknowledgments

We would like to thank the staff members of the Department of Nuclear Medicine and PET/CT-MRI Centre, the First Affiliated Hospital of Jinan University, for their excellent technical support.

## Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## Patient consent

The patient has agreed to the use of his examination images for publication, and we have obtained informed consent for this.

## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.radcr.2021.12.040](https://doi.org/10.1016/j.radcr.2021.12.040).

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