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Authors
Raslan, Osama A
Muzaffar, Razi
Shetty, Vilaas
et al.

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Image findings of cranial nerve pathology on [18F]-2- deoxy-D-glucose (FDG) positron emission tomography with computerized tomography (PET/CT): a pictorial essay

Osama A. Raslan1*, Razi Muzaffar1, Vilaas Shetty2 and Medhat M. Osman1

Abstract

This article aims to increase awareness about the utility of 18F-FDG-PET/CT in the evaluation of cranial nerve (CN) pathology. We discuss the clinical implication of detecting perineural tumor spread, emphasize the primary and secondary 18F-FDG-PET/CT findings of CN pathology, and illustrate the individual 18F-FDG-PET/CT CN anatomy and pathology of 11 of the 12 CNs.

Background

Conventional CT and MRI have been the imaging modalities of choice for evaluation of cranial nerve (CN) pathology. However, CN pathology can also be detected on [18F]-2- deoxy-D-glucose (FDG) positron emission tomography with computerized tomography (PET/CT) imaging [1–3]. As FDG PET/CT is increasingly being used for oncologic imaging and more specifically for evaluation of head and neck (HN) cancer [4], PET/CT interpreters need to familiarize themselves with the image findings of CN involvement, which will greatly impact the staging and management of these patients.

Tumor related PET/CT findings include the perineural spread of HN tumors which represents a rare contiguous metastatic extension of tumor along a cranial nerve that portends to poor prognosis, even if the patient is asymptomatic [2, 5]. If present, treatment can be changed to include neck dissection, a larger radiation field, or adding adjuvant therapy [6–8]. Facial nerve involvement (CN VII) in parotid tumors may preclude facial nerve-sparing surgery or require additional treatment modality [9]. Patients with skin cancer and perineural invasion will require adjuvant radiation therapy even when clear margins are achieved with Mohs surgery [10, 11]. Also the degree of FDG uptake by the tumor as measured by the SUV max is an important prognostic marker for locally advanced nasopharyngeal cancer. High FDG uptake reflects more aggressive tumors that may require more aggressive treatment and carries a worse prognosis, as compared to the less aggressive low FDG tumors [12].

Non-tumor related benign and malignant cranial nerve pathology can also be incidentally detected during PET/CT oncologic imaging including schwannomas [13], optic nerve glioma [14], meningioma [15], and melanoma [15]. Gallium 68 (68Ga) 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA)-octreotate (DOTATATE, GaTate), has been shown to be more sensitive than FDG-PET/CT in detection of low grade somatostatin receptor positive tumors namely meningioma, esthesioneuroblastoma and schwannoma [16].

The purpose of this article is to describe the primary and secondary FDG-PET/CT findings of CN pathology and to provide a comprehensive illustration of the PET/CT cross-sectional anatomy and pathology of almost each individual CN, thus raising awareness and familiarity about incidental CN lesions seen on PET/CT, which will directly reflect on patient staging and management.

Primary and secondary PET/CT findings of CN pathology

The primary sign of CN pathology includes linear thickening or linear increased/decreased FDG activity along...
the expected course of the CN (Fig. 1). For this purpose, all three planes (axial, coronal and sagittal) and maximum intensity projection (MIP) images must be evaluated and correlations with all other available imaging modalities, e.g. (CT or MRI) which will often confirm the abnormality.

The secondary signs of CN pathology include widening or destruction at the corresponding skull base foramen, asymmetric atrophy or abnormal activity in the muscles supplied by the CN, or increased FDG activity related to synergistic/antagonistic muscle overcompensation to maintain function (Table 1).

**Case presentation**

Olfactory nerve (CN I)

Direct visualization of the CN I lesion is beyond the resolution of PET/CT, however CN I involvement
Table 1 Clinical, primary and secondary findings of CN pathology

| Symptoms/signs that trigger search pattern for CN pathology | Which CN to suspect? | What to look for and where to look for it on PET/CT? |
|------------------------------------------------------------|----------------------|---------------------------------------------------|
| Abnormality along course of CN | Abnormal skull base foramen/bone | Muscle atrophy | Over compensation |
| Abnormality along course of CN | Abnormal skull base foramen/bone | Muscle atrophy | Over compensation |

Anosmia

| CN I (Olfactory) | Roof of nose and anterior cranial fossa | Cribriform plate of ethmoid | – | – |

Visual loss

| CN II (Optic) | Orbit, suprasellar cistern | Optic canal | – | – |

Diplopia

| CN III (Oculomotor) | Cavernous sinus | Superior orbital fissure (SOF) | Extraocular muscles (except superior oblique and lateral rectus muscles) | – |

Vertical diplopia

| CN IV (Trochlear) | Cavernous sinus | SOF | Superior oblique | – |

Trigeminal Neuralgia

| CN V (Trigeminal, main trunk) | Pons, preopticine cistern, Meckel's cave. | – | – | – |

Paresthesia over forehead and eye

| CN V1 (Ophthalmic division) | Cavernous sinus | SOF | – | – |

Paresthesia over cheek

| CN V2 (Maxillary division) | Cavernous sinus, cheek | Foramen rotundum, pterygopalatine fossa and infraorbital canal /foramen | – | – |

Paresthesia over chin, trismus

| CN V3 (Mandibular division) | Masticator space | Foramen ovale, mandibular canal and mental foramen | – | – |

Lateral gaze diplopia

| CN VI (Abducens) | Cavernous sinus, clivus | SOF | Lateral rectus | Ipsilateral Medial rectus |

Facial palsy

| CN VII (Facial) | Cerebellopontine angle, parotid space | Petrous bone, internal auditory canal (IAC), and stylomastoid foramen | – | – |

Hearing loss/imbalance

| CN VIII (Vestibulocochlear) | Cerebellopontine angle | Petrous bone and IAC | – | – |

Hoarseness

| CN X (Vagus nerve, recurrent laryngeal branch) | Carotid space, | tracheoesophageal grooves, around aortic root | – | – |

Jugular foramen

| CN XI (Spinal accessory) | Ipsilateral vocal cord | Contralateral vocal cord | – | – |

Shoulder drooping

| CN XII (Hypoglossal nerve) | Occipital condyles, Carotid space, base of tongue | JF, Hypoglossal canal | Ipsilateral hemitongue | Contralateral hemitongue |

should be suspected in lesions involving the superior sinonasal and anterior cranial fossa region. The differential considerations include olfactory neuroblastoma (Esthesioneuroblastoma), sinonasal carcinoma and melanoma (Fig. 2).

**Optic nerve (CN II)**

The main differential considerations for CN II lesion include optic pathway glioma (OPG), optic nerve sheath meningioma, idiopathic orbital inflammatory pseudotumor, and optic neuritis. FDG activity in Optic nerve glioma
is variable depending on its histological grade [17, 18]. Some authors suggested the use of FDG-PET/CT in monitoring malignant transformation of OPG in children with neurofibromatosis type 1 syndrome [17, 19]. Optic meningioma is a benign tumor that typically demonstrates minimal to no FDG uptake on PET [15] and can be associated with bony sclerosis/destruction as in our case (Fig. 3). Orbital pseudotumor could be both hyper or isometabolic on FDG PET [18]. Xie et al. described a 56-year-old female with elevated FDG activity in several cranial and peripheral nerves suggestive of multiple neuritis, with patient’s symptoms improving following treatment [3].

Oculomotor, trochlear and abducens nerves (CN III, IV, VI)

Direct visualization of CNs III, IV and VI is usually beyond the resolution of PET/CT, however large brain stem or cavernous sinus lesions along the course of these nerves may indicate cranial nerve involvement by these lesions. Also, extraocular muscle atrophy or asymmetric decreased uptake could represent denervation injury, which should prompt a search for a lesion along the course of the innervating CN. In an attempt to compensate for the paralyzed muscle, the non affected extraocular muscles may show increased FDG activity, further confirming the CN involvement (Fig. 4c–e).
Trigeminal nerve, maxillary and mandibular divisions (CNV, V2 & V3)

FDG-PET/CT can detect perineural tumor spread along the trigeminal nerve and its main divisions; most commonly arising from head and neck squamous cell carcinoma, adenoid cystic carcinoma, mucoepidermoid carcinoma, skin cancer and melanoma as well as lymphoma [1] and neurolymphomatosis [20] (Fig. 5).

Facial/vestibulocochlear nerve complex (CNVII and VIII)
The most common cerebellopontine angle lesions are vestibular schwannoma and meningioma. Vestibular schwannoma is typically described as a hypometabolic lesion [21], however in our experience they were...
hypermetabolic (Fig. 6c-f), which may be related to the large size of the lesions. Vestibular schwannoma is differentiated from meningioma by extension into the internal auditory canal (Fig. 6f). The less common facial nerve schwannoma is diagnosed when the lesion extends along the labyrinthine segment of CNVII (Fig. 6g, h). Perineural spread form parotid gland lesions should be suspected with abnormal activity extending superiorly along the stylomastoid foramen or within the temporal bone [2, 22, 23]. Rare CN melanoma metastasis along CNs VII and VIII has also been described [24].

Vagus and spinal accessory nerves (CNs X and XI)
The most common jugular foramen (JF) lesions that my involve CN X and XI are glomus jugulare, schwannoma, meningioma and skull base metastasis. Looking at the bone margins of the JF on the bone window of PET/CT may help differentiate glomus tumors which tend to have a permeative destructive margins from schwannoma which tend to cause smooth expansion of the JF (Fig. 7e) and meningioma, which may have permeative sclerotic margins [25]. If the recurrent laryngeal branch of CNX is involved, it will be seen as a hypometabolic ipsilateral paralyzed vocal cord with a hypermetabolic overcompensating contralateral vocal cord (Fig. 7c, d). Ipsilateral shoulder dropping on MIP images (Fig. 7g), with atrophy of the trapezius and sternomastoid muscles on the axial images (Fig. 7c, d), signifies CNXI involvement, which could be secondary to CNXI sacrifice during neck dissection.

Hypoglossal nerve (CN XII)
Injury of CNXII could occur by the aforementioned JF lesions [25]. Further distally it could be secondary to hypoglossal foramen lesions (CNXII Schwannoma [25, 26]), clival tumor (chordoma, chondrosarcoma and plasmacytoma) [25], or rarely could be secondary to retrospective perineural tumor spread from tongue base tumor or radiation injury. An atrophic sagging fatty infiltrated ipsilateral tongue will be seen with hypometabolism on PET/CT (Fig. 8 b, d, e) [25].

Conclusion
Crani al nerve pathology can be detected on FDG PET/CT. With the increased reliance on PET/CT in patient staging and follow-up, PET/CT interpreters should familiarize themselves with these findings as it may change patient staging and management.

Consent
“This retrospective study was approved by the Saint Louis University IRB board”.
Fig. 7 A 32 year-old-female presenting with a hoarse voice. Axial fused (a) and unfused (b) PET/CT images of the skull base showing a hypometabolic soft tissue mass centered on the left jugular foramen with smooth osseous expansion suggestive of schwannoma of cranial nerve IX, X or XI which all exit the skull base through the jugular foramen. Axial fused (c) and unfused (d) PET/CT images at the level of the glottis show no 18F-FDG uptake in the left vocal cord (blue arrow) with compensatory increased activity in the right vocal cord, consistent with laryngoscopy proven left vocal cord paralysis due to tumor involvement of left CN X and its recurrent laryngeal branch. Asymmetric atrophy of the left sternomastoid and trapezius muscles is consistent with chronic denervation due to tumor involvement of the left cranial nerve XI (spinal accessory nerve) (red arrows). Axial CT scan of the skull base with bone window settings (e) and axial post-contrast fat-suppressed T1 MRI (f) at the same level show the enhancing left cranial nerve IX/X/XI mass pathologically proven to be a schwannoma. g Coronal MIP image of a 50-year-old male with HIV presenting with worsening right facial weakness and pathologically proven squamous cell carcinoma of the neck, with perineural tumor invasion along the jugular foramen (not shown), showing right shoulder drooping compared to the left one (red line), secondary to atrophy of the right trapezius and sternomastoid muscles, confirming CN XI involvement. Also note the bulky hypermetabolic cervical adenopathy (arrow) in the right neck involving lymph node levels 1 through 4 consistent with metastatic lymph nodes.

Fig. 8 A 41 year-old-male patient diagnosed with left sided nasopharyngeal carcinoma and intracranial involvement. Axial CT of the neck (a) at the time of diagnosis (5/2005) showing normal posterior contour of the tongue (red line). The patient received radiotherapy and chemotherapy ending in 2006. Follow-up axial fused PET/CT images of the neck region (b) on (8/2013) shows interval atrophy of the left hemi-tongue, with abnormal posterior contour (green line). Post contrast coronal T1 WI before treatment (c), coronal fused PET/CT and coronal contrast enhanced MRI T1W images after treatment (d, e) confirming the left hemi tongue atrophy (arrow). Clinically, the patient’s tongue deviates to the left. The constellation of findings is consistent with post radiation hypoglossal neuropathy.
Abbreviations

FDG: [18 F]-2-deoxy-D-glucose; PET/CT: Positron emission tomography with computerized tomography; CN: Cranial nerve; RN: Head and neck; CPA: Cerebellopontine angle lesion; IAC: Internal auditory canal; JF: Jugular foramen; OI: Olfactory nerve; CN II: Optic nerve; CN III: Oculomotor nerve; CN IV: Trochlear nerve; CN V: Trigeminal nerve; CN VI: Abducens nerve; CN VII: Facial nerve; CN VIII: Vestibulocochlear nerve; CN IX: Glossopharyngeal nerve; CN X: Vagus nerve; CN XI: Spinal accessory nerve; CN XII: Hypoglossal nerve; FIESTA: Fast imaging employing steady-state acquisition; MPR: Multiplanar reformatted images; SSFP: Steady state free precession; STIR: Short tau inversion recovery; MIP: Maximum intensity projection.

Competing interests

Dr. Osman: Speaker, Koninklijke Philips NV. All other authors have no financial disclosures.

Authors’ contributions

All Authors: 1) Have made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; 2) have been involved in drafting the manuscript or revising it critically for important intellectual content; 3) have given final approval of the version to be published; and 4) agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All authors read and approved the final manuscript.

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Author details

1 Department of Radiology, Division of Nuclear Medicine, St. Louis University, 3635 Vista Avenue, Saint Louis, Missouri 63110, USA. 2 Department of Radiology, Division of Neuroradiology, St. Louis University, 3635 Vista Avenue, Saint Louis, Missouri 63110, USA.

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