

¹⁸F-fluoroethyl-L-tyrosine positron emission tomography-guided diagnosis of a malignant intramedullary spinal cord tumor

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Abstract. Diagnosis in patients with a suspected malignant intramedullary lesion that requires biopsy for definitive diagnosis may be challenging, as spinal cord surgery carries the risk of irreversible neurological deficits. The current study presents the first case of ¹⁸F-fluoroethyl-L-tyrosine (¹⁸F-FET) positron emission tomography (PET) imaging in a patient with a spinal cord tumor. The patient was unsuitable for magnetic resonance imaging due to his implanted cardiac defibrillator. ¹⁸F-FET PET indicated a high-grade malignancy of the spinal cord, justifying tumor biopsy. Histological analysis was compatible with a malignant melanoma. This is also the first report demonstrating the FET-PET appearance/metabolic phenotype of a malignant melanoma of the spinal cord.

Introduction

Malignant spinal cord tumors make up ~22% of all primary spinal cord tumors (1). Intramedullary spinal cord tumors are the rarest of these neoplasms and can severely impair the neurological function and quality of life of patients (2). Therefore, the accurate and early diagnosis of these tumors is essential to obtain an optimal outcome. Diagnosis is based on contrast-enhanced magnetic resonance imaging (MRI) of the spine, which is considered the diagnostic method of choice,

enabling excellent delineation of the spinal cord and adjacent structures (3). However, diagnosis in patients with spinal cord diseases may be challenging, particularly in patients with a suspected malignant spinal cord disease, which requires biopsy for definitive diagnosis; this is because spinal cord surgery carries the risk of irreversible neurological deficits (4,5).

New imaging techniques that help to provide additional justification for spinal cord biopsy/surgery are desperately required. With improved spatial resolution of positron emission tomography (PET) techniques, PET using the tracer ¹⁸F-fluorodeoxyglucose (¹⁸F-FDG) has been explored in small series to assess neoplastic spinal cord lesions (6,7). ¹⁸FDG-PET, however, does not allow the reliable differentiation between neoplastic and inflammatory lesions (8). Thus, new imaging techniques are necessary to achieve this differentiation.

¹⁸F-fluoroethyl-L-tyrosine (¹⁸F-FET) PET may particularly lend itself for this purpose because of its potential for differentiating between neoplastic and inflammatory lesions (9,10). In this regard, it has been shown to be a promising tool for the detection of pseudoprogression in glioblastoma patients (11), and for the identification of patients with radiation necrosis in brain metastases (12). The current study presents the first case of ¹⁸F-FET PET imaging in a patient with a malignant tumor of the spinal cord.

Case report

A 74-year-old male presented at the Department of Neurology, University of Bonn Medical Center on April 28, 2014 with a progressive symmetric distal numbness and dysesthesia of the legs. The patient reported no associated back pain or weight loss, and no pre-existing neoplastic disease. Due to a disconnected electrode wire in his implanted cardiac defibrillator, the patient was unsuitable for MRI.

A contrast-enhanced computed tomography (CT) scan of the whole spine, and a CT scan with myelogram did not show any evidence of a tumor mass or spinal cord or root compression. A CT scan of the brain was also

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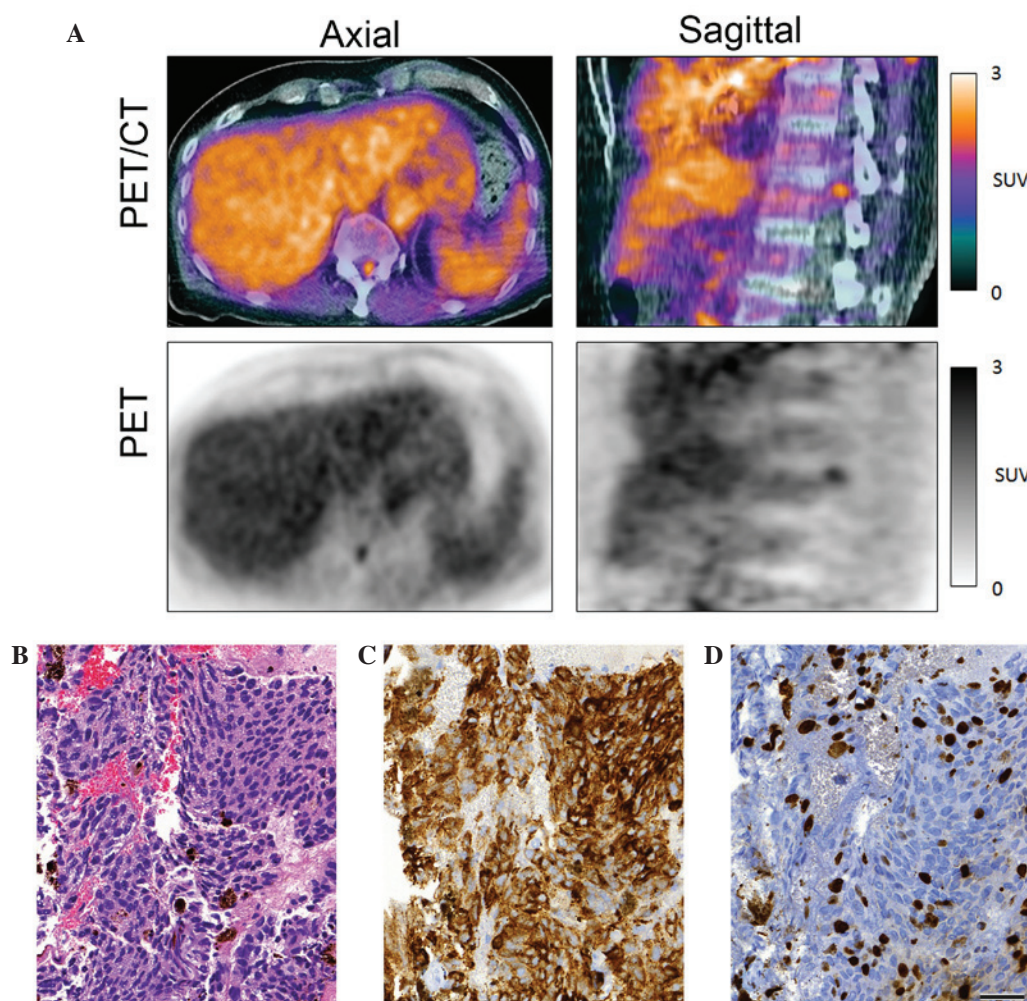


Figure 1. (A) ^{18}F -fluoro-ethyl-tyrosine PET with and without CT scans showing marked elevation of intramedullary tracer uptake at the 12th thoracic vertebra. (B-D) Histomorphological and immunohistochemical findings. (B) Hematoxylin and eosin staining revealed a tumor with increased cellularity, cytological atypia and cytoplasmic as well as extracellular melanin pigment. The cytomorphological aspect was dominated by epithelioid cells arranged in nests or fascicles. Mitotic figures were observed. (C) Immunohistochemical examinations revealed strong immunoreactivity for HMB45. (D) ~10% of the tumor cell nuclei expressed the proliferation-associated antigen Ki-67 (MIB-1; scale bar, 50 μm). The lesion was classified as melanocytic tumor with increased proliferative activity, compatible with a malignant melanoma. PET, positron emission tomography; CT, computed tomography; SUV, standardized uptake value.

unremarkable. Cerebral spinal fluid analysis, an infectious disease screening (including human immunodeficiency virus, Epstein-Barr virus, varicella-zoster virus, cytomegalovirus and herpes simplex virus screening), onconeural antibodies and full blood analysis did not reveal any relevant pathological findings. Staging with contrast-enhanced CT scan of neck/chest/abdomen, as well as fundoscopic and skin evaluations did not show an extraspinal tumor. Despite the use of corticosteroids, symptoms progressed to paraplegia with an ankle clonus and pathological Babinski's sign on the left side. ^{18}F -FDG PET revealed a pathologically accumulating intramedullary lesion, indicating elevated focal glucose metabolism at the 12th thoracic vertebra (Th12). Considering that the ^{18}F -FDG PET had insufficient ability to differentiate between inflammatory and neoplastic lesions, an additional ^{18}F -FET PET was performed to aid in ruling out an inflammatory lesion; preclinical data have previously indicated no significant accumulation of ^{18}F -FET in inflammatory spinal cord lesions, as opposed to ^{18}F -FDG (13).

^{18}F -FET PET confirmed focal tracer accumulation at Th12, indicating a high-grade malignancy of the spinal cord

(Fig. 1A). The ratio of the maximal standardized uptake value (SUV) of the tumor to the SUV of the surrounding normal tissue, which is referred to as the tumor-to-normal tissue ratio (TNR), was 2.21. The mean TNR was 1.82. Based on these findings, the patient underwent a diagnostic biopsy. Intraoperative localization of the tumor area was performed under the guidance of ^{18}F -FET PET data. The biopsy material was fixed with formaldehyde overnight, embedded in paraffin, cut into 4- μm sections and mounted on slides. The neuropathological analysis involved immunostaining with mouse anti-Ki67 (cat. no. M70240; 1:1,000; Dako Denmark A/S, Glostrup, Denmark) and anti-melanosome (HMB45) monoclonal antibodies (cat. no. M0634; 1:100; Dako Denmark A/S). Histological analysis revealed a melanocytic tumor with high proliferative activity and cellularity, compatible with malignant melanoma (Fig. 1B-D).

After stereotactic irradiation of the spinal cord (at the Th12 level) with 42.65 Gy in 16 fractions, the patient's clinical status improved gradually over a period of 6 months until he was able to walk a few steps independently. The patient is currently alive at 2-years following a spinal cord tumor diagnosis.

Written informed consent was obtained from the patient prior to the publication of this study.

Discussion

To the best of our knowledge, this is the first report of the utilization of ^{18}F -FET PET imaging in a patient with a malignant spinal cord tumor. ^{18}F -FET PET in this patient was shown to provide valuable information to differentiate between inflammatory and neoplastic lesions of the spinal cord and to warrant surgery/biopsy in such eloquent areas.

These findings are in accordance with the findings in brain tumors, where a growing body of evidence supports the role of ^{18}F -FET PET imaging in discerning between neoplastic tumors and inflammatory lesions and/or post-treatment effects (12,14). If MRI is contraindicated, ^{18}F -FET PET and ^{18}F -FDG PET resolution in conjunction with CT imaging may be sufficient to map a spinal cord biopsy site. However, as has been demonstrated in preclinical studies, ^{18}F -FDG has inferior capability in distinguishing neoplastic from inflammatory or treatment-related lesions as opposed to an amino-acid PET tracer (13,15). ^{18}F -FET, a commonly used radiolabeled amino acid, is characterized by a long half-life and is thus suitable for widespread clinical usage (16). However, despite its promising properties, ^{18}F -FET PET has not yet gained a foothold in imaging of suspected spinal cord neoplasms.

The current study is the first case demonstrating the metabolic phenotype of a malignant melanoma of the spinal cord, as detected by ^{18}F -FET PET. The intense metabolic activity is likely what makes this tumor amenable to ^{18}F -FET PET imaging. Based on the findings of the presented case, ^{18}F -FET PET imaging should be explored further in malignant spinal cord disease and melanoma.

In summary, this is the first report of ^{18}F -FET PET imaging in a patient with a malignant spinal cord tumor. ^{18}F -FET PET in this patient was shown to provide valuable information to differentiate between inflammatory and neoplastic lesions of the spinal cord and to warrant surgery/biopsy in eloquent spinal cord areas. This is the first case demonstrating the metabolic phenotype of a malignant melanoma of the spinal cord, as detected by ^{18}F -FET PET. In patients unable or unsuited to have an MRI, in whom a spinal cord tumor is suspected, ^{18}F -FET PET provides valuable information to determine whether a tumor is likely to be malignant. In this scenario, ^{18}F -FET PET may assist in deciding whether a patient should be subjected to biopsy/resection.

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