Case Report: Evaluation of Neurofibromas on ^{18}F-FDG PET/MRI in a Patient with Neurofibromatosis Type 1

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Introduction

Neurofibromatosis Type 1 (NF-1), a disease with autosomal dominant inheritance, has an incidence of 1 in 3000 [1]. NF-1 is characterized by various clinical manifestations, including café au lait spots, Lisch nodules, skeletal deformities, neurofibromas, and plexiform neurofibromas. Plexiform neurofibromas can undergo transformation into a malignant peripheral nerve sheath tumor (MPNST), the primary cause of mortality in this patient population [2]. It is an aggressive lesion, with a poor prognosis. Clinical findings such as pain and rapid enlargement sentinel signs of malignant transformation. Currently, 18-fludeoxyglucose* positron emission tomography/computed tomography (^{18}F-FDG PET/CT) is a sensitive imaging modality for detection of MPNSTs [3]. ^{18}F-FDG PET/MRI may be a better imaging modality for assessment of neurofibromas in this patient population, by combining metabolic data from PET with superior soft tissue contrast and radiation dose reduction of MRI by omitting the CT exam.

*The full prescribing information for the Fludeoxyglucose F^{18} injection can be found at the end of the article.

Patient history

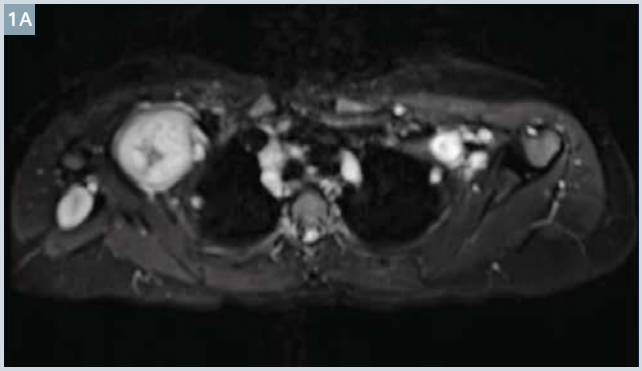
20-year-old female with known NF-1 presented to the outpatient clinic with a palpable right axillary mass, progressively enlarging and increasingly painful over the past two years. She also complained of numbness and paresthesias in her right hand, mainly along the middle, fourth and fifth fingers, as well as right hand weakness. She denied any family history of neurofibromatosis. Physical examination revealed a large tender mass in the right axilla with associated right hemihypotrophy, as well as an additional superficial smaller mass overlying the right scapula, multiple café au lait spots, and bilateral axillary freckling. Neurologic examination revealed cognitive impairment, mild atrophy and mild flexor/extensor motor weakness in both hands, right greater than left.

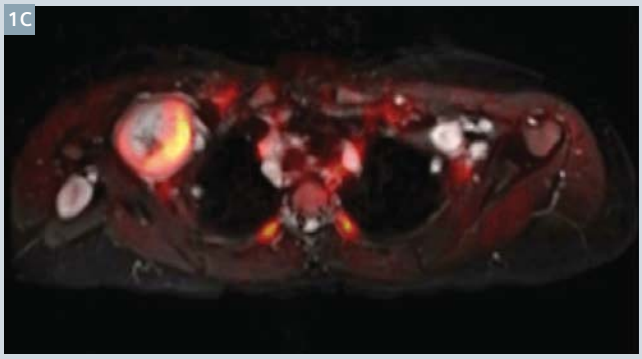
Sequence details

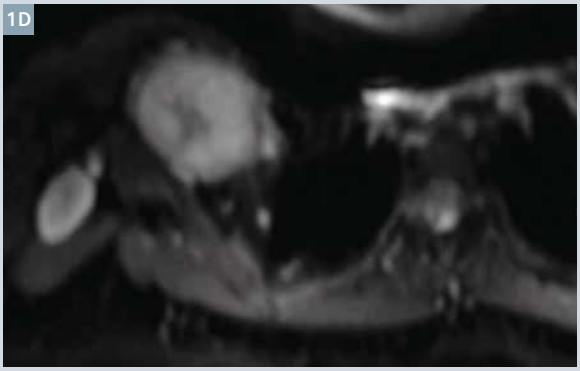
Simultaneous PET and MRI were acquired (Biograph mMR, Siemens Healthcare, Erlangen, Germany) using the same tracer injection from a PET/CT (Biograph™ mCT) exam performed on the same day. Diagnostic MR sequences included axial STIR, coronal STIR and diffusion-weighted imaging (DWI) using 3 b-values (0, 350, 750 s/mm^2). PET was acquired simultaneously covering 4 beds from upper legs through thorax (6-minute sinogram acquisition).

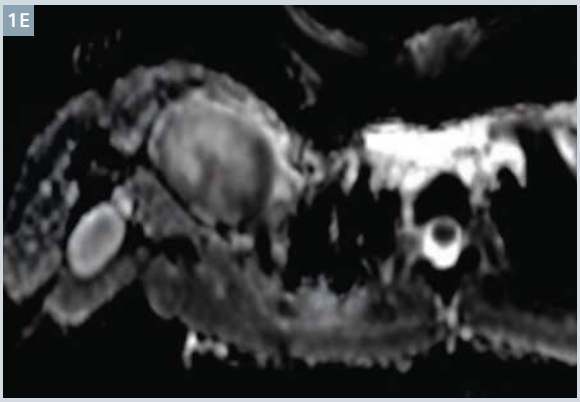
Imaging findings

Initial MRI of the cervical spine and right arm reportedly demonstrated a dominant large soft tissue mass in the right axilla extending into the brachial plexus, as well as extensive bilateral plexiform neurofibromas. At the time of initial presentation around 2 years prior, a biopsy of the right axillary mass was done and showed a "WHO 1 low-grade plexiform neurofibroma without evidence of malignancy". Subsequent ^{18}F-FDG MR/PET examination was performed showing focal intense FDG uptake in the dominant enlarging well-circumscribed right axillary mass with a maximal standardized uptake value (SUV_{max}) of 5.7, demonstrating heterogeneous increased T2 signal intensity with a central cystic area, as well as diffusion restriction at the periphery of the mass (Fig. 1). Additional neurofibromas with low-grade metabolism without diffusion restriction were also detected in the left gluteus maximus muscle with SUV_{max} of 3.7 (Fig. 2) as well as in the right iliacus muscle with SUV_{max} of 3.3 and right gluteus maximus muscle with SUV_{max} of 2.1 (Fig. 3). Based on the significant progression of clinical symptoms and worrisome imaging features of enlargement, elevated SUV_{max} value, and peripheral diffusion restriction, patient underwent ultrasound-guided biopsy of the right axillary mass. Histopathology was consistent with a MPNST.









1 Axial STIR **(1A)**, PET **(1B)**, fused post-hoc **(1C)**, DWI **(1D)** and ADC **(1E)** images demonstrate a hyperintense right axillary mass with central cystic component, intense peripheral FDG uptake (SUV_{max} 5.7) and diffusion restriction. Tumor was malignant at surgery.

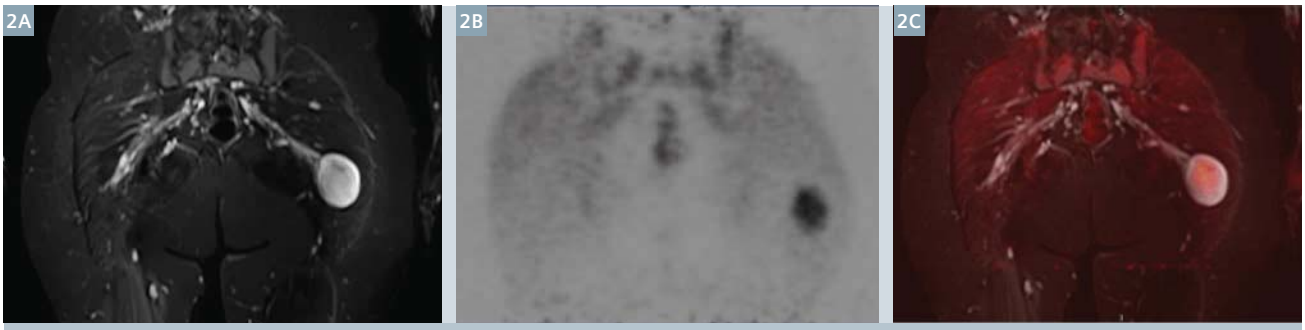
Indications

Fludeoxyglucose F^{18} Injection is indicated for positron emission tomography (PET) imaging in the following settings:

- **Oncology:** For assessment of abnormal glucose metabolism to assist in the evaluation of malignancy in patients with known or suspected abnormalities found by other testing modalities, or in patients with an existing diagnosis of cancer.
- **Cardiology:** For the identification of left ventricular myocardium with residual glucose metabolism and reversible loss of systolic function in patients with coronary artery disease and left ventricular dysfunction, when used together with myocardial perfusion imaging.
- **Neurology:** For the identification of regions of abnormal glucose metabolism associated with foci of epileptic seizures.

Important Safety Information

- **Radiation Risks:** Radiationemitting products, including Fludeoxyglucose F^{18} Injection, may increase the risk for cancer, especially in pediatric patients. Use the smallest dose necessary for imaging and ensure safe handling to protect the patient and healthcare worker.
- **Blood Glucose Abnormalities:** In the oncology and neurology setting, suboptimal imaging may occur in patients with inadequately regulated blood glucose levels. In these patients, consider medical therapy and laboratory testing to assure at least two days of normoglycemia prior to Fludeoxyglucose F^{18} Injection administration.
- **Adverse Reactions:** Hypersensitivity reactions with pruritus, edema and rash have been reported; have emergency resuscitation equipment and personnel immediately available.



2 Coronal STIR **(2A)**, PET **(2B)**, and fused post-hoc **(2C)** images of a left gluteus muscle mass demonstrating high T2 signal intensity and mild FDG uptake (SUV_{max} 3.7).

Discussion

^{18}F-FDG PET/CT has developed into a well-recognized highly sensitive imaging modality for detection of MPNST, which is the leading cause of morbidity and mortality in patients with neurofibromatosis type 1 (NF1) [1-6]. Moreover, ^{18}F-FDG PET/CT may be potentially useful in preoperative tumor staging, guiding biopsies to the region of highest diagnostic yield within the tumor, or even directly influence management, either by reducing the number of unnecessary surgeries for benign plexiform neurofibromas or suggesting early intervention in tumors with imaging features suspicious for malignancy [7-9]. The most recognized parameter of PET/CT to differentiate between benign and malignant tumors in these NF1 patients is the maximum standardized uptake value (SUV_{max}). Despite the variation in the SUV_{max} cutoff value to differentiate between benign and malignant neurogenic tumors in patients with NF1, ranging between 1.8 [10] and 7.0 [1], the most widely used value is 3.5, where tumors with $SUV_{max} < 2.5$ are considered to be benign, tumors with $SUV_{max} > 3.5$ to be malignant, and those with values between 2.5 and 3.5 to be equivocal, in which case clinical correlation is suggested, and clinical/radiologic follow-up accordingly. Most studies have reported some degree of overlap between benign and malignant lesions on PET/CT, especially in the 2.5-3.5 SUV_{max} range.

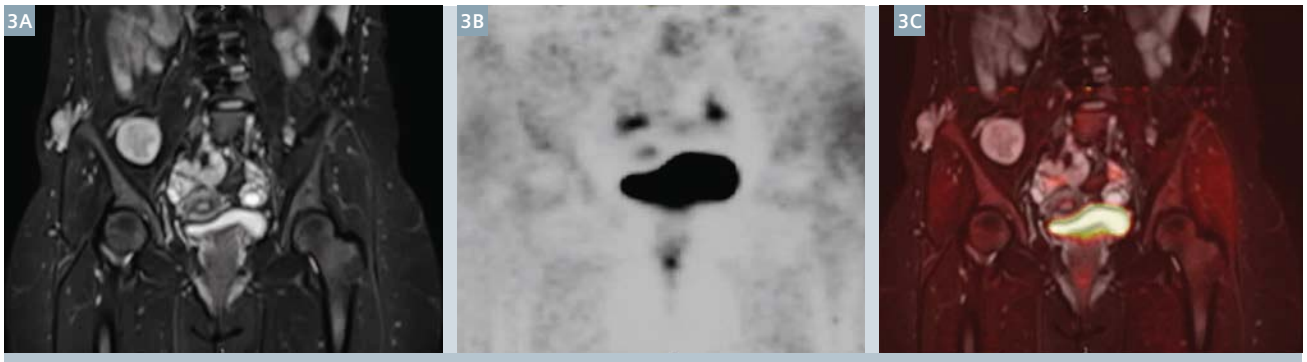
Several MRI features have been described as favoring MPNSTs, such as ill-defined margins, irregular enhancement, intratumoral lobulation and perilesional edema, all of which however have much lower sensitivity compared to PET/CT [2, 11, 12]. Whole-body MRI has been used to determine the burden of disease and extent of tumors in patients with NF1, without proven accurate differentiation between benign and malignant lesions. Tumor density measured by ADC and quantitative measures of perfusion measured by dynamic contrast-enhanced MRI (DCE-MR) require further study as potential diagnostic biomarkers for MPNSTs.

The above literature demonstrates that PET/CT and MR alone are not sufficiently reliable in differentiating benign, atypical and malignant PNST histologies and there is a need to develop better non-invasive imaging signatures to guide patient management. This case is an example of the potential utility of MR/PET in these lesions, with an excellent correlation between worrisome imaging features including an elevated SUV_{max} value (> 3.5) and diffusion restriction, and the eventual pathologic diagnosis on MPNST. The additional lesions in the pelvis area were presumed to be benign, mainly based on their low-grade metabolism and absence of other worrisome imaging features, as well as the absence of clinical symptoms.

Conclusion

Hybrid MR/PET is a promising new imaging modality which can potentially address the current limitation of existing knowledge by combining two of the most advanced imaging modalities (MR and PET) in an attempt to better diagnose malignancy in patients with this very serious disease that causes significant morbidity and mortality among Americans, at a significantly reduced radiation exposure by omitting clinically unnecessary imaging such as CT.

*The statements by Siemens' customers described herein are based on results that were achieved in the customer's unique setting. Since there is no "typical" setting and many variables exist there can be no guarantee that other customers will achieve the same results.



3 Coronal STIR **(3A)**, PET **(3B)**, and fused post-hoc images **(3C)** of right gluteus maximus and right iliacus lesions also demonstrating high T2 signal intensity and mild ^{18}F-FDG uptake (SUV_{max} 3.3 and 2.1 respectively).

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