^{18}F-FDG PET/CT in Malignant Peripheral Nerve Sheath Tumours: Insights and Clinical Implications

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Abstract

Malignant peripheral nerve sheath tumours (MPNSTs) are very rare, aggressive soft-tissue neoplasms developing from and involving the peripheral nerve sheath. MPNSTs are difficult to diagnose and treat and they contribute to significant morbidity and mortality for patients. ^{18}F-FDG PET/CT is valuable in diagnosing and staging as well as guiding therapeutic interventions, especially therapy response assessment in MPNST. As the incidence is very low, a valid statement at this point with respect to its role in patient management and optimal care is not defined. The current review will venture to use the available literature to define a role of this modality in the various aspects of management of MPNST.

Keywords: ^{18}F-FDG PET/CT; Malignant peripheral nerve sheath tumours; PET/CT; neurofibromatosis; soft-tissue sarcoma

DOI: https://doi.org/10.47391/JPMA.25-39

Introduction

Malignant peripheral nerve sheath tumours (MPNSTs) are very rare, aggressive soft-tissue neoplasms developing from and involving the peripheral nerve sheath.[1] The overall incidence is extremely low, approximately 0.001 % of the population although MPNSTs represent 5–10% of all soft tissue sarcomas and are more prevalent in neurofibromatosis type 1 (NF-1). The lifetime risk of developing MPNST in a patient with NF-1 syndrome is 8%–13%.[1] MPNSTs carry an ominous prognosis with a 5-year survival of up to 60% due to delayed diagnosis, early metastasis, and poor response to systemic therapy.[2] The diagnosis of MPNST with conventional radiological methods before sarcomatous transformation is quite difficult.[5] ^{18}F-FDG PET/CT is a promising technique used for staging, surveillance, treatment response evaluation and differentiation between benign and malignant pathologies in somatic malignancies.

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Review of Evidence

Radiological imaging serves as a useful non-invasive component in the diagnosis and management of MPNST, while the physical examination can indicate the involvement of peripheral nerves, imaging usually helps to locate these neurogenic tumours. Non-enhanced computed tomography (CT) can detect features of MPNST but the major contribution of CT lies in the demonstration of bony involvement. Magnetic resonance imaging (MRI) is optimal for assessing the local involvement of soft-tissues and exhibiting features diagnostic of MPNST.1 Moreover, positron emission tomography-computed tomography (PET/CT) with ^{18}F-fluorodeoxyglucose (FDG), which is being increasingly utilized nowadays, can greatly influence the diagnosis, staging, and follow-up of MPNSTs. ^{18}F-FDG PET/CT plays significant role in differentiating benign from malignant lesions as CT and MRI have limited role. Initial staging includes imaging of the primary lesion by using MRI and local CT. ^{18}F-FDG PET/CT is the best method to image the primary tumour in the periphery and to exclude metastasis.

^{18}F-FDG PET/CT plays a crucial role in the evaluation and management of (MPNSTs). These highly aggressive soft tissue sarcomas are highly FDG avid and have high maximum standardized uptake values (SUVmax) of 3.4-16.5, with a reported sensitivity of approximately >90%. 18F-FDG PET/CT has a potential role in the evaluation of the distribution of the primary lesion, loco-regional extension, and distant metastatic.

^{18}F-FDG PET/CT has a potential role in assessing the extent of the primary tumour, guiding biopsies and identifying potential metastatic lesions, which is essential for accurate staging and treatment planning.[1] The National Comprehensive Cancer Network (NCCN) guidelines suggest using 18F-FDG PET/CT scans for diagnosing MPNSTs due to their ability to detect increased metabolic activity associated with these tumours.[2] ^{18}F-FDG PET can help differentiate MPNSTs from benign nerve sheath tumours, such as neurofibromas. MPNSTs tend to be more

FDG avid, with SUVmax values generally higher than those of BPNSTs. However, some benign schwannomas can sometimes exhibit intense heterogeneous FDG activity, mimicking MPNSTs, so a low threshold for biopsy is recommended in such cases. Geitenbeek et al., found that ideal threshold values for SUVmax, SUVpeak, TLmax, and TLmean can achieve high sensitivity and specificity in detecting MPNSTs with SUVmax values above 5.8 being particularly indicative of malignant tumours, while SUV max values below 5.8 suggestive of benign nerve sheath tumours.[2] A systemic review by Tovmassian D et al., describes that the 18F-FDG -PET/CT is a useful, noninvasive diagnostic tool for the assessment of malignant transformation of PNSTs in adults and children.[2] It is able to predict with excellent sensitivity and negative predictive value, whether malignant transformation has occurred. It does however have shortcomings in that there is no ideal SUVmax cut-off value that has been found and substantiated. Further prospective trials are required in order to establish an ideal SUV max cut-off, to determine the use of tumour-to-liver ratio, other normalized values and to increase the pool of data available in this area and this should be performed in a uniform fashion. ^{18}F–FDG plays crucial role in diagnosis of distant metastases with its ability for whole body imaging in one stop (Figure 1).

^{18}F-FDG PET-CT can provide earlier detection of local disease recurrence and distant sites of metastases in patients with post-chemoradiation shrinkage. It can guide the treating oncologist by helping in dose escalation and expansion in the recurrent or residual tumour. ^{18}F-FDG has a potential role in differentiating high-grade and dedifferentiated lesion types of MPNSTs. 18F-FDG PET imaging can help distinguish residual or recurrent tumour from post-treatment inflammatory changes or scar tissue, as malignant lesions typically exhibit higher metabolic activity compared to non-malignant lesions.

Although there is not much published in support of utility of ^{18}F-FDG PET/CT for therapy response assessment for MPNST, ^{18}F-FDG PET imaging contributes considerably in monitoring the response to therapy after chemo or radiation therapy, by detecting changes in metabolic activity within the tumour (Figure 2). The sensitivity of ^{18}F-FDG PET/CT in the assessment of response after the completion of treatment regimens has been studied in the past with good results in diverse tumour types.[2] The time interval is likely to depend on the rate of restoration of glucose utilization in survived tumour cells after therapy. Although there are no uniformly recognized quantitative criteria for predicting response at interim PET, ^{18}F-FDG PET/CT has a potential role in the assessment of treatment response and aids in the early identification of patients with a favourable prognosis.

^{18}F-FDG PET/CT can be used for prognostication in MPNSTs. Yadav et al., report that the quantitative ^{18}F-FDG PET/CT parameters can help in prognostication at both baseline and relapse and additionally, the heterogeneity observed in lesions on textural analysis show high risk of recurrence and progression.[2]

Since many of the studies dealing with ^{18}F-FDG PET/CT in

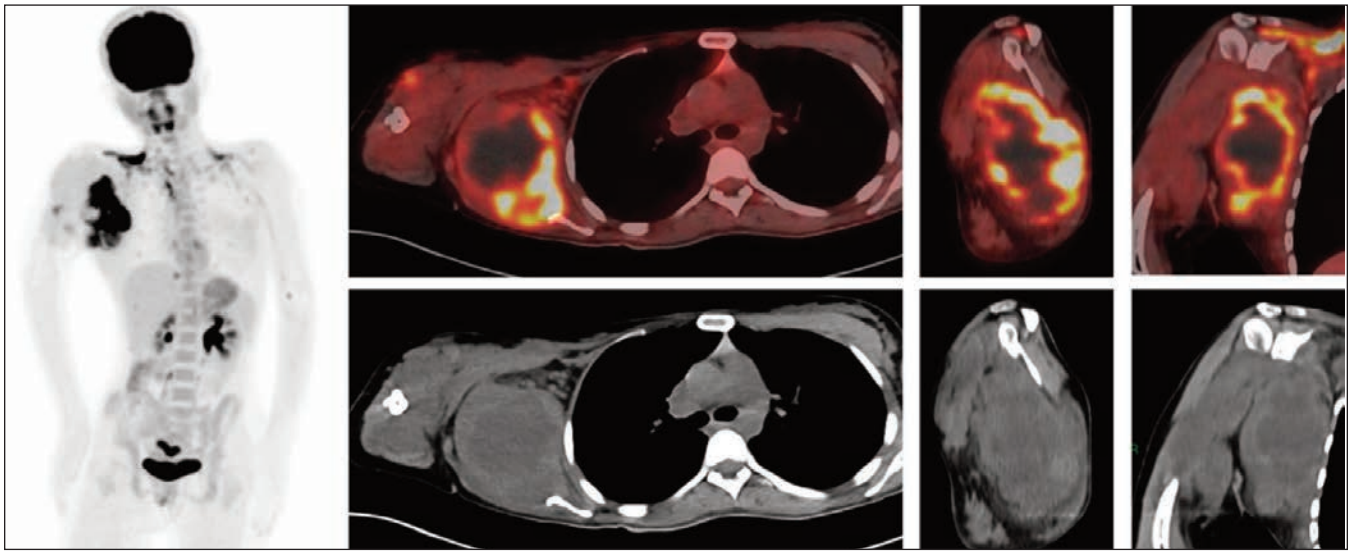

Figure-1: A 20-year-old is known case of neurofibromatosis type 1, presented with large right axillary mass. ^{18}F-FDG PET/CT images show ^{18}F-FDG avid lobulated soft tissue lesion (SUV max- 12.8) in right axillary region with areas of hypodensity suggestive of necrosis. The lesion is involving the muscles anterior to scapula. Hypodense lesions with no significant ^{18}F-FDG uptake are also seen in muscular and subcutaneous planes of adjacent right axilla and right shoulder region. Few areas of focal uptake are seen at this site. Biopsy from large ^{18}F-FDG avid axillary mass showed malignant peripheral nerve sheath tumour on the background of the neurofibroma. Hypodense lesions with no significant uptake in right shoulder were benign fibromas.

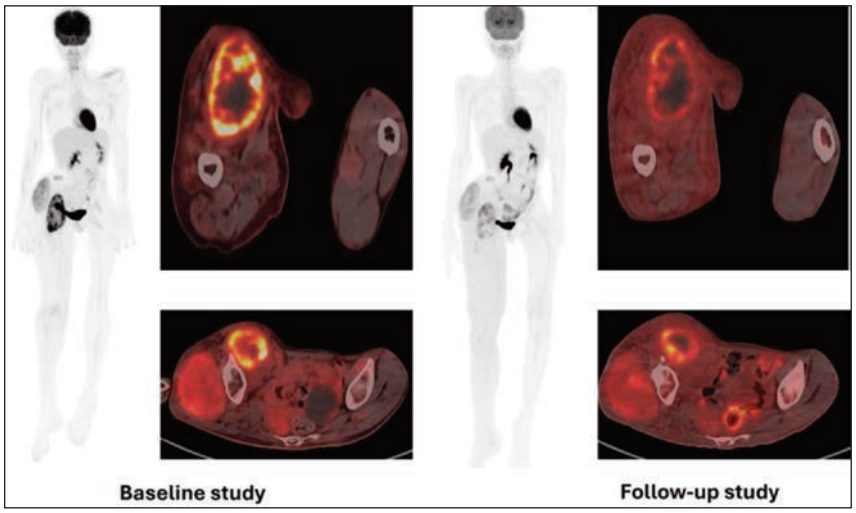

Figure-2: There is mild time interval reduction in size of right proximal thigh region with no significant change seen in size of right gluteal region and right pelvic region soft tissue masses suggesting stable disease, however there is significant reduction in metabolic activity in these 3 lesions (SUV max 12.4 reduce to SUV max 4.5) suggestive of partial metabolic response.

MPNST are case reports or small case series, large studies with comparison with other imaging modalities can help in better prognostication and improvements in diagnosis and management. The limited accuracy of [18]F-FDG PET/CT in small tumours or tumours with lower FDG uptake can be overcome by the simultaneous use of small molecules like amino acid that have shown good tracers for neurogenic tumours.[1] PET/MR is an emerging technique that could offer advantages due to its lack of ionizing radiation and enhanced soft tissue contrast. Future research might explore how combining PET/MR with PET/CT could potentially reduce radiation exposure for patients with known MPNST during follow-up scans.

Conclusion

[18]F-FDG PET/CT is a valuable tool for the detection and characterization of MPNSTs, with quantitative metrics and providing useful diagnostic and prognostic information. [18]F-FDG -PET/CT has been shown to be a useful, noninvasive diagnostic tool to differentiate benign from malignant peripheral nerve sheath tumours, monitor response to systemic therapy, and as a non-invasive way to detect/confirm malignant transformation. As the incidence is very low, definitive trials with adequate sample size are required to establish its potential role of [18]F-FDG PET/CT.

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