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Original Article

Diagnostic accuracy of 18-F FDG-PET/CT in evaluation of malignant neuronal involvement in neurologically manifested cancer patients

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ABSTRACT

Aim and objectives: The aim of this study was to assess the role of 18-F FDG-PET/CT in evaluating the peripheral malignant neuronal affection as well as perineural tumoral spread that occurs in patients with cancers.
Methodology: 50 patients with clinical symptoms of neurological deficits (34 male and 16 female) were included, their ages ranged from 17 to 74 with a mean of 45 years. PET/CT was done for all patients followed by clinical correlation after anti-inflammatory drugs and chemotherapy.
Results: Interpretation of the PET/CT studies and clinical correlation revealed 10 true positive cases with malignant neuronal involvement, 4 false positive cases diagnosed clinically as radiotherapy-induced neuropathy, 34 true negative cases and 2 false negative cases with negative PET/CT study and clinical evidence of nerve affection with sensitivity 83.33%, specificity 89.47%, PPV 71.43%, NPV 94.44% and diagnostic accuracy 88%. P-value $>$ 0.05 was considered statistically significant.
Conclusion: PET/CT has a significant role in detection of neuronal involvement by malignancy in cancer patients. Correlation between PET/CT and clinical outcome after chemotherapy improves the accuracy of diagnosis.

1. Introduction

Many types of malignant tumors as lymphoma, head and neck, breast, lung, prostate, colorectal, gynaecological and skin cancers can involve in their pathology peripheral nerves either by direct invasion or by extension of tumor cells along the tissue of the nerve sheath which is known as perineural spread (PNS) [1].

The most common tumors affecting peripheral nerves are lymphoma and head and neck cancers. Neuronal involvement in lymphoma patients occurs by direct extension form a nearby nodal or extra-nodal lymphomatous infiltrations or by systemic dissemination. Also, the cranial nerves as trigeminal and facial nerves are mainly affected by perineural spread in patients with head and neck cancers most commonly those arising from salivary glands (as adenoid cystic carcinoma), squamous cell carcinoma (SCC), melanoma and sarcoma [2,3].

The assessment of peripheral nerves involvement by malignancy is challenging to the clinicians and the radiologists because it can be asymptomatic and overlooked clinically even the surgeon cannot recognize it and it can be underestimated by imaging techniques [4].

Additionally, whether it is symptomatic or not, it has a poor prognosis as it decreases survival and increases the risk of recurrence and metastasis as it can extend beyond the fields of radiation and surgical treatment. So, the undiagnosed neuronal involvement by malignancy or perineural spread has a negative effect on the efficiency of disease treatment [5,6].

In the last few decades, Magnetic resonance imaging (MRI) with gadolinium-based contrast material enhancement was the first choice imaging modality used in recognization and diagnosis of peripheral nerves involvement by malignancy and perineural spread mainly when suspected clinically. Despite being non-invasive method, it has many disadvantages as difficulty in interpretation due to anatomical distortion by radiation or surgery, contraindication to contrast agent in renal patients, as well as contraindication of MRI to metallic devices, pain and claustophobia [7,8].

Nowadays, the introduction of positron emission tomography (PET)/computed tomography (CT) which is a combination of PET and CT imaging modalities has advanced the knowledge of the pathophysiology of cancer. It can observe metabolic processes by detecting

Abbreviations: 18F, fluorine-18; CT, computed tomography; FDG, fluorodeoxyglucose; GBM, glioblastoma multiformis; MIP, maximum intensity projection; MRI, magnetic resonance imaging; NHL, Non-Hodgkin's lymphoma; PET, positron emission tomography; PNS, perineural spread; SCC, squamous cell carcinoma; SUV, standardized uptake value

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gamma rays emitted indirectly by a positron-emitting radionuclide (Fluorine 18) which is introduced into the body on a biologically active molecule (Fluorodeoxyglucose) and add it to the anatomical information obtained from CT during the same session [9,10].

So, 18-F FDG-PET/CT helps in evaluation of neuronal involvement by malignant tumors and perineural spread to a great extent. Although it has low specificity due to radiotracer uptake in cases of radiation or chemotherapy-induced plexopathy or other inflammatory neuropathy, it gives high suspicion of neuronal involvement by malignancy and perineural spread in clinically-silent patients and confirm the diagnosis when correlated either clinically in symptomatic patients or with MRI [1,11].

Furthermore, PET/CT facilitated directing biopsy form the metabolic activity detected along the course of certain nerve, and when it is malignant, it can be used in follow up for assessment in treatment response [1].

2. Patients and methods

2.1. Patients

Fifty patients (34 male and 16 female) with different types of pathologically proven cancers and different neurologic manifestations suspecting neuronal involvement had done 18-F FDG-PET/CT examinations during the period from November 2016 to November 2017. Approval of Research Ethics Committee (REC) and informed consent were obtained from all participants in this study after explanation of the benefits and risks of the procedure as well as accurate informing of the duration of the PET-CT examination. Privacy and confidentiality of all patients' data were guaranteed. All data provision were monitored and used for scientific purpose only.

Inclusion criteria:

- Patients with histologically confirmed malignancy with neurological complaint on taking history.
- No age/sex predilection.
- Exclusion criteria:
- Pregnant females.
- Patients with hyperglycemia (blood glucose level ≥ 200 mg/dL).
- Patients with organ failure or active infection.

2.2. Methods

All patients were subjected to the followings

2.2.1. Data collection

- Personal history: name, date of birth, age, sex, and gynecological history of female patients to avoid heedless exposure of the fetus.
- History of any systemic disease as diabetes, recent inflammation or infection, organ failure.
- Past history of prior malignancy, neurological disease or/ and any operations.
- Present history, focused upon the type and site of malignancy, dates of diagnosis and treatment (biopsy results, surgery, radiation, and chemotherapy), current medications, the recent symptoms. The studied 50 patients were selected after thorough data collection including suspecting symptoms of neurological deficits; either sensory or motor disturbances or combination between both. The symptoms in this study included pain in most of patients, muscle weakness, numbness, tingling, urinary incontinence and constipation as well as facial symptoms as burning sensation, numbness, spasm and tongue weakness in patients with head and neck cancer, they were asked about its onset, course, duration, taken medication for it and its course in relation to chemotherapy (if received). Also, all the previous imaging studies, histopathological findings and any other investigations.
- The accurate time for PET/CT scanning was one week post-biopsy, 4 weeks post-surgery, 2–4 weeks post-chemotherapy, and 1–3 months post-radiation.
- Recent creatinine level and history of allergies to contrast material or any allergy were known from the patients.
- The patients were asked about their ability to lie for the duration of the scan (30–45 min) and history of claustrophobia.

Table 1
The indications of PET/CT in the studied 50 patients.

The indication for PET/CT studies	No. of patients	Percentage %
Primary staging	4	8%
Identifying unknown primary tumor	6	12%
Follow up	24	48%
Assessment of treatment response	16	32%

Table 2
The total result of the 50 PET/CT studies.

Cases	−ve		+ve		χ^2	^{FE}p
	No.	%	No.	%		
−ve	True –ve		False –ve		23.980*	< 0.001*
	34	68	2	4		
+ve	False +ve		True +ve			
	4	8	10	20		

* Statistically significant at $p \leq 0.05$.

2.2.2. Patient preparation

- Dietary preparation including complete food fasting as well as no intravenous fluids containing dextrose or parenteral feedings for approximately 4–6 h prior to scanning. Only 2 liters of plain water was permitted for well hydration to increase 18F-FDG excretion; flavored water, sugar or carbohydrate intake, caffeine, alcohol, and nicotine products were not allowed 12 h before scan. A high-protein, low-carbohydrate and low-fat diet was taken 24 h before scan.
- Activity restriction 24 h before study. No gum chewing.
- Diabetic patients (number = 21 in this study) on regular insulin were advised to take their normal amount of insulin with breakfast by 6 AM.
- Blood glucose level was checked at the day of examination before 18F-FDG injection, it ranged between 65 mg/dl and 215 mg/dl. Target blood sugar is 150–200 mg/dl.
- The weight of the patients was also measured which ranged between 45 kg and 115 kg and then the dose of the radiopharamaceutical (18F-FDG) was calculated for each patient (0.1 mCi/kg body weight). The height of the patients was also measured; it ranged between 155 cm and 185 cm. All these data were noted in a worksheet.
- IV line set up for the radiopharmaceutical injection, either in the anterior forearm, dorsal hand, radial aspect of the wrist, or the antecubital space.
- On arrival of the radiopharmaceutical, it was calibrated by the physicians in hot lab. Then, the patient name and medical record number were reviewed. The IV line in each patient was checked using normal saline prior to administering the radiopharmaceutical. The patients were injected with 18F-FDG. The dose of 18F-FDG injected ranged between 5.5 mCi and 11 mCi. 18F-FDG injection was followed by flushing with 10–20 cc of normal saline.
- Patients were isolated in the dedicated uptake warm quite rooms and rested for 45–60 min before imaging.
- The bladder was emptied by voiding just before being positioned on the PET-CT table.