Original article

Positron Emission Tomography in Mucosal Melanomas of Head and Neck: Results from a South Asian Tertiary Cancer Care Center

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Abstract

To evaluate the accuracy of fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT) in staging and restaging of patients with mucosal melanomas (MM) of head and neck. Patients who underwent PET/CT at our institution, with a biopsy proven diagnosis of MM of the head and neck between March 2006 and December 2013 were included in the study. Nineteen patients with MM of the nasal cavity, paranasal sinuses, and oral cavity were included, of which 12 were for staging and seven for restaging. PET/CT had 100% sensitivity (SN), specificity (SP), positive predictive value (PPV), and negative predictive value (NPV) for detection of the primary. SN of 91.7%, SP of 100%, PPV of 100%, and NPV of 87.5% were seen for nodal metastases. For distant metastases, SN of 85.7%, SP of 100%, PPV of 100%, and NPV of 92.3% were noted. The disease was upstaged from loco-regional to metastatic in 32% leading to treatment change in 25% in the staging group and 43% in the restaging group. PET/CT demonstrates good overall accuracy in evaluation of patients with MM of the head and neck. The main strength of PET/CT lies in detection of distant metastatic disease due to extended whole-body field of view.

Keywords: Computed tomography, head and neck, mucosal melanoma, positron emission tomography, positron emission tomography/computed tomography

Introduction

Mucosal melanomas (MM) arise in extracutaneous sites from melanocytes present in mucosal membranes of the respiratory tract, gastrointestinal and urogenital tract. In the head and neck, the MM arises from the mucosal lining of the nasal cavity, sinuses, and in the oral cavity. Apart from mucosal membrane, they can also arise from the melanocytes present in the eye and leptomeninges.[1]

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Primary MM are rare, aggressive tumors accounting for 0.4–2% of all malignant melanomas and 4–10% of melanomas of head and neck.[2-4] MM are usually detected late because they occur in occult sites, and there is the absence of signs and symptoms in early disease. All these lead to even poorer prognosis in this aggressive malignancy.

The etiopathogenesis of this malignancy is not well-known. Unlike in cutaneous melanomas where

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exposure to the sun is a well-known risk factor; it is not the case in MM as these arise on mucosal lining which are not exposed to sun.[5] Because of the rarity of MM and lack of knowledge about their etiopathogenesis, there are no well-established staging systems and evidence-based treatment protocols.

The role of positron emission tomography/computed tomography (PET/CT) in the evaluation of distant metastases, response evaluation and recurrence of squamous cell carcinoma head and neck has already been established.[6-8]

We undertook this retrospective evaluation to study the role of fluorodeoxyglucose (FDG) PET/CT in the evaluation of MM of the head and neck.

The aim of our study was to report our experience in evaluating the accuracy of FDG PET/CT in staging and restaging of patients with MM of the head and neck.

Materials and Methods

Patients with biopsy proven MM of the head and neck who underwent a PET/CT between March 2006 and December 2013 were included in the study. A total of 19 patients, 12 males and seven females with age range of 36–81 years were included. Patients with MM of the nasal cavity, paranasal sinuses, and oral cavity were included. There were 12 patients for staging and seven for restaging [Table 1]. All the PET/CT studies were evaluated for the ability to detect the primary disease, nodal, and other sites of metastases. The sensitivity (SN), specificity (SP), positive predictive value (PPV), negative predictive value (NPV), and accuracy were calculated for each site at 95% confidence interval.

Table 1: Patient demographics

Characteristics	*n*
Gender	
Male	12
Female	07
Age (years)	
Median	60
Range	36-81
Location of tumor	
Nasal cavity	9
Paranasal sinus	2
Alveolus	5
Hard palate	3
Indication	
Staging	12
Restaging	07

Patient preparation and positron emission tomography/computed tomography imaging protocol

All patients were asked to fast for 4–6 h before the study and blood glucose levels were checked and confirmed to be <150 mg/dl. The studies were performed 60–90 min following intravenous administration of 5 MBq/kg of ^{18}F-FDG. Imaging was performed on a discovery ST PET/CT system (GE Medical Systems). It combines a 16 slice CT scanner with a dedicated PET (BGO plus crystal, dimensions 3.8 mm × 3.8 mm × 3.8 cm).

CT was performed over 5–8-bed positions from the skull base to the mid-thigh; using multislice (16 slice) CT component of the system. CT parameters included 140 kV, 110–210 mA, 0.8 s/rotation, pitch of 1.75:1, field of view (FOV) 50 cm, the length of scan 1.0–1.6 m, 0.625 spatial resolution, and slice thickness of 3.75 mm. The intravenous and oral contrast were not routinely administered in all patients unless there was a specific indication. This was followed immediately by acquisition of PET data in the same anatomic locations with 15.4 cm axial FOV acquired in three-dimensional mode with 3 min/bed position.

Image reconstruction and interpretation

The images were reconstructed using a standard vendor provided reconstruction algorithm which incorporated ordered subset expectation maximization. Image fusion was performed using coordinate-based fusion software and subsequently reviewed at a workstation that provided multiplanar reformatted images and displayed PET images, CT images, and PET/CT fusion images.

The images were evaluated by two experienced nuclear medicine physicians. Any area with intensity greater than background that could not be identified as physiological activity or which on CT correlation did not fit into benign (infective/inflammatory/degenerative) was considered to be suggestive of tumor on the PET study. For pulmonary lesions, the morphologic characteristics of metastases on CT were taken as positive even in the absence of ^{18}F-FDG uptake. The diagnostic accuracy of FDG PET/CT for detection of the primary tumor/recurrence and the metastatic lesions was correlated with either histopathology or subsequent follow-up scan.

Statistical analysis

All the PET/CT studies were evaluated for the ability to detect the primary disease, nodal, and other sites of metastases. The SN, SP, PPV, NPV, and accuracy were calculated for each site at 95% confidence interval.

Results

The results of PET/CT were analyzed for 12 patients who were for staging and seven for restaging [Tables 2 and 3].

The primary tumor/recurrent lesion was detected in 18 out of the 19 patients as one patient referred for restaging had only metastatic disease. In all patients, histopathological correlation was available for the primary (SN, SP, PPV, NPV - 100%) and cervical nodal disease [Figure 1]. Nodal metastases were detected in 11 out of the 19 patients and was falsely negative in one patient (SN 91.7%, SP 100%, PPV 100%, NPV 87.5%). Distant metastatic lesions were detected in six patients of whom five patients had metabolically active disease [Figure 2] and in one patient non-FDG avid lung nodules were detected [Table 2, patient no. 8]. A metastatic brain lesion in the frontal lobe [Table 2, patient no. 17] was not detected on PET, which was detected by magnetic resonance imaging (MRI) and confirmed by histopathology (SN 85.7%, SP 100%, PPV 100%, NPV 92.3%). A second primary in the kidney was detected in one patient [Table 2, patient no. 18]. In all patients who

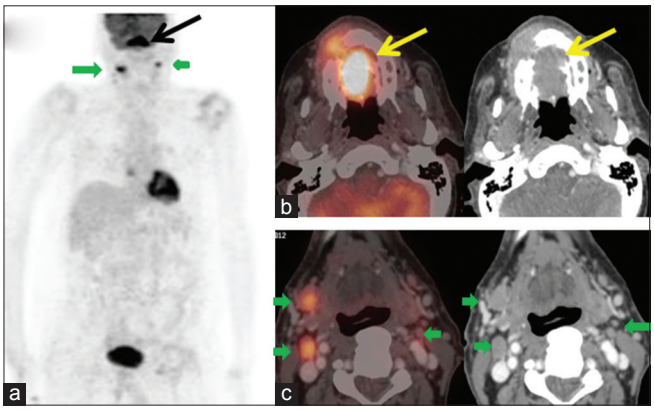

Figure 1: (a) Maximum intensity projection image showing hypermetabolic focus in the hard palate (arrow) and cervical nodes (block arrows), (b) axial fused positron emission tomography/computed tomography and computed tomography images showing fluorodeoxyglucose avid primary mass in the hard palate (arrow), (c) axial fused positron emission tomography/computed tomography and computed tomography images showing fluorodeoxyglucose avid bilateral cervical nodes (block arrows) [Patient no. 11 from Table 2]

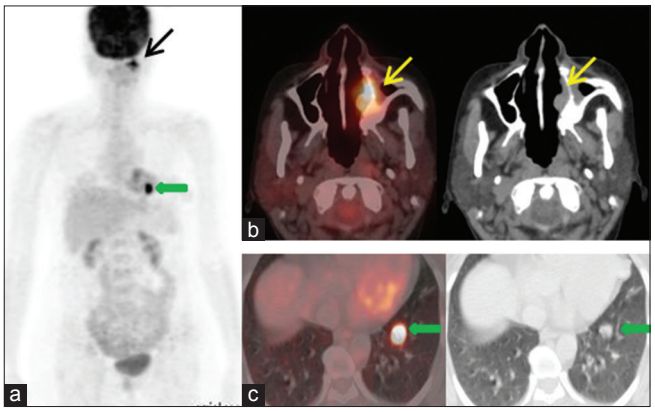

Figure 2: (a) Maximum intensity projection image showing hypermetabolic recurrent focus in left nasal cavity (arrow) and another hypermetabolic focus in left lung (block arrow), (b) axial fused positron emission tomography/computed tomography and computed tomography images showing fluorodeoxyglucose avid recurrent mass in left nasal cavity (arrow), (c) axial fused positron emission tomography/computed tomography and computed tomography images showing fluorodeoxyglucose avid nodule in lower lobe of the left lung (block arrow) [Patient no. 15 from Table 2]

Table 2: Indication and PET/CT scan result

Age/gender	Primary site	Indication	Primary	Nodal metastases	Distant metastases	upstaged
80/male	Nasal cavity	S	TP	TP	TN	No
72/female	Nasal cavity	S	TP	TP	TP	Yes
70/male	Nasal cavity	S	TP	TN	TN	No
74/male	Nasal cavity	S	TP	TN	TN	No
55/female	Nasal cavity	S	TP	TN	TN	No
66/male	Maxillary sinus	S	TP	TN	TN	No
46/female	Upper alveolus	S	TP	TP	TP	Yes
48/male	Upper alveolus	S	TP	TP	TP	Yes
					Non-FDG avid lung nodules	
65/female	Upper alveolus	S	TP	TP	TN	No
55/male	Lower alveolus	S	TP	FN	TN	No
81/male	Hard palate	S	TP	TP	TN	No
60/male	Hard palate	S	TP	TP	TN	No
59/male	Nasal cavity	RS	TP	TP	TP	Yes
55/male	Nasal cavity	RS	TP	TN	TN	No
60/female	Nasal cavity	RS	TP	TP	TP	Yes
61/male	Nasal cavity	RS	TP	TP	TP	Yes
42/female	Maxillary sinus	RS	TN	TN	FN (brain metastasis)	No
65/male	Lower alveolus	RS	TP	TN	TN	Yes
						2nd primary in the kidney
36/female	Upper alveolus	RS	TP	TP	TN	No

S: Staging; RS: Restaging; TP: True positive; TN: True negative; FP: False positive; FN: False negative; FDG: Fluorodeoxyglucose

Table 3: Result

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Primary	100	100	100	100	100
Nodes	91.7	100	100	87.5	94.7
Metastases	85.7	100	100	92.3	89.5
Overall	92.5	100	100	93.3	94.7

PPV: Positive predictive value; NPV: Negative predictive value

were upstaged to metastatic disease by PET/CT; none had clinically evident metastatic disease.

The overall SN, SP, PPV, NPV, and accuracy were 92.5%, 100%, 100%, 93.3%, and 94.7%, respectively.

Among the 12 patients for initial staging 25% were metastatic at initial presentation (three out of 12). Fifty-four percent had cervical nodal metastases at initial presentation (seven out of 12). The disease was upstaged from clinically loco-regional disease to metastatic disease in 32% (six out of 19). This lead to a treatment change in 25% (three out of 12) in the staging group and 43% (three out of 7) in the restaging group.

Discussion

Mucosal melanoma of the head and neck carries an extremely dismal prognosis with 5-year survival of localized MM being only 24%.[9] For early and localized MM, the primary modality of treatment is surgery with or without adjuvant radiotherapy (RT) postoperatively.[10]

In spite of adequate local control, recurrences are common due to aggressive nature of MM.[11] It is thought that high rates of local recurrence are likely because of multifocal nature of the disease or due to clinically obscured lymphatic spread.[12]

In such a scenario, PET being metabolic whole body imaging tool appears ideal for accurate staging of MM before undertaking curative resection.

Melanoma cancer cells are known to be extremely FDG avid due to up-regulation of glucose transporter proteins, and this forms the basis of imaging melanoma with FDG PET.[13] Combination of CT with PET is an added advantage and makes it possible for anatomic localization as well as to distinguish between pathological and physiological/benign uptake of FDG thus increasing the SN and SP of the imaging modality.

Moreover, FDG PET/CT is one of the best modalities for evaluation of distant metastases in head and neck and many other cancers of the body.[14,15]

In our study, the primary lesion was detected in all patients, nodal metastases were correctly identified in 11 patients out of 19. In one patient, the surgical specimen was positive for nodal metastasis which was not evident on the scan. It is well-known that micro-metastasis can be missed on PET/CT and is beyond the resolution of the imaging scanners for detection.

The overall SN for distant metastases was 86%. Twelve sites of metastatic lesions were correctly identified in six patients. In one patient, a frontal lobe lesion was not identified on PET. PET is not an ideal modality for detection of brain metastases due to high physiological uptake of FDG in the brain.

In our study, we have seen that PET/CT has high SN, SP and diagnostic accuracy in detection of MM of head and neck and thus may play an important role in staging of these melanomas and thus stratifying the choice of treatment in patients with distant metastatic disease and in patients with recurrent disease. Patients with disease at the primary site with loco-regional lymph nodes are treated with surgery and RT whereas patients with distant metastatic disease or with inoperable disease are treated with biochemotherapy or targeted therapy.[16]

The results of our study were similar to the study done by Haerle *et al*., where PET/CT in initial staging was compared with CT or MRI in ten patients. Regional nodal disease and distant metastases were detected in all patients except in one with brain metastasis.[17]

In another study done by Lamarre *et al*., role of PET/CT was evaluated in patients with sinonasal neoplasms.[18] Total number of patients in this study were 31 with only six patients of mucosal melanoma. This study showed a high NPV and low PPV due to high rate of false positive results. Most false positive results were seen in the restaging group at the primary site, which also led to unnecessary surgical interventions. However, this was not the case in our study as all MM are extremely FDG avid where in the study by Lamarre *et al*., there was a heterogeneous group of sinonasal neoplasms which included olfactory neuroblastomas, squamous cell carcinoma, sinonasal undifferentiated carcinomas and salivary gland tumors apart from MM. The FDG avidity varies from high to low in this mixed population. This could be the reason for more number of false positives.

Moreover, in our study, low-grade FDG uptake in normal/reactive appearing neck nodes which were morphologically elongated, nonenhancing with fatty hilum with standardized uptake value (SUV) value below 2.5 were reported as benign nodes. Nodes which were rounded, enhancing with SUV >2.5 were considered to be involved by the disease. There were no false positive neck nodes in our study.

PET/CT can also be used for response assessment and a predictor of prognosis.[19]

The first limitation of our study is the small number of patients, but MM is a rare disease and is important that such series are reported to strengthen the existing literature on MM. The second limitation was that histopathological validation for all the distant metastases was not done. This may not be technically feasible each time and may not be ethically correct. However, this was substantiated by follow-up imaging.

Conclusion

PET/CT demonstrates good overall accuracy in evaluation of patients with MM of the head and neck. The main strength of PET/CT lies in detection of distant metastatic disease due to extended whole body FOV.

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Conflicts of interest
The authors declare no conflicts of interest.

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