Research Article

18F-FDG PET/CT in Identifying Primary Site in Patients with Neck Secondaries: A Cross Sectional Study

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Abstract

Purpose: The detection of the primary site in patients with carcinoma unknown primary neck is always a challenge. This study was conducted to assess the role of 18F-FDG PET/CT in detecting the primary in patients with neck secondaries. This study also aimed to compare its diagnostic sensitivity with computed tomography and triple endoscopy.

Materials and Methods: We prospectively evaluated thirty two patients of carcinoma of unknown primary who presented with cervical lymphadenopathy. Inclusion criteria were all patients who had a fine-needle aspiration of cervical lymph node suggestive of squamous cell carcinoma without clinically detectable primary site. We did a clinical and radiological evaluation for all patients. All patients were subjected to further assessment by a triple endoscopy and 18F-FDG PET/CT. Following 18F-FDG PET/CT, we took a biopsy from the suspicious site in all patients. The biopsy reports were collected.

Results: The primary detection rate was 18.8%. With the help of PET CT, biopsy confirmed primary site was detected in 6 patients. The sensitivity, specificity, positive predictive value, negative predictive value of PET-CT were 100%, 34.6%, 26.1%, 100% respectively.

Conclusion: 18F-FDG PET/CT has higher sensitivity, detection rate and negative predictive value as compared to computed tomography and triple endoscopy.

Keywords: 18F-FDG PET/CT; Unknown Primary; Carcinoma; Neck Secondaries

Introduction

Carcinoma of unknown primary (CUP) is proven metastatic neck lymphadenopathy, without identifying a primary site within a subsequent five year period. The diagnosis is by exclusion, after a complete history and physical examination, necessary laboratory studies, computed tomography (CT) scans and additional directed studies indicated by positive findings during the initial workup [1]. Carcinoma with the unknown primary consist of 5% - 10% of all cancer patients [2]. Around 1 - 2% of these patients account to head and neck malignancy [2]. The primary detection rate of

18 Fluorodeoxyglucose Positron Emission Tomography Computed Tomography ([18]FDG PET-CT) reported varying from 10% to 47% in the literature [3-5]. There are high morbidity and mortality of cancer of unknown primary due to lack of knowledge of primary tumour. Still, there are not many prospective studies showing the role of 18F-FDG PET/CT in cancer of unknown primary and its comparison with conventional CT. Therefore, this study is conducted to assess the role of 18F-FDG PET/CT in detecting primary malignant site in patients with carcinoma neck unknown primary and to compare with other modalities like Computed tomography and Triple endoscopy.

Materials and Methods

This is a prospective cohort study. We obtained institute ethics committee approval before commencing the study. All patients included in the study had undergone Fine needle aspiration of cervical lymph nodes and had proven squamous cell carcinoma on cervical nodes whose primary site was unidentified. Patient who refused to give written informed consent, pregnant and lactating mothers, patients with uncontrolled diabetes and claustrophobia were excluded from the study.

After obtaining consent, patients were evaluated in our outpatient department. We did a complete detailed clinical examination. Chest Xray, Barium swallow and Contrast-enhanced computed tomography of the neck were done. Radiologists reviewed Contrast-enhanced Computed Tomography (CECT) neck of all patients. Thirty two patients who had no evidence of primary, after clinical and radiological evaluation, were recruited into the study. We did 18F-FDG PET/CT and triple endoscopy for all patients recruited in the study. Two experienced nuclear medicine physicians evaluated the 18F-FDG PET/CT scan findings independently, who were blinded to the clinical and structural imaging findings. Any focal areas with increased uptake in 18F-FDG PET/CT were considered suspicious. The biopsy was taken from those sites in patients who had a suspicious 18F-FDG PET/CT. Patients who had negative biopsy reports and in whom no primary site was able to identify were treated as like unknown primary with secondary neck, as per their staging. In patients whose PET-CT had no suspicious site, a biopsy was taken from the clinically suspected primary site. Any biopsy suggestive of malignancy was considered as the primary site. Histopathology reports were collected. We compared the histopathology reports with 18F-FDG PET/CT findings. All patients were treated as per institutional protocols.

Results

We recruited thirty two patients who did not have any primary site identifiable in clinical examination or CECT. All patients included in this study had squamous cell carcinomas (SCCAs) cervical nodal metastasis which was either cytology or histology proven. The mean age was 55.03 years. Twenty five were men, and 7 were women. Majority of patients were of above the age of 50 (24 patients). Majority of patients belonged to N2 (18 patients) as compared to the N3 stage (14 patients). Focal uptake in 18FDG PET-CT was seen in 23 (71.9%) of 32 patients. The site with focal uptake was considered as the probable site of primary and biopsy was taken from these sites. While in remaining patients (28.1%), there was no area of focal uptake.

Among 23 patients in whom biopsy was taken from suspicious areas, six patients had biopsy proving squamous cell carcinoma.

In patients whose CECT and 18F-FDG PET/CT failed to reveal any primary site, underwent random biopsies from clinically suspected sites. Among these nine patients, 4 underwent biopsy from tonsil, two from the base of tongue, one each from pyriform sinus, nasopharynx and tonsillolingual sulcus. All these patients histopathology did not report any malignant pathology. Hence, we infer that 18F-FDG PET/CT had a high negative predictive value (100%).

The 18F-FDG PET/CT scan was able to detect a biopsy-confirmed primary site in 6 patients. The biopsy sites in those patients are given in the following table (Table 1).

		95% confidence interval
Sensitivity	100% (6/6)	51.7 - 100
Specificity	34.6% (9/26)	17.9 - 55.6
Positive predictive value	26.1% (6/23)	11.1 - 48.7
Negative predictive value	100% (9/9)	62.9 - 100

Table 1: Diagnostic accuracy of 18FDG PET CT in the study.

*: The biopsy was taken from one suspected site only even when PET-CT did not show any abnormality.

Biopsy of all patients, who had negative 18FDG PET-CT scan for detection of primary, were negative. These patients were classified as unknown primary carcinoma as all these cases were also negative on CECT Scan and panendoscopy. These patients were presented at our multidisciplinary head and neck tumour board and were treated as per standard protocol.

Hence, we infer that the primary tumour detection rate 18FDG PET-CT is 18.8% (6 of 32). There were 17 false positive PET-CT results. The overall primary tumour detection rate (PET plus pan endoscopy plus CT scan) was still 18.8% (6 of 32 cases) as pan endoscopy, and CECT scan did not reveal any primary. The validity of 18FDG PET-CT in our study has been summarized in table 1.

Discussion

Carcinoma of the unknown primary site (CUP) represents a group of heterogeneous tumours that share the unique clinical characteristic of metastatic epithelial disease with no identifiable origin at the time of diagnosis. The management of these tumours is a challenge in oncology. Identification of the primary and histology of the tumour forms the basis for assigning appropriate therapy for the patients [6].

We reviewed the literature and found that most of the studies published in the literature are done with Positron Emission Tomography (PET) alone and with a lesser number of patients. Now it has been well established that PET alone has lower sensitivity as compared to 18F-FDG PET/CT. 18F-FDG PET/CT has higher sensitivity and specificity compared to PET as it has better localization of abnormal FDG uptake [3]. 18F-FDG PET/CT has been less evaluated in patients with cervical metastases and results are very heterogeneous. Therefore, the present study was aimed to find out the role of 18F-FDG PET/CT in detecting primary malignant site in patients of unknown primary tumours, presenting with cervical lymph node squamous cell carcinoma metastases.

All patients included in this study had squamous cell carcinomas and an upper neck presentation with the bulk of the metastatic adenopathy in level 2 and level 3. The false positive rate of FDG PET-CT was relatively high in our study (17 out of 32 patients), similar to a study by Roh., et al [7].

Nine of 32 patients did not show any focal uptake on PET-CT. The biopsy was done from clinically suspicious areas in those patients, but all biopsies were negative for malignancy. Therefore, we can infer PET-CT has a high negative predictive value (100%).

Whole-body 18F-FDG PET/CT reduced the number of unidentified primary lesions by 18.8% in our series of patients. These lesions were small and were missed during the initial conventional diagnostic evaluation. Even though the number appears to be minor, the benefit to patients should be measured by an increase in survival or improvement in the quality of life.

18F-FDG PET/CT was beneficial in patients in whom we were able to find a primary site, especially in cases where nasopharynx was found as the primary site. Even though the nodal status was high in those patients, the patients were considered for curative therapy.

Sengupta., et al. [8] investigated 18F-FDG PET/CT as a means of detection of primary tumours in 15 patients with unknown primary tumours. They opined that 18F-FDG PET/CT might be a more accurate and cost-effective method for detecting hidden primary tumours than a conventional diagnostic approach. However, for our group of patients, the average costs of a traditional diagnostic workup were relatively low as compared to 18F-FDG PET/CT. Therefore, it may not be cost-effective for our group of patients.

Our experience would suggest that in patients with a complete negative workup (negative PET and negative panendoscopy), the risk of a primary tumour is low, indicated by high negative predictive value (100%) of PET-CT.

In our series, 50% of the patients belonged to N3 nodal status. The N3 neck patients form a difficult group due to advanced disease to manage. The overall poor prognosis for the N3 neck has been demonstrated in multiple studies. It should also be realized that 18F-FDG PET/CT is an expensive investigation. False-positive 18F-FDG PET/CT rates were high in our series.

Regardless of its ability to detect an unknown primary tumour, another critical aspect of 18F-FDG PET/CT that should be considered is its ability to identify or rule out additional metastatic sites, which may have important implications for patient management. The utility of 18F-FDG PET/CT may mainly be of interest in patients with carcinoma with unknown primary, who present with lymph node metastatic disease only. In case any distant metastasis site is noted, the patient management differs. One of our patients was found to have lung metastasis following 18F-FDG PET/CT.

A recent meta-analysis done by Burglin., et al. found that the detection rate of primary with 18F-FDG PET/CT is 40.3%. They also added that ¹⁸FDG PET-CT has been promising as a single accurate modality of diagnosis in cases of carcinoma with unknown primary [9].

Compared to other diagnostic procedures that are often used in patients with unknown carcinoma primary (e.g. CT alone and endoscopic procedures), 18F-FDG PET/CT is both non-invasive and a very sensitive tomographic whole-body imaging modality. 18F-FDG PET/CT may allow detection of a primary tumour and complete tumour staging in a single examination. It can be argued that if 18F-FDG PET/CT fails to detect a primary tumour, other diagnostic procedures are also likely to fail. Therefore, we would like to advocate 18F-FDG PET/CT as a first-line imaging modality in all patients with the metastatic disease rather than using it after other diagnostic procedures. But still, we need to have more prospective studies with long term follow up.

Conclusion

18F-FDG PET/CT plays an essential role in detecting primary malignant site in patients of unknown primary tumours presenting with cervical lymph node metastasis. 18F-FDG PET/CT was found to have higher sensitivity, detection rate and negative predictive value as compared to conventional diagnostic modalities like contrast-enhanced computed tomography of neck and triple endoscopy in patients of unknown primary tumours. In our study, 18F-FDG PET/CT had the highest sensitivity in patients with N3 neck

nodes. Therefore, patients with higher nodal status have a better chance of detection of the primary site by 18F-FDG PET/CT. Still further prospective studies may be required for considering 18F-FDG PET/CT as the primary modality for identifying the primary site in patients with carcinoma with unknown primary.

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Conflict of Interest

There is no conflict of interest among the authors.

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