Original Article

Role of [18F]FDG – PET/CT Scan in Cervical Tuberculosis

Sanjeev Kumar, Pankaj Singh, Survesh Kumar Gupta[1], Ajay Kumar Verma[2], Suresh Kumar

Departments of General Surgery, [1]Paediatric Surgery and [2]Respiratory Medicine, King George's Medical University, Lucknow, Uttar Pradesh, India

Abstract

Background: Distribution and quantification of extra-pulmonary tuberculosis and elicitation of response antitubercular therapy via F18–Fluorodeoxyglucose Positron Emission-based Tomography/ Computed Tomography(F18–FDG PET/CT) . **Materials and Methods:** This was a prospective Pilot study. In this study 30 patients of age between 15 to 36 years(mean 26.8±6.13years) were included. PET/CT scan was performed at the time of presentation(baseline) and after 2 months of anti-tubercular therapy to evaluate bacterial activity in different levels of cervical lymph nodes and changes in various parameters of lymph nodes such as size, conglomeration and abscess formation were included in the evaluation. **Result:** In this study, 18 patients were of 18 to 30 years(60.0%), 3 patients were below 18 years(10.0%) and 9 patients above 30 years(30%). The female proportion was higher in our study population(53.3%). Node-positive status, conglomeration, and abscess were evaluated clinically. Maximum percentages were found in level II and level V groups. While minimum percentage was found in level I and level VI. We also found that in all patients of tubercular cervical lymphadenopathy, tubercular bacterial activity was found at some distant sites also the common sites were the lung(56.7%), mediastinum(53.3%), abdomen(36.7%) and bone(23.3%). The response of antitubercular therapy by F18 - FDG PET/CT scan after 2 months of treatment was checked. There was a significant change in standardized uptake value(SUV-max) pre-treatment and post-treatment at all distant sites except the bony site. **Conclusion:** F18-FDG PET/CT scan is a non-invasive tool in monitoring the response of antitubercular chemotherapy in patients of extrapulmonary and multiorgan lymphadenopathy.

Keywords: *Antitubercular chemotherapy, extrapulmonary tuberculosis, fluorine-18-fluoro-2-deoxy-D-glucose, standardized uptake value max*

Introduction

Tuberculosis (TB) is an infectious disease caused by the bacillus *Mycobacterium tuberculosis* and is still a leading cause of mortality and morbidity worldwide. In 2015, approximately 10.4 million new cases and 1.8 million mortalities were reported by the WHO.[1] It typically affects the lungs (pulmonary TB) but can also affect other sites (extrapulmonary TB). The most common site of TB in the head-and-neck region was observed to be cervical lymph nodes (LNs).[2] Diagnostic tests for TB disease include sputum smear microscopy, rapid molecular tests, and culture methods.

Positron emission-based tomography (PET) with glucose analog 2-(Fluorine-18)-fluoro-2-deoxy-D-glucose (F 18-FDG) is well-proven and extensively used in malignant disease.[2] In infectious diseases role of FDG remains to be explored.

The use of F 18-FDG is essentially based on its detection of increased glucose metabolism, which in TB is mainly due to increased macrophage and neutrophil activity.[3] F 18-FDG PET was unfortunately limited by its well-documented lack of specificity and inability to clearly distinguish the granulomatous disease from malignant involvement based on SUV max. However, there was a scarcity of studies on FDG PET/CT in TB patients. F 18-FDG PET integrated with computed tomography (CT) was a noninvasive tool capable of early detection and assessment of disease extent.[4]

In previous studies, FDG-PET/CT allowed an accurate pretherapeutic mapping of lymph node tuberculosis (LNTB) and helped with early TB confirmation. The SUV_{max} follow-up is a potential tool for monitoring the treatment response.[5]

The present study aimed to know the distribution and quantification of extrapulmonary (cervical nodal) TB as

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Address for correspondence:
Dr. Suresh Kumar, Department of General Surgery, King George's Medical University, Shah Mina Road, Chowk, Lucknow - 226 003, Uttar Pradesh, India.
E-mail: sureshkgmc45@gmail.com

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well as the elicitation of response to antitubercular therapy through F 18-FDG PET/CT.

Methodology

After ethical clearance from the institutional ethical committee, the prospective pilot study was conducted in the Department of General Surgery, and collaboration with Department of Pulmonary Medicine, Pathology and Microbiology, KGMU, Lucknow, and the Department of Nuclear Medicine, SGPGIMS, Lucknow. Patients between 14 and 60 years of age, with definite signs and symptoms of cervical TB, cytologically and pathologically proven were included in the study. Patients were undergoing antitubercular treatment according to drug-sensitive TB (DSTB) as per the Revised National TB Control Programme (RNTCP) guidelines.

Chronically sick and moribund patients, pregnant and lactating patients, patients not willing to participate were excluded from the study.

PET/CT scan was performed at the time of presentation (baseline) and second scan after 2 months of antitubercular therapy (ATT), i.e., at the end of the initial phase of antitubercular therapy (category DSTB).

Bacterial activity through FDG PET scan was evaluated in different levels of cervical LNs and changes in various clinical parameters of LNs such as size, conglomeration, and abscess formation as evaluated using high-resolution ultrasonography of the neck were included. ATT was given according to RNTCP guidelines. Standardized uptake value (SUV_{max}) levels were compared (baseline and after 2 months of treatment).

The data were expressed as mean and standard deviation or median, range, and percentage as appropriate. All the categorical data were compared using Chi-square test. Variables were analyzed by one-way ANOVA. The $P < 0.05$ was considered statistically significant. The statistical analysis was done using IBM SPSS Statistics for Windows, version 21.0 (IBM Corp., Armonk, N.Y., USA).

Imaging

The images were acquired after 50–70 min of injection using SIEMENS Biograph PET/computed tomography (CT) (molecular CT/positron emission tomography True Point, Germany) scanner. Appropriate scanning parameters were applied during the imaging procedure.

Results

In this study, 30 patients with cytopathologically proven cervical TB were evaluated aged between 15 and 36 years with a mean age was 26.8 ± 6.13 years. Most of the patients were between 18 and 30 years of age. There were 18 patients of 18–30 years (60.0%), three patients below 18 years (10.0%) and nine patients were above 30 years (30%). The female proportion was higher in our study population (53.3%).

Table 1: Cervical lymph node level-wise clinical outcome

Cervical lymph node level	Positive lymph nodes, *n* (%)	Conglomeration, *n* (%)	Abscess, *n* (%)
I	2 (6.7)	2 (6.7)	1 (3.3)
II	21 (70)	19 (63.3)	17 (56.7)
III	19 (63.3)	17 (56.7)	16 (53.3)
IV	8 (26.8)	7 (23.3)	7 (23.3)
V	19 (63.3)	17 (56.7)	17 (56.7)
VI	3 (10)	1 (3.3)	1 (3.3)

Node-positive status, conglomeration, and abscesses were evaluated using high-resolution ultrasonography of the neck. Maximum percentages were found in the level II and level V groups with the above characteristics whereas minimum percentage was found in level I and level VI with the above characteristics [Table 1].

In our study, we found that in all patients of tubercular cervical lymphadenopathy tubercular bacterial activity was found in some other distant sites such as the lung, mediastinum, abdomen, and bone in order of their frequency [Table 2].

We also checked for the response of antitubercular therapy by F 18, FDG PET/CT after 2 months of treatment. There was a significant change in SUV_{max} pretreatment and posttreatment at all distant sites except the bony site [Table 3].

Discussion

A lot of studies have been performed on the role of F 18-FDG PET in malignant lesions and also some benign lesions. Efforts have been made to use F 18-FDG PET to distinguish the benign lesion from malignant lesions and results have generally not been encouraging. Active TB avidly takes up F 18-FDG, at both pulmonary and extra-pulmonary sites. Thus, F 18-FDG PET was very useful to assess the extent of active TB. The detection of extrapulmonary lesions was particularly useful, as obtaining tissue or fluid for analysis may not always be possible and at times, invasive. Many studies have been conducted to distinguish avid TB from malignancy and other granulomatous conditions.[6,7]

Jha *et al*. found that the maximum number of affected patients was in the 2nd and 3rd decades with female predominance but the number of patients having cervical abscesses or sinus was quite low. Age of susceptibility and female predominance was comparable but patients having cervical abscess or sinus were much higher in our study.[8]

The separate studies found that the most involved group of LNs was level V followed by level II.[9] Another study found the level II group of LNs was most commonly

Table 2: Association of enlarged tuberculous cervical lymph nodes with other sites of tuberculosis in the body

	n (%)
Abdominal	11 (36.7)
Pulmonary	17 (56.7)
Mediastinal	16 (53.3)
Bone	7 (23.3)

Table 3: Statistical observation of SUV_{max} pretreatment (1) and posttreatment (2) (one-way ANOVA test)

	Number of patients	Mean of SUVmax±SD	*P*
Pair 1			
Cervical 1	30	6.68±2.34	0.001*
Cervical 2	30	4.64±1.80	
Pair 2			
Abdomen 1	11	3.75±5.56	0.006*
Abdomen 2	11	2.63±4.04	
Pair 3			
Mediastinal 1	16	4.69±5.10	0.001*
Mediastinal 2	16	2.90±3.16	
Pair 4			
Bone 1	7	1.68±3.65	0.442
Bone 2	7	1.50±3.35	
Pair 5			
Pulmonary 1	17	4.02±5.43	0.004*
Pulmonary 2	17	2.69±3.99	

SD: Standard deviation

involved and the results supported our data.[8,10] We found that the level II was the most commonly involved group.

When patients were subjected to the whole body F 18-FDG PET/CT scan, we found that none of the patients had bacterial activity confined only to the cervical area, but also associated with other areas of the body. Associated lesions were most commonly found in the lungs followed by mediastinal and least commonly associated with bone. In a previous study of active cases of pulmonary TB, 48.6% of patients had more than one organ involved.[11]

In our study, we observed and found that there was a significant decrease in SUV_{max} in all the affected areas of the body except bone. In a previous study done on three patients, PET/CT was used to predict the response and helped in response monitoring in multisite nonpulmonary TB by a change in SUV uptake value.[12]

In our study, we concluded that the maximum decrease in SUV_{max} was observed in mediastinal TB and lowest in bony TB after 2 months of ATT, i.e. rapid and early response to treatment was observed in mediastinal TB. This inference was applied in predicting the duration of treatment based on distant sites of involvement, i.e. mediastinal TB could be treated with a shorter duration of ATT (since SUV_{max} fall rapidly) as compared to bony TB. The LNs responding to ATT could be differentiated from the nonresponding LN using SUV_{max} as a cutoff. This might assist in early diagnosis and differentiate tubercular LNs from malignancy.

Conclusion

Our study demonstrated that FDG PET CT is a noninvasive tool for monitoring the response to antitubercular chemotherapy in patients of tubercular cervical lymphadenopathy. Early detection of distant or multiorgan involvement was also a novel outcome that was demonstrated in the study. In addition, it may aid in deciding the duration of treatment based on other sites of involvement by the disease.

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Conflicts of interest

There are no conflicts of interest.

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