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ORIGINAL RESEARCH / ÖZGÜN ARAŞTIRMA

Potential false positive active extra pulmonary tuberculosis lesions on FDG PET/CT imaging in malignancy

Kanser FDG PET/CT görüntülemesinde olası yanlış pozitif aktif akciğer-dışı tüberküloz lezyonları

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ABSTRACT

Objectives: Integrated fusion imaging modality Positron Emission Tomography Computed Tomography (PET/CT) using 18Fluorine-Fluoro Deoxy Glucose (18F-FDG) is commonly utilized in imaging oncology. We expand the role of this imaging modality in our study to demonstrate the appearance of active extra pulmonary tuberculosis (TB) lesions.

Materials and methods: This study involved prospective evaluation of 8 patients using 18F-FDG PET/CT with confirmed diagnosis of extra pulmonary TB infection. Visually high intensity lesions in abnormal areas were studied where the mean and maximum standardized uptake value (SUV_{mean} and SUV_{max}) were tabulated. The diagnosis of TB infection was confirmed by isolation of TB bacillus from these lesions or evidence of responding to anti TB treatment during post treatment evaluation using FDG PET/ CT at follow up.

Results: The genders are equally affected. Majority of the group falls within young age below 50 years. Number of PET/CT studies demonstrating lesions either singly or multiple were equal in distribution. Nodal involvement is commonest in our study including mediastinum, paraaortic and inguinal groups. Other sites of infection include spine and bowel. The average SUV_{max} and SUV_{mean} for all lesions were 7.7 and 5.2 respectively.

Conclusion: Active TB lesions are FDG avid. Thus, FDG avid lesions should be interpreted with extra careful when FDG PET / CT is utilized in managing malignancy.

Keywords: extra pulmonary tuberculosis, 18F-FDG PET/CT, SUV_{max}, false positive, malignancy

ÖZET

Amaç: 18Florin-Floro-Deoksi-glukoz (18F-FDG) kullanılarak yapılan, Pozitron emisyon tomografi bilgisayarlı tomografisi (PET/CT) birleşik füzyon görüntülemesi onkolojik görüntüleme için sıklıkla kullanılır. Biz çalışmamızda, bu görüntüleme yönteminin rolünü genişleterek, aktif akciğer dışı tüberküloz (TB) lezyonlarını göstermek amacıyla kullandık.

Gereç ve yöntem: Bu çalışam doğrulanmış akciğer dışı TB enfeksiyonlu 8 hastada 18F-FDG PET/CT kullanılarak prospektif bir değerlendirme şeklinde gerçekleştirildi. Anormal bölgelerdekki görsel yüksek yoğunlukklu lezyonlar ortlama ve maksimum standardize tutlum değerleri (SUVort ve SUVmaks) elde edildi ve tabloalştırıldı. Tüberküloz tanısı, lezyonlardan TB basili izolasyonu veya tedavi sonrası takipte FDG PET/CT lezyonlarının tedavi cevabının görülmesiyle doğrulandı.

Bulgular: Her iki cinse eşit oranda etkilenmişti. Her iki gruptakilerin çoğu 50 yaş altında idi. Lezyonları gösteren PET/CT çalışma sayısı hem tek hem de çoğul olarak eşit dağılım gösterdi. Çalışmada nodal tutulum en sık mediastinal, paraaortik ve inguinal bölge lenf bezlerinde görüldü. Diğer enfeksiyon bölgeleri, omurga ve barsaklar idi. Ortalama SUVmaks ve SUVort değerleri tüm lezyonlar için sırasıyla 7.7 ve 5.2 idi.

Sonuç: Aktif TB lezyonları FDG'yi tutma eğilimindedir. Bu nedenle FDG PET/CT görüntülemesi kanser tedavisinde yol gösterici olarak kullanılıyorsa, elde edilene FDG tutullum görüntüleri çok dikkatle yorumlanmalıdır.

Anahtar kelimeler: Akciğer dışı tüberküloz, PET, SUV, yanlış pozitif, malignite

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INTRODUCTION

Tuberculosis infection has become a global health concern. Human migration is a major contributing factor causing TB spread in regions where the disease was uncommon in the past. Despite costly multiple eradication programs, the incidence of TB infection continued to be on a rising trend. World Health Organisation (WHO) estimated over 9.0 million newly diagnosed cases with 1.7 million deaths in the year 2006[1]. Global TB burden is increased with the discovery of the new multidrug resistance (MDR) strain. This is partly caused by low socioeconomic status and education level of affected populations leading to non compliance to treatment. The increasing incidence of new extreme multidrug resistance (XMDR) TB strain is closely related to ever increasing incidence in Human Immunodeficiency Viral (HIV) cases[2].

The clinical features of extra pulmonary TB infection are generally non-specific. The diagnostic work out is complicated. Despite endless challenges, early diagnosis is essential to ensure successful treatment preventing further spread of this transmissible disease by droplets inhalation.

Routine workout using total white counts, erythrocyte sedimentation rate, C-reactive protein often failed in identifying cases early. Tuberculin skin tests, which need careful interpretation, may be misleading. Quantiferon B tests are specific for latent infection but not readily available[3].

Cross sectional imaging features of extra pulmonary TB infection on ultrasound, CT and MRI are non specific and require isolation of organism in confirming the diagnosis. Attempt in cultivating TB bacillus is time consuming owing to slow growth of colony[4]. Invasive procedures often fail in obtaining low yield specimens. In addition, poor general conditions of affected patients, as a result from prolonged illness, prevent further interventional approach in treating these patients.

Combined morphological and functional PET/CT imaging study is an integrated diagnostic imaging modality commonly utilized in major institutions mainly in managing patients with malignancy. To a lesser extent, this imaging modality is also utilized in imaging infection[5,6,7,8,9,10,11,12,13], neurology[14,15] and cardiology[16,17,18]. We observed the pattern of FDG uptake in active extra pulmonary TB lesions in this study utilizing integrated PET / CT modality.

MATERIALS AND METHODS

Our patients presented with a variety of generalised symptoms like malaise, low grade temperature, generalised ache or clinically asymptomatic. They were investigated for clinical diagnosis of infection. The laboratory and basic imaging tests were inconclusive for TB infection. 18F-FDG PET/CT examination was done in view to identify the source of infection.

Standard acquisition protocol was observed in all patients. We acquired the PET/CT images using Siemens's Biograph with LSO crystal. All patients were required to be fasted overnight. Body weight in kilogram and height in centimetre were incorporated into SUV calculation and fasting blood sugar level were obtained to ensure patient was in fasted state prior to 18F-FDG injection. Immediate post intravenous administration of 18F-FDG, patients were given instruction to rest in a quiet room for 30 minutes to reduce background uptake before the scanning procedure.

We performed whole body imaging protocol from base of the skull to mid thigh in supine position. Low dose unenhanced CT was performed for attenuation correction. CT and PET images were integrated to obtain the most accurate anatomical fused location. The images were reviewed using Siemen's Symbia workstation. Three dimensional image reconstructions in axial, coronal and sagittal were displayed on separate segments of the screen in three different thresholds for CT, PET and fused PET/CT.

During image analysis, high FDG uptakes evident by visual increase intensity were considered abnormal. Region of interest (ROI) was drawn over these lesions to derived the SUV_{mean} and SUV_{max}

RESULTS

In all patients, the diagnosis of TB infection was achieved through isolation of TB bacillus by aspiration procedure or evidence of treatment response following anti TB drugs treatment between 6 to 9 months interval.

The results from our study are tabulated in table 1.

Table 1. Extra pulmonary tuberculosis lesions and semi quantitative evaluation using maximum and mean standardized uptake value (SUV).

ID	Sex	Age	Diagnosis confirmed By	Site	Semiquantitative Evaluation SUV_{max}	SUV_{mean}
°	°	°	°	°	°	°
1	F	26y	Isolation	Rt Paratracheal	10.8	6.8
				Rt Infraclavicular	7.3	5.3
				Rt Retro trachea	8.5	5.7
				Rt Supraclavicular	8.0	4.5
2	M	56y	Response to anti TB	Dorsal 10^{th} vetebra	6.9	5.5
3	F	22y	Response to anti TB	Submandibular	9.6	6.0
4	M	28y	Isolation	Left Psoas	9.5	7.8
				Left Inguinal	7.4	4.1
				Left axilla	7.5	4.1
				Rt Paratracheal	5.5	3.0
				Rt Para-aortic	9.5	6.1
5	M	53y	Isolation	Rt Hip	7.6	6.4
6	F	19y	PCR	Rt Axilla	10.5	7.2
7	F	24y	Isolation	Preaortic	6.1	3.8
				Retrosternum	4.7	2.7
8	M	17y	Isolation	Para-aortic	7.0	4.7
				Lesion in RIF	5.9	5.5

M= Male; F= Female; Rt= Right; Lt= Left; Ant= Anterior; RIF= Right iliac fossa; PCR –polymerase chain reaction

Majority of them had no pulmonary lesions (62%). Two of our patients had disseminated TB infection involving two or more systems in addition to lung lesions. Majority of FDG avid lesions involved lymph nodes. One patient presented with lesion in axial skeleton and another with intestinal involvement.

Our data was collected from a total of 8 PET/CT examinations, where we found 17 localisations of active extra pulmonary TB lesions. Five patients were diagnosed by isolation of mycobacterium from tissue samples and aspirates. Two patients showed complete remission upon anti TB treatment at follow up and 1 patient was diagnosed through a positive polymerase chain reaction result from aspirate of anterior chest wall collection.

Semiquantitative evaluation of lesions was done by means of SUV_{max} and SUV_{mean} readings which were obtained through calculated Region Of Interest (ROI) drawn within the area of visually high intensity lesional uptake. The readings were plotted in a distribution graft representing each active TB lesions (figure 1).

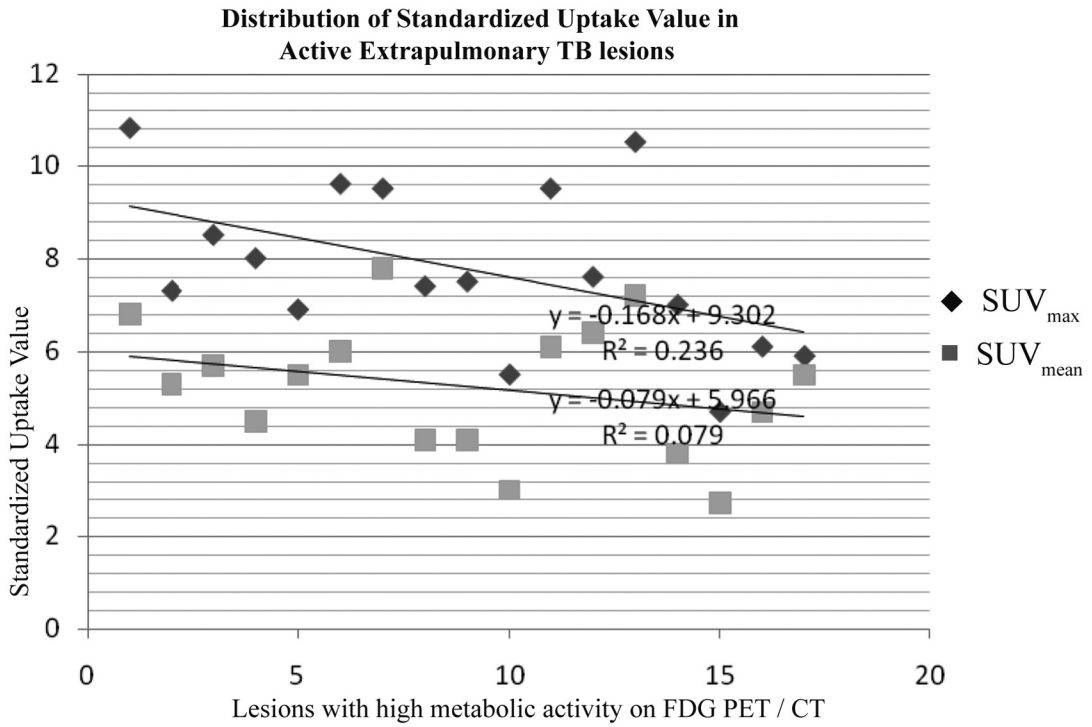

Figure 1. Illustration of SUVmax and SUVmean distribution for active extrapulmonary TB lesions obtained in this study.

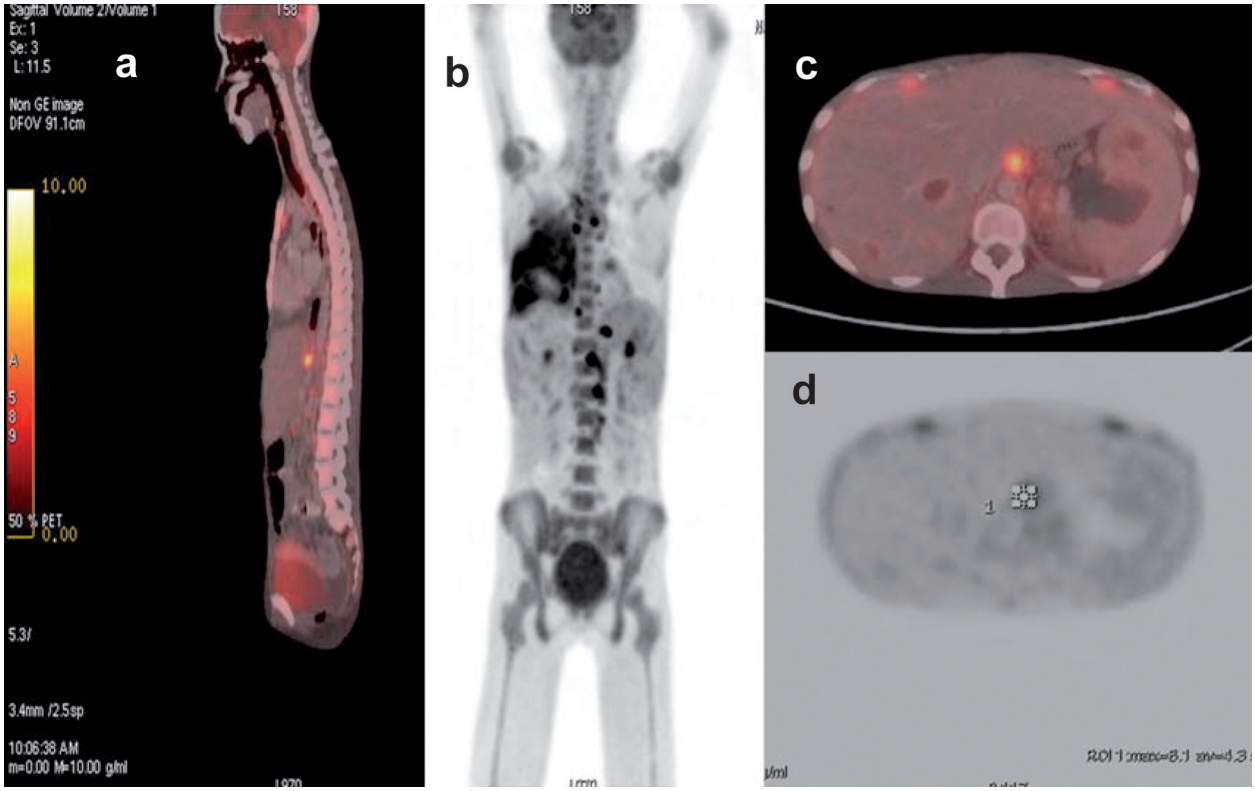

Figure 2 (a-d). This 24 year old lady presented with generalised vague illness for several months prior to admission to the hospital. FDG PET CT demonstrated multi focal FDG avid lesions. Multiplanar image projection (MIP in 3b) demonstrated visually high intensity lesions in the right lung and along paravetebral region. These lesions resembling malignancy demonstrating SUV_{max} above 2.5. TB was isolated from her sputum culture.

Table 2. The SUV_{max} and SUV_{mean} of active extrapulmonary TB lesions in this study.

°	SUV_{max}	SUV_{mean}
Minimum	4.7	2.7
Mean	7.7	5.2
Maximum	10.8	7.8

All active TB lesions from this study demonstrated SUV_{max} ranging from 4.7 to 10.8 with mean $SUV_{max.}$ 7.7. The SUV_{mean} ranges betwen 2.7 to 7.8 with mean 5.2 (Table 2).

DISCUSSION

The pathway for FDG metabolism is being elaborated in many previous publications[19-21]. At molecular level, FDG which resembles glucose molecules are being taken up in proportion to the rate of tissue metabolism. In general, malignancy is known to has higher rate of tissue metabolism, thus at PET / CT imaging, malignancy showed high FDG uptake as compare to the surroundings. In inflammatory conditions such as TB infections there is also higher rate of tissue metabolism. They also tend to exhibit similar findings at PET/CT imaging[22-24]. This explains visually high intensity active TB lesions in our study. Despite being an established metabolic tracer for FDG avid tumours, our results showed that active extrapulmonary TB lesions demonstrated high intensity lesions at imaging using FDG PET / CT with $SUV_{max} > 4.7$ and $SUV_{mean} > 2.7$

Since extra pulmonary TB infection can involve any parts of the body, mediastinal avid lesions should be interpreted with caution since metastasis may look similar to an active TB lymphadenitis on FDG PET / CT. In such situation, other clues for TB infection should be looked for including typical lung changes on CT scan. During image interpretation, maximum effort should be made to optimized information gathered from both imaging modalities. Otherwise, tissue biopsy should be recommended to confirm the diagnosis.

Combined integrated PET / CT modality is also an excellent tool in the investigation of spinal infection. Superior spatial resolution of CT makes precise localisation of a FDG avid lesions on PET image[25,26]. CT can also play an important role in a guided procedure for lesion confirmation. We utilized this method to confirm the diagnosis of our patient (no.2) where TB was isolated and the patient responded to anti TB treatment during follow up scan 6 months later.

Our observation in this study found FDG PET / CT as a potential tool in navigating clinicians in the management of active TB patients. The initial SUV_{max} can be a valuable base line surveillance in monitoring response to treatment[27,28,29] and providing information on disease extension. However, its routine utilization needs to be justified owing to its limited availability and high costs. Nevertheless, The result of this pilot study granting further investigations to be carried out in justifying the utilization of FDG PET / CT in the field of infection involving larger cohort group.

Conclusion

FDG PET/CT is a potential tool in demonstrating active extrapulmonary TB lesions. Thus, FDG PET / CT avid findings should be interpreted with extra careful when being utilized in the management of patients with malignancy.

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