18F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography in the Assessment of Occult Involvement in Widespread Granulomatosis with Polyangiitis (Wegener's Granulomatosis)

Abstract

Granulomatosis with polyangiitis (GPA) can be classified as classic triad of organ involvement consisting of lungs, upper respiratory tract/sinuses, and kidneys; limited which is not having the full triad; or widespread with additional organ involvement for example prostate, spleen, skin, eyes or peripheral nervous system and occasionally other organs. GPA is associated with increased 18F-fluorodeoxyglucose (FDG) uptake on positron emission tomography/computed tomography (PET/CT). PET/CT has the advantages of whole-body imaging and detecting metabolic abnormality before structural changes. FDG PET/CT is used to assess the extent of the disease in GPA and can detect site of occult disease involvement where there are metabolic evidence of defined organ involvement with no CT or clinical evidence. This may result in upgrading of the disease from limited to classic triad or from classic triad to widespread.

Keywords: *18F-fluorodeoxyglucose, granulomatosis with polyangiitis, occult involvement, positron emission tomography/computed tomography, widespread*

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Introduction

Granulomatosis with polyangiitis (GPA) is associated with increased 18F-fluorodeoxyglucose (FDG) uptake on positron emission tomography/computed tomography (PET/CT). In comparison to CT, PET/CT has the advantages of whole-body imaging and detecting metabolic abnormality before structural changes.[1] The role of 18F-FDG PET/CT to detect lesions in GPA has been published in several previous case reports.[2,3] However, to our knowledge, this is the second reported 18F-FDG PET/CT case showing widespread GPA. The first case was reported by Almuhaideb *et al*. in 2011.[4] In their case report, FDG PET/CT successfully detects occult areas of disease activity with no radiological or clinical evidence of involvement.

Case Report

A 41-year-old male presented with fever, shortness of breath, bilateral parotid swelling, and cough started 10 days earlier treated with azithromycin with partial response. There are bilateral parotid gland swelling and tenderness, but there were no enlarged cervical or supraclavicular lymph nodes (LNs). Routine laboratory analysis showed increased erythrocyte sedimentation rate (46 mm/h), elevated C-reactive protein (189 mg/L), and positive antinuclear antibodies. Infectious serology was negative. Chest X-rays revealed airspace shadowing in left upper zone, with infiltrative markings and obscured left cardiophernic (CP) angle [Figure 1].

CT showed left apicoposterior lung mass with collapse consolidation [Figure 2b], pericardial and small left pleural effusions, left lower lobe nodule (LLL) with mildly enlarged meditational LN, bilateral renal masses [Figure 3h], and left adrenal adenoma. On head-and-neck CT, there was bilateral markedly enlarged parotids [Figure 3b and d], enlarged right submandibular and bilateral lacrimal glands, multiple bilateral enlarged cervical LN, and extensive paranasal sinus disease.

PET/CT [Figures 2 and 3] done 60 min after intravenous injection of 357.8 MBq of 18F-FDG demonstrated enlarged FDG-avid parotid and right submandibular glands [Figure 3c] with maximum standardized uptake value (SUV_{max}) of 7.6 in the left parotid, multiple bilateral small

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How to cite this article: Saleh Farghaly HR, Alqarni AO, Nasr HA. 18F-fluorodeoxyglucose positron emission tomography/computed tomography in the assessment of occult involvement in widespread granulomatosis with polyangiitis (Wegener's granulomatosis). Indian J Nucl Med 2019;34:153-6.

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Access this article online

Website: www.ijnm.in

DOI: 10.4103/ijnm.IJNM_151_18

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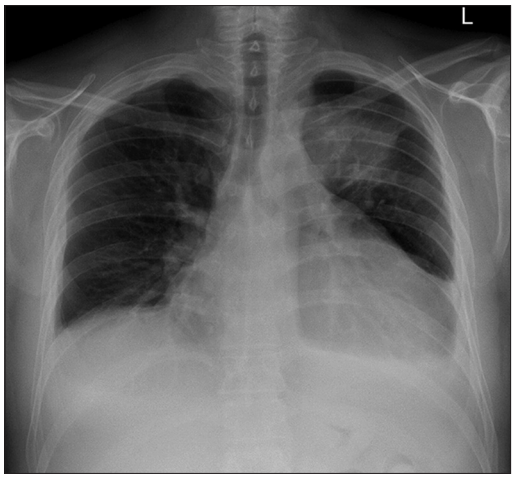

Figure 1: Chest X-ray showing airspace shadowing in left upper zone with infiltrative markings and obscured left CP angle angel

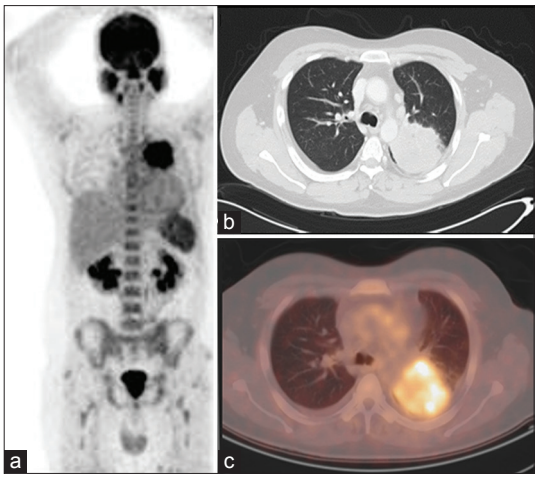

Figure 2: Anterior projection of Maximum Intensity projection (MIP) images is shown (a), large left upper lobe pulmonary heterogeneous enhancing mass on axial computed tomography (b) with high fluorodeoxyglucose uptake on axial positron emission tomography/computed tomography (c) and standardized uptake value of 7.7

cervical LN with variable FDG uptake with highest SUV_{max} = 3.5, high nasal FDG uptake [Figure 3a], bilateral FDG-avid maxillary sinus mucosal thickness more on the left side, left apicoposterior heterogeneous lung opacity with high FDG uptake (SUV_{max} = 7.7) [Figure 2c], multiple enlarged hypermetabolic mediastinal LN with highest SUV_{max} = 3, LLL hypermetabolic nodule (SUV_{max} = 3.6), heterogeneously high splenic metabolic uptake [Figure 2a] (SUV_{max} = 4.9) with no focal splenic lesions, multiple bilateral renal hypodense hypermetabolic lesions, mild FDG avid pericardial effusion with $SUV_{max}$of 1.7 [Figure 3e and 3f], the largest seen in the right kidney (SUV_{max} = 8.7) [Figure 3g and h], intense diffuse prostatic hypermetabolism (SUV_{max} = 12.8) [Figure 3i and j], hypermetabolic heterogeneous bone marrow (BM), and small left adrenal lesion with low-FDG uptake (SUV_{max} = 1.2) and mean HU = −15, suggestive of adrenal adenoma.

Biopsy of left upper lobe lung mass showed granulomatous noncaseating inflammation with small foci of necrosis with no evidence of malignancy. BM biopsy revealed reactive BM. Suggested differential diagnoses were infection, sarcoidosis, vasculitis, and others. Additional analysis done demonstrated a positive antineutrophil cytoplasmic antibody (ANCA) titer with elevated c-ANCA and anti-PR3 titers (119 units) while negative myeloperoxidase antibodies.

Based on the above clinical, laboratory, radiological, and histopathological findings, diagnosis of GPA was proposed.

Five months after prednisolone and rituximab treatment, there was a significant improvement in clinical, laboratory (c-ANCA titer 48 units), and radiological findings [Figure 4].

Discussion

It is proven that FDG PET/CT is able to accurately detect active sites of GPA, including patients in whom other diagnostic markers have been inconclusive. Multiorgan involvement is often seen on PET/CT in patients with relapsing disease. Overall, functional PET imaging is a sensitive tool to establish disease distribution and guide diagnostic biopsies in GPA.[5] The classic triad of organ involvement consists of lungs in 95% of cases, upper respiratory tract/sinuses in 75%–90%, and kidneys in 80%.

In terms of extent, GPA can be classified as:

- Classical: Full triad
- Limited: Not having the full triad[6]
- Widespread: Additional organ involvement (skin [50%], eyes [45%,] peripheral nervous system (35%), and occasionally other organs as the heart and gastrointestinal tract).[7]

In our case, CT showed evidence of classical GPA with involvement of lungs, upper respiratory tract/sinuses, and kidneys. On FDG PET/CT, however, there is prostatic, splenic, and BM in addition to classical triad, upgrading the case from classical to widespread GPA.

The role of 18F-FDG PET/CT to detect lesions in GPA has been published in several previous case reports.[2,3] However, to our knowledge, this is the second reported 18F-FDG PET/CT case showing widespread GPA. The first case reported by Almuhaideb *et al*. showed FDG-avid right maxillary sinus/nasal cavity, right parotid, mediastinum, lungs, and prostate lesions,[4] compared to our case which showed FDG-avid involvement in lungs, upper respiratory tract/sinuses, kidneys, prostate, spleen, BM, and possibly pericardium. Although the brain and kidney lesions are not easy to be detected on FDG PET/CT, it is reported that renal cortical involvement can be depicted[8] as in our case.

In the current case, prostatic involvement was detected only on FDG PET/CT without concurrent CT or clinical evidence. Stillwell *et al*. reported that symptomatic granulomatous prostatitis is not common in GPA and only reported in 2% of cases.[9] The incidence of antemortem splenic involvement in GPA is very low. This is mostly due to asymptomatic nature in majority of the cases.[10] As

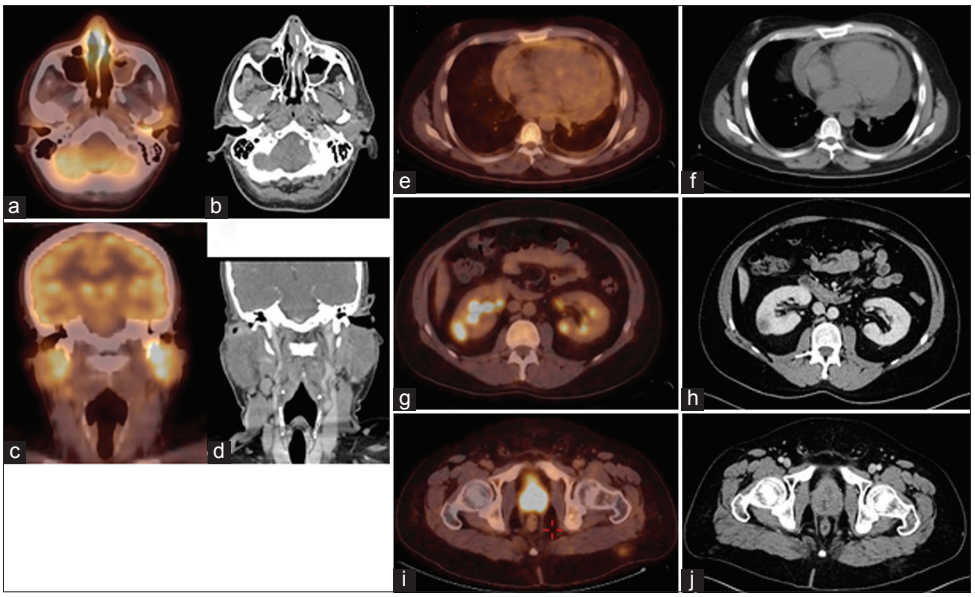

Figure 3: Fluorodeoxyglucose positron emission tomography/computed tomography and computed tomography head and neck, chest, abdomen, and pelvis revealed high metabolic uptake in nasal region (a) with mucosal hypertrophy on computed tomography (b), high uptake in enlarged parotids (c and d), pericardial effusion (e and f), focal hypermetabolic bilateral hypodense renal cortical lesions (g and h), and hypermetabolic enlarged prostate (i and j)

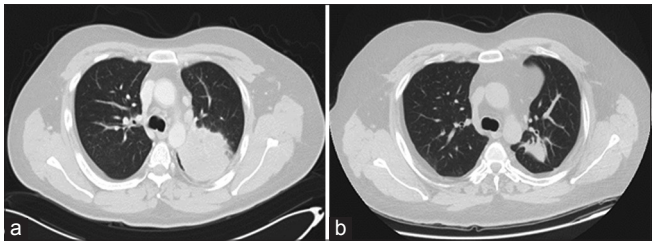

Figure 4: Pretherapy contrast-enhanced computed tomography chest demonstrating the left lung mass (a) and posttherapy computed tomography (b) showed significant interval regression in size

in the current case, the spleen showed abnormally diffuse hypermetabolism with no corresponding CT changes and no related symptoms.

We detected diffuse BM FDG uptake in axial skeleton, concordant with Nelson *et al*., who found diffuse BM and spleen uptake in 1/8 cases with GPA alone and 1/4 cases with concurrent malignancy.[11] In terms of GPA extent, our case can be classified as widespread GPA, based on FDG PET/CT findings, showing additional occult areas of disease activity in spleen and prostate with no related or corresponding radiological or clinical evidence.

Thus, this case report highlights the utility of 18F-FDG PET/CT for the assessment of disease extent in GPA and upgrading the disease from classic triad based on clinical and CT findings to rare form of widespread disease by detecting metabolically active occult areas of disease activity.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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