Case Report

Fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography in idiopathic pulmonary fibrosis: A new ray of hope!

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ABSTRACT

Idiopathic pulmonary fibrosis (IPF) is a progressive interstitial lung disease with median survival of 2–3 years. It is described as fibroproliferative rather than pro-inflammatory disorder with limited treatment options. IPF diagnostics and therapeutics are a hot topic of current research. We describe a case elaborating the utility of the whole body positron emission tomography with 2-deoxy-2-(fluorine-18) fluoro-D-glucose (F-18 FDG) integrated with computed tomography technique in IPF. The area of most intense pulmonary F-18 FDG uptake corresponded to regions of honeycombing suggesting metabolically active disease amenable to pharmacologic intervention. Additional F-18 FDG uptake was seen in mediastinal nodes implying an extrapulmonary component of disease.

Keywords: Fluorine-18 fluoro-D-glucose, honeycombing, idiopathic pulmonary fibrosis, positron emission tomography/computed tomography

INTRODUCTION

Idiopathic pulmonary fibrosis (IPF) is a progressive interstitial lung disease (ILD) occurring primarily in older adults, limited to the lungs, and associated with the radiologic and/or histopathologic pattern of usual interstitial pneumonia (UIP).[1] Clinical and radiological correlation is sufficient to establish the diagnosis of IPF. Limited treatment modalities and poor survival have made researchers integrate newer diagnostics and therapeutics in search of effective therapy. Role of positron emission tomography (PET) with 2-deoxy-2-(fluorine-18) fluoro-D-glucose (F-18 FDG) integrated with computed tomography (CT) has been studied recently in patients with IPF. We describe a case elaborating the findings of this noninvasive radiology technique in IPF.

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CASE REPORT

A 70-year-old man ex-smoker was referred to our outpatient department with symptoms of progressive exertional dyspnea and dry cough since 1 year. On general examination, he had the presence of exercise desaturation from of 95% to 75% and Grade III clubbing. On chest auscultation, bibasilar fine crackles were noted.

Chest X-ray showed a bilateral reticulonodular pattern with right upper lobe fibrosis [Figure 1]. Hematological and biochemical blood investigations were within normal limits. High-resolution computed tomography (HRCT) of thorax showed bilateral reticular opacities with honeycombing in peripheral subpleural areas and interlobular, intralobular septal thickening with traction bronchiectasis, and few ground-glass opacities (GGOs) most marked in lower lobes. Spirometry showed severe restrictive abnormality with forced vital capacity

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of 0.85 L (26% of predicted). Diffusion capacity of lungs for carbon monoxide could not be performed. F-18 FDG PET/CT showed moderate grade F-18 FDG avid (maximum standardized uptake value (SUVmax) - 4.35) uptake in bilateral reticular opacities [Figure 2a] with relatively high grade F-18 FDG (SUVmax - 6–6.6) uptake in honeycombed areas [Figure 2b]. Low-grade FDG uptake was noted in the ground glass areas with multiple F-18 FDG avid (SUVmax - 8.72) mediastinal lymph nodes [Figure 2c]. His two-dimensional echocardiography showed a pulmonary artery systolic pressure as estimated by tricuspid regurgitation jet method of 35 mmHg. Dual-energy X-ray absorptiometry scan showed osteopenia.

With clinicoradiological correlation, the patient was diagnosed as a case of IPF with mild pulmonary hypertension and osteopenia. He was initiated on therapy with pirfenidone and offered pulmonary rehabilitation.

DISCUSSION

A specific UIP pattern has been described with respect to HRCT of the chest in IPF. Clinical history and characteristic HRCT pattern are the key to diagnosis with a multidisciplinary approach for the treatment of these patients.[1] HRCT has a positive predictive value of 96% and has made the role of surgical lung biopsy obsolete in IPF.[2] However, HRCT is a purely structural imaging on which only indirect inferences regarding metabolism can be made based on degrees of fibrosis and GGO. Hence, newer diagnostics and therapeutics have been explored in IPF. Advances in molecular biology and technology have opened a Pandora's box. One of the newer modalities, F-18 FDG PET/CT is recently studied in IPF. The principle of F-18 FDG uptake in the disease process by tissues is a marker of glucose utilization, correlating with certain types of tissue metabolism (malignancy, infection, and inflammation). Glucose transporter-1 (Glut-1), the predominant Glut in the lung, is responsible for F-18 FDG uptake. Studies have shown F-18 FDG PET to be more sensitive than HRCT in detecting early disease in IPF, and also allow early detection of therapeutic response.[3] The first few studies of F-18 FDG PET/CT evaluation in IPF were by Meissner *et al*.[4] and Kim *et al*.[5] They concluded that SUV ratio reflected disease activity of IPF, and it had a positive correlation with fibrosis score or total score on HRCT.[6] Groves *et al*.[6] documented novel findings of intense pulmonary F-18 FDG uptake corresponding to regions of honeycombing on HRCT of IPF patients and increased F-18 FDG in mediastinal nodes implying an extrapulmonary component of disease. Both of these were seen in our case. The prevailing ILD hypothesis states that chronic inflammatory process injures the lung and modulates the lung fibrogenesis, leading to the end-stage fibrotic scar.[7] Honeycombing is pathognomonic of this irreversible established fibrotic disease; hence, F-18 FDG-PET evidence of increased Glut-1–mediated glucose metabolism at these sites is an interesting contradictory finding. Whether honeycombing represents burnt-out disease or a metabolically active fibrotic process has been debated on by the authors.[6] They postulated that the raised F-18 FDG uptake in patients with changes of honeycombing was a reflection of increased fibroblast metabolism that expresses Glut-1.

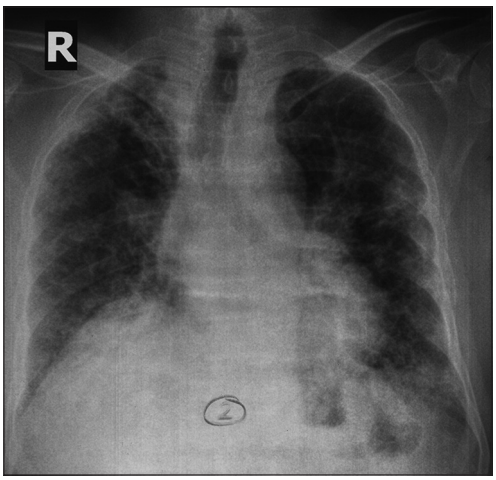

Figure 1: Chest X-ray (posteroanterior view) showing a bilateral reticulonodular pattern with right upper lobe fibrosis

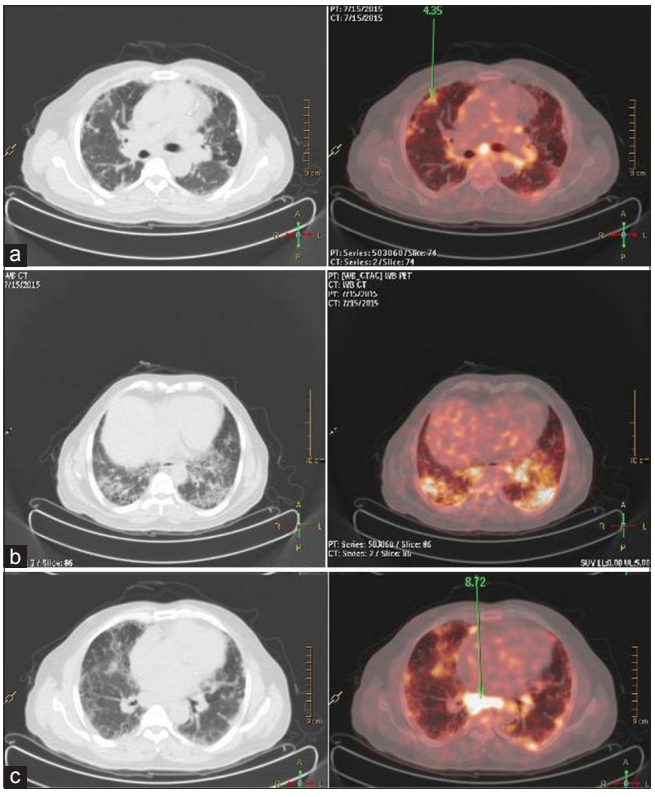

Figure 2: (a) High-resolution computed tomography and corresponding fluorine-18 fluoro-D-glucose positron emission tomography/computed tomography image showing moderate grade fluorine-18 fluoro-D-glucose avid (maximum standardized uptake value - 4.35) uptake in bilateral reticular opacities. (b) High-resolution computed tomography and corresponding fluorine-18 fluoro-D-glucose positron emission tomography/computed tomography image showing high-grade fluorine-18 fluoro-D-glucose (maximum standardized uptake value - 6–6.6) uptake in honeycombed areas. (c) High-resolution computed tomography and corresponding fluorine-18 fluoro-D-glucose positron emission tomography/computed tomography image showing multiple fluorine-18 fluoro-D-glucose avid (maximum standardized uptake value - 8.72) mediastinal lymph nodes

Another theory states F-18 FDG-PET uptake in fibrotic lung diseases is due to inflammatory cells and erythrocytes within regions of neovascularization and not by an increased metabolic rate of epithelial cells.[8] Turner-Warwick first implicated aberrant vascular remodeling in the pathogenesis of IPF, demonstrating anastomoses between the systemic and pulmonary microvasculature, and extensive neovascularization within areas of fibrosis.[9] Keane *et al.*[10] proposed that in IPF, an imbalance in the expression of angiogenic chemokines (CXCL5 and CXCL8) versus angiostatic factors (CXCL10) existed, favoring net angiogenesis. Fibroblasts appeared to be the predominant source of CXCL8 in the interstitium of IPF supporting their role in the angiogenic activity in this disease. Although the explanation for the raised F-18 FDG uptake at sites of honeycombing remains unclear, the findings suggested that effective pharmacologic intervention is possible in these. In a recent study,[11] it was shown that SUVmax was higher in IPF patients with disease progression than in those with stable disease suggesting that F-18 FDG PET/CT may play a role in predicting the progression of IPF.

To conclude, implications of F-18 FDG uptake on F-18 FDG PET/CT in IPF are still under research, and no robust evidence is yet available on its exact use. However, F-18 FDG PET/CT has shown interesting results in early diagnosis, predicting therapy response, and progression of disease. Further studies are required to explore and establish its utility.

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Conflicts of interest
There are no conflicts of interest.

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