

# <sup>18</sup>F-FDG PET imaging of granulomatosis with polyangiitis - Wegener's Syndrome

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Keywords: Granulomatosis with  
polyangiitis-Wegener's disease  
-<sup>18</sup>F-FDG PET -PET/CT

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## Received:

7 December 2015

## Accepted revised:

8 January 2016

## Abstract

**Objective:** Granulomatosis with polyangiitis (GPA), formerly called Wegener's syndrome, is a vasculitis associated with antineutrophil cytoplasmic antibody and may occur in all ages but mostly in older adults. The organs most frequently involved are the ear, nose and throat (rhinitis, sinusitis, oral ulcers, chondritis), the lungs (nodules, sometimes cavitating, infiltrates, hilar adenopathy) and the kidneys (glomerulonephritis). As patients typically present with constitutional symptoms, the diagnosis can be challenging. We report the findings on positron emission tomography/computed tomography (PET/CT) with fluorine-18-fluorodeoxyglucose (<sup>18</sup>F-FDG) in a patient with a limited form of GPA. **Conclusion:** None of the findings on PET are specific for GPA, but in a given clinical context, they may contribute to early diagnosis. They may guide biopsy taking, and may determine the extent of the disease. During and after treatment, PET can be used to monitor disease activity.

*Hell J Nucl Med 2016; 19(1):53-56*

*Epub ahead of print: 1 March 2016*

*Published online: 1 April 2016*

## Introduction

Granulomatosis with polyangiitis (GPA), formerly called Wegener's syndrome, is one of several vasculitides that are associated with antineutrophil cytoplasmic antibody (ANCA). Other entities in this group are microscopic polyangiitis, Churg-Strauss syndrome and renal limited vasculitis. Granulomatosis with polyangiitis is an immune mediated disorder that is probably initiated by infection or drugs on a suitable genetic background. The immune response is directed in part against previously shielded epitopes of neutrophil granule proteins, and most commonly against proteinase 3. This immune response involves T-cells, neutrophils, endothelial cells and B cells [1].

The distinction between GPA and microscopic polyangiitis is not sharply defined, but in clinical practice, patients are classified as having GPA if they have destruction in their upper respiratory tract and/or nodules or cavities in the lower respiratory tract, and/or have granulomatosis on biopsy of any organ [2].

Granulomatosis with polyangiitis mostly occurs in older adults, but may occur at all ages. Patients typically present with constitutional symptoms including fever, migratory arthralgias, malaise, anorexia and weight loss. These may last for weeks to months without evidence of specific organ involvement. The organs most frequently involved are the ear, nose and throat (rhinitis, sinusitis, oral ulcers, chondritis), the lungs (nodules, sometimes cavitating, infiltrates, hilar adenopathy) and the kidneys (glomerulonephritis), but the skin, the eyes, the nervous system and less commonly, the gastrointestinal tract, the heart, the genitourinary tract, the parotid glands, the thyroid, the liver or the breast may all be involved [2]. Prompt diagnosis of GPA is important to permit initiation of therapy that may be life-saving and organ-sparing [3]. Treatment may consist of glucocorticoids with methotrexate, cyclophosphamide, or rituximab, depending on the severity of the disease [4].

In the present report we describe the findings on PET/CT with <sup>18</sup>F-fluorodeoxyglucose (FDG) in a patient with the limited form of GPA, which occurs in about one-fourth of cases, with clinical findings restricted to the upper respiratory tract and/or the lungs at diagnosis. Most of these patients will eventually develop glomerulonephritis if left untreated [2].

## Case Report

A 47 years old male patient presented with severe and invalidating pain and stiffness proximally in the limbs. The pain had started two months earlier after an upper airway infection with a persistent cough for which the patient had been treated with azithromycin. During a short episode, concomitant otalgia at the left had been present. The patient gave no history of fever, arthritis, eye infection, weight loss, skin lesions or blood loss. He mentioned hay fever with pollen allergy. At home he kept no pets.

On physical examination no tachypnea or cyanosis were found. No fever was present. The cardiopulmonary examination was normal. No swollen lymph nodes were palpated in the neck and supraclavicular regions.

Routine laboratory analysis showed an increased erythrocyte sedimentation rate (58 mm/h) and a slightly elevated C-reactive protein (CRP). Additional analyses demonstrated a positive antineutrophil cytoplasmic antibody (ANCA)-titer with elevated c-ANCA and proteinase-3 titers. Rheuma factor, anti-cyclic citrullinated peptide (anti-CCP), anti-streptolysin O (ASLO) and anti-nuclear factor (ANF) were negative. Infectious serology was negative. Tumor markers carcinoembryonic antigen (CEA) and neuron specific enolase (NSE) were within normal limits. Urinalysis was normal.

Chest X-rays showed bilateral multiple nodules (Figure 1).



**Figure 1.** Chest X-rays at presentation shows bilateral lung nodules.

Computed tomography of the chest additionally revealed bilateral lung nodules with central necrosis and excavation (Figure 2).

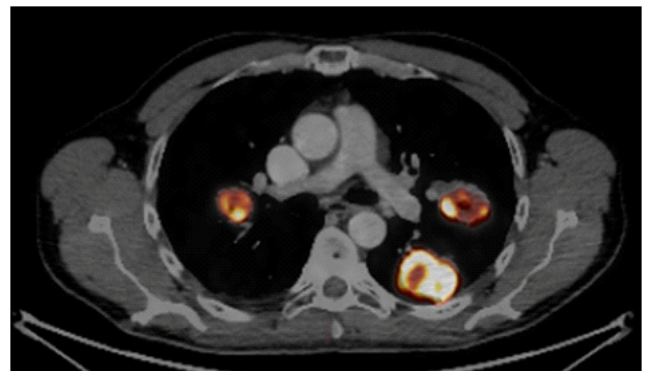
A differential diagnosis was proposed consisting of multifocal lung neoplasia, central necrotising metastasis of non-pulmonary origin, infections such as tuberculosis or aspergillosis, and systemic disease with vasculitis, type Wegener

granulomatosis.

A positron emission tomography/computed tomography PET/CT (Discovery Lightspeed ST, General Electric Medical Systems, Milwaukee, Wisconsin, USA) was performed 87 minutes after intravenous injection of 206.9MBq of  $^{18}\text{F}$ -fluorodeoxyglucose (FDG) and demonstrated increased uptake in the lung nodules with a maximum standard uptake value (SUV) of 15.2 (Figure 3). No other abnormalities were present, in particular not in the upper respiratory tract.



**Figure 2.** Thorax CT at presentation reveals bilateral lung nodules with central necrosis and excavation.



**Figure 3.** PET/CT at presentation demonstrates increased uptake in the lung nodules.

Transthoracic lung biopsy revealed non-caseous necrotizing granulomatous inflammation including giant cells, histiocytes, neutrophils, and eosinophils as well as infiltration of lymphocytes, plasma cells and histiocytes in the surrounding tissue with vasculitis, compatible with Wegener granulomatosis. High doses of corticosteroids were started together with cyclophosphamide in function of body weight. Symptoms improved dramatically.

Chest X-rays four months later showed a spectacular remission of the lung nodules (Figure 4). Nearly three years after diagnosis, and 1.5 year after termination of the treatment, the patient remains well.



**Figure 4.** Chest X-rays after 4 months of therapy shows that the lung nodules have disappeared.

## Discussion

In the patient described in this report, pulmonary nodules were present that avidly took up  $^{18}\text{F}$ -FDG (maximal SUV 15.2) and at biopsy turned out to be due to granulomatosis with polyangiitis, formerly called Wegener's disease. Uptake of  $^{18}\text{F}$ -FDG in pulmonary nodules due to this disease has been frequently reported [5-15], like in paranasal or sinus involvement [5, 7, 11-15]. In a small case series of 12 patients, maximal SUV in pulmonary nodules ranged from 3.53 to 19.51, with a mean of 12 [13]; in another series of 8 patients, the maximal SUV for lung lesions varied between 0.69 and 7.10 [15].

Although the  $^{18}\text{F}$ -FDG PET findings in the present and previously published cases are not specific for GPA, GPA should be considered in the differential diagnosis of  $^{18}\text{F}$ -FDG uptake in organs that may be involved with GPA, in particular in nodular lung lesions. It could even be considered as a differential diagnosis for any tumoral lesion with  $^{18}\text{F}$ -FDG uptake, since ANCA vasculitis may present with tumor-like masses outside the lung [16]. Histopathologic evidence is crucial to establish a final diagnosis. It is recommended that whenever possible, the diagnosis should be confirmed by tissue biopsy at a site of active disease [2]. In this respect, PET, and combined PET/CT in particular, could be helpful to select a site to be biopsied, as has been described in a few patients [11, 14], because this may avoid sampling error. In those cases where GPA presents with constitutional symptoms only,  $^{18}\text{F}$ -FDG PET may help to identify the underlying cause. In one case,  $^{18}\text{F}$ -FDG PET/CT findings preceded elevation of serum proteinase 3-ANCA [15], contributing to an earlier diagnosis.

Moreover, PET findings may help to determine the extent

of the disease and may reveal locations that are potentially life threatening, such as in the case of periaortitis [5, 17].

Fluorine 18-fluorodeoxyglucose (FDG) positron emission tomography (PET) can also be used to monitor disease activity after treatment. In one patient with GPA affecting the lungs and kidneys, clinical improvement and decrease of ANCA titers to normal levels was accompanied by a decreased  $^{18}\text{F}$ -FDG uptake in one lesion and disappearance of the other lung lesions. CT, on the other hand, remained abnormal. Moreover, at a recurrence two years later,  $^{18}\text{F}$ -FDG PET showed multiple areas of increased uptake in the lungs, whereas the CT showed a decrease in the size of the original lesions [6]. In 5 more patients,  $^{18}\text{F}$ -FDG PET/CT was used to evaluate treatment efficacy. Five upper respiratory tract lesions disappeared and 5 lung lesions showed diminished activity on PET after completion of chemotherapy for Wegener's in spite of residual lesions on CT [14]. Two patients underwent  $^{18}\text{F}$ -FDG in follow-up after treatment, one because of fever, the other to stage esophageal cancer. In both patients, results were negative [14]. Another case series described complete resolution of previously active lesions (including bilateral adrenal gland involvement) after immunosuppressive therapy in one patient and low activity in remaining pulmonary mass lesions in another patient on maintenance therapy [13]. It follows from these observations that functional imaging is better suited to assess disease activity than is anatomic imaging. The interest of this may lay in the fact that ANCA titers, which are monitored to assess disease activity, are not consistently parallel to the course of the vasculitis and may rise without a relapse occurring [18-20]. Moreover, one could envisage PET as a means to monitor disease activity in an organ specific way.

*In conclusion*,  $^{18}\text{F}$ -FDG PET/CT may contribute to the initial diagnosis of GPA by indicating biopsy sites, may evaluate the extent of the disease, assess treatment efficacy and monitor patients.

*The authors declare that they have no conflicts of interest*

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