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Case Report

Positron Emission Tomography in the management of five cases with granulomatosis with polyangiitis

Granülamatosis Polianjitis tanılı beş olgunun Pozitron Emisyon Tomografisi ile değerlendirilmesi

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ABSTRACT

Granulomatosis with polyangiitis (GPA) formerly Wegener's Granulomatosis, is characterized by granulomatosis necrotizing vasculitis that primarily involves upper respiratory tracts, lung and kidney. There are two types of disease, 'limited' and 'generalized'. Radiological findings are seen as multiple bilateral nodules that change from a few millimeters to centimeters in size or parenchymal infiltrations, cavitations or nodules presented with cavitations. These nodules sometimes can be confused with malignancy in terms of the size and appearance. In this study, we discussed the role of positron emission tomography/computerized tomography (PET/CT) in the initial evaluation of patients with the diagnosis of GPA mimicking malignancy.

Keywords: Wegener's Granulomatosis, lung, kidney, positron emission tomography

ÖZ

Granülomatöz Polianjitis (GPA) eski adıyla Wegener Granülomatozu, öncelikle üst solunum yolları, akciğer ve böbrekleri tutan, granülomatöz nekrotizan vaskülit ile karakterizedir. Hastalığın 'sınırlı' ve 'yaygın' olmak üzere iki formu vardır. Radyolojik bulguları birkaç milimetreden santimetreye kadar değişen çok sayıda bilateral nodüller veya parankimal infiltrasyonlar, kavitasyonlar veya kavitasyonlarla karakterize nodüller olarak görülür. Bu nodüller bazen boyut ve görünüm açısından malignite ile karışabilir. Bu çalışmada, maligniteyi taklit eden GPA tanısı alan 5 olgunun ilk değerlendirmesinde pozitron emisyon tomografisi / bilgisayarlı tomografinin (PET / BT) rolünü tartışmayı amaçladık.

Anahtar Kelimler: Wegener Granülomatozu, Akciğer, böbrek, pozitron emisyon tomografisi

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Introduction

Granulomatosis with polyangiitis (GPA) formerly Wegener's Granulomatosis is a relatively rare disease characterized by granulomatous necrotizing vasculitis that primarily involves upper respiratory tracts, paranasal cavity, lungs, kidneys and the other body segments [1, 2]. Typically, GPA is most seen vasculitis with 10% ratio which effects lung among vasculitic diseases [3]. Pulmonary involvement is observed in 90-95% of cases. Size of nodules can range from a few millimeters to 10 centimeters which are usually presented with cavitations [4]. In few cases, these nodules are misdiagnosed radiologically as malignancy [5]. There are two forms of disease, 'limited' and 'generalized'. Kidney involvement is presented in 'generalized' form. Both alveolar hemorrhage and kidney insufficiency indicate poor prognosis [6]. The definitive diagnosis of GPA has been made by granulomatous involvement of upper airways, lungs and kidney. Especially, lung biopsy is recommended [7]. In active cases, the presence of circulating antineutrophil cytoplasmic antibodies [ANCA] is an important noninvasive diagnostic criteria.

Positron Emission Tomography (PET) with using radyopharmaceutic agents such as F-18 fluorodeoxyglucose (FDG), functional images of glucose uptake and metabolism in the body is a noninvasive imaging method [8]. Especially, the role of FDG-PET in oncology is very respectable but with recent, follow up and diagnosis of inflammatory disease such as vasculitis begin to see more accepted [9-11]. This dilemma leads to confusion. In this study, we discussed the role of positron emission tomography/computerized tomography (PET/CT) in the initial evaluation of patients with the diagnosis of GPA mimicking malignancy.

Case 1: A 63-year-old woman presented with shortness of breath for 1.5 months. A nodular opacity was detected in left upper zone in chest X-ray. There was a 20 mm spiculated nodule in left lingula inferior segment in chest tomography. She was referred to our clinic pre-diagnosis of malignancy. Her physical examination was normal. Laboratory tests showed increased C-reactive protein (CRP: 10,7 mg/dl) and erythrocyte sedimentation rate (ESR: 87 mm/h) and anemia (Hb: 10.6 g/dL). No pathology was detected in fiberoptic bronchoscopy (FOB), direct examination and culture sputum acid-fast bacilli [AFB] were negative. PET/CT imaging for diagnosis and staging of malignancy showed collapse/consolidation near major fissur in left upper lobe apicoposterior segment and in this field increased FDG uptake (SUVmax: 7.84). The bigger one that approximately 1.5x2 cm in size in right lung apical segment and multipl nodules in both lungs with increased FDG uptake (SUVmax: 8.26) (Figure 1). cANCA detected positive, subsequent CT- guided fine needle aspiration biopsy of lung nodules yielded vasculitis.

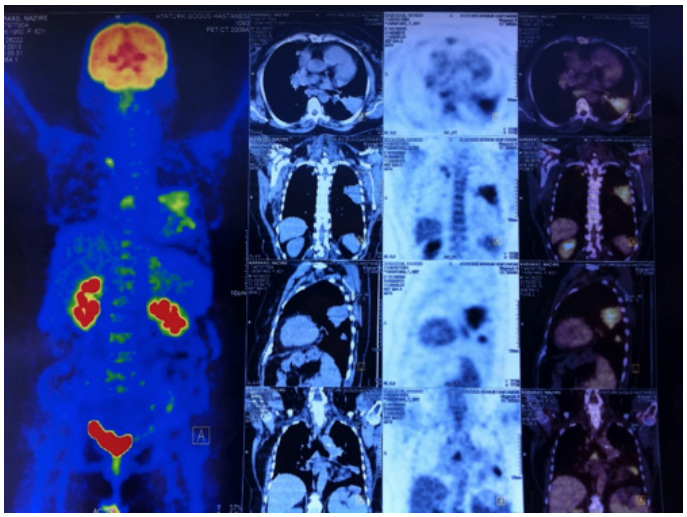

Figure 1. Collapse/consolidation near major fissur in upper lobe apicoposterior segment and in this field increased FDG uptake (SUVmax: 7.84). Multipl nodules in both lungs with increased FDG uptake (SUVmax: 8.26).

Case 2: A 37-year-old man presented with common joint pain and cough for 3 months. Nodules with multipl regular margin were seen in chest X-ray. Physical examination was normal. Laboratory tests showed decreased hemoglobinemia (Hb: 9.2 g/dL), increased platelet count (Plt: 1.193.000), CRP: 24.4 mg/dl and ESR: 120 mm/h. Hematuria and proteinuria were dedected at urine analysis. Excisting multipl nodularities in chest X-ray, patient was referred for FDG PET scan. It was demostrated that both maxillary sinus were partially oblitared with soft tissue and air level liquid in left maxillary sinus. Besides this area, more pronounced in the left nasal cavity, bilateral nasal cavities showed metabolic uptake images (SUVmax: 16.95). Also in the right posterior segment of palate showed increased FDG uptake (SUVmax: 16.95). The bigger one 3 cm in size with both lungs increased FDG uptaake (SUVmax: 14.95) (Figure 2). FOB biopsy was performed and the result was consistent with vasculitis. c-ANCA also detected positively.

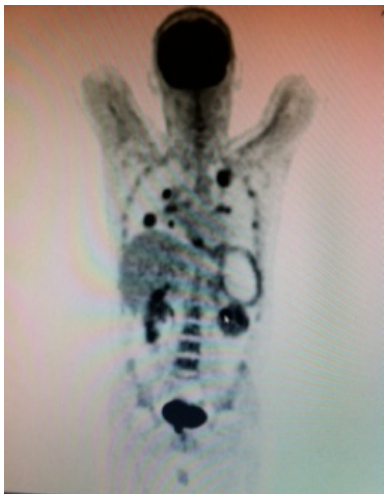

Figure 2. The bigger one 3 cm in size with both lungs with increased FDG uptaake [SUVmax: 14.95]. Bilateral nasal cavities showed metabolic uptake images (SUVmax: 16.95). Also in the right posterior segment of palate showed increased FDG uptake (SUVmax: 16.95) (Patient only had fusion image).

Case 3: A 79 year-old-man, presented with cough for 6 months. A chest x-ray showed a mass in right lower zone. A chest CT demonstrated a 8 cm mass in middle lob. Physical examination was normal and no abnormality was observed in bronchoscopy. A PET/CT demonstrated about 87x71 cm mass with collapse and consolidation increased FDG uptake (SUVmax: 19.53). Focal collaps and consolidation in laterobasal segment and lower lobe posterobasal segment of right lung that significantly increased FDG uptake (SUVmax: 20.21). Focal collaps/consolidation viewed in lingula and lower lobe of left lung basal segment metabolic uptake (SUVmax: 13.52) were presented (Figure 3). Transthorasic fine needle aspiration was performed and consisted with GPA.

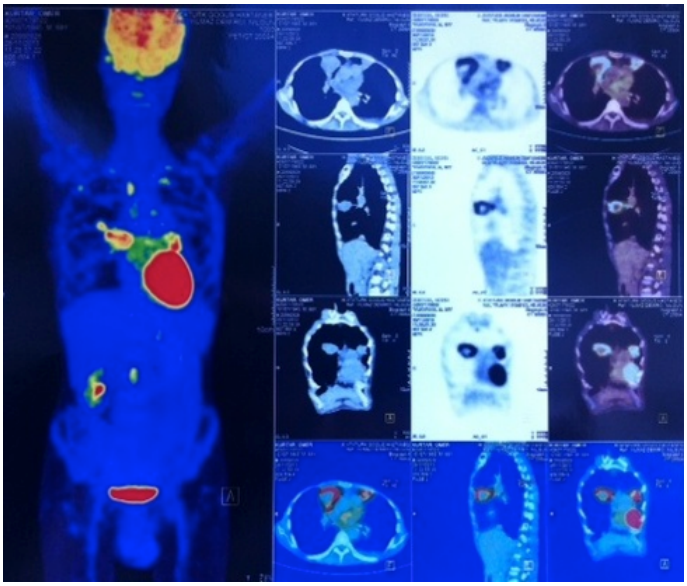

Figure 3. An 8.7x7.1 cm mass with increased FDG uptake (SUVmax: 19.53) in the middle lob. Focal collaps/consolidation viewed in lingula (SUVmax: 13.52).

Case 4: A 35 year-old–man refered to emergency department with symptoms of influenza for a week. A Mass was detected in chest X-ray. A chest CT demonstrated a pleural based mass in left upper lobe. Both phyical examination and laboratory tests were normal. With pre-diagnosis of malignancy PET/CT demonstrated subpleural, approximately 3.4x2.9 cm lesion with increased metabolic activity (SUVmax: 5.66) (Figure 4). Since transthoracic fine needle aspiration was non diagnostic, wedge biopsy was performed. Histopathology was consistent with vasculitis. c-ANCA was positive.

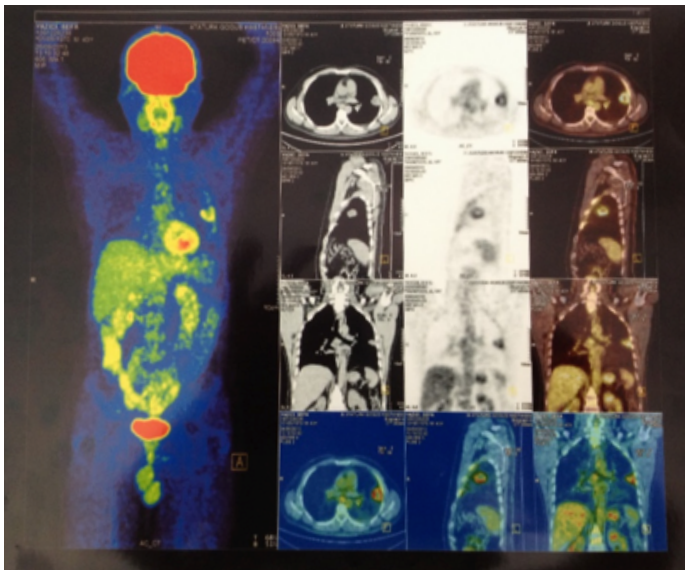

Figure 4. Approximately 3.4x2.9 cm lobular lesion with increased FDG uptake (SUVmax: 5.66).

Case 5: A 62 year-old- woman presented with cough and shortness of breath. A nodul was determined in chest X- ray. A Chest CT demonstrated nodules in both lower lobes and afterwards she referred to our clinic. Physical examination and laboratory tests were normal. A PET/CT showed two lesions and the bigger one was in posterobasal segment of left lung and approximately 2x3.5 cm in size and increased FDG uptake (SUVmax: 6.5) (Figure 5). FOB was non-diagnostic. The patient was not suitable for transthorasic fine needle aspiration, so right thoracotomy and wedge biopsy was performed. Histopathology was consistent with granulomatous vasculitis. c-ANCA was positive.

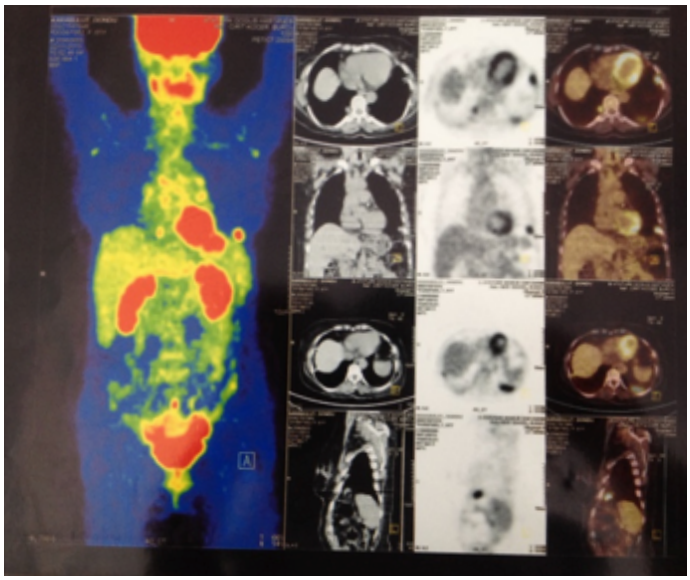

Figure 5. Approximately 2x3.5 cm lesion in posterobasal segment of left lung with increased FDG uptake (SUVmax: 6.5).

All patients consultated to rheumatology department and three of them received prednisolone and cyclophosphamide combination and one of them received prednisolone and metothrexate combination and one of them received only prednisolone therapy. All of them cured after treatments.

Discussion

GPA is a relatively rare disease characterized by granulomatous necrotizing vasculitis that primarily involves small and medium sized vessels [12]. Estimated prevelance is 0.003% [6]. The ethiology is unknown, but silica dust exposure increased the prevelance seven fond [7,13]. GPA is seen rare in adeloscent age, mostly common in fifth decade. The male/female ratio is 1:1 [6,14]. American College of Rheumatology Association has established the following criteria for the diagnosis of GPA: 1) nasal and oral inflammation [painful or painless ulcers or bloody nasal discharge], 2) nodules in chest X-ray, fixed infiltrates, cavities, 3) abnormal urinary sediment (the red cells with or without microscopic cylinder hematuria), 4) biopsy of artery showing granulomatous inflammation in perivascular area. The presence of two or more of these four criteria was associated with an 88 % sensitivity and 92% specifity [4]. Our 4 cases had 2 criterias, one of them had 4 criterias. The most common symptoms are sinusitis, purulent or bloody discharge, rhinologic symptoms such as epistaxis and otitis media [6,15,16]. Systemic symptoms such as fever, night sweats, weight loss, and weakness may also ocur. Cough, shortness of breath, lower respiratory tract symptoms such as hemoptysis also seen 90% of cases and 11% of cases have isolated lung involvement. [17,18]. One of our patients had upper respiratory complaints, four had cough, two had shortness of breath. None of the patients had renal failure.

In GPA patients, nonspecific laboratory tests, increased sedimentation rate, leukocytosis, thrombocytosis and normocytic normochromotic anemia are seen [6,19]. GPA is one of the small vessel vasculitis, ANCA assay used in differentiating, c-ANCA used in diagnosis and evaluation of activity. c-ANCA is positive 80-90% in generalized type, 55-66% in limited type [20]. Besides, negativity can not provide to exclude the disease [21,22]. c-ANCA levels of untreated active cases are high over 90%, levels decrease in remission [4,23]. In our report c-ANCA was positive in 4 of 5 cases.

Involvement of lung is characterized with multiple nodular lesions that sizes ranging from 1-10 cm and cavity in half of them. Inflammation rarely reaches to bronchi that can lead secondary atelectasis [4,24]. The principle of PET-CT displays of the biological activity of tumor cells that distinguish between malign and benign tissue. FDG is not spesific for malignancy, also in cases of various infections such as tuberculosis and histoplasmosis, granulomatous diseases like sarcoidosis and vasculitis FDG increases [25]. In our cases, PET-CT was demanded to evaluate malignancy or metastases. Walter et al. reported that FDG PET-CT imaging has 99.7 % sensitivity and 99.8% specifity in the evaluation of disease extention in large vessel vasculitis [26]. Similarly, Bertagna et al. showed that FDG is highly effective in detecting large vessel vasculitis anywhere in the body and in diagnosis of patients with fever of unknown origin [27].

Nonspesific clinical symptoms of GPA frequently cause a delay in the diagnosis. Computed tomography findings are nonspesific due to the variety of the lesions. PET imaging in multiple pulmonary nodules may give false positive results mimicking malignancy. Increased involvement may remain hing in follow up.

The sensitivity of the central nervous system and kidney lesions are limited. However, it is also valuable for diagnosis of difficult cases [28,29]. A few published case reports show that FDG PET/CT can detect soft tissue involvement earlier compared to other imaging modalities such as CT and it is reliable in the diagnosis of disease relapse particularly in GPA [25,29]. Ito et al indicated that GPA lesions in the upper respiratory tract were easier to detect by FDG uptake during PET/CT than by nonenhanced CT alone [30]. Besides, it is valuable in terms of showing unexpected involvement of the body. Ozmen et al showed that FDG PET/CT determined in 46% of patient population unexpected involvement areas such as great vessels, ear, spleen, kidney, duodenum, trachea and skin which were difficult to detect by conventional imaging procedures [31]. In our study, expect upper and lower respiratory tract and kidney, FDG PET/CT detected palata and prostate involvement. In spite of clinical and laboratory findings, tissue biopsy is required for definitive diagnosis of the GPA. However, a definitive histopathological diagnosis could not obtain over 50% of cases so, FDG PET/CT is a complemantory modality via indication of suitable biopsy sites [30]. Definitive diagnosis is usually made based on the pathologic findings of the lung and kidney. In our patients, 3 patients diagnosed with transtorasic fine needle biopsy, 2 patients diagnosed with wedge biopsy.

FDG PET/CT imaging findings including SUVmax is useful for diagnosis and treatment efficacy in patients with malignancy and inflammation. Ozmen et al found that 13 patients had either solitary or multiple pulmonary nodular/mass lesions with marked increased FDG uptake mean SUVmax 12± 4, range 3.53- 19.51 on PET/CT [31]. In the study of Ito et al, the interquartile range of SUVmax for the 6 patients with upper respiratory tract lesions and 4 with lung lesions of the 6 patients was 3.86-8.03 [median 5.28] [30]. In our study, 5 patients with lung involvement SUVmax was 5.66- 20.21 [median 19.19] on PET/ CT. One of 5 patient had extra pulmoner involvement with SUVmax palatine 16.95, nasal cavity 15.48, kidney 12.03 and prostate 14.95 on PET/CT.

As a conclusion GPA is a rare disease. None of the findings on PET are specific for GPA, but in a given clinical context, they may contribute to early diagnosis. Also PET/CT may guide biopsy taking, and since it is a whole body examination, may determine the extent of the disease. Also in patients presenting with multiple pulmonary nodules GPA should be considered in differential diagnosis with intensed FDG uptake.

Declaration of conflicting interests

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