Clinical Implication of $^{18}$F-FDG-PET in Diagnosing and Monitoring Disease Activity in a Case of Subclinical Stage of Giant Cell Arteritis

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Giant cell arteritis (GCA) is a systemic vasculitis which typically occurs in persons over 50 years old. GCA is closely related to polymyalgia rheumatica (PMR). A temporal artery biopsy is the gold standard test for the diagnosis of GCA. Recently, there is increasing evidence for the role of $^{18}$F-fluorodeoxyglucose positron emission tomography ($^{18}$F-FDG-PET) in diagnosis of vasculitis. Here, we report on a case of a 67-year-old Korean male who was diagnosed with atypical GCA in subclinical stage concomitant with PMR by $^{18}$F-FDG-PET. After treatment, abnormal findings of $^{18}$F-FDG-PET were improved. (J Rheum Dis 2015;22:382-386)

Key Words. Giant cell arteritis, Polymyalgia rheumatica, Positron emission tomography

INTRODUCTION

Giant cell arteritis (GCA) is a vasculitis of large and medium-sized vessels causing critical ischemia [1]. GCA affects primarily the extracranial branches of the carotid artery and the most common manifestations of GCA are constitutional symptoms, headache, visual symptoms, jaw claudication, and polymyalgia rheumatica (PMR) [2]. PMR is an inflammatory disorder of unknown etiology characterized by pain and stiffness in the neck, shoulder, and pelvic girdles. GCA and PMR are closely related inflammatory syndromes that affect persons older than 50 years and frequently occur together [3]. In the diagnosis of GCA, a temporal artery biopsy (TAB) is the gold standard test. Recently, there are increasing numbers of studies that report the usefulness of $^{18}$F-fluorodeoxyglucose positron emission tomography ($^{18}$F-FDG-PET) in GCA, particularly in cases with non-specific presentation such as fever, malaise and weight loss. Here we present the case of a Korean man who was diagnosed with atypical GCA in subclinical stage concomitant with PMR by $^{18}$F-FDG-PET.

CASE REPORT

In June 2013, a 67-year-old Korean man was admitted to our hospital with persistent high fever for 10 days. He also had been suffering from the headache on the occiput area, morning stiffness more than one hour and pain and stiffness in the neck and both shoulders for one month. He had no history of hypertension, diabetes, cardiovascular disease, peripheral vascular disease, pulmonary tuberculosis, viral hepatitis or malignancy. At physical examination, he looked chronically ill and there was tenderness on posterior area of the neck and both shoulders. No heart murmur or vascular bruit in the neck, chest, or abdominal area could be heard. Blood pressure was 126/66 mmHg and body temperature was 38.2°C. Laboratory examinations showed an elevated erythrocyte sedimentation rate (ESR) of 120 mm/h (normal range: 0 to 10 mm/h) and C-reactive protein (CRP) of 14.0 mg/dL (0 to 0.5
mg/dL). Rheumatoid factor (RF), anti-cyclic citrullinated peptide antibody (ACPA), antinuclear antibody and anti-neutrophil cytoplasmic antibody were negative. A chest radiograph, abdominal-pelvic computed tomography (CT), brain magnetic resonance imaging (MRI), cervical spine MRI and echocardiography didn’t reveal anything that would explain a cause of fever.

He underwent 18F-FDG-PET for further evaluation. 18F-FDG-PET showed increased glucose metabolism in the walls of the ascending aorta, aortic arch, thoracic descending aorta, both subclavian arteries, both common carotid arteries, and particularly severe in both common femoral arteries and their large branches with wall thickening (Figure 1). Under the impression that this might be systemic vasculitis, we examined aorta CT, but that didn’t show any evidence of vasculitis.

He was diagnosed with atypical GCA in subclinical stage concomitant with PMR and started on a medium dose of prednisolone treatment (35 mg/d, 0.5 mg/kg/d) and azathioprine. After one week of treatment, CRP decreased from 14.0 mg/dL to 2.6 mg/dL and fever was relieved. After 4 weeks, CRP was in the normal range. After 6 weeks of treatment with azathioprine, serum liver enzyme elevated to 6 times of normal range. So we stopped the treatment with azathioprine. After 2 weeks, level of liver enzyme was within normal range. We started the treatment with methotrexate. After that, level of liver enzyme has been maintained within normal range. Currently, he has been treated for 15 months with no specific symptoms, including pain and stiffness of the neck. Prednisolone has been tapered to 5 mg/d and methotrexate (12.5 mg/wk) has been maintained. ESR decrease to 10 mm/h and CRP has been maintained within normal range. In addition, follow up 18F-FDG-PET was done to evaluate the state of vasculitis after 12 months of treatment (Figure 2).

There are several qualitative and quantitative measures to monitor treatment response and disease activity. We used a semi-quantitative measure that compare arterial wall and liver uptake by defining vessel and hepatic region of interest (ROI) and quantifying the maximal standardized uptake value (SUVmax). The liver is a reference organ because of the homogeneous 18F-FDG distribution.

Figure 1. 18F-fluorodeoxyglucose positron emission tomography before treatment. There are increased glucose metabolism in the walls of the ascending aorta, aortic arch, thoracic descending aorta, both subclavian arteries, both common carotid arteries and especially both common femoral arteries and their large branches with wall thickening.
Cut off ratio is 1.0. This ratio led to a sensitivity of 88.9%, a specificity of 95.1%, and an accuracy of 94.4% [4]. The ratio before treatment was 1.49 and that after treatment was 0.98 (Figure 3). Follow up 18F-FDG-PET showed the improvement of arteritis.

**DISCUSSION**

The incidence of GCA varies widely in different populations from less than 0.1 per 100,000 to 77 per 100,000 in persons aged 50 years and older [2]. GCA is more common in Caucasians, particularly in those of Scandinavian descent, but infrequent in Asian populations [1]. GCA is closely related to PMR and the presence of biopsy-proven GCA has been demonstrated in 16% to 21% of patients with PMR, and symptoms of PMR are present in 40% to 60% of patients with GCA [5]. GCA concomitant with PMR is predominantly seen in the elderly, with cases under the age of 50 being rare and the incidence increasing with age [6]. A TAB is the gold standard test for the diagnosis of GCA [3,7]. However, TAB may be normal in 42% to 61% of the patients [8]. Recently, several reports showed that 18F-FDG-PET accurately and safely identifies the multiple vessels involved in GCA [9]. A smooth linear or long segmental pattern of 18F-FDG uptake in the aorta and its main branches is thought to be a characteristic pattern of GCA [10]. In Korea, some cases that 18F-FDG-PET was used in the diagnosis of GCA were reported [11,12].

In accordance with age (50 years or older), bilateral shoulder aching, elevated ESR and CRP, morning stiffness more than one hour (> 45 min), absence of RF or ACPA and absence of other joint involvement, the patient in our case was classified as PMR based on 2012 provisional classification criteria for PMR [13]. No definite diagnostic criteria exist for GCA. From criteria for the classification of GCA by the American College of Rheumatology in 1990, the presence of 3 or more of 5 criteria (age greater than or equal to 50 years at disease onset, new onset of or new type of localized pain in the head, tenderness or decreased pulse of temporal artery, elevated ESR greater than or equal to 50 mm/h and abnormal findings on bi-
opsy of temporal artery) was associated with a sensitivity of 93.5% and a specificity of 91.2% [14]. He satisfied 3 criteria (age, headache, elevated ESR). $^{18}$F-FDG-PET showed increased vascular uptake but it didn’t show the increased uptake of shoulder, hip and the spinous process and bursa of the vertebra that can be seen in patients with PMR [15]. He didn’t experience visual symptom, jaw and tongue claudication and scalp pain. Moreover there was no temporal artery abnormality, scalp tenderness and bruit. So we think him as the patient with atypical GCA in subclinical stage concomitant with PMR. He was treated with prednisolone and other immunosuppressive agents for GCA. After 12 months of treatment, follow up $^{18}$F-FDG-PET was done and that showed the improvement of arteritis.

This is a case of GCA that demonstrates the usefulness of $^{18}$F-FDG-PET not only for diagnosis but also for therapeutic monitoring. There are several limitations of $^{18}$F-FDG-PET and it may be difficult to replace TAB. But it may be a useful diagnostic tool in GCA, especially in atypical cases and subclinical stage and it can help patient be treated in early stage. In addition, it can be used to monitor disease activity and response to treatment, especially in the case without definite vessel stenosis. And
based on this case, we hypothesize that there may be more cases of atypical and subclinical stage of GCA among Asians. They might be diagnosed with fever of unknown origin (FUO) or PMR without being diagnosed with GCA. Therefore, we think that large studies using \textsuperscript{18}F-FDG-PET should be conducted to determine how many patients with FUO or PMR have GCA.

**SUMMARY**

We report a case in which \textsuperscript{18}F-FDG-PET was used to diagnose GCA and to confirm improvement after treatment. \textsuperscript{18}F-FDG-PET can be a useful diagnostic and therapeutic monitoring tool in GCA, especially in atypical cases and subclinical stage.

**CONFLICT OF INTEREST**

No potential conflict of interest relevant to this article was reported.

**REFERENCES**