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SHORT COMMUNICATION

Diagnosing polymyalgia rheumatica on ^{18}F-FDG PET/CT: typical uptake patterns

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Abstract

Objective The diagnosis of polymyalgia rheumatica (PMR) is often challenging, since similar clinical features and laboratory findings can be observed in several inflammatory conditions. PMR involves affected sites in a specific manner, and ^{18}F-FDG PET/CT has the advantage for assessing the disease activity of each site. The purpose of this study was to identify the patterns of ^{18}F-FDG uptake that suggest the diagnosis of PMR.

Methods We studied 60 patients who had undergone ^{18}F-FDG PET/CT scans for workup of suspected PMR, arthritis, enthesitis, or myopathy. Final diagnoses were made by board-certified rheumatologists. The incidence of significant ^{18}F-FDG uptake, higher than mediastinal blood pool, of the following sites were compared among PMR patients and patients with other diseases: wrists, elbows, shoulders, sternoclavicular joints, acromioclavicular joints, spinous processes, ischial tuberosities, and greater trochanters. For the spinous processes, the incidence of "Y"-shaped uptake along the interspinous bursae was also evaluated.

Results A definitive diagnosis of PMR was given to 16 of 60 patients. The incidence of significant ^{18}F-FDG uptake in the definitive PMR group was 6% for wrists and for elbows, 88% for glenohumeral and sternoclavicular joints, 25% for acromioclavicular joints, 81% for spinous processes, 69% for ischial tuberosities, and 81% for greater trochanters. Patients with PMR showed a significantly higher incidence of "Y"-shaped uptake along the interspinous bursae than the other patients (38 vs. 9%) ($P=0.016$).

Conclusion ^{18}F-FDG uptake distribution patterns and morphology can contribute to the diagnosis of PMR. Significant ^{18}F-FDG uptake in the sternoclavicular joints is one of the characteristic findings in patients with PMR as well as the uptake in the shoulders, ischial tuberosities, and greater trochanters. "Y"-shaped spinous process uptake may be one of the specific findings for PMR.

Keywords Polymyalgia rheumatica · ^{18}F-FDG PET/CT · Spinous processes · Interspinous bursa · Sternoclavicular joints

Introduction

Polymyalgia rheumatica (PMR) is a rheumatic disease characterized by widespread aching and stiffness. It tends to affect elderly people. The symptoms of PMR seem to be related to synovitis of proximal joints and extra-articular synovial structures [1]. The diagnosis is often challenging, because the clinical features and laboratory findings can also be observed in other various inflammatory conditions, such as elderly onset rheumatoid arthritis (RA), spondyloarthropathy (SpA), remitting seronegative symmetrical synovitis with pitting edema (RS3PE) syndrome, and several infectious diseases.

PMR has a specific site pattern and ^{18}F-FDG PET/CT is advantageous for assessing the disease activity of each site. In typical cases of RA and PMR, abnormal accumulation can be seen in the shoulders. In RA, the other affected sites are the fingers, wrists, and elbows [2]. In PMR, the ischial tuberosity, vertebral spinous processes, and iliopectineal bursa are typically affected [3].

In cases of Baastrup's disease, linear uptake along the interspinous ligament is the typical ^{18}F-FDG accumulation pattern (Fig. 1) [4]. Considering the etiology, PMR is speculated to have some distinct and unique ^{18}F-FDG accumulation patterns, though it has not fully been investigated. The

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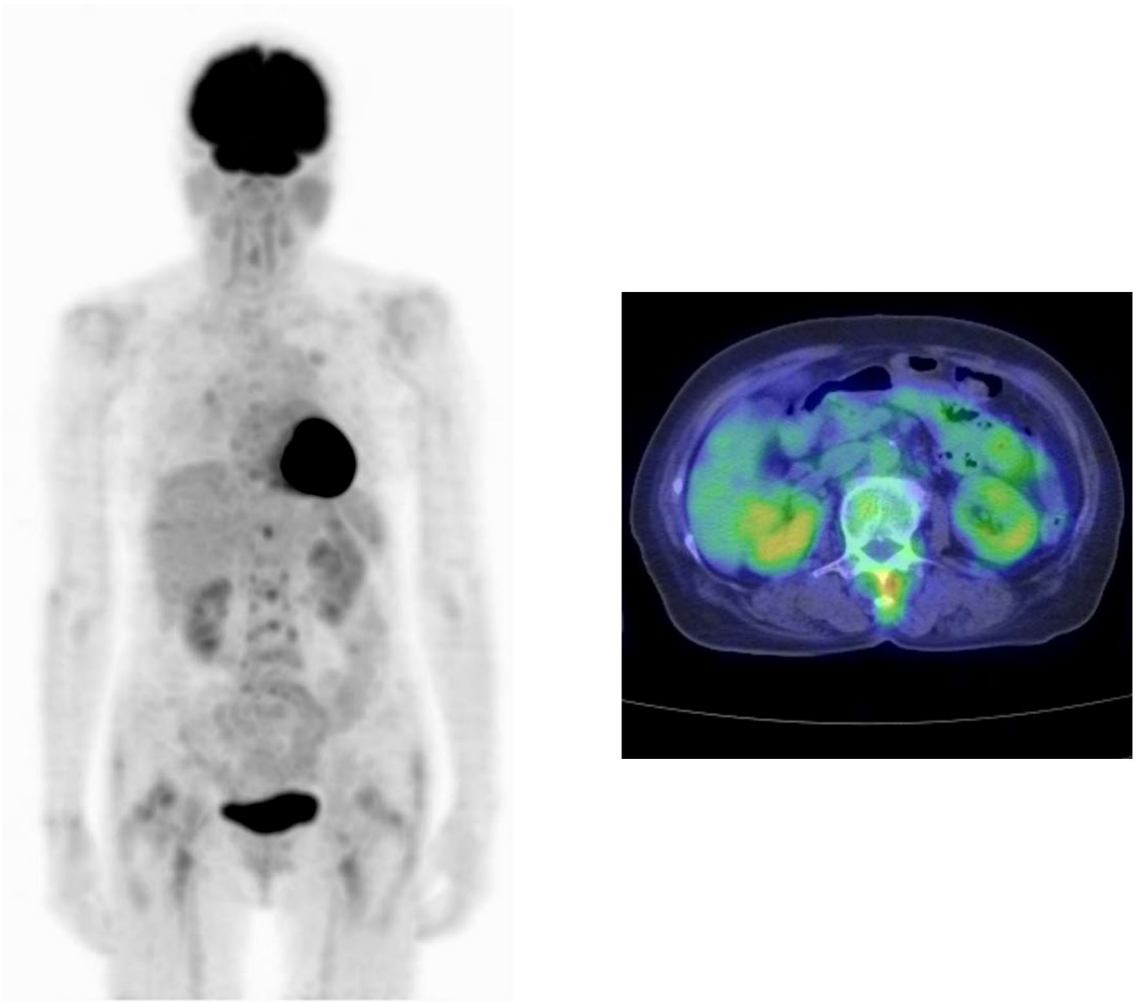

Fig. 1 ^{18}F-FDG PET/CT images of an 81-year-old female with suspected Baastrup disease. There is linear FDG uptake along the interspinous ligament

purpose of this study was to identify the specific patterns of ^{18}F-FDG uptake that contribute to the diagnosis of PMR.

Methods

The retrospective study design was approved by our ethics committee. The study population included all 60 patients (mean age = 72 ± 10, male/female = 20/40) who underwent ^{18}F-FDG PET/CT scans for workup examination of suspected PMR, arthritis, enthesitis, or myopathy between July 2007 and March 2016. There was no case under medical treatment. All patients were asked to fast for at least 4 h before intravenous ^{18}F-FDG administration. Administered ^{18}F-FDG activity for each patient was 185 MBq at calibration date (^{18}F-FDG scan injectable; Nihon Medi-Physics, Tokyo, Japan). PET/CT images were acquired approximately 1 h after the administration of ^{18}F-FDG. 34 of the 60 studies were performed using a Siemens Discovery mCT TOF (time-of-flight) PET/CT scanner (Siemens Healthineers, Erlangen, Germany) and the remaining 26 studies were performed using Aquiduo-16 non-TOF PET/CT scanner (Canon Medical Systems, Otawara, Japan). PET emission scanning was performed after the transmission CT scans with an acquisition time of 2 min per bed position, and then the images were reconstructed using a 3D iterative reconstruction algorithm: 3D-OSEM + point-spread function (PSF) + TOF for the Discovery mCT scanner and FORE + OSEM for the Aquiduo scanner.

Visual assessment of the individual joints for all patients: wrists, elbows, glenohumeral joints, sternoclavicular joints, acromioclavicular joints, spinous processes, ischial tuberosities, and greater trochanters were made by. ^{18}F-FDG accumulation higher than mediastinal blood pool was considered significant for each lesion.

For the spinous processes, the unique ^{18}F-FDG accumulation pattern along the interspinous bursa, being expected to be specific for the PMR patients, we named "Y"-shaped uptake (Fig. 2). "Y"-shaped uptake was also considered significant when the accumulation was higher than mediastinal blood pool.

The final diagnosis of definite PMR was made by either the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) provisional classification criteria in 2012 [5] or Bird's criteria [6] which were exclusively based upon the physical examinations of the board-certified rheumatologists and laboratory data. The rheumatologists adopted these two different criteria because currently PMR diagnostic criteria have not been unified or standardized yet. Then, the incidence of significant ^{18}F-FDG accumulations in the abovementioned individual joints were compared between the patients with the definite diagnosis of PMR by the rheumatologists and the remaining patients, who did not satisfy either of these PMR diagnostic criteria. The incidence of "Y"-shaped uptake was also compared between the two groups. The difference was statistically analyzed using Fisher's exact test (cutoff for significance: $p < 0.05$).

Results

A definitive diagnosis of PMR by the rheumatologists was made in 16 of 60 patients (mean age = 75 ± 10, male/female = 1/15). As shown in the profiles of the remaining 44 patients who were not diagnosed with PMR (Table 1). The incidence of significant ^{18}F-FDG uptake in the definite PMR patients vs. the incidence in the remaining patients is summarized in Table 2. Significant differences between the two groups were observed in the glenohumeral joints (14/16 vs. 22/44; $p = 0.015$), sternoclavicular joints (14/16 vs. 11/44;

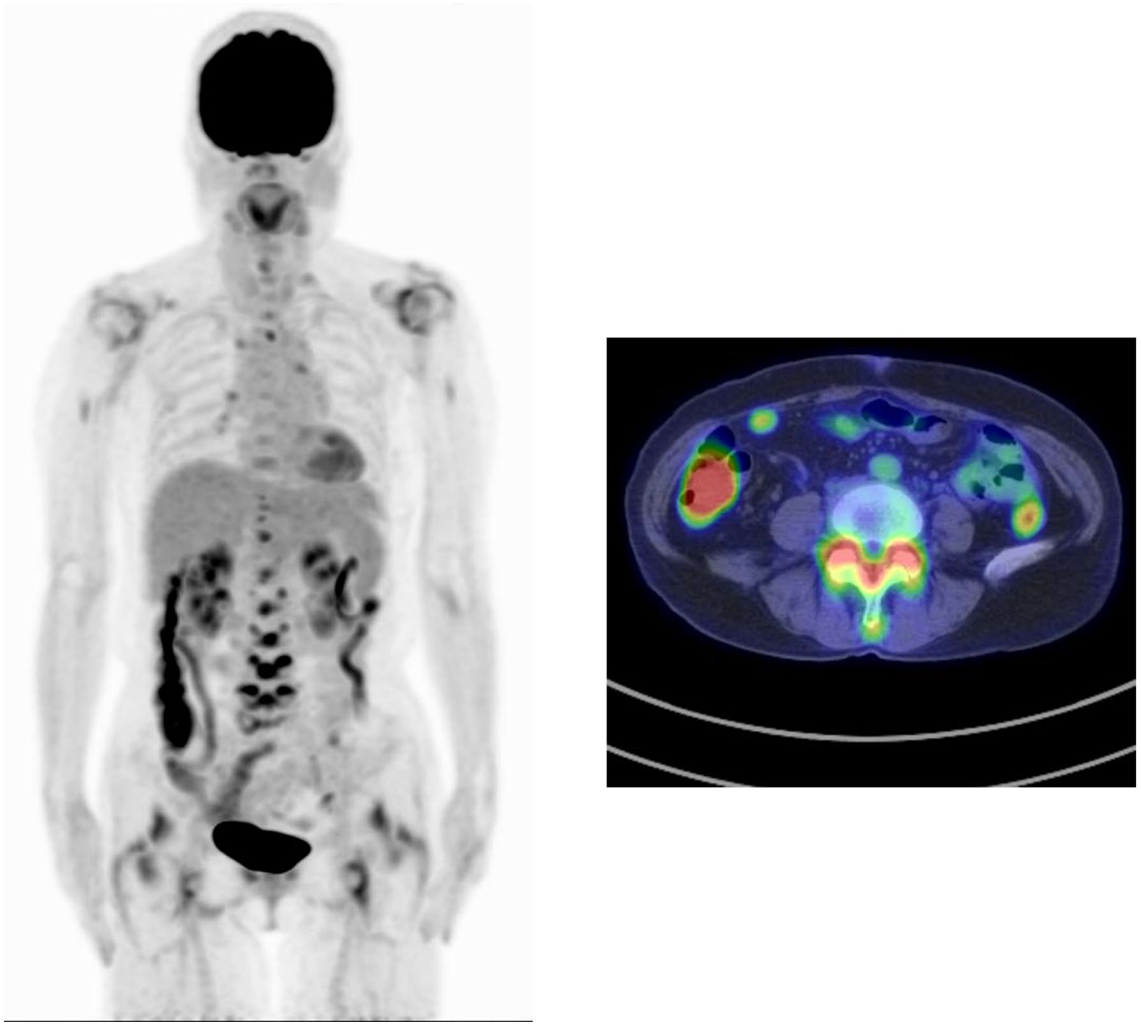

Fig. 2 ^{18}F-FDG PET/CT images of a 67-year-old female with PMR. PET/CT reveals abnormal accumulation in the shoulders, the ischial tuberosity, vertebral spinous processes, and iliopectineal bursa. There is the "Y-shaped uptake" pattern in the spinous processes

Table 1 The profiles of the 44 patients who did not have the diagnosis of PMR

	Total ($n=44$) (%)
RA	7 (16)
SpA	4 (9)
SAPHO syndrome	2 (5)
Takayasu arteritis	3 (7)
Paraneoplastic syndrome	3 (7)
Undifferentiated connective tissue disease	7 (16)
Infection	2 (5)
Osteoarthritis or nothing particular	9 (20)
Non-diagnosed patients[a]	7 (16)

[a]The non-diagnosed patients were those who had some PMR-like symptoms but who satisfied neither PMR diagnostic criteria nor the other diagnostic criteria for any specific diseases

Table 2 The incidence of significant ^{18}F-FDG uptake for individual joints

	Definite PMR group ($n=16$) (%)	The other group ($n=44$) (%)	p value
Wrists	1 (6)	10 (23)	0.26
Elbows	1 (6)	8 (18)	0.42
Glenohumeral joints	14 (88)	22 (50)	0.015
Sternoclavicular joints	14 (88)	11 (25)	<0.001
Acromioclavicular joints	4 (25)	8 (18)	0.72
Spinous processes	13 (81)	23 (52)	0.072
Ischial tuberosities	11 (69)	12 (27)	0.006
Greater trochanters	13 (81)	21 (48)	0.037

Table 3 The incidence of "Y-shaped uptake" in the spinous processes

	Definite PMR group ($n=16$) (%)	The other group ($n=44$) (%)	p value
"Y-shaped" spinous process uptake	6 (38)	4 (9)	0.016

$p<0.001$), ischial tuberosities (11/16 vs. 12/44; $p=0.006$), and greater trochanters (13/16 vs. 21/44; $p=0.037$). As for the spinous processes, the difference was not statistically significant (13/16 vs. 23/44; $p=0.072$); however, when looking at the morphology of ^{18}F-FDG accumulation, the patients with definite PMR were found out to have significantly higher incidence of "Y"-shaped uptake than the other patients (6/16 vs. 4/44; $p=0.016$) (Table 3). Namely, the sensitivity of this finding for PMR was calculated as 38%, the specificity as 91%, the positive predictive value (PPV) as 60%, and the negative predictive value (NPV) as 20% of the findings. Moreover, three out of four patients with a "Y"-shaped uptake pattern who belonged to the second group were those who had some PMR-like symptoms but who did not satisfy either PMR diagnostic criteria. The other was a RA patient.

Discussion

Highlighting the combination of the affected sites is often helpful for the diagnosis of systemic disorders. Several inflammatory disorders and collagen vascular diseases have their specific affected patterns at multiple site. In the present study, "Y"-shaped spinous process ^{18}F-FDG accumulation was observed with significantly higher incidence in the definite PMR patients. Moreover, the patients who had shown "Y"-shaped spinous process uptake in the not diagnosed with PMR group also left open a possibility of PMR. Therefore, "Y-shaped" spinous process ^{18}F-FDG uptake is considered to be a specific finding for PMR.

Several authors have already reported the characteristic ^{18}F-FDG PET/CT findings that suggest the diagnosis of PMR. Yamashita et al. showed that significant ^{18}F-FDG accumulation is seen in the ischial tuberosities, greater trochanter, and spinous process, and the sensitivity (85.7%) and specificity (88.2%) of diagnosing PMR were high when ^{18}F-FDG uptake in at least two of these sites was found [7]. In the present study, the ischial tuberosity, greater trochanter, spinous processes, glenohumeral joints, and sternoclavicular joints were the most common affected sites for the PMR patients. Abnormal ^{18}F-FDG accumulation in the glenohumeral joints was also observed in a patient with elderly onset RA and osteoarthritis, so there is still a differential diagnosis based just on these findings [8]. Dasgupta et al. have stated that the specificity of glenohumeral findings for discriminating RA from PMR was not high (70%) even when ultrasound findings were included in the scoring algorithm of the ACR/EULAR criteria [5]. As for the sternoclavicular joints, our data indicated that PMR may potentially or asymptomatically affect this site frequently. However, these findings are typically observed in patients with synovitis, acne, pustulosis, hyperostosis, osteitis (SAPHO) syndrome, and can also be observed in those with RA, and so these lesions are not considered to be specific for PMR.

The present study found that "Y"-shaped uptake is characteristic of PMR. It is considered to be the manifestation of bursitis around the spinous process. The structures around the spinous process are forming the posterior ligamentous complex: intraspinous bursa, bilateral facet joint space, and retrodural space of Okada. The retrodural space of Okada is located dorsal to the ligamentum flavum in the interlaminar space, providing the communication between bilateral facet joints and intraspinous bursae [9]. It is a potential space, difficult to identify unless there is fluid or inflammation within this area. Our speculation is that "Y"-shaped uptake in PMR

patients may be the manifestation of bursitis extending from the interspinous bursa to the retrodural space of Okada to the bilateral facet joints. However, linear uptake along the spinous processes is a known finding in Baastrup's disease. Baastrup's disease, also called "kissing spine," is characterized by the close approximation and the contact of adjacent spinous processes [4]. In the cases of ^{18}F-FDG PET/CT study in Baastrup's disease, there is linear accumulation along the interspinous ligament, and this kind of accumulation is speculated to reflect inflammation or rupture of the interspinous ligament, or bursitis [10].

Local ^{18}F-FDG accumulation pattern, such as "Y"-shaped spinous process uptake in the present study, should be important for the differential diagnosis. When the accumulation patterns in the shoulders and femurs are carefully observed, elderly onset RA patients and PMR patients seem to have different ^{18}F-FDG accumulation patterns, as proposed by Yamashita et al.: those with elderly onset RA typically show circumferential yet linear ^{18}F-FDG accumulation surrounding the humeral head, reflective of synovitis, whereas those with PMR shows nonlinear localized accumulation, reflective of bursitis [3]. High-resolution PET images might solve their problem by the more precise assessment about the local accumulation pattern in the future.

Our study has several limitations. This is a retrospective study. We used two different PET/CT scanners, and only one scanner had time-of-flight and point-spread function (TOF + PSF) reconstruction techniques. Accordingly, we have just evaluated visual uptake difference between each joints and mediastinal blood pool without calculating standardized uptake value (SUV). Each joint investigated are not as small as bringing underestimation. The diagnosis of PMR may not fully be objective, since the criteria were partly based upon the rheumatologists' physical examinations. Since our study has small number of the cases, our study population has somewhat different gender ratios from the general morbidity ratio of PMR (male:female = 1:2–3). In spite of these limitations, we believe that this pilot study could emphasis the superiority of visual assessment using FDG PET/CT for the diagnosis of PMR.

Conclusion

It is necessary to be aware of ^{18}F-FDG uptake distribution patterns and morphology. Significant uptake at the sternoclavicular joints is one of the common findings, as well as the uptake at the glenohumeral joints, ischial tuberosities, and greater trochanters. "Y"-shaped spinous process uptake should be a specific finding for PMR. These ^{18}F-FDG PET/CT finding can contribute to the diagnosis of PMR.

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Compliance with ethical standards

Conflict of interest The authors have no potential conflicts of interest to disclose.

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