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Original article

Similarities and differences in fluorodeoxyglucose positron emission tomography/computed tomography findings in spondyloarthropathy, polymyalgia rheumatica and rheumatoid arthritis

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ABSTRACT

Objectives: We assessed fluorine-18 (^{18}F)-labelled fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) findings in patients with seronegative spondyloarthritis (SpA), polymyalgia rheumatica (PMR), and rheumatoid arthritis (RA).
Methods: We studied 53 patients with SpA (n = 21), PMR (n = 16), or RA (n = 16) admitted to our hospital between 2006 and 2011. Disease activity in the ischial tuberosities, greater trochanters, spinous processes, vertebral bodies, and sacroiliac joints (SIJ) were evaluated by determining FDG accumulation using maximum standardized uptake values (SUV_{max}) and FDG scores.
Results: SUV_{max} for ischial tuberosities was significantly higher in PMR than SpA or RA. SUV_{max} for greater trochanters and spinous processes was significantly higher in PMR than RA ($P < 0.001$) and significantly higher in SpA than in PMR or RA for SIJ ($P = 0.01$). No significant difference in vertebral scores was observed among groups ($P = 0.488$). FDG scores yielded similar results. X-ray findings were consistent with PET/CT findings in 3/15 (20%) patients with sacroiliitis, whereas magnetic resonance imaging findings were consistent with PET/CT findings in 4/7 (57.1%) patients.
Conclusions: PET/CT detection of inflammation in the ischial tuberosities, greater trochanters, and spinous processes discriminated between PMR and RA, but not between SpA and PMR. PET/CT findings can distinguish SpA from RA and PMR and are useful for the early diagnosis of sacroiliitis.

1. Introduction

Seronegative spondyloarthritides (SpA) are a family of diseases that share certain clinical features, including enthesitis, asymmetric oligoarthritis, and inflammation of the axial joints, particularly the sacroiliac joints (SIJ), with spinal inflammation [1].

Plain radiographs of the spine, SIJ and involved peripheral joints, and entheses are helpful in documenting longstanding disease, but are less diagnostically informative regarding changes in early or undifferentiated spondyloarthritis (USpA). After a diagnosis of USpA has been made, considerable time is required before the condition is classified as either ankylosing spondylosis (AS) or psoriatic arthritis (PsA) [2,3].

According to the European Spondyloarthropathy Study Group (ESSG) and Amor criteria, the only plain radiographic findings that are specific for SpA are those of sacroiliitis [4,5]. However, radiographic sacroiliitis becomes apparent only several years after disease onset. Magnetic resonance imaging (MRI) can be helpful in the diagnosis of SpA in patients without plain radiographic evidence of sacroiliitis [6–9]. Nevertheless, the application of MRI for the evaluation of multiple lesions is limited.

The fluorine-18 (^{18}F)-labelled fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) technique has practical applications in patients with multilocular inflammatory manifestations in the spine, joints, and entheses, particularly in locations that are difficult to examine clinically, such as the intervertebral discs, apophyseal joints, costovertebral and costotransverse joints, anterior chest wall, symphyses, and entheseal sites.

The usefulness of PET in ^{18}F-labelled FDG-PET/CT has been well established for the diagnosis, staging, and evaluation of therapy for various types of cancer throughout the body. However, elevated glucose metabolism is observed in inflammatory cells as well as in cancer cells [10,11]. Although this phenomenon is a source of false-positive results in oncological diagnoses, it may be used for the diagnosis of inflammatory disease [12]. FDG-PET/CT scans have

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been used to detect inflammatory rheumatic disorders including rheumatoid arthritis (RA) [13,14], polymyalgia rheumatica (PMR) [15], and large vessel vasculitis [16]. However, few reports have described the use of whole-body PET/CT for the diagnosis of SpA [17–19].

Using PET/CT in patients with active SpA, Taniguchi et al. [17] demonstrated enthesitis manifesting as the inflammation of the spinous processes, SIJs, hips, and ischial tuberosities. Blockmans et al. [15] performed FDG-PET scans in 35 patients with PMR and observed abnormal FDG accumulation in the vertebral spinous processes in 51% of patients and in the hips in 89% of patients. Proximal symptoms similar to PMR can be seen in patients with late-onset SpA [20]. Axial skeletal involvement, oligoarthritis, distal pitting edema, and constitutional symptoms such as fever, anorexia, and weight loss may be present in these patients, together with an elevated ESR [21].

Elderly-onset SpA and RA can be difficult to distinguish from PMR, and the FDG-PET/CT images of SpA and PMR may be similar, as discussed above. Thus, the present study examined the similarities and differences among PET/CT findings in patients with SpA, PMR, and RA, and investigated the applicability of the image findings to the early diagnosis of SpA.

2. Methods

2.1. Patient characteristics

We reviewed all medical charts for patients admitted to our institute's Division of Rheumatic Diseases between January 2006 and September 2011. We identified 21 patients with SpA, 16 with RA, and 16 with PMR who had undergone FDG-PET/CT in the Department of Radiology to exclude other diseases. FDG-PET/CT was carried out on all patients hospitalized with SpA symptoms. In the present study, PMR patients included both patients at the onset of PMR and those hospitalized with a chief complaint of PMR symptoms. Regarding RA, only the cases in which an inflammatory response indicated RA activity were selected from those in which FDG-PET/CT was carried out to evaluate malignancy or infection resection. Laboratory findings were evaluated within 5 days of PET/CT examination.

SpA was diagnosed when a patient's condition met the Amor diagnostic criteria [5]. Diagnoses of PMR were based on the criteria suggested by Chuang et al. [22] and on the exclusion of other inflammatory diseases. All 16 PMR patients also met Healy's criteria for retrospective assessment [23]. Patients with RA fulfilled the 1987 criteria outlined by the American College of Rheumatology (ACR) [24]. All patients with SpA and PMR were negative for both rheumatoid factor (RF) and anti-cyclic citrullinated peptide (CCP) antibodies.

The ages (mean ± standard deviation [SD]) of patients with SpA, PMR, and RA were 50.8 ± 18.0, 76.2 ± 8.9, and 70.9 ± 10.0 years respectively, and the number of males/females were 7/14, 4/12, and 2/14 respectively. The mean serum C-reactive protein (CRP) levels for the SpA, PMR, and RA groups were 4.26 ± 3.81, 7.91 ± 3.54, and 7.54 ± 4.78 mg/dL, and the mean erythrocyte sedimentation rates (ESR) were 104.1 ± 19.9, 74.4 ± 43.9, and 87.9 ± 29.7 mm/h respectively. Disease durations were: SpA: 158.4 ± 369.1 (1–1356) weeks; PMR: 8.1 ± 5.9 (4–24) weeks; RA: 324.5 ± 314.0 (3–939) weeks. Disease activity was evaluated using the modified health assessment questionnaire (MHAQ), which measures the patient's functional status and quality of life. The MHAQ scores were 3.9 ± 2.5, 5.8 ± 3.0, and 6.7 ± 1.6, respectively for the SpA, PMR, and RA groups. We found no significant difference in gender ($P = 0.344$) or ESR ($P = 0.276$) among the three patient groups; however, the age ($P \leq 0.001$) and CRP levels ($P \leq 0.01$) were significantly lower in patients with SpA compared with those of the other two groups. The mean disease duration in the PMR group was significantly shorter than that in the SpA and RA groups ($P \leq 0.01$). The mean MHAQ score in the RA group was significantly higher than that in the SpA group ($P \leq 0.01$). The medications prescribed during the period when PET imaging was performed were: SpA group: steroids (prednisolone [PSL] at 5–17.5 mg daily; $n = 3$), methotrexate (MTX; $n = 1$), sulfasalazine (SSZ: $n = 1$), non-steroidal anti-inflammatory drugs (NSAIDs; $n = 4$), and infliximab ($n = 1$); PMR group: no treatment ($n = 14$), NSAID ($n = 1$) and colchicine ($n = 1$); RA group: steroids (PSL 6.4 ± 2.4 [mean ± SD] mg daily, range [3–10 mg daily]; $n = 11$), SSZ ($n = 3$), MTX ($n = 4$), cyclosporine ($n = 1$), tacrolimus ($n = 1$), bucillamine ($n = 1$), and etanercept ($n = 1$).

Of the 21 patients with SpA, 15 underwent the human leukocyte antigen (HLA) test. HLA-B27 was demonstrated in three (20.0%), and HLA-B39 in two (13.3%) of the 15 patients.

The present study was approved by the ethics committee of our hospital.

2.2. FDG-PET/CT imaging

After a 5-hour fast, blood glucose levels were measured and patients received an intravenous injection of 370 MBq of FDG. One hour after FDG injection, PET/CT imaging was performed from the vertex to the knee joints or from head to foot using a PET/CT scanner (Biograph 16; Siemens Medical Solutions, Forchheim, Germany) with a 3-minute emission scan/bed and CT attenuation correction. A dedicated workstation was used to evaluate FDG uptake for characteristic findings, such as sacroiliitis, spondylitis, and enthesitis in patients with SpA, or bursitis in the ischial tuberosities, greater trochanters, and spinous processes in patients with PMR [4,25,26]. FDG uptake was not measured in major joints such as the shoulder, elbow, and knee because arthritis, enthesitis, and bursitis in these joints cannot be readily distinguished using the FDG-PET/CT technique. For example, it is difficult to differentiate omarthritis from subacromial bursitis on FDG-PET images because the subacromial bursa is located between the rotator cuff and the acromion and the deltoid muscle and is adjacent to the shoulder joint. The bursae in the popliteal fossa are generally referred to as popliteal cysts, and approximately 97% of suprapatellar bursae communicate with the knee joint. Thus, when synovial fluid is retained in the knee joint, a similar synovial fluid retention is detected in the suprapopliteal bursa. Bursitis of another site in the knee is adjacent to the knee joint and is difficult to differentiate from synovitis on FDG-PET images. Moreover, enthesitis in the same region is adjacent to the joint and difficult to distinguish from synovitis or bursitis on FDG-PET images.

Regions of interest were drawn around each site and maximum standardized uptake values (SUV_{max}) were calculated. FDG uptake into these sites was evaluated visually using the following scoring system, modified from Goerres et al. [14]: 0: no uptake (same as bone); 1: slight uptake; 2: moderate uptake (same as liver); 3: higher uptake than liver. SUV_{max} and FDG scores for each site were then calculated. Total SUV_{max} and FDG scores were recorded for each site, and each site with an FDG uptake score greater or equal to 2 was considered to show positive PET/CT findings.

Among the 21 patients with SpA, 20 had undergone X-ray examination and 11 had undergone MRI scans to evaluate the SIJs and enthesopathy.

2.3. Statistical analyses

All statistical analyses were performed using Stata software (version 11.2; StataCorp, College Station, TX, USA).

The medians and SDs of the SUV_{max} and FDG scores and proportions of positive FDG uptake were calculated for each body part. We