PET-CT findings in patients with polymyalgia rheumatica without symptoms of cranial ischaemia

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PET-CT findings in patients with polymyalgia rheumatica without symptoms of cranial ischaemia

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ABSTRACT
INTRODUCTION: Polymyalgia rheumatica (PMR) is an inflammatory disorder that affects the elderly. At present, evidence is limited regarding the usefulness of positron emission tomography-computed tomography (PET-CT) in the diagnosis of PMR. This study aimed to compare patient characteristics and symptoms with PET-CT findings in a Danish population of PMR patients without clinical symptoms of giant cell arteritis.

METHODS: The medical records of 50 Danish PET-CT-scanned patients with PMR were reviewed. Symptoms, characteristics and PET-CT findings were registered from the medical records.

RESULTS: Fluorodeoxyglucose (FDG) uptake was seen at the shoulders and/or hips of about 80%, and at the spinous processes of about 50% of the patients. Furthermore, 14% of the patients showed no FDG uptake at any of the studied locations. A sensitivity of 79% for PMR was found if there was FDG uptake at any two of the following three locations: the shoulder, the hip and the spinous processes. Vascular FDG uptake was seen in 7% of the patients. No significant correlations between any symptoms and any PET-CT findings were found. C-reactive protein was significantly lower in patients receiving glucocorticoids, and completely normal scans were seen significantly more often in patients receiving steroid treatment.

CONCLUSIONS: PET-CT is a sensitive imaging technique in PMR patients. Symptoms and PET-CT findings do not correlate in PMR. Steroid treatment prior to PET-CT reduces the scan’s ability to demonstrate inflammation in PMR patients.

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TRIAL REGISTRATION: not relevant.
tional symptoms (i.e. fever, weight loss, night sweats, malaise) and musculoskeletal system symptoms (e.g. pain, morning stiffness) was registered. The nuclear medicine physician’s description of the PET-CT was scrutinised, and if more than one PET-CT scan had been made, the findings in the one closest to the date of the patient’s PMR diagnosis were used. The descriptions were made by various nuclear medicine physicians over a course of 3.5 years, and were based on a visual examination of the PET-CT. We registered FDG uptake at the shoulder, the hip, the spinous processes at any level, the ischial tuberosity, the vasculature and the sternoclavicular joint. Additionally, presence of pathological FDG uptake at any other location was registered.

### TABLE 1

<table>
<thead>
<tr>
<th>Patient characteristics.</th>
<th>All patients (N = 50)</th>
<th>Steroid naive patients (N = 29)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex, n (%)</td>
<td>31 (62)</td>
<td>18 (62)</td>
</tr>
<tr>
<td>Age at diagnosis, yrs, median (range)</td>
<td>74 (46-88)</td>
<td>76 (46-88)</td>
</tr>
<tr>
<td>Time from 1st consultation to diagnosis, days, median (range)</td>
<td>27 (0-333)</td>
<td>21 (0-333)</td>
</tr>
<tr>
<td>Time from PET-CT to diagnosis, days, median (range)</td>
<td>9 (–83-322)</td>
<td>10 (–13-322)</td>
</tr>
<tr>
<td>CRP before treatment with glucocorticoids, mg/l</td>
<td>67 (± 55.0)</td>
<td>64 (± 62.8)</td>
</tr>
<tr>
<td>Median (range)</td>
<td>57 (2-246)</td>
<td>49 (2-246)</td>
</tr>
<tr>
<td>On glucocorticoid treatment at the time of PET/CT, n (%)</td>
<td>21 (42)</td>
<td>0</td>
</tr>
</tbody>
</table>

Clinical suspicion triggering PET-CT, n (%)

- Cancer: 31 (62)
- Infection: 7 (14)
- Vasculitis/PMR: 11 (22)
- Other: 1 (2)

CRP = C-reactive protein; PET-CT = positron emission tomography-computed tomography; PMR = polymyalgia rheumatica; SD = standard deviation.

### TABLE 2

<table>
<thead>
<tr>
<th>Symptoms or clinical manifestations related to polymyalgia rheumatica in patients. The values are n (%).</th>
<th>All patients (N = 50)</th>
<th>Steroid naive patients (N = 29)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper extremity pain yes INP/II</td>
<td>49 (98) 1 (2)</td>
<td>29 (100) 0</td>
</tr>
<tr>
<td>Lower extremity pain yes INP/II</td>
<td>44 (88) 3 (6)</td>
<td>25 (86) 1 (3)</td>
</tr>
<tr>
<td>Back and/or neck pain yes INP/II</td>
<td>35 (70) 12 (24)</td>
<td>22 (76) 6 (21)</td>
</tr>
<tr>
<td>Morning stiffness yes INP/II</td>
<td>12 (24) 38 (76)</td>
<td>7 (24) 22 (76)</td>
</tr>
<tr>
<td>Constitutional symptoms yes INP/II</td>
<td>32 (64) 17 (34)</td>
<td>22 (76) 7 (24)</td>
</tr>
<tr>
<td>Rapid response to glucocorticoids yes INP/II</td>
<td>29 (58) 10 (20)</td>
<td>15 (52) 9 (31)</td>
</tr>
<tr>
<td>Clinical evidence of arthritis yes INP/II</td>
<td>9 (18) 6 (12)</td>
<td>3 (10) 3 (10)</td>
</tr>
<tr>
<td>US evidence of bursitis yes INP/II</td>
<td>2 (4) 45 (90)</td>
<td>1 (3) 26 (90)</td>
</tr>
<tr>
<td>Ischaemic symptoms yes INP/II</td>
<td>0 45 (90)</td>
<td>0 27 (93)</td>
</tr>
<tr>
<td>Healey criteria fulfilled [5] yes INP/II</td>
<td>23 (46) 22 (44)</td>
<td>14 (48) 12 (41)</td>
</tr>
</tbody>
</table>

INP/II = information not provided/insufficient information; US = ultrasonographic.

Statistical analysis was made using Excel 2013, with the RealStats and Solver add-ins. For analysis of continuous variables, the Kruskal-Wallis test was used as these variables could not be assumed to be normally distributed. For comparison of binary variables, Fisher’s exact test was used. Medians are presented with the range in parentheses.

**RESULTS**

The median age of the patients was 74 (range: 46-88) years, 62% were female. The patients had a median diagnostic delay of 27 (range: 0-333) days (Table 1). The median CRP before treatment was elevated to 57 (range: 2-246) mg/l. Almost all patients had upper extremity pain (98%), most had lower extremity pain (88%) and many had neck/back pain (70%). The diagnostic criteria for PMR, proposed by Healey [5], were met in 46% of the patients (Table 2). PET-CTs were performed due to suspicion of malignant disease in slightly more than half of the patients. FDG uptake was found primarily in the shoulders, hips, spinal column, ischial tuberosities and in the sternoclavicular joints (Table 3). A temporal artery biopsy was made in nine (31%) cases, one was inconclusive, the rest were negative. A total of 21 patients were receiving glucocorticoid treatment at the time of their PET-CT, and seven (33%) of these patients had normal PET-CTs. In contrast, no steroid-naïve patients had completely normal PET-CTs (p = 0.001). CRP at the time of the PET-CT was significantly lower in patients receiving glucocorticoid treatment than in steroid-naïve patients; the median CRP was 7 (range: 0-57) mg/l versus 40 (range: 2-255) mg/l, p < 0.0001. Because of these findings, indicating that glucocorticoid treatment might introduce bias, the remainder of the statistical analyses were made on the glucocorticoid-naïve patients exclusively.

No significant correlations were found between any localised pain and FDG uptake in the corresponding region of interest (ROI). Furthermore, presence of constitutional symptoms did not correlate with vascular FDG uptake (Table 4). No significant correlations between CRP values and FDG uptake could be found at any ROI. Sensitivity of the FDG-positive PET-CT for the diagnosis of PMR was calculated when combining the following three ROIs: shoulder, hip and spinous processes. A sensitivity of 48% was achieved if there was FDG uptake at all three locations simultaneously. Furthermore, if there was FDG uptake at any two of these three locations, a sensitivity of 76% was achieved. Conversely, only 14% of patients had a finding of only “other pathological uptake” or no uptake at all. As this study did not include a control group, no specificities could be calculated.
DISCUSSION

In the Danish PMR patients included in this study, increased FDG uptake in the shoulders and hips was very common, whereas FDG uptake at the spinous processes was less frequent. Increased FDG uptake at the sternoclavicular joint and the ischial tuberosity was occasionally seen, whereas vascular FDG uptake was rare. Surprisingly, other pathological uptake than what is typically found in PMR was found in roughly three out of five patients. Most of these findings were non-specific, but in a few cases the PET-CT findings warranted further investigation (e.g. colonoscopy and biopsy).

The patients were given their PMR diagnosis by a rheumatologist, but only half of the patients fulfilled the criteria proposed by Healey [5]. This was primarily because the data required to fulfill these criteria were missing in the patients’ medical records. This probably reflects the records being every-day clinical tools and not data gathered for scientific purposes, a well-known problem in the retrospective study design. It is not known to which degree the results of the PET-CT influenced the rheumatologist when the PMR diagnosis was given, as it was not specified in the medical records.

A clear majority of the 29 steroid-naive patients had a very low time delay (days to a few weeks) from PET-CT to a PMR diagnosis was established. Only four patients had a considerable time delay exceeding two months. This patient number is too low to have skewed the results.

The very high frequencies of FDG uptake at the shoulders and at the hips in this study are similar to the frequencies reported by Yamashita et al [4], Blockmans et al [6], Rehak et al [7], Palard-Novello et al [8] and Wakura et al [9], confirming a high prevalence of this finding in PMR patients. However, a history of upper or lower extremity pain does not seem to correlate with these findings. In the present study, there were several patients without upper and/or lower extremity pain who had an increased FDG uptake at these locations. To our knowledge this has not yet been investigated elsewhere. The findings are in contrast to the rather low frequency of FDG uptake at these sites reported by Sondag et al [10] (58% had FDG uptake at the shoulders, 38% at the hips), but 44% of the PMR patients in that study were treated with corticosteroids, which may lower FDG uptake. The findings of the present study also confirm the findings by Camellino et al [11] that FDG uptake at the spinous processes is fairly common (48% of patients), but no connection to columnar pain could be made. Hence, increased FDG uptake detectable by PET-CT might not demonstrate the inflammatory changes responsible for the reported regional pain symptoms.

Similarly, an imaging study including 57 PMR patients revealed that US evidence of subacromial bursitis remained in nearly 60% of patients, even after clinical remission or low disease activity was achieved [12].

Our finding of a sensitivity of 76% when combining the PET-CT findings at the hips, shoulders and spinous processes is not surprising as a high frequency of FDG uptake at these locations in PMR patients has also been found in other studies [4, 6-8, 13, 14]. However, some authors have reported that FDG uptake at the hips and shoulders is unsuitable for distinguishing between PMR and similar diseases (e.g. rheumatoid arthritis), as the specificity is low [13], unless the pattern of FDG uptake at these locations is considered [14].

The finding of a significant negative effect of glucocorticoid treatment on PET-CT findings is similar to findings reported by Blockmans et al. The authors were able to demonstrate a significant reduction in FDG uptake at the shoulders, hips and spinous processes after three months of methylprednisolone therapy [6]. Similarly, in a study of GCA patients, previously abnormal PETs were normalised in eight out of 22 patients after three months of methylprednisolone treatment [15]. Sondag et al also found that FDG uptake was significantly lower in PMR patients receiving steroid treatment [10].

A potential connection between CRP values and PET-CT findings could not be demonstrated in this study. Similarly, Stellingwerff et al were unable to establish a
CONCLUSIONS
A majority of PMR patients have an increased uptake at specific locations. Neither regional nor constitutional symptoms correlate with PET-CT findings in PMR. This study supports previous evidence that steroid treatment prior to FDG PET-CT reduces the ability of the scan to demonstrate inflammation in PMR patients. Large prospective studies of PET-CT findings in PMR patients with inclusion of relevant control groups are warranted as PET-CT at present remains an expensive, not readily available imaging modality.

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CONFLICTS OF INTEREST: Disclosure forms provided by the authors are available with the full text of this article at www.danmedj.dk

LITERATURE
