New arguments for a vasculitic nature of polymyalgia rheumatica using positron emission tomography


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Abstract

Objective. To study the possible contribution of fluorodeoxyglucose (FDG)-positron emission tomography (PET) in the diagnosis of giant cell arteritis and polymyalgia rheumatica.

Methods. A consecutive case series consisting of five patients with polymyalgia rheumatica, six patients with temporal arteritis and 23 age-matched patients with other inflammatory conditions were evaluated with FDG-PET. Studies were performed before therapy with steroids was started.

Results. A total of 4/6 patients with giant cell arteritis and 4/5 patients with polymyalgia had increased FDG uptake in their thoracic vessels, compared to 1/23 controls (P < 0.001). Increased vascular FDG uptake in the upper legs was seen in 8/11 patients with giant cell arteritis or polymyalgia compared to 8/23 control patients (P < 0.05), and in the lower legs in 6/11 patients compared to 6/23 controls (P = not significant).

Conclusions. FDG-PET scan is the first non-invasive technique which may indicate large-vessel vasculitis and which can show its extension throughout the body. It strongly suggests that polymyalgia rheumatica is a form of vasculitis.

Key words: Vasculitis, Polymyalgia rheumatica, Giant cell arteritis, FDG-PET scan.

Polymyalgia rheumatica is a clinical syndrome of proximal muscle pain and stiffness in older patients without pathognomonic diagnostic tests [1–3]. It is closely related to arteritis temporalis and many patients with this type of vasculitis have polymyalgia-like complaints. Polymyalgia rheumatica is diagnosed by exclusion of other disorders which can give rise to similar complaints and by the rapid relief of symptoms by low-dose corticosteroid treatment.

Except for surgical biopsy, arteriography, von Willebrand’s factor antigen and anti-neutrophilic cytoplasmic antibody measurement [4], no non-invasive techniques are available for diagnosing vasculitis. Imaging techniques such as gallium scintigraphy [5], indium-labelled leucocyte scans [6] and three-phase Tc-99m pyrophosphate scintigraphy [7] have been used in selected patients with vasculitis, yet inflamed vessels have never been visualized with these techniques.

Positron emission tomography (PET) with radioactive labelled fluoro-18-deoxyglucose (FDG) makes in vivo measurement of metabolic processes possible. FDG is a glucose analogue which is transported across the capillary and sarcolemmal membranes in proportion to the rate of glucose uptake. Increased FDG uptake can be observed in various conditions such as ischaemically threatened myocardial tissue [8], cancer [9] or inflammatory processes [10]. Since polymyalgia rheumatica and temporal arteritis are characterized by impressive laboratory signs of inflammation, we evaluated the use of FDG-PET in these conditions.

Methods

Patients

All patients with giant cell arteritis or with a clinical syndrome of polymyalgia rheumatica who were admitted to the General Internal Medicine Department of the University Hospital Gasthuisberg in Leuven, Belgium, between April 1996 and June 1998, underwent a FDG-PET scan. Diagnosis of giant cell arteritis was established when temporal artery biopsy revealed vasculitis in patients who fulfilled ACR criteria for this form of vasculitis [11]. Diagnosis of polymyalgia rheumatica was established when the patients fulfilled the Hunder and Healey criteria for polymyalgia [2, 3] and when a
temporal artery biopsy was normal. Patients who were already treated with corticosteroids were excluded from the study. The control group consisted of patients, 50 yr of age or older, admitted during the same time period with a long-lasting fever or an inflammatory syndrome which could not be ascribed to vasculitis.

**FDG imaging**

Patients fasted for at least 6 h before the examination. Whole-body images were obtained using a CTI-Siemens 931/08/12 scanner, with an axial field of view of 10.1 cm. A total of 6.5 Mbq/kg were injected i.v., 1 h before the start of the acquisition. Whole-body imaging was performed using 5 min/bed position for head, thorax and abdomen, and 4 min/bed position for the lower extremities. Total acquisition time was ~90 min.

PET results were examined by two teams of two nuclear medicine specialists who were not aware of the diagnosis in these patients. Their results were compared and, if deviating, a consensus was reached after discussion. The blood vessels of the lower legs (tibial arteries), the upper legs (femoral and popliteal arteries) and the thoracic arteries (aorta, subclavian arteries, carotid arteries) were individually assessed. A zero score meant that there was absolutely no visualization of blood vessels, a score of 1 stood for minimal FDG uptake in the vessels, at score 2 there was a clearly increased vascular FDG uptake and at score 3 FDG uptake in the vasculature was markedly pronounced. Scores 0 and 1 were regarded as negative, scores 2 and 3 as positive.

**Statistics**

Vascular FDG uptake in patients was compared with controls using \( \chi^2 \) testing. Bonferroni correction was used when polymyalgia patients and giant cell arteritis patients as separate groups were compared with controls. Numerical data are followed by the standard deviation, whenever applicable.

**Results**

**Patients**

A total of 34 patients were included in the study. Six patients (three males, three females, mean age 70 ± 6 yr) had giant cell arteritis. Five patients (all female) had a clinical diagnosis of polymyalgia rheumatica, their mean age was 63 ± 6 yr. There were no clinical signs of temporal artery involvement in these polymyalgia patients (no jaw claudication, no headache, no visual disturbances).

In 23 patients (17 male, six female, mean age 65 ± 10 yr), the fever and/or inflammation was not due to vasculitis or polymyalgia. In 10 patients, no explanation for the fever or inflammatory syndrome was found, but in seven of them there was a spontaneous recovery, which makes a transient infectious cause plausible. The following diagnoses were made in the remaining 13 cases: tuberculosis and sarcoidosis in two patients each, and monoclonal gammopathy of unknown significance, chronic pyelonephritis, bronchiectasias, chronic myelomonocytic leukaemia, infectious arthritis, systemic lupus erythematosus, rheumatoid arthritis, cytomegalovirus infection and encephalitis in one patient each.

**FDG-PET results**

Table 1 summarizes the findings of vascular FDG uptake in the upper and lower legs, and in the thoracic arteries. An example of a normal FDG-PET scan and a FDG-PET scan in giant cell arteritis is given in Figs 1 and 2, respectively.

Only one patient with giant cell arteritis had no increased vascular FDG uptake. The sole polymyalgia patient without vascular FDG uptake had a much lower C-reactive protein concentration compared to the four patients with strong vascular FDG uptake (27 mg/l vs 122 ± 39 mg/l).

In four of these five polymyalgia patients, a control PET scan was performed during steroid treatment, at a time when inflammatory parameters had normalized and patients had become asymptomatic. Vascular FDG uptake had clearly decreased at that time (Fig. 3).

In control patients, increased FDG uptake in the upper legs was seen in eight cases. Six of these eight patients also displayed increased FDG uptake in the vessels of the lower legs. In one of these patients (a 55-yr-old man with pneumonia), there was increased FDG uptake in the thoracic arteries as well. Only two of these eight patients had evidence of atherosclerosis; the only patient with temporal arteritis and negative FDG-PET, in contrast, suffered from pronounced atherosclerosis.

**Discussion**

We have evaluated the possible role of FDG-PET in the diagnosis of giant cell arteritis and polymyalgia rheumatica. We could demonstrate that these patients have an increased FDG uptake in their larger thoracic arteries. This pattern was seen only once in the control group. Owing to high uptake in the brain, the small diameter of the vessel and the relatively high background of the skin, direct evaluation of the temporal arteries is not possible on whole-body PET investigation. The high uptake in the brain also prevents judging of the brain arteries. FDG uptake in the arteries of the upper and lower legs was less specific, since these features were found in 35 and 26%, respectively, of the control population as well. We speculate that atherosclerosis might also contribute to an increased FDG uptake by the vessels, particularly in the light of recent findings suggesting an important inflammatory component in the pathogenesis of atherosclerosis [12, 13]. However, the abdominal aorta or the iliac arteries, which are frequently involved in atherosclerosis in an older population, were never visualized on FDG-PET scan. The single control patient with increased thoracic FDG uptake had no striking signs of atherosclerosis. This was also the case in five other patients with increased vascular FDG uptake in the legs. In contrast, the single patient with giant cell arteritis who had no increased vascular
Table 1. Number of patients and controls with increased vascular FDG uptake

<table>
<thead>
<tr>
<th></th>
<th>Upper legs</th>
<th>Lower legs</th>
<th>Thoracic vessels</th>
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<tbody>
<tr>
<td>Giant cell arteritis</td>
<td>5/6</td>
<td>4/6</td>
<td>*</td>
</tr>
<tr>
<td>Polymyalgia rheumatica</td>
<td>3/5</td>
<td>2/5</td>
<td>**</td>
</tr>
<tr>
<td>Controls</td>
<td>8/23</td>
<td>6/23</td>
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*P < 0.05; **P < 0.001.

FDG uptake suffered from marked atherosclerosis. In addition, if atherosclerosis were to give rise to increased FDG uptake in the vessel wall, we would expect to find local hot spots, corresponding to inflammatory plaques, rather than the smooth, linear picture found in the temporal arteritis and polymyalgia patients (Figs 2 and 3a). The normalization of FDG uptake in the subclavian arteries in patients with polymyalgia rheumatica during steroid therapy strongly argues against atherosclerosis as a cause of increased FDG uptake. Therefore, we believe that the increased FDG uptake in the thoracic blood vessels of our patients is truly due to inflammation, namely vasculitis. This suggests that polymyalgia is, in fact, a manifestation of an underlying vasculitic process, as has already been suggested by Weyand et al. [14, 15]. These authors found very similar levels of mRNA for inflammatory cytokines in temporal artery biopsies of patients with giant cell arteritis and in patients with isolated polymyalgia, clearly different from patients without these diseases. Our findings suggest that FDG-PET scan, like measurement of mRNA for inflammatory cytokines, is a more sensitive technique in the vessels of the legs (arrows) in a patient with arteritis temporalis.

The ‘whole-body’ FDG-PET scan offers the extra advantage that all foci of vasculitis are visualized with one examination. The increased FDG uptake in the
aorta, the subclavian arteries and the arteries of the upper legs in giant cell arteritis confirms that this vasculitic process expands far beyond the temporal arteries, a sufficiently known finding from the literature [16, 17]. Other causes of increased FDG uptake, such as activation of the endothelium, cannot be excluded as a possible cause for our results. In conclusion, we suspect that this relatively new, non-invasive technique may become a useful tool in the investigation of patients with inflammatory conditions and suspicion of polymyalgia rheumatica or temporal arteritis. Positive findings, particularly in the thoracic arteries, might yield the basis for a judicious empirical treatment with corticosteroids. Further studies in larger groups of patients with other types of vasculitides are wanted. Our findings add new arguments for the hypothesis that polymyalgia rheumatica represents a vasculopathy.

References