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PICTORIAL REVIEW

^{18}F -FDG PET/CT in polymyalgia rheumatica—a pictorial review

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ABSTRACT

Polymyalgia rheumatica (PMR) is one of the inflammatory rheumatic diseases that can potentially be detected by positron emission tomography/CT. High fluorine-18 fludeoxyglucose (^{18}F -FDG) accumulation around the shoulders, sternoclavicular and hip joints are the most common pre-treatment features of patients with PMR. Another common sign is increased ^{18}F -FDG uptake in extra-articular regions between columnal spinous processes, near ischial tuberosities and in the praepubic area. Some patients also present with high ^{18}F -FDG uptake in main arteries, corresponding to the characteristics of giant cell arteritis. It is possible to observe a decrease or even a disappearance of ^{18}F -FDG uptake after effective therapy, an event which may be useful for the monitoring of treatment as well as for detection of PMR relapse.

INTRODUCTION

Polymyalgia rheumatica (PMR) is the most common inflammatory rheumatic disease of the elderly. PMR typically develops in patients older than 50 years and is more common in females; however, the cause, development mechanisms and targets of inflammatory damage are still elusive.¹

PMR shares many pathogenetic and epidemiological features with giant-cell arteritis (GCA) and both have the potential to be detected by positron emission tomography (PET)/CT. With the exception of ultrasound, there is currently a paucity of imaging guidelines in PMR, nevertheless, the diagnosis of PMR is usually straightforward based on clinical findings and raised inflammatory markers. Our previous observations confirm that fluorine-18 fludeoxyglucose (^{18}F -FDG) PET/CT may be an advantageous one-step diagnostic modality for detecting different variants of PMR, for assessing extent and severity. There are several barriers to routine implementation of PET/CT in the evaluation of patients with PMR including: (1) unproven cost effectiveness, (2)

scanner capacity issues and (3) radiation exposure considerations. On the other hand, PET/CT provides a more holistic assessment of disease activity than more limited assessment with ultrasound.

The most illustrative cases out of 115 ^{18}F -FDG PET/CT examinations performed on 89 patients with PMR at our institution were selected for this pictorial essay.

Periarticular accumulation

Periarticular accumulations (highlighted in yellow in all figures in this essay) represent the most common pattern of ^{18}F -FDG uptake in patients with PMR (Figure 1). In pioneering ^{18}F -FDG PET examinations reported by Blockmans et al,² high ^{18}F -FDG uptake was detected in shoulders in 33/35 (94%) patients and in hips in 31/35 (89%) patients. In another hybrid PET/CT study published in 2012, high ^{18}F -FDG uptake in shoulders and hips was detected in 12/14 (86%) patients with relatively low specificity, 24.9% for shoulders and 64.7% for hips.³ A high incidence (>70%) was also observed in other cohorts as summarized

in Table 1.^{4–6} Moreover, it is possible to observe ^{18}F -FDG accumulation not only in shoulders and hips but, with focused detailed analysis, also in the near bursae with radiotracer uptake at the front of the hip joint indicating iliopsoas bursitis.^{6,8} A focal and non-linear uptake pattern is more consistent with the diagnosis of PMR than a circular and linear uptake pattern in elderly patients with onset rheumatoid arthritis.⁸ The other prominent site exhibiting increased ^{18}F -FDG accumulation is the sternoclavicular joints, presenting positivity in 43–72% patients (Table 1).^{3–6}

Extra-articular accumulation—interspinous and ischiogluteal bursitis

PMR can be accompanied by extra-articular involvement (highlighted in green in all figures in this essay), as in bursitis.

Blockmans et al² were the first to describe high ^{18}F -FDG uptake surrounding vertebral spinous processes in approximately half of their PMR patient cohort (18/35). Increased ^{18}F -FDG-uptake near the cervical and lumbar spinous processes was confirmed by other groups including our cases presented in Figure 1.^{4–6,8,9} Furthermore, radiotracer uptake was detected in intervertebral joints.⁶ Other published case reports of patients examined on PET/CT scanners noted high ^{18}F -FDG uptake in other extra-articular synovial structures (bursae around ischial tuberosities and femoral trochanters, highlighted in Figure 1).^{3–6} Bursitis detected using ^{18}F -FDG PET/CT appears to be typical for patients with PMR, with reasonable sensitivity (85.7%) and specificity (88.2%) determined by high ^{18}F -FDG uptake in at least two of three locations (ischial tuberosities, greater trochanters and spinous processes).^{10,3}

Figure 1. Fluorine-18 fludeoxyglucose (^{18}F -FDG) distribution in the torso of a patient with polymyalgia rheumatica with developed signs of coincidental giant-cell arteritis in a 78-year-old female. (a) Schema representing the left anterior oblique orientation, (b) maximum intensity projection positron emission tomography (PET) and (c) PET/CT fused axial and sagittal slices. Green colour/arrows, extra-articular ^{18}F -FDG uptake (cervical and lumbar interspinous bursae and ischiogluteal bursae) and praepubic ^{18}F -FDG uptake; red colour/arrows, vascular ^{18}F -FDG uptake (giant cell arteritis); yellow colour/arrows, articular/periarticular ^{18}F -FDG uptake (shoulders, hips and sternoclavicular joints).

Table 1. Studies observing sites of fluorine-18 fludeoxyglucose (¹⁸F-FDG) accumulations in patients with polymyalgia rheumatica

Author	Examination	n ^a	Age in years (range)	No. of patients with high positivity of ¹⁸ F-FDG uptake, n (%)								
				Shoulders	Hips	Sternoclavicular joints	Ischial tuberosities	Spinous processes			Symphysis	Subtrochanteric bursae
								Anywhere	Cervical	Lumbar		
Blockmans et al, ² 2007	PET	35	Mean 68.5 (61–76)	33 (94%)	31 (85%)			18 (51%)				11 (31%)
Yamashita et al, ³ 2012	PET/CT	14	Mean 72.6 (56–84)	12 (86%)	12 (86%)	6 (43%)	12 (86%)	11 (79%)	1 (7%)	11 (79%)	10 (71%)	9 (64%)
Camellino et al, ⁹ 2014	PET/CT	65	Median 73 (50–87)					31 (48%)	6 (9%)	30 (46%)		3 (5%)
Takahashi et al, ⁸ 2015	PET/CT	27	Mean 77.3 (67–87)				26 (96%)	22 (82%)				
Rehak et al, ⁴ 2015	PET and PET/CT	67	Median 70 (51–83)	58 (87%)	47 (70%)	31 (46%)	35 (52%)		13 (19%)	38 (57%)		27 (40%)
Palard-Novello et al, ⁵ 2016	PET/CT	18	(50–80)	16 (89%)	17 (94%)	13 (72%)	17 (94%)		10 (56%)	13 (72%)		0
Sondag et al, ⁷ 2016	PET/CT	50	Median 69.3 (49–89)					24 (48%)	5 (10%)	19 (38%)		1 (2%)
Wakura et al, ⁶ 2016	PET/CT	15	Median 72 (55–85)	12 (80%)	11 (73%)	9 (60%)	14 (93%)		7 (47%)	11 (73%)	14 (93%)	
Rehak et al, ¹¹ 2017	PET/CT	15	Median 70 (53–78)	15 (100%)	15 (100%)	14 (93%)	14 (93%)	14 (93%)	4 (27%)	13 (87%)		5 (33%)

PET, positron emission tomography.

In the Sondag et al⁷ cohort, 22 out of 50 (44%) patients were treated with corticosteroids during study evaluation.^aNumber of patients.

Figure 2. A 73-year-old female with newly diagnosed polymyalgia rheumatica. High praepubic fluorine-18 fludeoxyglucose uptake is marked by green arrows. Targeted MRI confirmed enthesitis of pectineal and adductor longus muscles (oedematous inflammation of the surrounding muscle tissue and oedema of the bone marrow). Follow-up control positron emission tomography/CT as well as MRI examination after steroid treatment reveals the absence of additional inflammation. PD SPAIR, proton-density spectral attenuated inversion recovery.

High sensitivity (92.6%) and specificity (90%) were also observed for PMR diagnoses when at least three of the following five items were satisfied: characteristic findings of shoulder and iliopsoas bursitis, ^{18}F -FDG uptake near ischial tuberosities and spinal spinous processes and lack of ^{18}F -FDG uptake in the wrists.^{8,10}

Extra-articular accumulation—enthesitis and tenosynovitis

The other sign of PMR in PET/CT is increased accumulation of ^{18}F -FDG in the front of pubic bones (Figures 1 and 2).^{4,6,7,11} Correlated MRI findings of inflammation in front of the symphysis related to enthesitis and tenosynovitis of the pectineus

and adductor longus muscles in patients with PMR were published in 2015.¹² In patients with well-developed signs of disease, it is sometimes possible to detect increased ^{18}F -FDG uptake in front of the anterior inferior iliac spine related to enthesitis of the rectus femoris muscle as recently observed by Wakura et al⁶ in 2016. Together with ischiogluteal bursitis, enthesitis of the biceps femoris may be a correlate of ^{18}F -FDG uptake near ischial tuberosities (Figures 1 and 3).

Monitoring of therapy

Decreasing ^{18}F -FDG accumulation, as a reaction to effective treatment (corticosteroids) being in concordance with clinical and laboratory remission (decrease of erythrocyte

Figure 3. Fluorine-18 fludeoxyglucose (^{18}F -FDG) positron emission tomography/CT scan in a 55-year-old female examined during polymyalgia rheumatica relapse in order to exclude co-incidental malignancy. Signs of metabolically active inflammation are present in the region of shoulders, hips and sternoclavicular joints near ischial tuberosities and lumbar spinous interspaces. Targeted ultrasonography confirmed corresponding inflammatory changes (pathological perfusion around subscapularis muscle tendon and long head biceps tendon (LHBT), pathologically increased content of subacromial (SA) bursae, perfusion in extended wall of bursae, increased perfusion around the ischial tuberosities and hamstring tendons).

Figure 4. Fluorine-18 fludeoxyglucose (^{18}F -FDG) positron emission tomography (PET)/CT images of axial and sagittal slices in a 68-year-old female. Signs of disease are present in the region of sternoclavicular joints (yellow arrows), ischiogluteal bursae (green arrows) and lumbar spinous interspaces (green arrowheads). The upper row represents the status prior to steroid therapy and is compared with findings after therapy as presented in the middle row. The lower row demonstrates polymyalgia rheumatica relapse 2 years after termination of steroid therapy, in which ^{18}F -FDG accumulation was observed around the right sternoclavicular joint, around the left ischiogluteal region and in one lumbar spinous interspace.

sedimentation rate and C-reactive protein levels), has been documented in separate case reports as well as in a cohort of patients examined using PET alone or PET/CT (Figures 2 and 4).^{2,3} Recently, this reaction was also described in a patient undergoing therapy with tocilizumab, a monoclonal antibody against the interleukin-6 receptor.⁵ Conversely, disease relapse may be mirrored by reaccumulation of ^{18}F -FDG (Figure 4).

Coincidence of polymyalgia rheumatica and giant-cell arteritis

A typical sign of GCA on PET/CT scans is increased accumulation of ^{18}F -FDG in the wall of the aorta including its rising branches (the subclavian and brachial arteries, brachiocephalic trunk, and iliac and femoral arteries). Synchronous PET/CT signs of GCA and PMR are observed in 31–64% of patients (Figure 5).^{2–4}

Figure 5. Fluorine-18 fludeoxyglucose (^{18}F -FDG) positron emission tomography (PET)/CT, maximum intensity projection PET scans of the torso of patients with giant-cell arteritis (GCA) and polymyalgia rheumatica (PMR). Cases A and B are typical for GCA; Cases D and E are typical for PMR cases; and Case C represents a mixture of features. Lesser mixtures of PMR and GCA signs are also seen in Cases B and D, with predominance of only a subset of components. This demonstrates that the characteristic signs of GCA (red arrowheads) and PMR (yellow and green arrowheads) are frequently not clear or exact.

CONCLUSION

It is possible to use ^{18}F -FDG PET/CT examination in treatment-naïve patients with PMR for assessment of extent of PMR disease. Most commonly, periarticular signs of pathology around the shoulders and hips as well as sternoclavicular joints have been reported. However, radiotracer accumulation also presents extra-articularly between spinous processes in the spine, in ischial tuberosities, in the praepubic region and, sometimes, in unique combination. Performance of PET/CT may be also useful to the differential diagnosis of occult malignancy or concurrent GCA. Nevertheless, PET-CT has a limited role at present and requires future prospective study to establish both cost effectiveness and clinical utility above and beyond standard assessment.

One of the main advantages in this examination is assessment of the whole body. In the regions described above, it is possible to

detect a decrease or even complete disappearance of pathological ^{18}F -FDG uptake in response to effective treatment, which may potentially be useful for monitoring treatment as well as for detection of PMR relapse.

PMR can be co-incidentally detected on ^{18}F -FDG PET/CT scans performed for others reasons, and this pictorial essay serves as a useful review for readers who may otherwise overlook or misinterpret these findings.

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