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ORIGINAL ARTICLE

Diagnostic performance of ^{18}F-FDG PET-CT for large vessel involvement assessment in patients with suspected giant cell arteritis and negative temporal artery biopsy

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Abstract

Objective The purpose of our study was to assess the diagnostic performance of ^{18}F-FDG PET-CT for large vessel involvement in patients with suspected giant cells arteritis (GCA) and a negative temporal artery biopsy (TAB).

Methods We conducted a retrospective study in a cohort of patients with suspected GCA and negative TAB who underwent an ^{18}F-FDG PET-CT. Ten vascular segments were studied using a visual score and a semi-quantitative method based on SUVmax ratio with respect to liver uptake. The diagnosis of GCA was established during a mean follow-up of 42 months, based on the presence of clinical symptoms, laboratory results, and imaging data compatible with GCA, good response to corticosteroid therapy, and no differential diagnosis after a follow-up of at least 18 months.

Results We included 63 patients (30 men and 33 women, aged 67 ± 12 years). ^{18}F-FDG PET-CT showed large vessel involvement in 22 patients, 14 of whom were finally diagnosed with GCA. Forty-one patients were ^{18}F-FDG PET-CT negative, 9 of whom were finally diagnosed with GCA. Overall, ^{18}F-FDG uptake by large vessel yielded 61% sensitivity, 80% specificity, 64% positive predictive value, 78% negative predictive value, and 73% diagnostic accuracy. A significant number of patients were treated by corticosteroids before ^{18}F-FDG PET-CT. However, corticosteroid therapy did not impact significantly the diagnostic performance, although there was a trend to a lower sensitivity in patients receiving corticosteroid therapy for more than 3 days.

Conclusions ^{18}F-FDG PET-CT is a useful imaging technique to assess large vessel involvement in patients with suspected GCA and negative TAB.

Keywords ^{18}F-FDG PET-CT · Giant cell arteritis · Temporal artery biopsy · Large vessel vasculitis

Introduction

Giant cell arteritis (GCA) is the main cause of large vessel vasculitis in elderly patients, affecting both large and medium size arteries [1]. Typical clinical manifestations are constitutional symptoms such as asthenia, anorexia and fever associated with cranial symptoms such as headaches, temporal artery anomalies, jaw claudication or visual impairment, consecutive to the involvement of the temporal artery and/or other branches of the carotid artery.

Positive diagnosis is usually obtained using temporal artery biopsy (TAB) which is expected to show a giant cell infiltrate associated with typical histological signs of vascular inflammation. However, this procedure is invasive and its sensitivity remains limited, with as much as 15% of false negatives in the study by Gonzalez-Gay et al. [2] and up to 40% in some other studies [3]. The diagnosis of GCA remains therefore challenging, especially in patients with extra-cranial vasculitis who often present with non-specific symptoms such as fever, fatigue and weight loss, and signs of inflammatory response, and for whom the median time to diagnosis is usually longer [4].

Although it is not mandatory in cases with typical clinical and imaging features, TAB remains an important

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examination for the diagnosis of GCA as emphasized in the last recommendations from the Japanese Circulation Society [5] and the European League Against Rheumatism [6].

ACR criteria were created in 1990 for GCA diagnosis with a positivity threshold of 3/5 criteria (age > 50 years, headache, temporal artery abnormality, elevated erythrocyte sedimentation rate, and abnormal TAB) [7]. However, its main purpose is to differentiate GCA from other types of vasculitis and these criteria are not well suited for routine use.

In clinical practice, the diagnosis of patients with negative TAB is made with a combination of clinical and paraclinical arguments including laboratory tests and imaging procedures. Large vessel involvement is frequent in GCA. It has been reported in 68% of patients in a study by Prieto-Gonzalez et al. using computed tomography (CT) angiography [8] and up to 83% in a study by Blockman et al. using ^{18}F-fluorodeoxyglucose positron emission tomography with computed tomography (^{18}F-FDG PET-CT) [9]. Some studies even suggest that GCA may concern exclusively large arteries without occurrence of cranial symptoms [4–10]. This large vessel involvement can be assessed by several imaging procedures such as CT angiography, magnetic resonance imaging (MRI), and ^{18}F-FDG PET-CT [11].

Recently, metabolic imaging using ^{18}F-FDG PET-CT has shown good diagnostic performance in large vessel vasculitis. A meta-analysis by Soussan et al. found 89.5% sensitivity and 97.7% specificity for the diagnosis of GCA [12].

To our knowledge, no study investigated specifically the diagnostic performance of ^{18}F-FDG PET-CT in patients with negative TAB, while it is the subgroup of patients in which the diagnosis is the most challenging. The purpose of the present study was to investigate the diagnostic accuracy of ^{18}F-FDG PET-CT in a population of patients referred to our institution for suspicion of GCA with negative TAB.

Materials and methods

Patients

We conducted a retrospective study at Montpellier University Hospital. All patients who benefited from a TAB and an ^{18}F-FDG PET-CT between January 2007 and January 2017 were reviewed to be potentially included. Inclusion criteria were a clinical suspicion of large vessel vasculitis and a negative TAB, without definite diagnosis by the time of the ^{18}F-FDG PET-CT examination. Patients with a positive TAB or with a follow-up duration of less than 18 months were excluded.

All patient data were reviewed using medical records including clinical history, laboratory findings, and imaging and histological results. ACR criteria were assessed for all patients.

The final diagnosis of GCA was established during follow-up based on the presence of clinical symptoms (including general syndrome, fever, cranial manifestation such as headache, jaw claudication, temporal artery abnormality or visual impairment, and symptoms evocative of polymyalgia rheumatica), laboratory results (elevated C-reactive protein level), and imaging data (increased vascular wall thickness on contrast-enhanced CT or MRI, increased vascular wall uptake on ^{18}F-FDG PET-CT) compatible with GCA, good response to corticosteroid therapy (from a clinical and biological point of view), and no differential diagnosis after a follow-up of at least 18 months.

The present study was approved by the institutional review board of our hospital. Due to the retrospective nature of the study, formal consent was not mandatory.

^{18}F-FDG PET-CT imaging protocol and interpretation

All PET-CT acquisitions were performed 60 min following IV injection of 3.5 MBq/kg of ^{18}F-FDG after a fasting period of at least 4 h. The PET axial field of view systematically encompassed the neck, thorax, abdomen, and pelvis.

PET examinations dating before June 2014 (32 patients) were performed using a Siemens Biograph 4 scanner. Images were reconstructed using the manufacturer's dedicated software and specifications (FORE + 2D OSEM using 8 subsets and 3 iterations followed by post-filtering with a 7 mm-wide Gaussian kernel). The acquisition time was 3 min per bed. Image matrices were sampled on a 128×128 grid with a voxel size of $5.3 \times 5.3 \times 3.4$ mm^3.

PET examinations dating after June 2014 (31 patients) were performed using a Siemens Biograph mCT 20 Flow scanner operated in time-of-flight mode. Images were reconstructed using the manufacturer's dedicated software and specifications (3D OSEM using 21 subsets and 2 iterations including PSF correction followed by post-filtering with a 3 mm-wide Gaussian kernel). The scanning speed was 1.1 mm per second. Image matrices were sampled on a 400×400 grid with a voxel size of $2 \times 2 \times 2$ mm^3.

The assessment of PET data was carried out by a nuclear medicine specialist using a Siemens Syngo.via viewer. The diagnosis of GCA was based on the presence of significant ^{18}F-FDG uptake in the vascular wall of aortic segments, carotid, vertebral, subclavian, or iliac arteries. The intensity of ^{18}F-FDG uptake in vascular walls was assessed visually using liver uptake as reference as described by Meller et al. [13] and as preconized in the joint procedural recommendation of the EANM, SNMMI, and ASNC [14] (0: no uptake; 1: uptake < liver;

2: uptake = liver; 3: uptake > liver). A semi-quantitative approach was also employed by computing the ratio between vascular wall SUVmax and liver SUVmax (SUVmax ratio). Alternative semi-quantitative approaches using arterial or venous blood pool as the reference tissue have also been proposed [15]. The use of target to blood pool ratio is however not recommended in clinical routine, mainly due to the lack of consensus regarding the positivity cutoff [14].

^{18}F-FDG PET-CT was considered positive for large vessel vasculitis if a segmental and circumferential pattern of increased ^{18}F-FDG uptake was observed in at least one vascular wall with a visual score of 2 or 3, and an SUVmax ratio above 1.

Statistical analysis

Categorical variables are presented as number (percentage), and continuous variables as mean ± standard deviation. Differences between groups were assessed using Student's *T* test for continuous variables and the Chi squared test (or Fisher's exact test when appropriate) for categorical variables. When estimating diagnostic performance indices, 95% confidence intervals (CI 95%) were computed using the Wilson score interval. All statistical computations were performed using Microsoft Excel.

Results

Sixty-three patients with clinical suspicion of GCA, negative TAB, and an ^{18}F-FDG PET-CT were included. The mean age was 67 ± 12 years; there were 30 men and 33 women. Ten patients were initially addressed for isolated constitutional syndrome, fever, or inflammatory syndrome, 26 for general symptoms with cranial manifestation or symptoms of polymyalgia rheumatica, and 27 for other non-specific symptoms.

Sixteen patients (25%) received corticosteroid therapy before TAB (median time 10 days, and more than 2 weeks before TAB in 7 cases). Twenty-six patients (41%) received corticosteroid therapy before ^{18}F-FDG PET-CT (median time 92 days, and more than 3 days before ^{18}F-FDG PET-CT in 24 cases). The mean CRP level was 94 mmol/L. The detailed characteristics of the study population are reported in Table 1.

After a mean follow-up of 42 ± 27 months (range 18–142), 23 (37%) patients were finally diagnosed with GCA. Among these 23 patients, 22 had general syndrome, fever, or biological inflammatory syndrome, 11 had cranial manifestation, 12 had symptoms evocative of polymyalgia rheumatica, and 3 had limb claudication. In 12 of them, an alternative imaging technique other than ^{18}F-FDG PET-CT was evocative of large vessel vasculitis (CT in 10 cases, MRI in 8 cases). All of them showed a good clinical and biological response to corticosteroid therapy. No differential diagnosis was found in these patients during follow-up.

Table 1 Patient characteristics in the whole population, in positive PET (PET+) and negative PET (PET−) subjects, and in subjects with (GCA+) and without (GCA−) final diagnosis of giant cell arteritis. CVRF: number of cardiovascular risk factors

	PET− (*n* = 41)	PET+ (*n* = 22)	GCA− (*n* = 40)	GCA+ (*n* = 23)	Total (*n* = 63)
Demographics					
Men (*n*)	24 (59%)	6 (27%) *	23 (58%)	7 (30%) ǂ	30 (48%)
Age (mean ± std dev)	70 ± 11	63 ± 11 *	67 ± 12	67 ± 10	67 ± 12
CVRF (mean ± std dev)	1.9 ± 1.1	1.6 ± 1.2	1.9 ± 1.1	1.7 ± 1.2	1.8 ± 1.1
Clinical					
General syndrome or fever (*n*)	38 (93%)	19 (86%)	35 (88%)	22 (96%)	57 (90%)
Cranial manifestation (*n*)	15 (37%)	8 (36%)	12 (30%)	11 (48%)	23 (37%)
Polymyalgia rheumatica (*n*)	13 (32%)	8 (36%)	9 (23%)	12 (52%) ǂ	21 (33%)
Limb claudication (*n*)	2 (5%)	1 (5%)	0 (0%)	3 (13%) ǂ	3 (5%)
Cortisteroid therapy before PET (*n*)	22 (54%)	4 (18%) *	17 (43%)	9 (39%)	26 (41%)
> 3 days (*n*)	20 (49%)	4 (18%) *	15 (37%)	9 (39%)	24 (38%)
CRP mg/L (mean ± std dev)	87 ± 80	107 ± 79	97 ± 87	88 ± 68	94 ± 80
ACR score ≥ 3 (*n*)	13 (32%)	7 (32%)	10 (25%)	10 (43%)	20 (32%)
Vascular complications (*n*)	13 (32%)	9 (41%)	12 (30%)	10 (43%)	22 (35%)
Aortic dilation or dissection (*n*)	4 (10%)	7 (32%) *	6 (15%)	5 (22%)	11 (18%)

*Significantly different compared to PET- subjects

ǂSignificantly different compared to GCA- subjects

Among the 40 remaining patients, 12 (19%) were diagnosed with other vasculitis, and 28 (44%) with other diagnosis.

^{18}F-FDG PET-CT was considered positive for large vessel involvement in 22 patients, 14 (64%) of whom were finally diagnosed with GCA after the follow-up of at least 18 months (Fig. 1 shows an example of true positive findings). In the eight (36%) remaining patients, the final diagnoses were: six spontaneously regressive vasculitis, one granulomatosis with polyangiitis (Wegener disease), and one cerebral vasculitis.

^{18}F-FDG PET-CT demonstrated involvement of 4.1 ± 2.6 vascular segments per patient, including ascending and descending thoracic aorta, aortic arch, abdominal aorta, iliac arteries, carotid arteries, and subclavian arteries (cf Table 2 for details). Thoracic aorta was involved in 86% of the cases, abdominal aorta and ilio-femoral arteries in 54% of the cases, and supra-aortic arteries in 54% of the cases. Mean SUVmax of the most hypermetabolic vascular focus was 4.8, corresponding to a mean SUVmax ratio of 1.43 with respect to liver. Of note, ^{18}F-FDG PET-CT also revealed shoulder, hip, or inter-spinal uptake evocative of polymyalgia rheumatica in three (14%) patients.

^{18}F-FDG PET-CT was considered negative for large vessel involvement in 41 patients. Among them 20 (49%) were on corticosteroid therapy more than 3 days before the examination, which is significantly more than in the ^{18}F-FDG PET-CT-positive group (4/22, 18%, $p = 0.02$). Nine negative PET patients (22%) were finally diagnosed with GCA (in 6 of these, corticosteroid therapy was initiated before ^{18}F-FDG PET-CT) and 32 (78%) with other diagnosis. The final diagnoses in non-GCA patients were: four other vasculitis, seven polymyalgia rheumatica, seven other rheumatic diseases, two cancers, four infections, and eight other diagnoses. ^{18}F-FDG PET-CT found a potential differential diagnosis in eight (20%) cases (polymyalgia rheumatica in four cases, other inflammatory rhumatism in two cases, digestive lymphoma in one case, metastatic prostatic neoplasm in one case).

Diagnostic performances of ^{18}F-FDG PET-CT are summarized in Table 3. Performances were also studied according to PET equipment and treatment status. No statistically significant difference was found between subgroups, although there was a trend toward a lower sensitivity in patients receiving corticosteroid therapy for more than 3 days (33% vs 79%, $p = 0.08$).

There were more women in the GCA group than in the non-GCA group (70% vs 42%, $p = 0.04$), consistent with the epidemiology of GCA, with a female to male sex ratio reported as 2.5 to 1 and more [16]. Women were also more represented in the ^{18}F-FDG PET-CT-positive group than in the ^{18}F-FDG PET-CT-negative group (73% vs 41%,

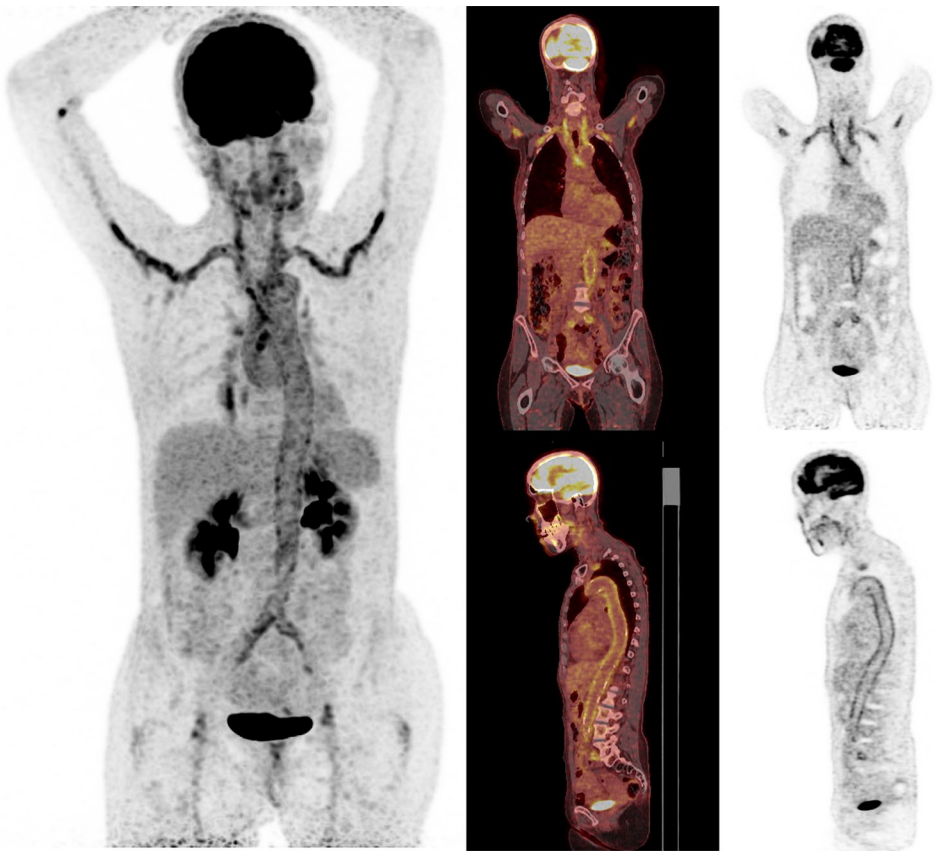

Fig. 1 Example of a 63-year-old patient presenting with constitutional syndrome, fever, and inflammatory syndrome, finally diagnosed with GCA. ^{18}F-FDG PET-CT showed intense uptake in the vascular wall of the thoracic and abdominal aorta, subclavian arteries, carotid arteries, and iliac arteries (grade 3)

Table 2 Description of arterial segments involved and corresponding semi-quantitative values in FDG PET-CT-positive patients. Last column (N) refers to the total number of vascular segments involved

Subject	Ascending aorta	Aortic arch	Descending aorta	Abdominal aorta	Right carotid	Lef carotid	Right subclavian	Left subclavian	Right iliac	Left iliac	Vascular SUVmax	SUVmax ratio	N
1	+		+	+[a]	+		+	+			6.2	1.48	6
2	+	+		+[a]					+	+	8.1	2.25	5
3	+[a]	+									5.7	1.02	2
4	+	+[a]	+								3.1	1.11	3
5		+	+[a]				+	+			2.1	1.00	4
6	+[a]	+		+					+	+	4.1	1.64	5
7	+[a]	+									3.7	1.00	2
8	+	+[a]	+								4.5	1.18	3
9								+[a]			4.4	1.69	1
10								+[a]			3.8	1.19	1
11	+[a]	+		+							3.6	1.20	3
12	+[a]	+	+		+						3.7	1.12	4
13			+[a]	+			+				7.1	1.45	3
14			+	+	+	+	+[a]				5.5	1.49	5
15		+	+	+[a]	+	+	+	+			5.7	1.78	6
16	+	+	+	+	+	+	+	+[a]	+	+	8.8	2.59	10
17	+	+	+[a]	+	+	+	+	+			4.8	1.23	8
18	+	+	+	+[a]			+	+			5.5	1.53	6
19	+	+	+[a]	+	+	+	+	+			4.3	1.54	8
20				+[a]							3.3	1.14	1
21			+[a]								5.3	1.77	1
22	+	+[a]	+								2.4	1.04	3
Total	14 (64%)	15 (68%)	14 (64%)	12 (55%)	7 (32%)	5 (23%)	9 (41%)	9 (41%)	3 (14%)	3 (14%)	4.8 ± 1.7	1.43 ± 0.41	4.1 ± 2.6

[a]Arterial segment showing the most intense vascular wall uptake (in each subject, vascular SUVmax and SUVmax ratios are detailed for that segment)

Table 3 Diagnostic performances of ^{18}F-FDG PET-CT according to PET equipment and to treatment status. The number of subjects is indicated between brackets

	Sensitivity	Specificity	Negative predictive value	Positive predictive value	Accuracy
Former PET (Siemens Biograph 4) ($n=32$)	64% (7/11)	76% (16/21)	80% (16/20)	58% (7/12)	72% (23/32)
Actual PET (Siemens mCT 20 flow) ($n=31$)	58% (7/12)	84% (16/19)	76% (16/21)	70% (7/10)	74% (23/31)
Corticosteroid > 3 days ($n=24$)	33% (3/9)	93% (14/15)	70% (14/20)	75% (3/4)	71% (17/24)
No corticosteroid or corticosteroid ≤ 3 days ($n=39$)	79% (11/14)*	72% (18/25)	86% (18/21)	61% (11/18)	74% (29/39)
Total	61% (14/23)	80% (32/40)	78% (32/41)	64% (14/22)	73% (46/63)

*$p=0.08$ compared to patients with corticosteroid therapy > 3 days

$p=0.02$), which was expected since there was more GCA patients in this group.

Patients in the ^{18}F-FDG PET-CT-positive group were significantly younger than patients in the ^{18}F-FDG PET-CT-negative group (mean age 63 years vs 70 years, $p=0.02$), likely due to the fact that corticosteroid therapy was initiated more often in frail older patients, inducing more false-negative findings in elderly subjects.

Occurrence of vascular complications was also reviewed, in particular aortic complications such as dilation (defined as aorta diameter superior to 40 mm) and dissection. In ^{18}F-FDG PET-CT-positive patients, there were six aortic dilations, two aortic dissections, one brachial artery thrombosis, and one cerebral stroke. In ^{18}F-FDG PET-CT-negative patients, there were four aortic dilations, two brachial artery stenosis, three retina central artery obliterations, two cerebral strokes, one visceral infarct, and one renal artery stenosis. No aortic dissection was observed in that group. The proportion of patients for whom aortic complication (dilation and/or dissection) was reported during follow-up was significantly higher in ^{18}F-FDG PET-CT-positive subjects ($n=7$; 32%) than in ^{18}F-FDG PET-CT-negative subjects ($n=4$; 10%; $p=0.04$).

Discussion

Diagnosing GCA remains a challenge for patients with negative TAB. There are many factors that may affect TAB sensitivity such as the segmental and focal pattern of histological lesions (influenced by sample size), previous corticosteroid therapy, or the absence of temporal artery involvement in GCA [17, 18, 19].

Moreover, several studies showed that GCA can be a heterogeneous disease, with multiple clinical patterns: Muratore et al. [20] showed that GCA patients with large vessel involvement on imaging were clinically different (younger, more negative TAB, less ophtalmic complications). On the other hand, patients with negative TAB often have a different clinical presentation, with less cranial symptoms and visual complications and a lower CRP level [2].

It is known that ACR criteria are not well suited for diagnosis of GCA in clinical practice [21]. The use of vessel imaging techniques has improved the diagnostic accuracy of GCA, especially in patients with negative TAB. In this study, ^{18}F-FDG PET-CT showed good diagnostic performance, revealing large vessel inflammations in 14/23 patients finally diagnosed with GCA.

^{18}F-FDG PET-CT is a marker of inflammation in the vascular wall, hence it is not specific of GCA and vascular ^{18}F-FDG uptake can be seen in other types of large vessel vasculitis or in atheroma mostly in elderly patients.

Interestingly, most false-positive findings were related to cases of spontaneously resolutive vasculitis (patients in whom symptoms and inflammatory syndrome resolved without corticosteroid therapy). This was observed in six patients, of whom three had evidence of vascular inflammation on another imaging technique (CT). In these six cases, no differential diagnosis was retained after a mean follow-up of 42 months (in particular, no infectious disease or other causes of large vessel vasculitis such as IgG4 syndrome, Behçet's disease, spondylarthritis, or paraneoplastic syndrome). It may be inferred that vascular wall inflammation visualized on ^{18}F-FDG PET-CT could be the cause of initial clinical manifestations in these patients. They have been classified as "false positive" in our study because of the absence of clinical impact on management and favorable outcome without treatment (Fig. 2 shows an example of false-positive findings). The etiology of these vasculitis remains uncertain and it can be hypothesized that they are forms of inflammatory vasculitis with a silent evolution.

Several post-mortem series have shown that vasculitis lesions in patients with no clinical symptoms (in the series from Gorel Ostberg, 16 out of 1097 necropsy patients showed histological signs of arteritis, of whom 14/16 (87,5%) were not diagnosed with vasculitis before their death) [22]. Few surgical series of patients with aortic replacement showed histological signs of aortitis (52 out of 1204 patients, 69% of whom had no clinical history or

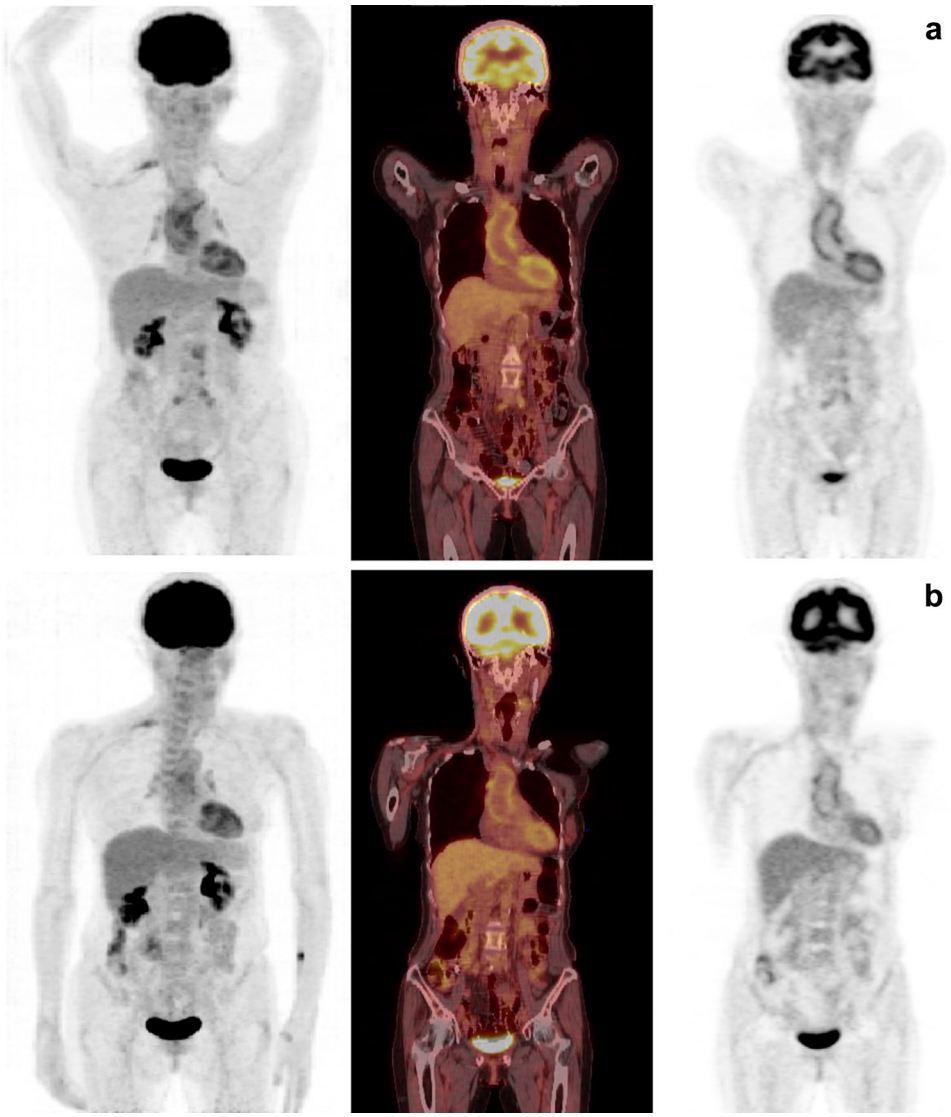

Fig. 2 Example of a 79-year-old patient presenting with fever, constitutional syndrome, anemia, and diffuse pain. Initial ^{18}F-FDG PET-CT (**a**) showed segmental hypermetabolism in the thoracic aorta (grade 3), subclavian arteries, and hypermetabolism of abdominal aorta and iliac arteries. Symptoms progressively regressed, whereas no corticosteroid therapy was undertaken. Control ^{18}F-FDG PET-CT 14 months later (**b**) showed a slight decrease in aortic wall uptake and disappearance of abdominal aorta and iliac uptake. The diagnosis of spontaneously regressive vasculitis was finally made since symptoms and imaging abnormalities regressed without any specific treatment, and no other differential diagnosis was found

symptoms of vasculitis or systemic disease in the series from Rojo-Leyva et al.) [23]. Some authors also reported several cases of spontaneously resolutive GCA [24, 25]. The necessity to treat or monitor these patients remains unclear. In our study, the rate of vascular complication during follow-up was relatively limited in these patients (aortic dilation was observed in 2 patients), but the conclusions remain limited by the small sample of our study.

In two patients, ^{18}F-FDG uptake in vessel walls was caused by other forms of vasculitis (granulomatosis with polyangiitis or Wegener disease, and cerebral vasculitis, respectively). They were considered as false-positive results for GCA, but ^{18}F-FDG PET-CT results allowed reinforcing the diagnosis of systemic vasculitis.

In our study, the specificity of ^{18}F-FDG PET-CT was 80% for the diagnosis of GCA with large vessel involvement. However all eight cases considered as false positive were cases of other large vessel vasculitis and ^{18}F-FDG PET-CT helped in the diagnosis of these patients by revealing large vessel inflammation and ruling out other pathology such as infection or neoplasm.

The sensitivity of 61% for GCA diagnosis in our study is in accordance with literature data. Large vessel involvement is not constant in GCA and is mainly assessed by imaging. Previous studies showed variable rates of large vessel involvement depending on the imaging modality and interpretation criteria [26]. For ^{18}F-FDG PET-CT, sensitivity ranged from 57% to 96% (pooled sensitivity 80%) in a meta-analysis by Besson et al. [27].

The relatively low sensibility could be explained by corticosteroid therapy initiated before examination in 6/9 patients diagnosed with GCA, but with negative ^{18}F-FDG PET-CT (all of them treated more than 3 days before examination). It is known that previous corticosteroid therapy is an important source of false-negative results [28]. Recently, Nielsen et al. showed in a prospective study that

corticosteroid therapy attenuates vascular ^{18}F-FDG uptake in GCA after 3 days of treatment, but with limited impact on diagnostic accuracy. However, after 10 days of treatment, sensitivity significantly decreased with only 35% of GCA patients still ^{18}F-FDG PET-CT positive [29]. In our study, there is a difference in sensitivity between patients who were not treated or treated for less than 3 days (79%) and patients treated for more than 3 days (33%), but did not reach statistical significance ($p = 0.08$), probably because of the small size of the population. Of note, this 33% sensitivity is similar to the 35% sensitivity reported by Nielsen et al. after 10 days of treatment.

Regarding vascular complications, there were significantly more aortic complications in ^{18}F-FDG PET-CT-positive patients. Moreover, among these complications, there were two aortic dissections (versus none in ^{18}F-FDG PET-CT-negative patients). Several studies have already shown that GCA patients with large vessel involvement had a higher risk of aortic complication, for example De Boysson et al. found 9% of aortic complications (9 dilations and 1 dissection out of 104 patients) in GCA patients with a positive ^{18}F-FDG PET-CT [30]. The incidence of aortic complication in their study was lower than in ours, likely due to differences in the definition of aortic dilation (for example, the cutoff diameter was 45 mm for ascending aorta in their study, while it was 40 mm in ours) and in patients characteristics (especially cardiovascular risk factor).

^{18}F-FDG PET-CT allowed to find differential diagnosis in 20% of non-GCA patients, emphasizing its usefulness in diagnosing inflammatory, infectious, or neoplastic diseases which can sometimes mimic GCA when it manifests as fever or inflammatory syndrome.

The main limitation of the present study is its retrospective design, with a lack of standardization in diagnostic procedures, treatment, and follow-up. ^{18}F-FDG PET-CT acquisitions were also not uniform because of the change in PET equipment, but no difference in terms of diagnostic performance was found between the former and current PET scanners. The relatively lower spatial resolution of the former PET did not significantly impact the diagnostic performances, probably because of the high vessel's wall activity in cases of active large vessel vasculitis. Studies using older generation PET demonstrated good diagnostic performances, with for example a sensitivity above 80% in most of the studies from the meta-analysis made by Besson et al. [27]. This supports the fact that difference of spatial resolution between the former and newer PET equipment does not significantly impact sensitivity for large vessel vasculitis.

The absence of histological gold standard can also be considered as a limitation, but it was the purpose of the study to evaluate these patients who can be subjects of difficult diagnosis in real life clinical practice, since no other histological examination is easily available to assess large vessel involvement. In addition, the long follow-up of at least 18 months allows a good confidence in the final diagnosis.

Conclusion

^{18}F-FDG PET-CT appears as a useful imaging procedure to help in the diagnostic assessment of patients with suspected GCA and negative TAB. It shows large vessel inflammation which can support the diagnosis of GCA or other types of vasculitis, and therefore help in therapeutic decision. Moreover, it may document potential differential diagnoses such as neoplasm, infection, or inflammatory rheumatism.

Importantly, corticosteroid therapy can negatively affect the sensitivity of ^{18}F-FDG PET-CT in large vessel vasculitis. If treatment has to be started, ^{18}F-FDG PET-CT should be performed as soon as possible (ideally within 3 days of treatment) to lessen the risk of false-negative results.

On the other hand, monitoring ^{18}F-FDG uptake during corticosteroid therapy could be interesting to assess response to therapy in GCA patients, since persistent uptake after treatment may indicate the persistence of large vessel vasculitis. Further studies are necessary to substantiate the relevance of ^{18}F-FDG PET-CT in treatment response assessment.

Compliance with ethical standards

Conflict of interest The authors declare they have no conflicts of interest and no funding was received for this study.

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