A case of fever of unknown origin: ^{18}F-FDG-PET/CT findings in Takayasu's arteritis

Abstract

This is a case of a 54 years old woman with fever of unknown origin. Physical examination showed nothing remarkable. Chest radiographs, abdominal ultrasound examination (US) and chest-abdominal-pelvic CT, showed segmental thickening of the wall of the aorta. On admission, the C-reactive protein level and the erythrocyte sedimentation rate were elevated. ^{18}Fluoro-fluorodeoxyglucose-positron emission tomography (^{18}F-FDG-PET/CT) showed increased uptake of the aorta wall and its main branches that could be indicative of arteritis. The temporal artery biopsy was negative for giant-cell arteritis. The patient responded well to prednisolone treatment. A second ^{18}F-FDG-PET/CT scan showed great improvement. ^{18}F-FDG-PET/CT scan early indicates arteritis of the great vessels that in this case was considered to be TA and contributes in monitoring disease activity.

Hell J Nucl Med 2008; 11(3): 172-174

Introduction

Takayasu's arteritis (TA) is a well-known, idiopathic, rare, systemic granulomatous disease, of large- and medium-sized vessels, leading to stenosis, occlusion, dilatation, and aneurysm formation in the aorta and its main branches and sometimes in the pulmonary artery [1]. The aetiology of Takayasu's arteritis is unknown but an association with rheumatic fever, tuberculosis and auto-immune diseases has been described [2]. The disease affects women more commonly than men. More than half the patients develop an initial systemic illness characterized by fever, anorexia, malaise, weight loss, night sweats, arthralgias, pleuritic pain, and fatigue [3].

The disease has various stages. The early disease is characterised by non-specific symptoms and clinical manifestations, resulting in delayed diagnosis, when irreversible vascular damage has occurred [4].

The diagnosis of TA and other large-vessels vasculitis and the assessment of their stage remains challenging, especially in patients with non-specific symptoms and laboratory tests. The standard diagnostic procedure includes: biopsy, angiography, ultrasound and magnetic resonance angiography. These procedures are largely operator-dependent or invasive or document only morphological changes, that mainly occur in the late stages of the disease [5, 6] ^{18}F-fluorodeoxyglucose positron emission tomography (^{18}F-FDG-PET/CT) may allow early diagnosis of vasculitis that may be TA and contribute to monitoring disease activity.

Case presentation

A 54-year-old woman was admitted with fever of unknown origin (FUO). At physical examination there was nothing remarkable. The blood pressure in both hands was normal, almost equal (110/60 mmHg) and no heart murmurs or vascular bruits in the neck, chest or the abdominal area could be heard. She had no history of cardiovascular disease, hypertension or hyperlipidaemia and had never suffered from rheumatic fever, tuberculosis or auto-immune diseases. On admission, the C-reactive protein (CRP) level was elevated (2 mg/dL, n<0.8 mg/dL) and the erythrocyte sedimentation rate was 80 mm/ (n<20 mm). Chest radiographs, abdominal US and chest-abdominal-pelvic CT, showed only segmental thickening of the aorta wall (Fig. 1). To identify the origin of the fever, ^{18}F-FDG PET/CT imaging was performed. The patient was asked to fast for 4-6 hours before the study in order to minimize glucose utilization in normal tissues. Serum glucose was less than 200mg/dL. The image acquisition started 60min after the intravenous administration of 370MBq ^{18}F-FDG. All acquisitions were performed by using an integrated PET/CT scanner (Discovery ST; GE Med-

Evangelia Skoura[1], **Chariklia Giannopoulou**[1], **Georgia Keramida**[1], **Maria Skilakaki**[2], **Ioannis Datseris**[1]

1. *Nuclear Medicine Department and*
2. *Radiology Department of Evangelismos Hospital, Athens, Greece*

Keywords: Fever of unknown origin – Takayasu's arteritis – ^{18}Fluoro-deoxyglucose – Positron emission tomography

Correspondence address:
Evangelia Skoura,
Nuclear Medicine Department,
Evangelismos Hospital, 45-47,
Ipsilandou street,
Athens 10676, Greece,
Tel: +30 210 7203006,
Fax: +30 210 72 59 305,
E-mail: lskoura@yahoo.gr

Received:
1 August 2008
Accepted revised:
11 November 2008

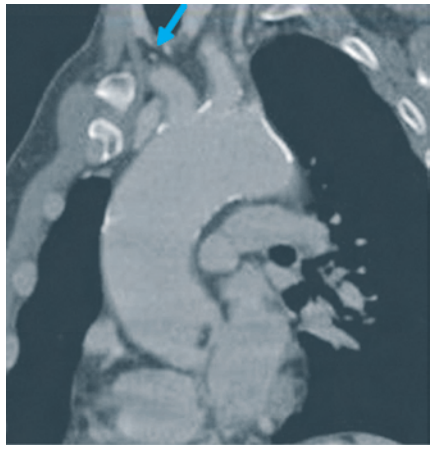

Figure 1. A CT scan showed calcifications and intense thickening of the wall of the thoracic aorta and its branches, especially in their proximal part.

ical Systems). Whole-body image from the mid femur to the base of the brain was obtained, divided in six bed positions. The PET emission images were acquired for a 4min acquisition period at each bed position. The imaging system enabled the simultaneous acquisition of 47 transverse PET images per field of view with intersection spacing of 3.27mm, for a total transverse field of view of 15.7cm. PET resolution was approximately 6.1mm full width at half maximum near the centre of the field of view. The PET/CT system also included a 4-detector row helical CT scanner (140kV and 80mA). The CT images were used not only for image fusion but also for generation of the attenuation map for attenuation correction. PET scan was acquired in the two-dimensional mode. The field of view and pixel size of the reconstructed images were 50 cm and 3.91 mm respectively, with a matrix size of 128x128. All images of ^{18}F-FDG PET/CT were viewed by the same two nuclear medicine physicians C.G. and E.S. blinded to the clinical and laboratory data.

^{18}F-FDG PET/CT demonstrated high glucose uptake in the wall of the aorta and its main branches (Fig. 2). For the semiquantitave evaluation of ^{18} F-FDG uptake in the great vessels wall we used a four point scale, proposed by Walter M et al (2005) [7]. According to this scale, large-vessel ^{18}F-FDG uptake graded from grade 0, grade I (lower than liver uptake), grade II (similar to liver uptake) and grade III (higher than liver uptake). In our patient ^{18}F-FDG uptake was grade III. The standardized maximal uptake value (SUVmax) was 4.5. The distribution of ^{18}F-FDG possibly indicated large-vessel's vasculitis. The temporal artery biopsy was negative, for giant-cell arteritis.

After high-dose steroid treatment (prednisolone 30 mg/day for a month and then gradually lowering the daily dose) the patient was afebrile and CRP and sedimentation rate returned to normal.

After six months, ^{18}F-FDG PET/CT scan was performed to evaluate treatment response (Fig. 3) and showed significantly decreased uptake. According to the four-point scale mentioned above, ^{18}F-FDG uptake in the wall of the aorta and its branches was of grade I and SUV max was 2.5.

The patient's history, her clinical condition with FUO, the above findings, her response to treatment and principally the findings on both ^{18}F-FDG PET/CT scans, suggested the diagnosis of TA.

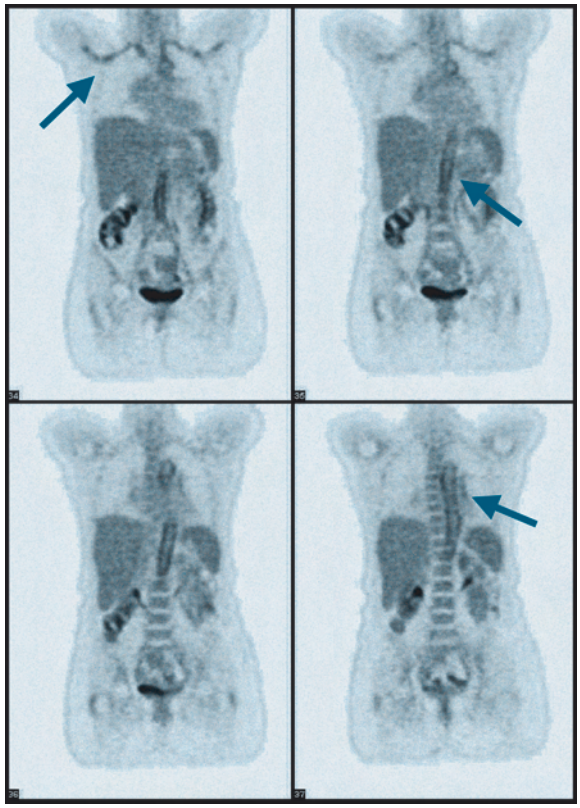

Figure 2. ^{18}F-FDG-PET/CT scan before treatment, demonstrated high uptake in the wall of the ascending aorta, the aortic arch, both subclavian arteries, both common carotid arteries, the descending and the abdominal aorta (grade III).

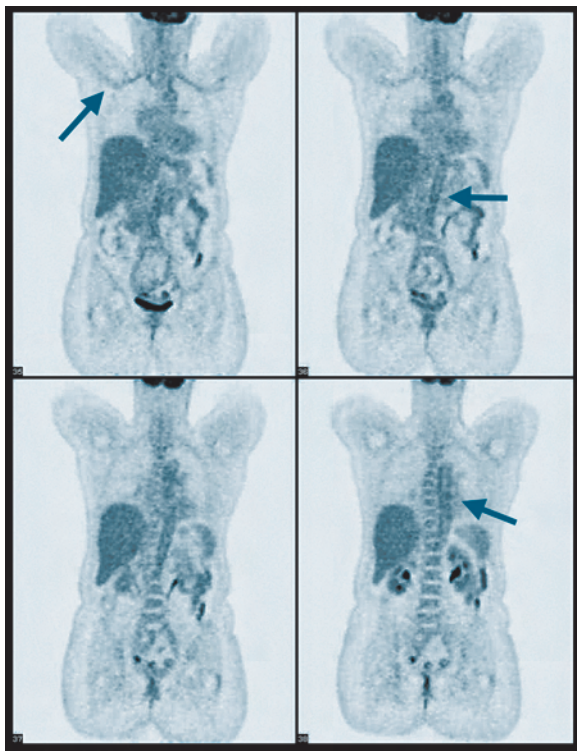

Figure 3. ^{18}F-FDG-PET/CT scan after treatment, demonstrated just a subtle increase of uptake in the wall of the ascending aorta, the aortic arch, both subclavian arteries, the descending and the abdominal aorta (grade I).

Discussion

In our patient, the diagnosis of TA, was suggested by clinical remission of the FUO normalization of the inflammation markers' and the findings in the ^{18}F-FDG PET/CT study before and after treatment with prednisolone. This is a case of early arteritis, thus temporal artery biopsy does not definitely exclude giant cell arteritis (GCA) in its early stages but it is highly indicative of absence of this disease.

Angiography is the gold standard for the diagnosis of TA but it has significant limitations. It is invasive, may aggravate local disease, provides data only on luminal anatomy, cannot evaluate changes in the arterial wall and may result in a normal angiogram in patients with early phase disease [8]. Biopsy is most useful, but it is usually impractical to obtain histological diagnosis, except in patients undergoing revascularization procedures [9]. In current clinical practice, clinical assessment when positive has greater diagnostic accuracy than inflammatory markers. It is therefore obvious that there needs to be a better and more reliable method for diagnosing TA and assessing disease activity [1]. PET, magnetic resonance imaging combined with angiography (MRI/MRA) and computed tomography combined with angiography (CT/CTA) are becoming widely available for the investigation of TA [8].

^{18}F-FDG is an increased glucolysis marker occurring either in tumour cells, or in activated inflammatory cells. Activated inflammatory cells express glucose transporter molecules and accumulate increased amounts of glucose and other structurally related substances such as ^{18}F-FDG; therefore ^{18}F-FDG-PET (or PET/CT) may become useful in the workup of large vessels' arteritis such as TA and giant cell arteritis [7]. Other studies have shown that ^{18}F-FDG PET has a sensitivity of 92%, a specificity of 100% and negative and positive predictive values of 85% and 100% respectively, in the initial assessment of active vasculitis in TA [1, 10].

Considering that early TA presents in a non-specific manner, with varying clinical manifestations and only the elevation of CRP and ESR, ^{18}F-FDG-PET (or PET/CT) can be used in diagnosing vasculitis and support the diagnosis of early TA [11].

Although ^{18}F-FDG-PET (or PET/CT) may also detect atherosclerosis, this disease exhibits a vascular distribution distinct from TA. For example, atherosclerosis is usually seen in the internal carotid arteries while TA usually affects the common carotid arteries and moreover, an intense linear uptake of ^{18}F-FDG is characteristic of active vasculitis in TA, as reported by others [8]. The above findings that support the diagnosis of TA were also found in our case.

In healthy subjects, with no large-vessels vasculitis, the ^{18}F-FDG uptake in the aorta wall and its branches is grade 0 or I and SUV max is up to 1.3 [7, 12]. On the contrary, in our case before treatment, the uptake of the great vessels wall was grade III and the SUVmax=4.5.

Several studies have shown that increased ^{18}F-FDG uptake in the affected arteries was observed in patients with active TA, indicating inflammation. In contrast, in patients with inactive TA, low or no ^{18}F-FDG uptake was observed in the great vessels wall [8, 12]. In the early stage of TA, inflammatory thickening of the aortic wall is the main pathologic finding as in our case, while in the advanced stage, the aorta exhibits stenosis, occlusion or aneurysmatic formation [4]. Thus, if TA is early diagnosed and treated, it may be possible to prevent or delay the onset of the occlusive stage of the disease [1, 7]. By performing a follow up ^{18}F-FDG-PET (or PET/CT) imaging, we and others, were able to show the effect of treatment on the disease activity [4, 13]. A major benefit of an ^{18}F-FDG PET (or PET/CT) scan in TA, is the accurate identification of the extent of the active stage of the disease, by detecting regions of inflammation in the great vessels [1].

Markers of inflammation such as C-reactive protein and erythrocyte sedimentation rate, are reported to be a rather unreliable surrogate for estimating the activity of inflammation in TA and assessing the efficacy of treatment [12]. Yet in our patient, CRP and ESR values correlated with clinical and imaging improvement in response to treatment.

In conclusion, in the appropriate clinical setting, ^{18}F-FDG-PET (or PET/CT) is sensitive and specific for the diagnosis of arteritis and the follow up of TA by assessing inflammation and its distribution in the aorta and its branches.

Bibliography

1. Webb M, Chambers A, Al-Nahhas A et al. The role of ^{18}F-FDG PET in characterizing disease activity in Takayasu arteritis. *Eur J Nucl Med Imaging* 2004; 31: 627-634.
2. Lupi-Herrera E, Sanchez-Torres G, Marcushamer J et al. Takayasu's arteritis: clinical study of 107 cases. *Am Heart J* 1977; 93: 94-103.
3. Eichhorn J, Sima D, Thiele B. et al. Anti-Endothelial Cell Antibodies in Takayasu Arteritis. *Circulation* 1996; 94: 2396-2401
4. Kaku B, Higuchi T, Kanaya H et al. Usefulness of Fluoro-deoxyglucose Positron Emission Tomography in a Patient with Takayasu's Arteritis Associated with Antiphospholipid Syndrome. *Int Heart J* 2006; 47: 311-317.
5. Blockmans D. Utility of imaging studies in assessment of vascular inflammation. *Cleve Clin J Med* 2002; 69 Suppl 2: SII 95-99.
6. Kissin EY, Merkel PA. Diagnostic imaging in Takayasu arteritis. *Curr Opin Rheumatol* 2004; 16: 31-37.
7. Walter M, Meizer R, Schindler C et al. The value of [^{18}F]FDG-PET in the diagnosis of large-vessel vasculitis and the assessment of activity and extent of disease. *Eur J Nucl Med Mol Imaging* 2005; 32:4-681.
8. Andrews J and Mason JC. Takayasu's arteritis-recent advances in imaging offer promise. *Rheumatology* 2007; 46: 6-15.
9. Johnton S, Lock R, Gompels M. Takayasu arteritis: a review. *J Clin Pathol* 2002; 55: 481-486
10. Bleeker-Rovers CP, Bredie SJ, van de Meer et al. ^{18}F-fluorodeoxyglucose positron emission tomography in diagnosis and follow-up of patients with different types of vasculitis. *Neth J Med* 2003; 61: 323-329.
11. Lorenzen J, Buchert R, Bohuslavski H. Value of FDG PET in patients with fever of unknown orign. *Nucl Med Commun* 2001; 22: 779-783.
12. Kobayashi Y, Ishii K, Oda K, et al. Aortic wall inflammation due to Takayasu arteritis imaged with ^{18}F-FDG PET Coregistered with enchanced CT. *J Nucl Med* 2005; 46: 917-922.
13. Meave A, Soto ME, Reyes PA et L. Pre-pulseless Takayasu's arteritis evaluated with ^{18}F-FDG positron emission tomography and gadolinium-enhanced magnetic resonance angiography. *Tex Heart Inst J* 2007; 34: 466-469.