PET/CT in Diagnosing and Evaluating Therapy in Vasculitis

2

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Contents

Vasculitides are defined by the presence of inflammatory leukocytes in vessel walls with reactive damage to mural structures. They are often categorised by the size of the vessels affected as large, medium and small vessel vasculitis. FDG PET/CT has shown to be an effective tool to investigate large vessel vasculitis. It is particularly useful because vasculitis can be difficult to diagnose given the absence of specific symptoms (e.g. fever, weight loss, malaise, fatigue, raised inflammatory markers). Morphological imaging shows anatomical changes and does not show inflammation in the early phase prior to structural changes. FDG PET/CT allows early detection of large vessel vasculitis before structural changes become detectable by conventional imaging. It is also difficult to distinguish active inflammatory lesions from residual anatomic changes due to previous inflammation [1, 2]. This book chapter will discuss the two most common causes of large vessel vasculitis, the criteria for

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PET positivity, differential diagnosis, the influence of immunosuppressive therapy, how PET can be used to change patient management, the evidence on PET for monitoring response to therapy, non-PET imaging used for the diagnosis of large vessel vasculitis and the role of FDG PET in medium and small vessel vasculitis.

2.1 Takayasu Arteritis

This rare disease mostly affects young women (80–90% of patients) with an age of onset of 10–40 years, with 1–3 new cases per million per year in the USA and Europe. Systemic symptoms include fatigue, weight loss and low grade fever. It primarily affects the aorta and its primary branches and subclavian artery involvement is common. A meta-analysis showed pooled diagnostic performance in estimating disease activity with sensitivity of 70.1% and specificity of 77.2%. FDG PET/CT compared to disease activity assessed by NIH criteria showed a sensitivity of 78% and specificity of 87%. The current literature is not clear on whether there is correlation between vascular uptake, disease activity and biological parameters [3–6]. Figure 2.1 is an example of a positive FDG PET/CT showing active large vessel vasculitis in a patient with Takayasu arteritis.

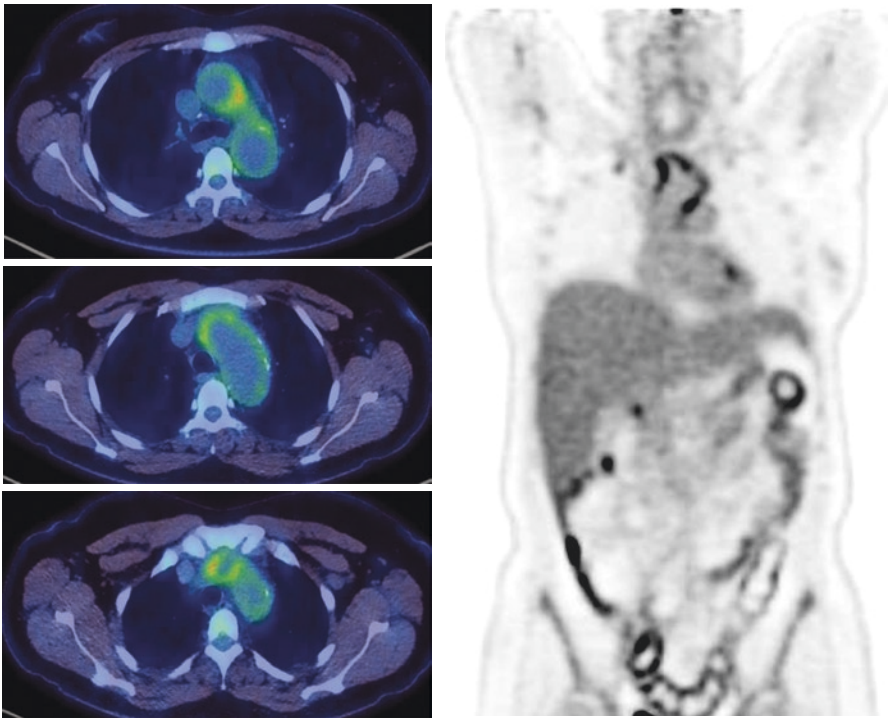

Fig. 2.1 Increased uptake in the aortic arch and the brachiocephalic trunk in a patient with Takayasu arteritis

2.2 Giant-Cell Arteritis

Mean age at diagnosis is 72 years. Prevalence is 1 in 500 adults >50 years. It affects predominantly the cranial branches of the arteries that originate from the aortic arch. Visual loss is a major complication. Temporal artery biopsy is the gold standard for diagnosis but has high false negative rates of 10–40%. There is a strong association with polymyalgia rheumatica. Pooled diagnostic performance for FDG PET is sensitivity 80%, specificity 89% and accuracy 84%. The main positive FDG vascular territories are the thoracic aorta, aortic arch, supra-aortic trunks and carotid arteries. There are discordant results for the correlation between vascular FDG uptake and serological markers (ESR, CRP) [7].

2.3 Criteria for PET Positivity

On visual analysis, a smooth linear or long segmental pattern of uptake in the aorta and its main branches with intensity higher than liver uptake is characteristic of giant-cell arteritis. A 4 point scale (0: no uptake, 1: uptake less than liver, 2: uptake equal to liver uptake and 3: uptake greater than liver uptake) showed that grade $\geq$2 for aorta and $\geq$1 for other arteries are positive for vasculitis [7–9].

Various teams have looked at semi-quantitative methods and compared uptake in vessel wall to blood pool, liver, lung and arterial uptake. The criterion that provided the optimal diagnostic performance was aortic arch SUVmax to venous blood pool SUVmax with a cut-off value of 1.53 that showed a sensitivity of 82% and specificity of 91% [10–14].

Figure 2.2 shows an example of diffuse smooth linear uptake in the wall of the aorta and its main branches, characteristic for large vessel vasculitis.

2.4 Differential Diagnosis

The main differential diagnosis of a positive PET for large vessel vasculitis is atherosclerosis, which can be quite difficult, especially in older patients in whom atherosclerosis is quite frequent. Typical findings for atherosclerosis are a patchwork of normal vessel wall, focal inflammation/uptake and calcifications. Typical findings for large vessel vasculitis are a smooth linear or long segmental pattern of uptake in the aorta and its main branches.

There have been anecdoctal reports of false positive findings with point spread function (PSF) reconstructions on the newer PET/CT cameras. The wall of large vessels is better delineated with PSF reconstructions and physiological uptake in the vessel wall is evident, which can make the vessel wall appear sharper and more intense. Careful attention to this finding is necessary when switching to a PSF reconstruction.

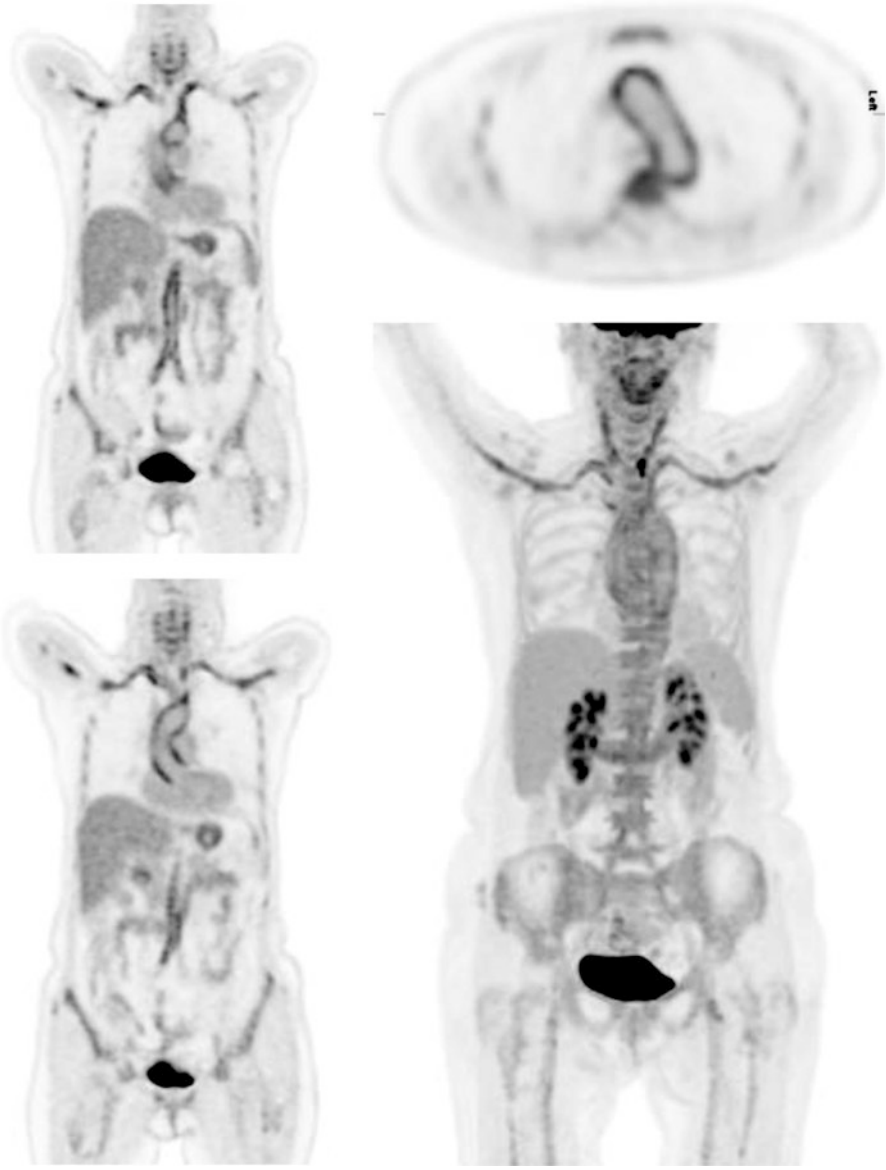

Fig. 2.2 Diffuse smooth linear uptake in the wall of the aorta and its main branches, characteristic for large vessel vasculitis

2.5 Impact of Immunosuppressive Therapy on Diagnostic Performance

The role of immunosuppressive therapy on the performance of FDG PET/CT was investigated in a study of 67 patients where a panel of experts determined the diagnosis and clinical management with and without the results of FDG PET. Large

vessel vasculitis was confirmed in 30 patients and ruled out in 31. Six patients with inconclusive data were excluded. In the 30 patients not on immunosuppression, sensitivity was 99.6%, specificity 86% and diagnostic accuracy 93%. There was no false negative PET finding. In the 31 patients on immunosuppression, sensitivity was 53%, specificity 79% and diagnostic accuracy 65%. There were eight false negative PET findings [15].

2.6 Role of FDG on the Management of Patients

The same study [15] investigated how FDG results changed patient management. The addition of FDG PET results changed diagnosis in 28% of patients, leading to a reduction of the number of patients scored as indeterminate from 20 to 10. The diagnostic accuracy was 54% without FDG PET and 71% with FDG PET. FDG PET had higher additional diagnostic value in confirming than in ruling out large vessel vasculitis. There was no significant change in the number of indications for temporal artery biopsy. There was a change in the treatment recommendation in 25% of patients.

2.7 Role of FDG PET on Monitoring Response to Therapy

There is no good evidence showing that FDG PET has a role in monitoring response to therapy.

In one study 35 patients were scanned at diagnosis, on steroid treatment and at relapse. FDG PET was positive at diagnosis in 29/35 patients. FDG uptake in the wall of the affected vessels was reduced at 3 months of treatment but there was no further reduction at 6 months of treatment. The patients who relapsed had similar FDG reduction of uptake between the baseline and treatment PET than patients who did not relapse. The authors concluded that FDG PET performed in patients on treatment is not predictive of relapse [10].

Another study assessed FDG PET and MRI in 25 patients with complicated giant-cell arteritis despite immunosuppressive therapy. There was no significant correlation between PET findings, CRP and ESR and clinical findings. The authors concluded that MRI and PET were unreliable for assessing large vessel inflammation in patients with complicated GCA and pre-existing immunosuppressive therapy [16].

2.8 Morphological Imaging

PET and morphological imaging are complementary. FDG PET will show vessel wall inflammation before morphological changes occur. Structural imaging will show arterial wall abnormalities, occlusions and aneurysms that can persist after the inflammatory phase.

Colour-Doppler US can show a hypoechoic oedematous wall swelling (halo sign). Sensitivity is 75%, specificity 83% with temporal artery biopsy as gold standard.

High resolution MRI can show mural thickening, oedema, stenosis and dilatation. Sensitivity is 89% and specificity 75% using biopsy-proven disease as a reference. CT and CT angiography can measure aortic diameter in cases of dilatation and are useful in detecting mural calcifications and to assess concentric mural thickening [17, 18].

2.9 Medium and Small Vessel Vasculitis

Because of the limited spatial resolution of PET (4–6 mm) the involvement of medium and small vessels cannot be accurately displayed. FDG PET can sometimes detect vessel wall inflammation in medium vessels. FDG PET can detect organ involvement in small vessel vasculitis [19, 20].

Key Points

- FDG PET/CT is a sensitive and specific non-invasive test to assess patients with a suspicion of large vessel vasculitis. Its use is complementary to CT and MRI. FDG PET/CT should be performed before steroid treatment is started or within 3 days of starting treatment. It is not sensitive to pick up small and medium vessel vasculitis. Its role in assessing response to treatment is not clearly defined at present.

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