**ABSTRACT**

A majority of the clinical use of positron emission tomography (PET)-computed tomography (CT) is related to cancer management. Its application in evaluating inflammatory diseases and pyrexia of unknown origin is becoming popular. We reviewed the fluorine-18-fluorodeoxyglucose PET-CT findings of an 80-year-old woman with nonspecific clinical presentation consisting of generalised malaise, moderately high fever and weight loss. Prior CT and magnetic resonance imaging were not helpful in providing a clinical diagnosis. The diagnosis was Horton’s arteritis, and the patient responded well to high-dose steroids.

**Keywords:** arteritis, fluorine-18-fluorodeoxyglucose positron emission tomography, Horton’s arteritis, hybrid imaging, positron emission tomography

**INTRODUCTION**

Despite Horton’s arteritis being rare, it is clinically important to detect this disease at an early stage, before complications resulting in permanent disability sets in. Application of the fused hybrid imaging technique, fluorine-18 (18F)-fluorodeoxyglucose (FDG) positron emission tomography (PET)-computed tomography (CT) in facilitating clinicians to diagnose arteritis has gained increasing importance. This technique enables the demonstration of high uptake in the wall of the arteries at an early stage, even in cases of non-infective or sterile inflammatory reaction. This special feature of imaging using FDG PET-CT can be recommended as a first-line investigating tool in patients with a vague clinical presentation of low-grade pyrexia of unknown origin.

**CASE REPORT**

An 80-year-old Caucasian woman was admitted to the hospital for generalised malaise, with moderate high fever and weight loss for several weeks prior to admission. Two years earlier, she had an episode of viral encephalitis with complete and uneventful recovery. She also had carcinoma of the vagina and was treated surgically 11 years prior to this event. Physical examination revealed no significant abnormalities, and clinically, the blood test showed a raised erythrocyte sedimentation rate (ESR) of 103 mm/hr. Chest radiograph showed diffused calcifications of the aortic wall with a tortuous aorta. CT (Figs. 1 & 2) and magnetic resonance (MR) imaging were also performed, but they only revealed extensive multifocal calcifications in the wall of the thoracic aorta and abdominal aorta up to its bifurcation. The carotid arteries were also involved bilaterally. No other additional information was obtained from the CT and MR imaging. At this juncture, the clinical diagnosis was inconclusive.

The patient underwent 18F-FDG PET-CT in view of suspected occult infection, resulting in the raised ESR. The examination was carried out at the Nuclear Medicine Department of Niguarda Hospital, Milan, Italy, using an integrated PET-CT system (Biograph, Siemens, Erlangen, Germany) that combines dual-slice spiral CT with a dedicated full-ring bismuth germanate crystal PET scanner. CT image acquisition was accomplished without intravenous contrast media administration. The following protocol was used: image acquisition started at 25 minutes after 18F-FDG injection. CT scanogram was performed to plan the PET-CT study. Low-dose CT acquisition was performed first with parameters of 2.5 mm slices, spiral mode at 50 mAs and 130 kV. CT was performed for anatomical correlation and attenuation correction for PET images. Immediately after CT image acquisition, the table was positioned for PET image acquisition (5 min/bed position). First acquisition was performed from the lung to the thighs in three-dimensional (3D) mode. Reconstruction of the emission data was performed by using an iterative algorithm with the software Somaris/5 VA40C and stored in a 128 matrix (FWHM 3.0 mm).
Fig. 1 Unenhanced axial CT images of the neck show multifocal calcifications of the wall of the major neck vessels. The left artery (short arrows) is more affected than the right artery (long arrows). Without intravenous contrast administration, the vessels are not easily distinguishable from the surrounding musculature structures.

Fig. 2 Unenhanced axial CT images of the thorax and abdomen show multifocal extensive calcifications (arrows) in the wall of the aorta until its bifurcation.

5 mm, zoom 1, pixel size 5.1, scatter correction). Volume projected images (transaxial, coronal and sagittal slices) and fusion images were generated for interpretation.

PET image acquisition (Figs. 3–5) revealed avid segmental 18F-FDG uptake with increased activity in the wall of the major vasculature of the neck, thorax and abdomen, as compared to background soft tissue uptake. However, the exact anatomical position cannot be precisely determined without CT anatomical correlation. The branching pattern which appears like a minified “underground map” in the neck vasculature in the coronal view is the best clue for vascular involvement in this region provided by these PET images. CT image acquisition is unable to conclude the findings other than focal or segmental calcifications.
Fig. 3  (a) Reconstructed multiplanar reconstruction (MPR) coronal CT image of the neck shows limited information with a focal calcification in the left superior mediastinum. There is a corresponding increased avid uptake of 18F-FDG on (b) fused, and (c) PET image at the same level (white arrow). The high FDG uptake in a “branching” pattern on the PET image gives an “underground map” appearance, and forms the best clue to vascular activity. The high activity along the right neck vasculature on the FDG-PET image (black arrows) is not seen on the CT image.

Fig. 4  (a) Reconstructed MPR sagittal CT image of the thorax and abdomen shows multifocal and segmental calcifications along the wall of arch and descending aorta. (b) The fused image confirms the location of increased 18F-FDG on the wall of the descending aorta, and the (c) PET image also shows avid activity along the wall of the descending aorta.

Fig. 5  (a) Reconstructed MPR coronal CT image of the thorax and abdomen shows multifocal calcifications along the wall of arch and abdominal aorta (white arrow). (b) Fused and (c) PET images show that the high uptake of 18F-FDG along the upper thoracic and lower abdominal vessels is as intense as, or more intense than, the liver activity.

The high uptake of FDG in the large vessels (thoracic aorta) was above 5.0. The sagittal view of the descending thoracic aorta provides the most information by demonstrating avid 18F-FDG activity along its wall (Fig. 4). The final diagnosis was arteritis (Figs. 3–5), as proven by the temporal artery biopsy, which revealed hyperplasia of the intima, with medium to moderate vasculitis of the vasa vasorum. Upon confirmation of the diagnosis, the patient underwent treatment using high-dose...
corticosteroids. She responded well, and no follow-up PET-CT was performed after that.

**DISCUSSION**

Various names have been associated with Horton’s arteritis, including Horton’s giant cell arteritis, Horton’s syndrome, Horton’s temporal arteritis, Horton-Gilmour disease, Horton-Magath-Brown syndrome and Hutchinson-Horton-Syndrome. The disease was described in several articles with the earliest at the initial stage of discovery in 1867. This rare clinical condition of generalised sterile inflammatory vasculitis affecting the medium- and large-sized arteries has the potential to result in permanent disability from its complications. Therefore, diagnosis and treatment should be instituted early. In fact, newly-recognised cases should be considered a true neuro-ophthalmic emergency, and prompt treatment with steroids can prevent blindness and other vascular sequelae.

The aetiology of Horton’s arteritis remains unknown. However, autoimmune reaction has been implicated in the pathogenesis. The histopathological findings suggest the presence of an antigen-driven disease, with local T-cell and macrophage activation in or near elastic tissue in the arterial walls. The degree and extension of arterial involvement depend on the presence of elastic lamina lining the endothelium of the vessels. This fact determines the type of arteries involved in the disease process. The clinical diagnosis is confirmed through a temporal artery biopsy with evidence of vasculitis characterised by a predominance of mononuclear infiltrates or granulomas, usually with presence of multinucleated giant cells.

In our case, despite the vague clinical signs and symptoms at presentation, two of the criteria in this patient fit into the diagnosis of Horton’s arteritis, which include the age of onset after 50 years, and raised ESR. However, these are not definitive and the importance of the generalised nonspecific clinical presentation was only recognised on retrospective evaluation. The average annual incidence of Horton’s arteritis in Europe is 10–20 cases per 100,000 population. Ostberg reported that the incidence of Horton’s arteritis may be more common than clinically evident. Despite the rarity of its occurrence, early recognition of the disease is important, in order to start early treatment to ensure arrest of the disease progression. Visual loss is one of the most significant causes of morbidity, and permanent visual impairment may occur in as many as 60% of patients.

Most imaging methods for investigating arteritis are more suggestive than diagnostic in value. Radiologically, calcification is generalised and nonspecific, and can be due to the normal ageing process. In the conventional radiological method of interventional arteriography, the findings in acute arteritis may be normal or show irregularity of the lumen of vessels, variation in calibre, thrombus or occlusion. Later, depending on the healing process, the vessel may exhibit segmental stenosis, dilatation, ectasia or aneurysmal formation. In many cases, arteriographical findings of arteritis are nonspecific as they can be produced by other disorders, such as infection. Furthermore, the demonstration of these changes may result in a vulnerable onset of complications. In our case, we found nonspecific focal and segmental calcifications along the major vessels in the walls of external carotids, thoracic aorta and abdominal aorta. These findings are also commonly seen among the elderly due to atherosclerosis.

In PET imaging, FDG accumulation in the walls of the arteries and aorta can be observed quite regularly, and some suggested that this is due to plaque formation as a result of atherosclerosis, which is known to be an immune inflammatory disease characterised by vascular calcification. In this case, arterial wall FDG accumulation greater than the adjacent blood pool activity was considered an inflammation, and arterial attenuation of > 100 Hounsfield units detected by CT was considered to be calcification. The FDG uptake tends to be diffused in the arterial wall inflammation, whereas in atherosclerosis, the uptake is predominantly focal and patchy along the vessels, depending on the stage of the evolution of the atherosclerosis development. However, at imaging, both clinical entities cannot be ascertained by just visual interpretation on PET-CT images. Incomplete clearing of FDG in the circulation has also been suggested as the cause. Thus, further studies to evaluate this situation utilising a modified delayed protocol to clarify this situation should be included in the future.

Premedication, which will alter the glucose level in the blood circulation, also has a role to play in the characterisation of the FDG uptake. von Schulthess suggested that extra precautions should be taken in interpreting PET images in cases of arteritis, due to the pitfalls of partial volumeing effect, which will reduce the appearance of high FDG activity and make the lesion appear less FDG active. Furthermore, because of the fine thickness of the arterial wall which cannot match the resolution of the PET equipment, even compared with the best resolution available commercially, there is always a tendency for partial voluming to occur. Steps that could be taken to minimise the pitfalls include determining the pre-imaging clinical status of the patient, including blood sugar level and potent anti-inflammatory drug therapy intake (e.g. dexamethasone and prednisolone). These should be taken into consideration as these may
influence the intensity by reducing FDG uptake by inflamed vessel walls. However, despite all the above-mentioned precautions that could be taken to improve the specificity, confirmatory biopsy remains the gold standard to diagnose this disease.

In our case, high uptake activity involving the walls of the arteries were not only confined to the regions of calcifications, but also to the rest of the walls where there were no obvious abnormalities observed on CT images (Figs. 3–5). These areas of activity corresponded with the inflammatory reaction, and appeared as intense as or slightly more than the liver activity. Furthermore, the use of this technique in managing giant cell arteritis has also been suggested, based on the results obtained by Blockmanns et al.(15) Scheel et al. found that 18F FDG-PET is an effective technique for detecting early aortitis and has a high correlation with laboratory inflammatory measures, in which during the follow-up examination, 18F FDG-PET uptake decreased in line with the clinical symptoms and inflammatory serum markers.(16) Finally, the diagnosis of Horton’s arteritis in this patient was confirmed through histopathological findings of the superficial temporal artery biopsy. The histopathological changes involving the calibre of the vessels were described in detail by Sewell and Lessell, and others.(15, 17–19)

While several authors feel the precise value of 18F FDG-PET in management of arteritis in the clinical setting is not yet defined, we feel that non-interventional and safer methods like FDG PET-CT should be employed early in managing patients clinically suspected to have arteritis.(20–22) In conclusion, in investigating cases of arteritis, nonspecific features on conventional method of imaging and nonspecific vague clinical presentations are the main concern in the management. PET-CT evaluation should be recommended as a routine diagnostic imaging tool in the earliest part of the management. This non-interventional method is more superior than other conventional methods of imaging arteritis, and is considered to be safer. It is a valuable method for early diagnosis, hence avoiding serious non-reversible fatal complications.

REFERENCES