Vasculitis Diagnosed on Fluorine-18 Labelled-2-Deoxy-2-Fluoro-D-Glucose Uptake in A Patient With Fever of Unknown Origin and A History of Non Hodgkin's Lymphoma

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Abstract: There are increasing data demonstrating the role of 18F-flourodeoxyglucose positron emission tomography with computerized tomography fusion (18F-FDG PET/CT) in the diagnosis of large vessel vasculitis, including Takayasu arteritis and giant cell arteritis. We report a case of large vessel vasculitis detected on 18F-FDG PET/CT; a 32-year-old woman with history of Non Hodgkin Lymphoma, admitted with fever of unknown origin (FUO) of 2-months duration and asthenia. To exclude FUO of malignancy, in the suspect of NHL relapse, 18F-FDG PET/CT imaging was performed. The images demonstrated significant 18F-FDG uptake in aortic arch and no signs of NHL relapse. This case report supports the role of 18F-FDG PET/CT as a useful and noninvasive tool in diagnostic evaluation of patient with FUO, both by excluding a malignant etiology and providing information about other possible causes such as inflammation, including vasculitis. 18F-FDG PET/CT is very useful in the early diagnosis of active inflammation including vasculitis and provides timely information for appropriate therapy.

Keywords: 18F-FDG PET/CT, Vessels inflammation, NHL, Takayasu arteritis, FUO.

INTRODUCTION

Vasculitis is an inflammatory condition of the blood vessels, characterized by a leukocyte infiltration of the vessel wall causing reactive destruction of the wall structures and surrounding tissue leading to infarction. It is classified according to the vessel size (large-size, medium-size and small-size vessel vasculitis) [1].

Fluorine-18-fluorodeoxy-glucose positron emission tomography with computerized tomography fusion (18F-FDG PET/CT) has a confirmed role in the diagnosis and management of oncological diseases, but literature evidence suggests a new role for 18F-FDG PET/CT also in the diagnosis of inflammatory processes such as vasculitis [2].

The diagnosis of vasculitis is challenging because clinical manifestations are non-specific, featuring fever, fatigue, weight loss, diffuse pain, myalgia, etc.; it is based on the history, clinical examination, and laboratory analysis and imaging findings. The role of imaging is to detect vasculitis and to guide biopsy, the gold standard for the definitive diagnosis [3].

18F-FDG PET/CT can be particularly useful in patients with a previous history of oncological diseases who develop fever of unknown origin (FUO). We report the case of a patient previously treated for Non Hodgkin's Lymphoma (NHL) referred to our attention for FUO and suspected NHL relapse.

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CASE REPORT

We report the case of a 32-year-old female hospitalized for a 2-months history of FUO and asthenia.

She had been previously diagnosed, in March 2011, with a large cell B NHL after right supraclavicular lymph node biopsy. A chemotherapy protocol with Aracytin + Bleomycin + Vincristine + Methotrexate was started and the patient achieved full remission in the same year.

On examination she appeared conscious, oriented, and well hydrated, with no skin lesions, BP 125/70 mmHg, a regular HR 85 per minute, an axillary temperature of 38.0 °C and blood sugar 115 mg/dl. Cardiac and pulmonary physical examinations were unremarkable. Abdominal examination showed no clinical signs of peritoneal irritation or masses other than mild spleen enlargement. Bilateral renal percussion was negative.

Further investigations showed normochromic normocytic anemia, with hemoglobin 8.9 g/dl (normal range for adult women 9-12 g/dl), WBC count $4.2x10^9$/L (normal range $4.3\text{-}10.8x10^9$/L), with 85.3% neutrophils, platelet count $185x10^9$/L (normal range $150\text{-}400x10^9$/L), ESR 125 mm/h (normal value <5mm/h), C-reactive protein 2.7 mg/dl (normal range 0–1 mg/dl) and beta2-microglobulin 2.63 mg/L (normal range 1.16-2.52 mg/L). Clotting indexes were within normal range. Renal function, serum electrolytes, lipid profile, liver indices, thyroid hormones, electrocardiogram and chest X-rays were normal.

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On the suspicion of NHL relapse, whole body 18F-FDG-PET/CT was performed with the Discovery STE scanner (General Electric Healthcare, Milwaukee, WI – USA). After at least 6 hours of fasting, an 18F-FDG dose of 265 MBq (4.2 MBq per kg of body weight) was administered intravenously and the PET/CT scans were recorded 45 minutes later.

A significantly increased 18F-FDG uptake (enhanced metabolic activity) was evident in a circumferential pattern along the aortic arch (Figure **1**). No 18F-FDG uptake was observed in the lymph nodes.

These findings excluded NHL relapse and suggested a vasculitis.

The patient was treated with a high dose corticosteroid regimen (1mg/kg). Her symptoms improved and the fever gradually resolved. Blood tests repeated on the 22nd day after the start of treatment showed normalization of the inflammation indexes.

DISCUSSION

We present the case of a patient with vasculitis, probably Takayasu's arteritis (TA), diagnosed with 18F-FDG-PET/CT. Large vessels vasculitis forms include giant-cell arteritis (GCA) and Takayasu's arteritis (TA). GCA is more common in elderly females, mainly affecting the supra-aortic arteries, most commonly the superficial temporal artery [4]; TA is predominantly observed in young women, most commonly involving the aorta and its branches [5].

The American College of Rheumatology has defined specific criteria to support the diagnosis, based on symptoms presenting in advanced disease. In initial TA the broad variety of non-specific symptoms, and variable severity and progression, often hamper a precise evaluation, delaying diagnosis [6-7].

The imaging techniques employed to diagnose vasculitis is Doppler ultrasound, MRI and CT angiography, which can show vessel wall thickening, thrombus, calcifications and luminal stenosis. Angiography, considered as the gold standard imaging technique, has high sensitivity but low specificity. It can detect an abnormal vascular anatomy but cannot define the reason for the vascular restriction (inflammation vs. fibrosis) [8]. Furthermore, it is invasive and associated with a high morbidity, exposure to radiation, as well as possible contrast toxicity [9].

18F-FDG PET/CT is a non-invasive diagnostic technique which can disclose, in patients with FUO, the disease onset earlier than traditional anatomical imaging techniques, thus allowing prompt treatment, which may delay or prevent the vessels stenosis. Webb *et al*., in patients with biopsy-proven TA who had undergone 18F-FDG-PET/CT, cross-sectional imaging

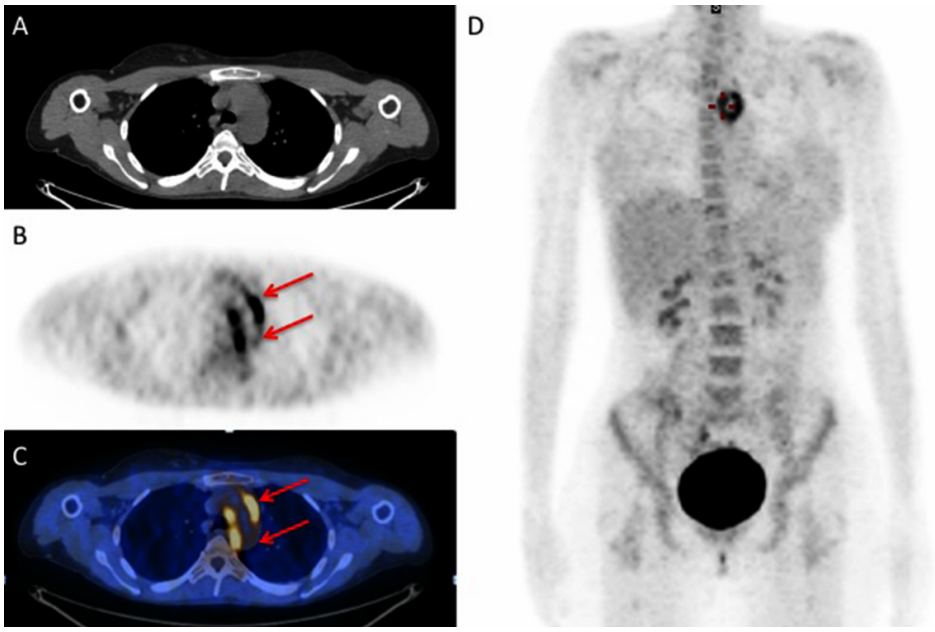

Figure 1: 18F-FDG PET/CT transaxial CT (**A**), PET (**B**), fusion (**C**) images show a significantly increased 18F-FDG uptake in a circumferential pattern along the aortic arch (red arrows). MIP images (**D**) do not show 18F-FDG uptake in lymph nodes and spleen.

(contrast-enhanced CT and MRI) and angiography, demonstrated 92% sensitivity, 100% specificity, and negative and positive predictive values of 85% and 100%, respectively, using 18F-FDG-PET/CT in the initial assessment of active vasculitis in TA [6].

18F-FDG PET/CT has already been validated to assess patients with different types of malignant tumors, including lymphomas. 18F-FDG PET/CT evaluates central metabolic pathways changes in cancer cells, which present higher levels of glycolysis, an elevated glucose uptake, and increased lactate production compared to non-malignant cells, a phenomenon known as "aerobic glycolysis" [10].

18F-FDG PET/CT scanning has been found useful in the staging and follow-up of Hodgkin's and non-Hodgkin's lymphoma [11-12], as well as in our patient who underwent 18F-FDG PET/CT for suspected NHL relapse.

The uptake of 18F-FDG in patients with NHL is firstly ascribable to neoplastic tissue, especially if the uptake is located in the lymph nodes and spleen. Occasionally 18F-FDG uptake is not specific for malignant tumors, because inflammation and infections can also trigger an increased glucose metabolism [13-14].

In fact, in our patient 18F-FDG-PET/CT did not reveal an altered uptake in lymph nodes or spleen, thus excluding NHL relapse, whereas there was 18F-FDG uptake in the aortic arch, indicating the intense metabolism associated with active inflammation, and thus suggesting an inflammatory disease. The final diagnosis was based on the combination of clinical signs, laboratory data and 18F-FDG-PET/CT findings, compatible with large vessel arteritis (probably TA).

CONCLUSIONS

This case report supports the role of 18F-FDG PET/CT as a useful and non-invasive tool in the diagnostic evaluation of a patient with FUO, both to exclude a malignant etiology and to gain information about other possible causes such as inflammation.

18F-FDG PET/CT is very useful in the early diagnosis of active inflammation, including vasculitis, and provides timely information supporting appropriate treatment decision-making.

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