Causes of ^{18}F-FDG uptake on white adipose tissue

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Abstract

White adipose tissue usually shows negligible fluorine-18-fluorodeoxyglucose (^{18}F-FDG) uptake. In certain clinical conditions this ^{18}F-FDG uptake has been reported to be increased like in HIV patients under treatment, in exogenous Cushing's syndrome, in cases related to premedication and other cases.

Introduction

Fluorine-18-fluorodeoxyglucose (^{18}F-FDG) uptake in positron emission tomography/computed tomography (PET/CT) imaging reflects the glucose metabolic activity of the tissue and usually human adipose tissue shows negligible ^{18}F-FDG uptake. The adipose tissue is comprised of brown and white tissue and it is well-known that brown adipose tissue, in response to cold temperatures and sympathetic stimulation, can demonstrate increased ^{18}F-FDG uptake typically in the neck, shoulders, and the paravertebral area of the thoracic spine . However, for the white adipose tissue, only a few recent studies have reported enhanced ^{18}F-FDG uptake in certain clinical conditions .

Patients infected with human immunodeficiency virus (HIV), treated with highly active anti-retroviral therapy and having osteodystrophy were reported to have significantly increased ^{18}F-FDG uptake in the subcutaneous fat . This finding was not found in HIV patients without osteodystrophy.

Another study reported a case with uterine cervical cancer and increased ^{18}F-FDG uptake in the subcutaneous and the visceral fat . This patient was treated by high-dose ascorbic acid and intravenous insulin shortly before the ^{18}F-FDG PET/CT scan and this medication could have induced increased white adipose tissue glycolytic activity. Intravenous infusion of high-dose ascorbic acid causes error in glucometer readings, resulting factitious hyperglycemia. Intravenous insulin was subsequently administered. Hypoglycemia induced by the administration of insulin mobilized liver glycogen and released energy stored in the white adipose tissue, resulting increased ^{18}F-FDG uptake in the white adipose tissue.

Another recent report demonstrated increased ^{18}F-FDG uptake in white adipose tissue after the administration of high-dose of glucocorticosteroids . The researchers suggested that glucocorticosteroids induced remodeling of white adipose tissue into the characteristic Cushingoid form, with catabolic lipolysis, anabolic lipogenesis, and adipogenesis. This remodeling process requires increased mitochondrial metabolism, resulting in increased ^{18}F-FDG uptake.

Increased ^{18}F-FDG uptake was also reported in children with lymphoblastic lymphoma after chemotherapy and very high doses of corticosteroids . These patients showed transiently increased facial uptake and decreased hepatic uptake of ^{18}F-FDG during therapy probably due to exogenous Cushing's syndrome.

The authors of this paper have experienced the case of a 61 years old woman with diffuse large B-cell lymphoma. Blood glucose level, before ^{18}F-FDG injection for the initial ^{18}F-FDG PET/CT scan was 92mg/dL also. Increased uptake showed in the lymphoma sites at the left palatine and tonsil, bilateral neck area, mediastinum, bilateral axillary area, abdomen, spleen, retroperitoneum, and right iliac area (Figure 1). Another, interim scan showed enhanced ^{18}F-FDG in the white adipose tissue during chemotherapy treatment with doxorubicin, cyclophosphamide, vincristine, and prednisone with rituximab (R-CHOP) (Figure 2). Twenty days after completion of the third cycle of R-CHOP, an interim ^{18}F-FDG PET/CT was performed to evaluate the patient's early treatment response (Figure 2).

It is of interest that although the patient had fasted for more than 6 hours prior to undergoing the PET/CT scan, her blood glucose level was 103mg/dL. Sixty minutes after ^{18}F-FDG injection, the PET/CT scan showed increased ^{18}F-FDG uptake in the

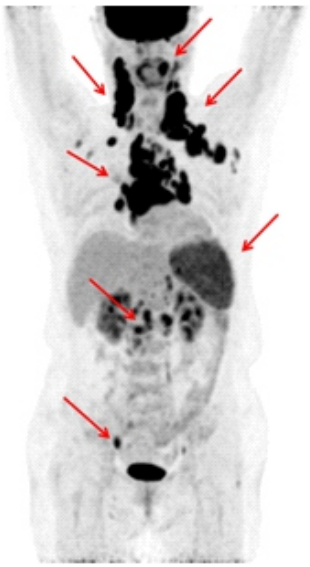

Figure 1. The maximal intensity projection of the initial ^{18}F-FDG PET/CT image of a 61 years old woman with diffused large B-cell lymphoma at the initial staging showed multiple lymphoma foci of increased ^{18}F-FDG uptake in the left palatine tonsil, bilateral neck, mediastinum, bilateral axillae, abdomen, spleen, retroperitoneum, and right internal iliac area with maximum SUV: 14.0. Over the heart the first SUVmax was 2.3.

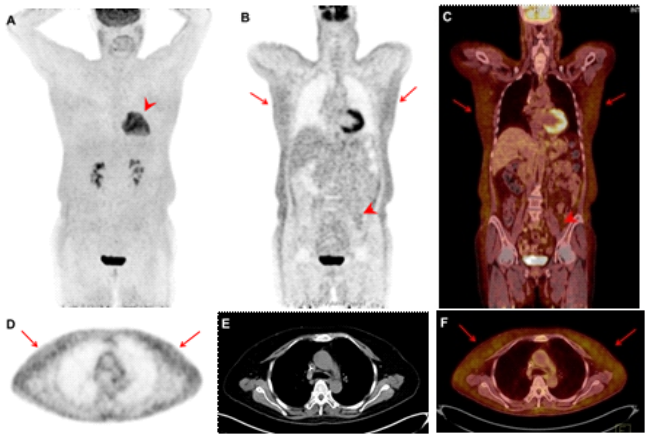

Figure 2. In the same case of Figure 1, the interim ^{18}F-FDG PET/CT scan performed after completion of the third cycle of chemotherapy showed: **A)** by maximal intensity projection diffusely increased ^{18}F-FDG uptake in the white adipose tissue with intensely increased ^{18}F-FDG uptake in the myocardium (arrowhead; SUVmax of 6.8). On the coronal PET **B)**, fused PET/CT **C)**, transaxial PET **D)**, transaxial CT **E)**, and fused PET/CT F) images, increased ^{18}F-FDG uptake in the subcutaneous white adipose tissue (arrow on B), C), D), and F); SUVmax of 2.2) is shown in the thorax, abdomen, and pelvis. The visceral white adipose tissue (arrowhead on B) and C)) also shows mildly increased ^{18}F-FDG uptake, while low ^{18}F-FDG uptake is seen in the liver (mean SUV of 1.1) and muscle tissue (SUVmax of 1.0).

subcutaneous and visceral white adipose tissue and the myocardium. In contrast, there was very low ^{18}F-FDG uptake in the liver and muscles. The patient denied of taking any medications before the diagnosis of lymphoma, except herbal medicine of unknown dose and content. Further tests revealed severely decreased serum levels of adrenocorticotropic hormone (ACTH) (<1.0pg/mL; normal range, 5.0-60.0pg/mL) and cortisol (0.73μg/dL; normal range, 6.7-22.6μg/dL), findings clinically suspicious for Cushing's syndrome induced by the administration of exogenous steroid medication. Following these test results, the patient was instructed to stop taking the herbal medicine and underwent the next cycle of R-CHOP. Fifteen days after the completion of the fourth cycle of R-CHOP, the patient underwent a second interim ^{18}F-FDG PET/CT scan (Figure 3), at which time she had a blood glucose level of 81mg/dL. The PET/CT images showed normal distribution of ^{18}F-FDG uptake and all lesions with intensely increased ^{18}F-FDG uptake on PET/CT had disappeared. Serum ACTH level measured the day after the PET/CT scan was 18.9pg/mL.

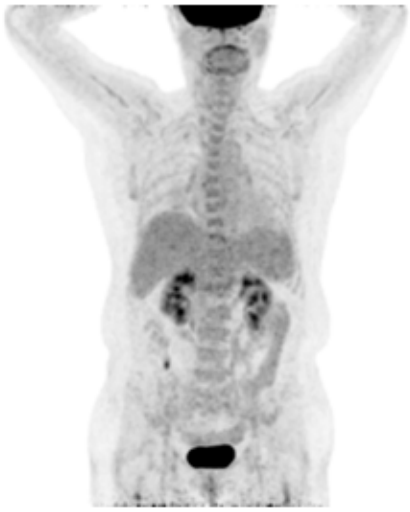

Figure 1. The same patient of Figure 1. Maximal intensity projection image of the second interim ^{18}F-FDG PET/CT scan showed normal distribution of ^{18}F-FDG uptake. All lesions with increased ^{18}F-FDG uptake had disappeared. The SUVmax over the heart was 2.3.

The patient received no anti-retroviral agents, insulin, or ascorbic acid, which have been reported as causes of enhanced white adipose tissue uptake of ^{18}F-FDG, but showed low serum levels of ACTH and cortisol that are suggestive of exogenous iatrogenic Cushing's syndrome. Prednisone, a synthetic glucocorticoid, is included in the R-CHOP treatment that the patient was receiving and could be the cause of enhanced white adipose tissue metabolic activity. However, considering the interval between R-CHOP treatment and the first interim ^{18}F-FDG PET/CT scan, as well as the normal distribution of ^{18}F-FDG uptake on PET/CT after the completion of chemotherapy which included prednisone, other factors could have also affected the biodistribution of ^{18}F-FDG uptake. Previous reports have stated that herbal medicinals as the one taken by the patient during the first three cycles of chemotherapy, could contain corticosteroids, resulting in exogenous iatrogenic Cushing syndrome .

In conclusion, increased metabolic activity and increased uptake of ^{18}F-FDG in white adipose tissue is scarce and among other factors can be due to corticosteroids, taken before by the patient.

The authors declare that they have no conflicts of interest.

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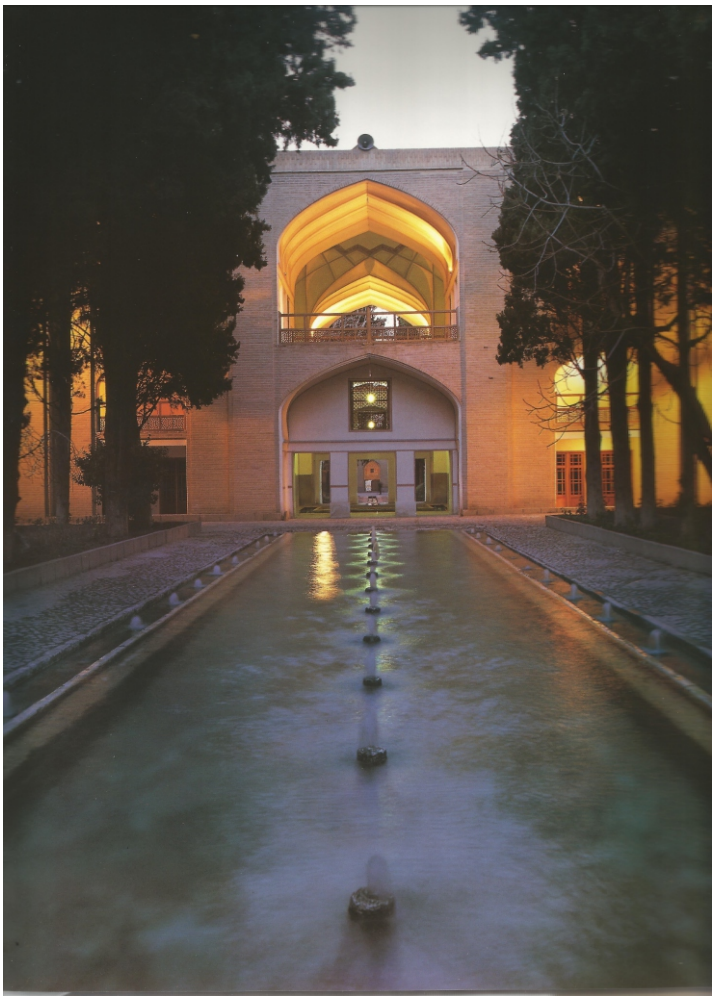

Bagh-e Fin, Kahan, a 19th century royal garden, Iran.