J of Nuclear Medicine Technology, first published online December 6, 2019 as doi:10.2967/jnmt.119.237545

Glucocorticoids Induced White Adipose Tissue Hypermetabolism in Cushing's Syndrome

Sasha O. Staack, M.D.[1], Allison C. Rosenthal, D.O.[2] Curtiss B. Cook, M.D.[3], Ming Yang, M.D*[1]

[1]Department of Radiology

[2]Department of Hematology/Oncology

[3]Division of Endocrinology

Mayo Clinic Arizona

***Corresponding author**

Ming Yang, MD

Assistant Professor

Department of Radiology

Mayo Clinic Arizona

Address:

13400 East Shea Boulevard

Scottsdale, AZ 85259

USA

Tel: 480-342-0988

Fax: 480-301-4303

Email: yang.ming@mayo.edu

Grant support: None

Number of words: 743

Abstract:

An adult lymphoma patient developed Cushing's syndrome following short-term, high-dose dexamethasone administration and presented with distinctive Cushingoid fat redistribution pattern and associated white adipose tissue increased ^{18}F-FDG uptake. Recognition of the unique ^{18}F-FDG uptake manifestation may aid in the diagnosis of this iatrogenic syndrome and avoid image misinterpretation.

Key words:

Cushing's syndrome; White fat; Glucocorticoids; PET/CT; FDG

Running title:

White Fat Hypermetabolism in Cushing's Syndrome

Introduction: In addition to regulation of glucose metabolism, glucocorticoids play an important role in adipose metabolism via multiple pathways. Exogenous high-dose glucocorticoids may cause Cushing's syndrome with resultant classical white adipose tissue redistribution. Although uncommon, the redeposited adipose tissue might show enhanced ^{18}F-FDG uptake in certain clinical conditions and lead to misinterpretation.

Case report: A 59-year-old woman with history of renal transplantation developed a post-transplant lymphoproliferative disorder involving the skin and brain, which was identified on ^{18}F-FDG PET/CT scan. She was treated with rituximab for chemotherapy and dexamethasone 8 mg/d for controlling cerebral edema. She also had been on low dose prednisone 5 mg/d for immunosuppression following her renal transplant. Six-weeks after initiation of chemotherapy and combined glucocorticoids therapy, a follow-up ^{18}F-FDG PET/CT scan was performed with fasting blood glucose level of 110 mg/dL. On ^{18}F-FDG PET/CT images, both the brain and cutaneous lesions had resolved. However, there was rapid proliferation of subcutaneous white adipose tissue with increased ^{18}F-FDG uptake at the face, neck and back (Figure 1). The posterior upper neck subcutaneous white fat tissue thickened from 2.1 cm to 5.1 cm with SUVmax increased from 1.2 to 2.6. At bilateral thighs, there was increased ^{18}F-FDG uptake of intermuscular adipose tissue (IMAT) beneath the fascia of wasting muscles, with SUVmax increased from 1.0 to 3.6 (Figure 2). Since there were no corresponding lesions in the redistributed fatty tissue, the hypermetabolism was considered as treatment-related false positive finding and a diagnosis of iatrogenic Cushing syndrome was achieved. A dexamethasone tapering protocol ensued given favorable response to therapy.

Discussion: Enhanced ^{18}F-FDG uptake in remodeled white adipose tissue has been sparsely reported in lymphoma patients receiving chemotherapy and glucocorticoids (1,2). It is well-

known that glucocorticoids play an important role in regulation of fat metabolism via stimulating lipolysis, lipogenesis and adipogenesis processes, which may lead to classical Cushingoid distribution of central white adipose tissue, i.e. moon face and buffalo back, etc. The increased ^{18}F-FDG uptake in white adipose tissue might be associated with up-regulated glycolytic mitochondrial metabolism and pro-inflammatory macrophage recruitment caused by dexamethasone administration (3). It also has been found that glucocorticoids promote differentiation of pre-adipocytes into mature adipocytes, which have relatively high GLUT1 expression (4).

Of interest, there is bilateral thighs IMAT showing increased ^{18}F-FDG uptake. The lower extremity IMAT is considered as an ectopic fat depot similar to visceral fat, which is part of central white adipose tissue family (5). Therefore, we believe that the IMAT hypermetabolism might carry the same mechanism of central subcutaneous white fat tissue aforementioned.

Conclusion: Redistributed white adipose tissue enhanced ^{18}F-FDG uptake in glucocorticoids induced Cushing's syndrome is a multifactorial phenomenon and might be related to age, sex, dosage and duration of glucocorticoid exposure, etc. Recognition of the uncommon ^{18}F-FDG uptake pattern in hypertrophic central white adipose tissue may raise awareness of iatrogenic Cushing's syndrome and avoid misinterpretation.

References

1. Hwang DY, Lee JW, Lee SM, Kim S. Causes of (18)F-FDG uptake on white adipose tissue. *Hell J Nucl Med. 2016;19:7-9*.

2. Kong MC, Nadel HR. 18F-FDG PET/CT With Diffusely High FDG Uptake Throughout Subcutaneous Adipose Tissues. *Clin Nucl Med. 2018;43:762-3*.

3. Pattison DA, Hofman MS, Lau E, Ware R, Hicks RJ. Enhanced white adipose tissue metabolism in iatrogenic Cushing's syndrome with FDG PET/CT. *J Clin Endocrinol Metab. 2014;99:3041-2*.

4. Gould GW, Holman GD. The glucose transporter family: structure, function and tissue-specific expression. *Biochem J. 1993;295 (Pt 2):329-41*.

5. Addison O, Marcus RL, Lastayo PC, Ryan AS. Intermuscular fat: a review of the consequences and causes. *Int J Endocrinol. 2014;2014:309570*.

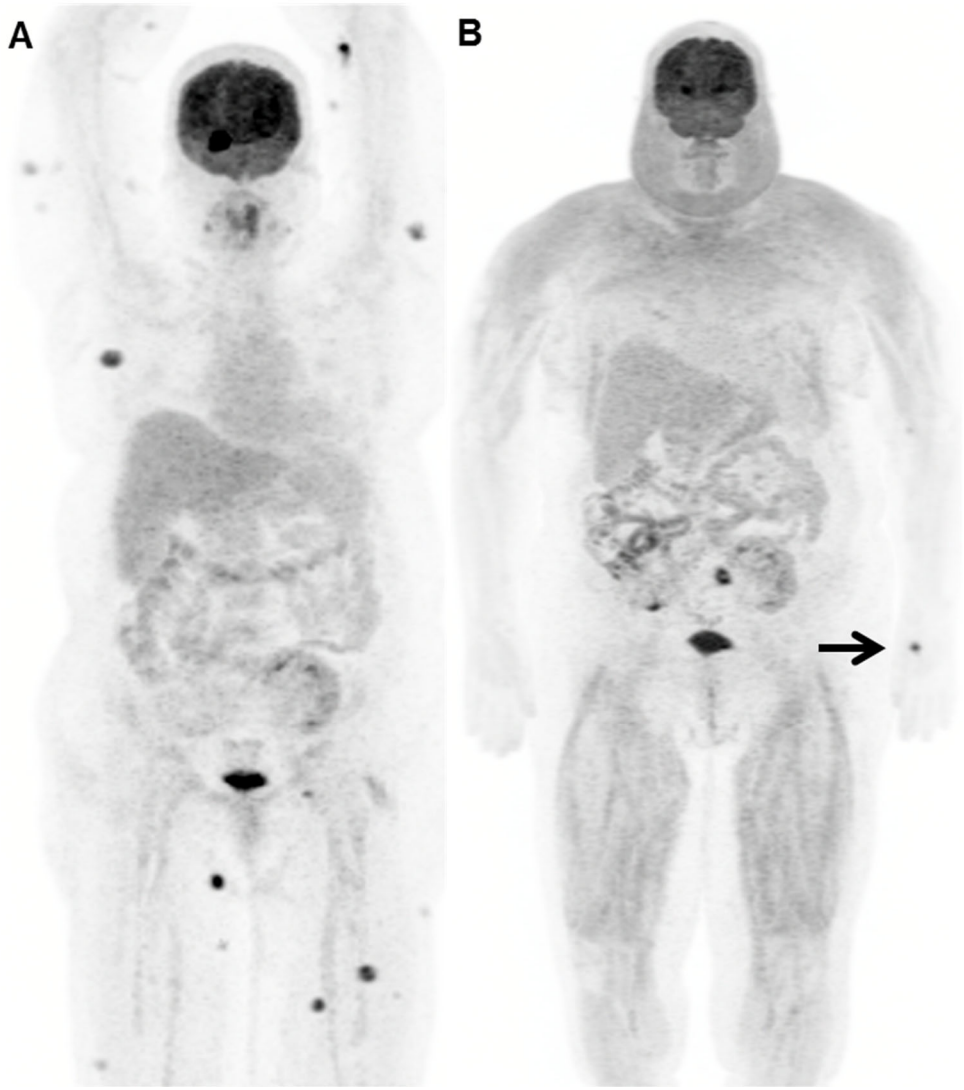

Figure 1. Maximum intensity Projection (MIP) images of baseline (A) and follow-up (B) ^{18}F-FDG PET/CT scan demonstrated resolution of numerous cutaneous and right temporal lobe tracer-avid lesions (Arrow in B indicates ^{18}F-FDG injection site).

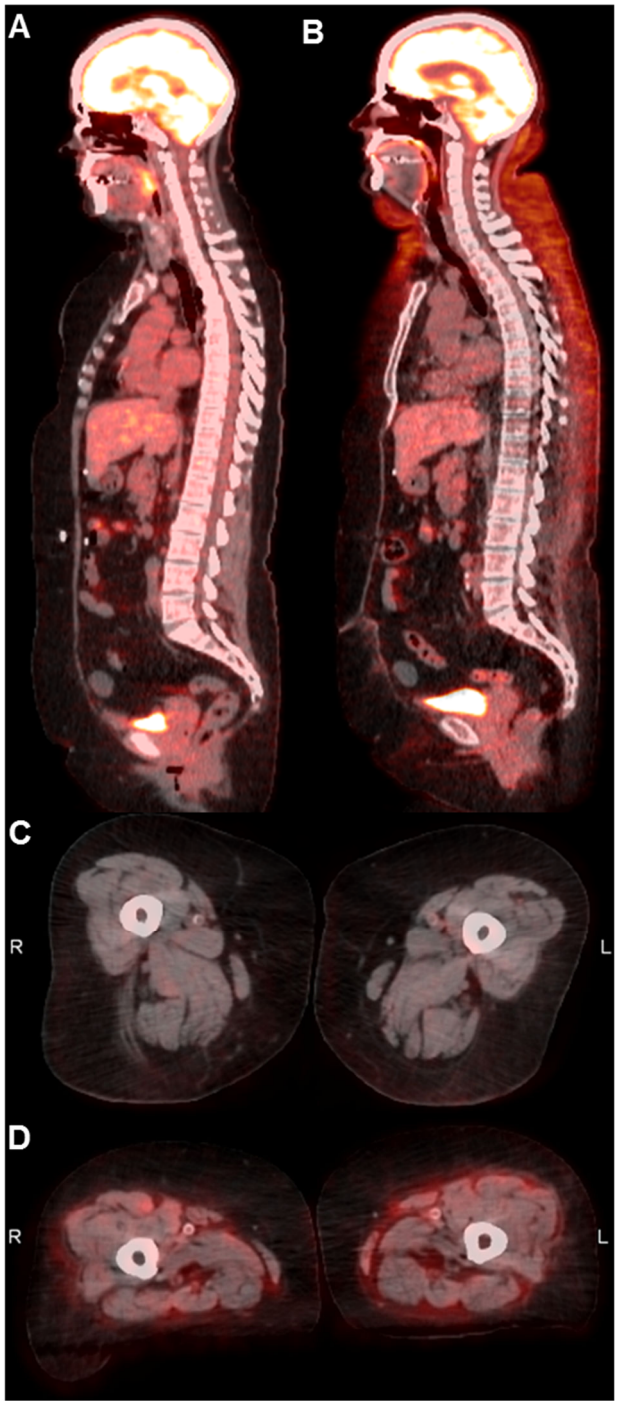

Figure 2. Sagittal fused images at baseline (A) and follow-up (B) showed thickened subcutaneous white adipose tissue with increased ^{18}F-FDG uptake at face, neck and back. Axial fused images of bilateral thighs at baseline (C) and follow-up (D) revealed muscle wasting and hypermetabolic intermuscular adipose tissue.