Tuberculosis With adrenal Insufficiency Mimicking Malignancy in FDG-PET images

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ABSTRACT

Addison's disease may result from adrenal tuberculosis (TB), malignancy, idiopathic adrenal atrophy, blastomycosis or histoplasmosis. Thus, adrenal masses are often characterized by fluorine-18 fluoro-2-deoxy-D-glucose positron emission tomography (18_F FDG-PET), which identifies tumors by their increased glucose metabolism. However, a large number of clinical conditions lead to false positives in PET, often related to inflammation or infection. Herein, we present a patient with adrenal insufficiency associated with bilateral masses and a history of TB. We identified elevated FDG uptake in both adrenal glands that could not be differentiated from primary bilateral adrenal lymphoma or other malignancies. Following adrenalectomy, a final diagnosis of adrenal TB was made. This uncommon case emphasizes that benign adrenal lesions can have increased FDG uptake leading to false-positive results.

Keywords: *Tuberculosis, adrenal insufficiency, malignancy, FDG-PET, adrenal mass.* **Nobel Med 2016; 12(3): 73-76**

FDG-PET GÖRÜNTÜLEMEDE MALİGNENSİYİ TAKLİT EDEN ADRENAL YETMEZLİK İLE BİRLİKTE TÜBERKÜLOZ

ÖZET

Addison hastalığının nedenleri olarak tüberküloz, malignite ve idyopatik adrenal atrofi gibi sebeplere sonradan metastatik tümörler, blastomikozis ve histoplazmozisi de içeren diğer nedenler eklenmiştir. FDG-PET görüntüleme adrenal kitlelerin karakterizasyonunda değerli bir yöntemdir. Enfeksiyon ve enflamasyon FDG-PET görüntülemede başlıca yanlış pozitiflik nedenleri arasında yer almaktadır. Biz de burada, adrenal yetmezliği ile birlikte bilateral adrenal kitlesi ve özgeçmişinde tüberküloz hikayesi olan vakayı sunmaktayız. Her iki adrenal bezde saptadığımız artmış FDG tutulumunu, primer bilateral adrenal lenfoma veya diğer adrenal malignitelerden ayırt edemedik. Adrenalektomi sonrası adrenal tüberküloz olarak kesin tanısı konuldu. Sık görülmeyen bu vakada olduğu gibi benign adrenal lezyonlarda artmış FDG tutulumu yalancı pozitif sonuçlara neden olabilmektedir.

Anahtar kelimeler: Tüberküloz, adrenal yetmezlik, malignite, FDG-PET, adrenal kitle. **Nobel Med 2016; 12(3): 73-76**

INTRODUCTION

Destruction of 90% of the adrenal cortex is the cause of primary adrenal insufficiency or Addison's disease. Autoimmune adrenalitis is presently the principal cause of Addison's disease in developed countries.[1] Other rare causes include histoplasmosis, blastomycosis, metastatic tumors, adrenal hemorrhage and various opportunistic infections due to acquired immunodeficiency syndrome (AIDS).[2,3] In developing countries, however, adrenal tuberculosis (TB) remains the major cause of Addison's disease.[4]

Imaging methods are a cornerstone in the initial diagnosis of adrenal TB. As the major cause of Addison's disease, TB can be initially diagnosed or excluded by imaging modalities such as computed tomography (CT) or magnetic resonance (MR).[5-7] Adrenal masses are often also characterized by fluorine-18 fluoro-2-deoxy-D-glucose (18_F FDG) positron emission tomography/computed tomography (PET/CT), traditionally used to detect tumors by labeling areas of high glucose metabolism. Conversely, a large number of clinical conditions lead to false positives in oncological PET, often related to inflammation or infection. For example, TB generates abnormal FDG uptake.[8,9] Herein, we present a case of bilateral abnormally increased 18_F FDG uptake in a patient with adrenal insufficiency associated with bilateral masses. Following adrenalectomy, a final diagnosis of adrenal TB was made.

CASE REPORT

A 53-year-old male patient was admitted to the outpatient clinic due to prostatism. An abdominal ultrasonography (USG) was performed, which showed a right spherical adrenal mass 40x20 mm in diameter. CT showed 36 HU right adrenal mass 45x27 mm in size and 36 HU left adrenal mass 40x29 mm in size. The patient was referred to the endocrinology department. In the patient's detailed history, no other symptoms were noted. The patient had a 20-pack year history of smoking. Additionally, he received three months of drug therapy due to TB pleurisy 45 years ago. Physical examination was unremarkable. Laboratory findings revealed hyponatremia (124 mmol/L, normal range 136-145 mmol/L) and hyperkalemia 5.6 mmol/L, normal range 3.5-5.1 mmol/L). On hormonal assessment, a low basal cortisol level of 3 µg/dL and high ACTH level of 1190 pg/mL (normal range 0-46 pg/mL) were observed. Therefore, an ACTH stimulation test was performed; the peak cortisol response was 3.9 µg/dL. Twenty-four hour metanefrin excretion was 11 mg/day (0-320) and 24 hour vanyl mandelic acid excretion was 4.2 mg/day (3.3- 6.5). On the basis of history, physical examination, laboratory and dynamic tests, the patient was diagnosed with adrenal failure (AF). The chest CT scan revealed non-specific nodules in the right and left upper lobes.

Whole-body 18_F FDG PET/CT was performed (Figure). Maximum-intensity projection (MIP) and coronal images showed intense uptake in the right adrenal mass (maximum standard uptake value (SUVmax), 6.82) and in the left adrenal mass (SUVmax, 6.68). There was no other pathological 18_F FDG uptake. Uptake patterns were consistent with benign adrenal hyperplasia or malignant invasive lesions.

Since the patient had a history of TB, bilateral adrenal masses and adrenal insufficiency, the possibility of TB was considered. However, due to the 18_F FDG PET/CT findings, malignancy could not been excluded. It was also discussed in a meeting with a surgeon, pathologist, and interventional radiologist. The decision was not to perform FNA as it might be inconclusive in this case. Therefore, the patient underwent bilateral adrenalectomy and the lesions were found to be caseified granulomas (TB) upon pathological examination.

Figure. Dual-modality PET/CT was performed using a Gemini TF TOF PET/CT scanner (Philips Medical Systems, USA). The patient fasted for at least 6 h prior to imaging. The fasting blood glucose level was measured as lower than 140 mg/dL prior to 18_F FDG (3.7 MBq/kg) intravenous injection, performed 60 min prior to scanning. Non-contrast whole-body CT was performed using a 16-slice helical CT. The CT scan data were collected at 50-120 mAs and 90-140 kV and adjusted for the patient's body weight. After the CT scan, an emission scan was obtained from the head to the feet at a rate of 20-60 sec per frame. Attenuation-corrected PET images with CT data were reconstructed using an ordered-subset expectation maximization algorithm (33 subsets, 3 iterations). CT and PET images were co-registered. The maximum standard uptake values (SUVmax) were calculated using the attenuation-corrected images. 18_F FDG PET/CT selected axial PET (A), axial plain CT (B), axial PET/CT fusion (C), coronal PET (D), coronal CT (E), coronal PET/CT fusion (F) images showed bilateral adrenal masses with intense 18_F FDG uptake (SUVmax right, 6.82; SUVmax left, 6.68).

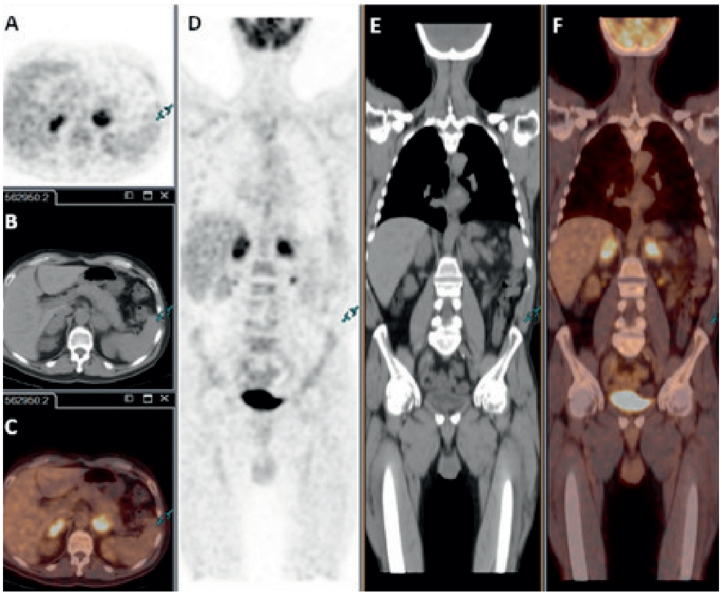

Figure.

DISCUSSION

Differential diagnosis of adrenal TB on the basis of imaging can be difficult, as bilateral adrenal lesions can also result from metastasis, lymphoma, chronic hemorrhage, pheochromocytoma or histoplasmosis. 18_F FDG-PET is generally used to differentiate benign from malignant adrenal masses.[10] In our TB patient, we identified elevated FDG uptake in both adrenal glands, which could not be differentiated from primary bilateral adrenal lymphoma or other malignancies.

Conventional imaging methods used to characterize adrenal lesions, such as unenhanced CT attenuation, enhancement washout CT or chemical-shift MRI, have several limitations for predicting malignancy, indicating the need for new imaging technologies. 18_F FDG PET/CT can assess glucose metabolism, which is accelerated in many cancers.[11] Metabolic imaging using PET is not only complementary to imaging with conventional modalities, but also may be more sensitive because alterations in the metabolism of cancer cells may precede gross anatomical changes. Conversely, 18_F FDG accumulates not only in malignant adrenal tumors but also in 5-10% of benign tumors that mimic metastasis and limit the specificity of 18_F FDG PET/CT imaging.[12-14]

The major cause of false-positive results varies among studies. In previous studies false-positive 18_F FDG PET/CT findings were mainly adrenal adenomas and pheochromocytomas.[13,14]

It has been suggested that the functional state of an adenoma could be a factor determining the intensity of 18_F FDG metabolism, but other researchers have found a lack of correlation between hormonal hypersecretion and F-18 FDG uptake. Several studies have shown that TB can produce high F-18 FDG uptake and limit the specificity of 18_F FDG PET/CT scans by mimicking metastases.[15-19] The findings of Kunikowska *et al*. confirmed that 18_F FDG accumulates in some benign adrenal masses.[20] In their series, an adrenal-to-liver (T/L) SUVmax ratio threshold >1.53 yielded six false-positive results, four adrenal TBs and two benign pheochromocytomas. The benign lesions related to TB showed a hypermetabolic pattern. In one patient with bilateral adrenal TB, 18_F FDG PET/CT showed low FDG uptake, which could have resulted from a lack of granulomatous inflammation due to the local suppressive effect of steroids secreted in the adrenal cortex.

TB still remains a cause of adrenal insufficiency in our country. Especially in patients with a history of TB FDG-PET positivity in bilateral adrenal masses has decreased possibility for malignancy.

CONCLUSION

The intense adrenal 18_F FDG uptake in our case underscores the necessity of considering adrenal TB as a possible differential diagnosis in bilateral adrenal masses in regions where TB is endemic. This is especially important when concurrent adrenal insufficiency is present.

*The authors declare that there are no conflicts of interest.

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