Non-Hodgkin's lymphoma of the testicle and bilateral adrenals detected by ^{18}F-FDG PET/CT

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Received February 23, 2011; Accepted May 11, 2011

DOI: 10.3892/etm.2011.300

Abstract. Lymphoma, particularly non-Hodgkin's lymphoma, may occur in sites other than the lymph nodes, i.e., extranodal lymphoma, which occurs in approximately 40% of total lymphoma cases. However, simultaneous detection of multiple extranodal involvements at presentation is quite uncommon. Here, we report a rare case of a 55-year-old Chinese man with non-Hodgkin's lymphoma of the left testicle and bilateral adrenals as determined by ^{18}F-FDG PET/CT imaging. FDG PET/CT has been successfully employed for lymphoma diagnosis, initial staging, restaging and therapy follow-up. It is useful for assessing both nodal and extranodal involvements. In the present case of lymphoma with involvement of the testicle and bilateral adrenals, ^{18}F-FDG PET/CT played an important role in the diagnosis and assessment of therapeutic response.

Case report

A 55-year-old Chinese male presented with a history of left lumbar pain for 1 month without frequency, urgency or dysuria. He had no fever, his appetite was normal, and no weight loss or gain was noted. The patient had no significant family history of illness. During the clinical examination, he appeared healthy. His blood pressure was 128/78 mmHg, his pulse 80 beats/min and his temperature was 36.2˚C. There was no skin or sclera icterus, and no superficial swollen lymph node was noted. The lungs were clear upon auscultation. The abdomen of the patient was soft and non-tender; there was no hepatomegaly or splenomegaly. Upon neurological examination, the patient appeared alert and orientated to time, place and people. Normal muscle bulk and tone with full strength in both arms and legs were noted.

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Key words: non-Hodgkin's lymphoma, bilateral adrenal, testicle, FDG PET/CT

Routine laboratory tests of blood, urine and feces were normal. CT scan of the abdomen demonstrated large bilateral adrenal masses with heterogenous enhancement. The left adrenal gland measured 6.81x8.78 cm and the right adrenal gland measured 8.22x6.15 cm in its greatest dimension (Fig. 1). Swollen lymph nodes were detected in the abdomen. Based on the CT findings, a provisional diagnosis of adrenal metastases or possible malignant tumor of the adrenals was made.

To further confirm the diagnosis and staging of the disease, an ^{18}F-FDG PET/CT scan was obtained per physician's request. The scan showed high FDG uptake in the bilateral adrenals with a max standard uptake value (SUV) of 29.0 (Fig. 2), high uptake in the retroperitoneal swollen lymph nodes with a max SUV of 24.0 and high focal uptake in the left testicle with a max SUV of 21.0 (Fig. 3), corresponding to a soft tissue nodule on CT. Based on the PET/CT findings, the diagnosis of a primary malignant tumor, e.g., lymphoma, was made and further work-up was recommended.

An ultrasound examination of the testis was subsequently performed and showed a hypoechoic area above the left epididymis, suspicious of a space-occupying lesion.

Finally, several days later, the patient underwent a left orchiectomy. Histopathological examination of the left testicle revealed diffuse large B-cell lymphoma (DLBCL); immunohistochemistry tested positive for cytoplasmic CD20, CD79α and CD117 (Fig. 4). Following the orchiectomy, the patient was treated with two cycles of CHOP chemotherapy (cyclophosphamide, doxorubicin, vincristine and prednisone) which was well tolerated. A mid-cycle ^{18}F-FDG PET/CT was performed 21 days after the first two chemotherapy cycles and demonstrated no abnormal FDG uptake in the regions of the bilateral adrenals and retroperitoneal lymph nodes, which were much smaller or disappeared on CT (Fig. 5). This was followed by another four cycles of chemotherapy.

The final clinical diagnosis of the patient was DLBCL stage IV E.

Discussion

Lymphomas are classified into two main groups, non-Hodgkin's lymphoma (NHL) and Hodgkin's lymphoma (HL). NHL is more common than HL and represents 85% of lymphomas (1). DLBCL constitutes approximately 30% of all NHL cases

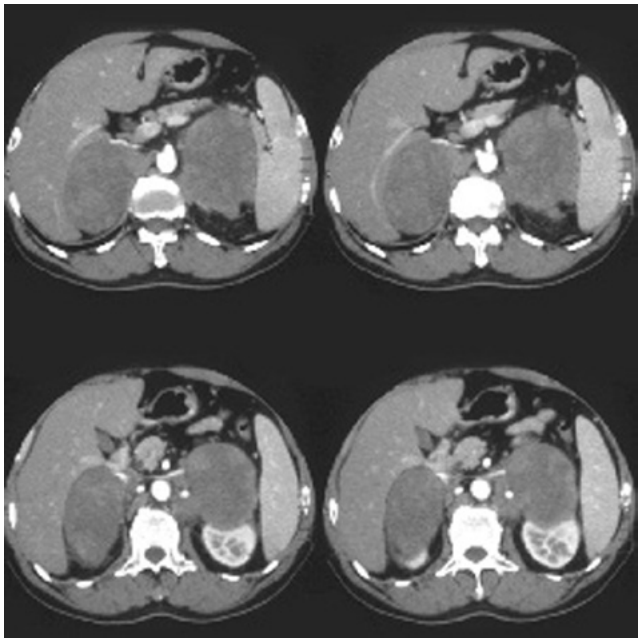

Figure 1. Enhanced CT scan of adrenals.

and typically presents with rapidly enlarging symptomatic masses, most usually due to nodal enlargement. Lymphoma, particularly NHL, may occur in sites other than the lymph nodes, i.e., extranodal lymphoma in approximately 40% of total lymphoma cases (2). Extranodal involvement may appear in various sites, including the lungs, thymus, chest wall, pericardium breast, spleen, pleura, liver, pancreas, gastrointestinal tract, peritoneum, omentum, genitourinary tract, adrenal gland, bone marrow or bone, and the central nervous system. Concurrent detection of multiple extranodal involvements at presentation is quite rare, and the majority of such cases are characterized by gastric or intestinal disease localization (3).

In the present study, the patient was found to have extranodal involvement of both the left testicle and bilateral adrenals, which is exceptionally rare.

A variety of neoplastic processes involve the testes. The most common germ-cell tumors include seminoma, embryonal carcinoma, teratoma, yolk-sac tumor and choriocarcinoma. Germ-cell tumors are the most common solid tumors in men between 20 and 35 years of age. Seminomas represent 50% of all germ-cell tumors and usually occur in men in their 30s. Non-seminomatous germ-cell tumors include Soki Leydig cell tumor, fibroma, fibrosarcoma, lymphoma and leukemia. Primary testicular NHL was first described as a clinical entity in 1866 (4). It is a rare disease and accounts for 1% of all NHLs, 2% of all extranodal lymphomas and 5% of all testicular neoplasms (5,6).

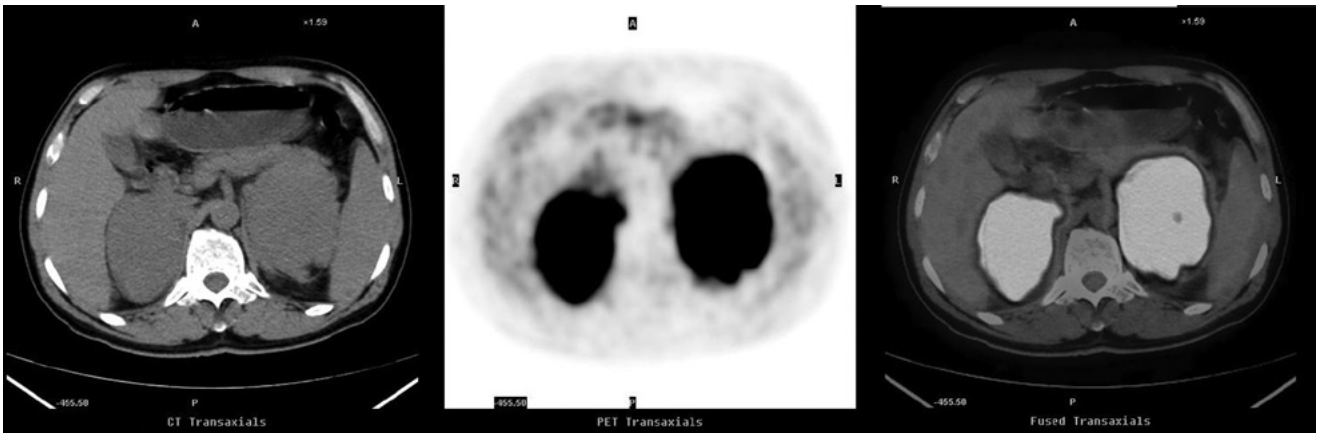

Figure 2. First ^{18}F-FDG PET/CT scan. High uptake of tracer in the bilateral adrenals with max SUV 19.5 and 29.0, respectively.

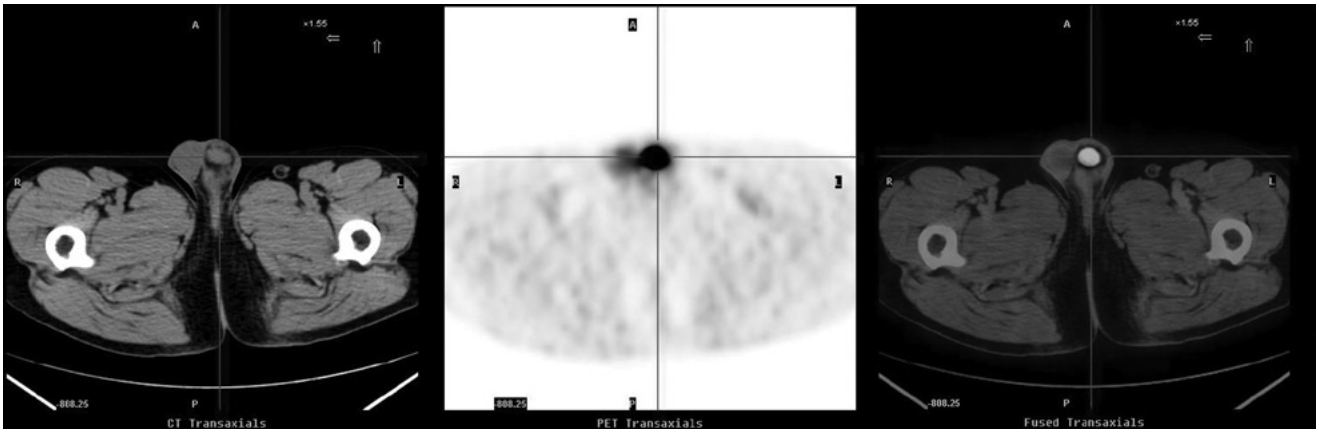

Figure 3. First ^{18}F-FDG PET/CT scan. High uptake of tracer in the left testicle with max SUV 21.0.

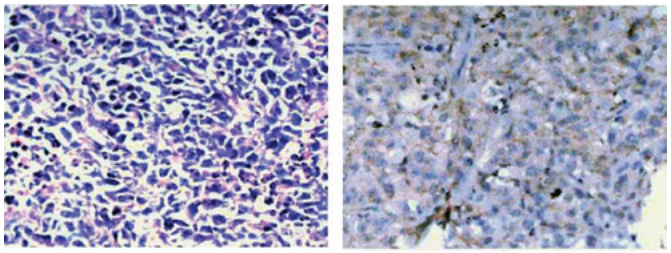

Figure 4. Immunohistochemistry of the left testicle: CD3(-), CD20(+), CD79α(+), PLAP(-), CD117(+), CD30(-) and CK(weak +).

Bilateral adrenal masses are commonly metastatic, but are also found in adrenal tuberculosis, pheochromocytoma and adrenal cortical carcinoma. NHL arising from endocrine glands represents only 3% of extranodal lymphomas (7). Secondary involvement of the adrenal gland with NHL has been reported to occur in up to 25% of patients during the course of the disease (8). However, primary adrenal lymphoma (PAL) is extremely rare. Most of the patients with PAL usually present with bilateral adrenal masses with no disease elsewhere.

In the present study, the patient was initially found to have bilateral adrenal masses by CT. CT scanning is considered the most important anatomic imaging modality for evaluating adrenal masses or masses in most other sites. The CT attenuation value has been helpful in differentiating a benign lesion from a malignant lesion (9). The sensitivity and specificity for characterizing a lesion display wide variability depending on the density of the lesion. A meta-analysis reported that the sensitivity for benign lesions ranged from 47% at a threshold of 2 HU to 88% at a threshold of 20 HU (10). Delayed enhanced CT can aid in analyzing the washout patterns noted in adrenal lesions (11). Mean CT attenuation of adrenal masses on contrast-enhanced CT has limited usefulness due to too much overlap between the benign and malignant lesions (9,12).

Unlike CT, FDG/PET measures glucose metabolism. It has been shown to play an important role in diagnosis, staging, monitoring response to treatment and detecting recurrence of various types of cancers. The first reports of ^{18}F-FDG PET for lymphoma imaging were published more than 20 years ago (13). As most lymphomas show high levels of ^{18}F-FDG uptake, subsequent studies investigating the value of ^{18}F-FDG PET in the diagnosis and staging of lymphomas have been carried out. These studies almost invariably demonstrated an extremely high sensitivity for HL and high-grade or aggressive NHL (14). ^{18}F-FDG PET consistently identified nodal and extranodal disease sites that were failed to be detected by conventional staging methods, including CT. ^{18}F-FDG PET also improved the characterization of lesions that were equivocal on other types of imaging. Thus, FDG-PET has become an established imaging modality for staging, restaging and monitoring therapy. PET/CT imaging is more accurate than PET or CT alone. PET/CT has evolved to become the modality of choice for the staging of nodal and extranodal lymphoma, for assessing therapeutic response and for establishing patient prognosis (15).

In the present study, simultaneous involvement of the bilateral adrenals and the left testicle was detected by ^{18}F-FDG PET/CT; therefore, the diagnosis of a primary malignant tumor, e.g., lymphoma, was made. It is well known that the final diagnosis of lymphoma is based on the pathological diagnosis. However, for ethical reasons, pathological diagnosis may not be possible for all lesions and abnormalities found. Thus, PET or PET/CT is useful for the diagnosis of lymphoma and usually detects unusual extranodal involvement (16,17), as illustrated in the present report. Assessment of early therapeutic response using PET/CT was also performed in our case.

In 2007, the consensus recommendations regarding the use of FDG/PET for the assessment of response after the treatment of patients with lymphoma were published by the Imaging Subcommittee of the International Harmonization Project (18). ^{18}F-FDG PET/CT is currently the standard procedure for assessment of the post-treatment response for most lymphoma subtypes. In addition, early response monitoring with ^{18}F-FDG PET is an effective tool for risk-adapted lymphoma therapy. This method may improve the outcome of patients who exhibit a poor respond to the initial therapy and who may benefit from an early modification of the treatment. ^{18}F-FDG PET may also allow individualized therapy for patients who have a low risk of treatment failure and who would otherwise be unnecessarily administered toxic treatment (19).

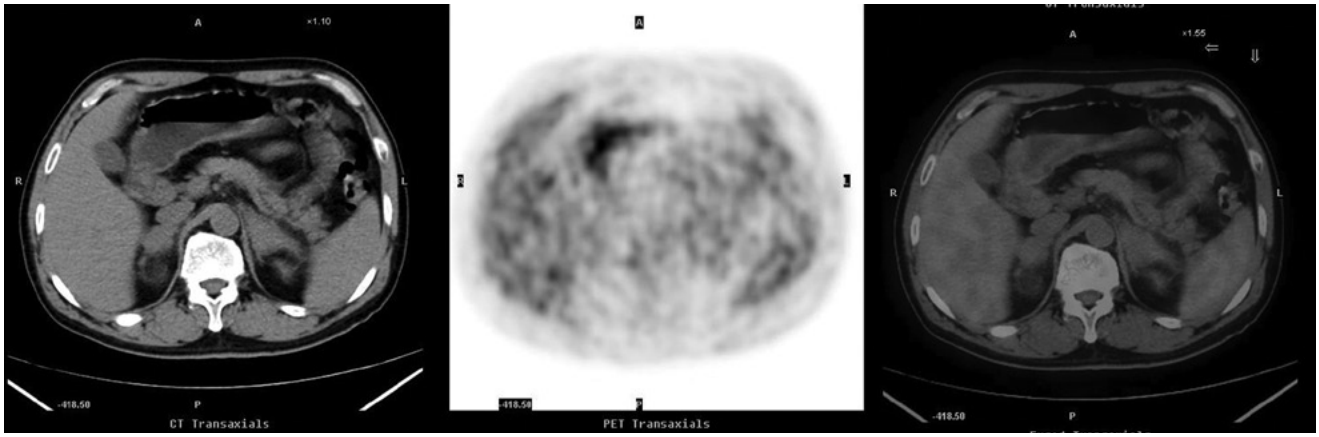

Figure 5. Second ^{18}F-FDG PET/CT scan after treatment: No high uptake of tracer in bilateral adrenals.

Additionally, the National Comprehensive Cancer Network has incorporated FDG-PET in the evaluation and management algorithm for most HL and NHL patients (20). The utilization of FDG-PET (PET/CT where available) is recommended in clinical settings as a baseline for lymphomas that are potentially curative (HL and DLBCL), as a baseline to exclude systemic disease in clinically localized lymphomas (HL, DLBCL, follicular lymphoma, mantle cell lymphoma, AIDS-related B-cell lymphoma, nodal and splenic marginal zone lymphoma, peripheral T-cell lymphoma and mucosa-associated lymphoid tumors), to evaluate residual masses and to monitor treatment of aggressive lymphomas (HL and DLBCL).

Over the last two decades, FDG PET or PET/CT has been successfully used to detect nodal and extranodal sites, to stage, restage, monitor therapy, detect recurrent lymphomas and establish patient prognosis (21).

In conclusion, a diagnosis of lymphoma should be considered when a patient shows a high metabolism of glucose in FDG PET or PET/CT imaging in two remote extranodal sites, e.g., bilateral adrenals and the testicle in our case. ^{18}F-FDG PET/CT is useful for the detection and assessment of the therapeutic response of lymphoma in addition to staging, restaging and detection of recurrent lymphomas.

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