Case Report

The diagnostic yield of fluorine-18 fluorodeoxyglucose positron emission tomography-computed tomography in recurrent testicular seminoma

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Abstract

The use of positron emission tomography-computed tomography (PET-CT) scan imaging is undoubtedly a significant evolution in oncological urology, although at present of limited use in every day urology practice. The aim of this study is to highlight the indication and diagnostic accuracy of fluorine-18 fluorodeoxyglucose PET/CT in the staging of a patient with metachronous bilateral testicular seminoma, elevated tumor markers, and equivocal conventional imaging findings.

Key Words: Bilateral seminoma, chemotherapy, fluorine-18 fluorodeoxyglucose positron emission tomography-computed tomography scan, testis tumors

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INTRODUCTION

Testicular cancer is the most frequent malignancy in men between 20 and 40 years of age, with an incidence of 4–10/100,000.[1] Germ cell testis tumors, generally, are classified to pure seminomas and to a more heterogeneous group of nonseminomatous tumors, which include teratomas, chorionic carcinomas, embryonal cell tumors, and mixed tumors.[2]

The incidence of seminomas has been on the rise over the last 30 years. About 25% of patients with seminoma present with advanced disease and around 15–20% of Stage I are harboring undetected metastatic disease, usually in the retroperitoneum that will likely cause tumor relapse after orchiectomy alone.[3]

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CASE REPORT

We report the case of a 32-year-old patient who underwent a left orchiectomy for a pT1 pure testicular seminoma in 2009. The patient did not consent to adjuvant chemotherapy at that time and opted for surveillance. His follow-up imaging with computed tomography (CT) scan and tumor markers were normal until September 2013, when he presented with a palpable mass in the right hemiscrotum and elevated

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tumor markers (β-human chorionic gonadotropin [β-hCG] 400 ng/ml, lactate dehydrogenase 125 IU/L). The chest CT scan was unremarkable. In the abdominal CT images, at the level of the kidney, in the retroperitoneal para-aortic space, there was soft tissue density that erased the suspicion of an abnormal lymph node [Figure 1]. In addition, given the highly elevated levels of β-HCG, a nonseminomatous tumor was also suspected and imaging with whole body positron emission tomography (PET)/CT was considered. A PET/CT scan was performed with a dedicated PET system, covering an axial field-of-view of 15.2 cm. PET images revealed an abnormal accumulation of fluorine-18 fluorodeoxyglucose (FDG) in the para-aortic space [Figure 2].

The patient underwent a right orchiectomy for what was considered a metachronous right testicular tumor and histology revealed a seminoma with syncytiotrophoblast elements. As the PET/CT findings together with the elevated β-HCG were considered evidence of retroperitoneal disease, we suggested a retroperitoneal lymph node dissection (RPLND). Taking into consideration that his disease was now upstaged to $T_1N_1M_0$, the patient denied RPLND and was scheduled for adjuvant chemotherapy with three cycles of bleomycin, etoposide, and cisplatin. The patient responded well to therapy and at 1-year follow–up, his tumor markers were within normal range, and the prechemotherapy enlarged lymph node was undetectable at follow-up PET/CT [Figure 3].

DISCUSSION

Germ cell tumors are the most frequent type of testicular tumors and the most common malignancies in men occur between the ages of 15 and 34 years. It has been well recognized that men who had one testicular germ cell tumor (TGCT) are at an increased risk of developing a germ cell tumor in the other testis,[4] with the incidence of bilateral tumors varying between 1% and 7.8%.[5,6]

Although it is a general rule that pure seminomas do not produce elevated tumor markers, approximately 30% of patients with pure seminoma of the testis present with mild elevation of β-hCG due to the presence of syncytiotrophoblastic giant cells, as in the case presented. However, in those cases, β-hCG levels are usually <500 IU/L and higher levels are rarely found.[7]

According to data from the M. D. Anderson Cancer Center, the incidence of bilateral testicular tumors is greater for seminoma patients compared to patients with nonseminoma. Moreover, patients presenting with seminoma at a younger age had an increased risk of developing a contralateral tumor while no significant concordance was found between the histologic type of the first and the second tumor.[8]

In the same study of 2431 men harboring testis tumors, there were 24 patients (1%) with bilateral testicular tumors, of which 14 (70%) had tumor recurrence within 5 years while the other 6 (30%) developed a second malignancy within a 10–15 years interval. Ondruš *et al*.[6] have described similar findings from 63 patients with metachronous testis tumors, where 21 men (33.3%) were diagnosed with a second testis tumor within 5 years, 20 patients (31.2%) after a follow-up period longer than 10 years, and 5 patients (7.9%) after a follow-up of 20 years.

In most men with bilateral TGCTs, common etiological factors likely predisposed them to both primary tumors. Begg in 2011[9] reasoned that if seminoma and nonseminoma tumors have distinct etiologies, then, among bilateral TGCT

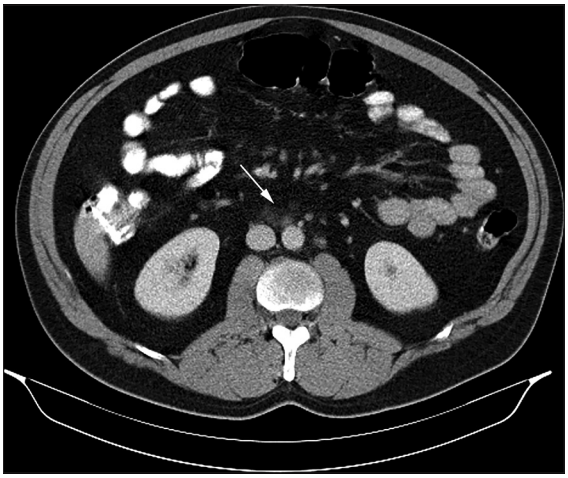

Figure 1: Abdominal computer tomography image with intravenous contrast administration, at renal level. In the retroperitoneal para-aortic space, it shows soft tissue density (arrow) that erased the suspicion of an abnormal lymph node

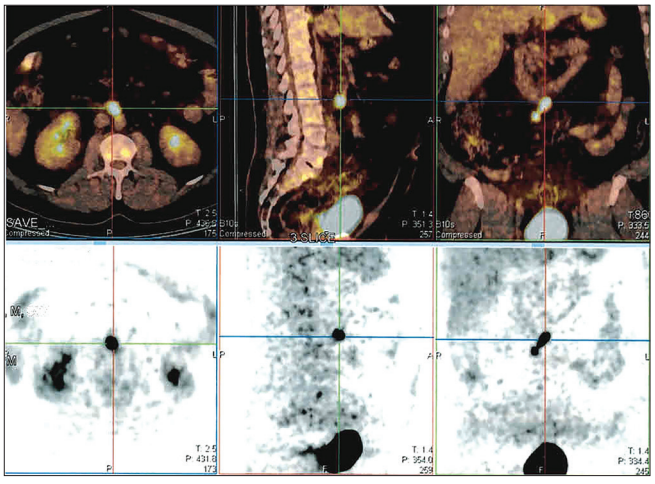

Figure 2: Prior to chemotherapy, positron emission tomography-computer tomography demonstrating an enlarged para-aortic lymph node confirming the site of testis tumor relapse

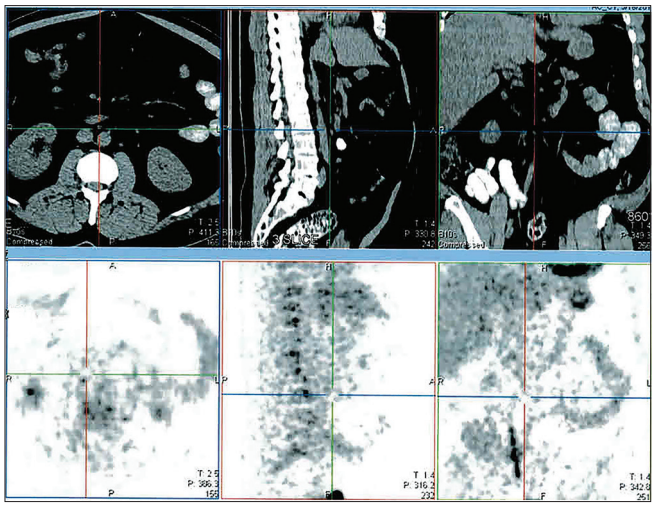

Figure 3: Follow-up positron emission tomography-computer tomography study clearly demonstrating no tracer uptake in the para-aortic lymph nodes following three cycles of chemotherapy

patients, a man's first and second TGCT are likely to be the same in accordance with a history of exposure to either seminoma-related or nonseminoma-related risk factors.

Regarding the time to recurrence of testicular tumors, Andreassen *et al*.[10] observed a significantly longer time interval between first and second cancers among patients with initial nonseminomatous germ cell tumors (NSGCTs) (6.3 years) compared to patients with a primary seminoma (4.6 years). However, in their analysis of 20 patients with metachronous tumors, the difference between these two intervals lacked significance (9.2 years vs. 6.9 years).

Tandstad *et al*.[11] in a study with 1003 patients with clinical Stage I, nonseminomatous testicular germ cell cancer (TGCC) demonstrated that 15% of patients with metachronous TGCC presented with metastatic disease, as in our case.

With regard to the effect of chemotherapy in the recurrence rates of TGCC, although data from the MRC TE19 trial indicate that the incidence of contralateral TGCC may be reduced in Stage I seminomatous patients treated with adjuvant carboplatin,[12] it is possible that adjuvant carboplatin only postpones the development of contralateral TGCC.[13] However, Andreassen *et al*.[10] were able to demonstrate that patients treated with cisplatin-based chemotherapy for metastatic disease may have a lower risk of developing contralateral testicular cancer and four or more courses of cisplatin-based chemotherapy seem to reduce the 5-year probability of developing contralateral TGCC in patients with untreated intratubular germ cell neoplasia.[14]

Follow-up guidelines: Stage I seminom

Based on the Spanish Society of Medical Oncology clinical guidelines for testicular tumors, published in 2011[15] after orchiectomy, the clinical staging should include serial tumor marker tests (with the alpha-fetoprotein to be negative), abdominal CT scan, and chest X-ray films. The European Society for Medical Oncology guidelines[16] recommend physical examination and tumors markers tests 3 times/year for 2 years and then once/year for the next 3 years, chest X-ray and abdominal CT twice/year for the first 2 years, and then once every 18 months for the next 3 years. In general, they suggest that the follow-up schedule needs to be adapted according to national and institutional requirements, but the trend is to limit the unnecessary CT scans and the exposure to radiation of the relatively young age of testicular cancer patients.

The criterion for the detection of positive nodal disease at CT is based on the size (>1 cm diameter of short axis) and morphology (round lymph nodes >0.8 cm) and, thus, lack the desired accuracy for characterizing lymph nodes,[14] leading to low sensitivity which is not >36%. On the other hand, standard magnetic resonance imaging (MRI) techniques (T1, T2, and T1+ contrast sequences) have higher sensitivity (45.5%) in the detection of metastatic lymph nodes while Harisinghani *et al*.[17] suggest that lymphotropic superparamagnetic nanoparticles contrast agents can lead to the increase of the sensitivity of MRI from 45.4% to 100%, with a specificity of 95.7%. However, MRI is not widely used in testicular cancer staging because of its cost, prolonged scanning time, its relative unavailability, and lack of radiologists with sufficient experience interpreting abdominal MRI.[18]

Furthermore at the moment, PET-CT scanning has no role in the routine follow-up of TGCT patients,[16] although it might be a useful tool in equivocal cases, where the conventional imaging erases the suspicion of metastatic disease in the retroperitoneal space, as it can identify metabolically active tissues in metastatic deposits. There are some papers in the literature where they study the clinical impact of PET/CT on the management of the testicular tumors, but the results are controversial as the number of patients are small and is difficult to draw safe conclusions.[19-23] In the question, if we can rely only on PET/CT in the follow-up of advanced seminoma patients, the answer is negative. However, Ambrosini *et al*.[24] showed in their paper that PET is superior for lymph node staging compared to CT (83% and 71%, respectively) with higher sensitivity and specificity and negative and positive predictive values (66%, 98%, 78%, and 95% for PET, and 41%, 95%, 67%, and 87% for CT, respectively) and it would be an useful examination in the evaluation of equivocal cases.

CONCLUSIONS

The case presented highlights the superiority of FDG PET/CT in depicting lymph node disease with greater

accuracy and sensitivity compared to conventional CT. Patients with testicular tumors are more likely to benefit from PET/CT in terms of accurate staging and treatment planning, although the PET/CT imaging is currently indicated in cases where CT findings are equivocal or inconclusive.

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Conflicts of interest

There are no conflicts of interest.

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