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Positive FDG-PET/CT Scans of a Residual Seminoma after Chemotherapy and Radiotherapy: Case Report and Review of the Literature

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Keywords

Residual seminoma; fluorine-18 deoxyglucose–positron-emission tomographic–computed tomographic scan; chemotherapy; radiotherapy

Introduction

Classical seminoma is exquisitely chemosensitive, and detecting viable residual disease after chemotherapy, even for high-volume disease, is uncommon. In the case of retroperitoneal seminoma, up to 80% of patients will have residual masses postchemotherapy,¹ so a primary concern is determining whether those residual masses contain viable tumor cells. This will dictate whether the patient needs further treatment or just active surveillance. Currently, fluorine-18 deoxyglucose (FDG)–positron-emission tomographic–CT (FDG-PET/CT) is the best noninvasive modality for predicting the presence of viable residual tumor in patients with post-chemotherapy residual masses.

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We describe here, to our best knowledge, the first case of a false positive FDG-PET/CT scan of a residual seminoma after chemotherapy followed by radiotherapy.

Case Report

A 44-year-old man had been experiencing intermittent symptoms of heartburn and abdominal discomfort for 6 months. In May 2008, a month before we first saw him, he had sought medical attention for a right abdominal mass. Abdominal and pelvic computed tomographic (CT) scans had shown a large (9.6×8.4 cm) retroperitoneal mass. The immunohistopathologic characteristics of a specimen obtained during a biopsy were consistent with seminoma (OCT3/4 and PLAP positivity).

The patient came to The University of Texas MD Anderson Cancer Center in early June 2008 for further evaluation. On CT scanning, the retroperitoneal mass had increased to 12×10 cm (Figure 1, transverse image, June 8, 2008). No evidence of metastasis was noted on brain magnetic resonance imaging (MRI) or chest CT. Testicular sonography revealed normal-size testes with no focal abnormalities. Serum analysis revealed high lactate dehydrogenase (LDH; 2,142 U/L) and beta human chorionic gonadotropin (β -hCG; 9.1 mIU/mL) and slightly elevated LDH isoenzyme 1 (39%) concentrations; α -fetoprotein was normal.

Treatment was initiated with four courses of etoposide and cisplatin. After the first cycle, the patient's heartburn and abdominal discomfort dissipated and his β -hCG decreased to less than 1 mIU/mL.

Four weeks after first-line chemotherapy was completed, FDG-PET/CT scanning showed a 7.7-cm residual tumor with a 9.8 maximal standardized uptake value (SUV). Serum LDH level was 544 U/L. A specimen of that mass obtained during biopsy revealed no viable tumor. However, given the continued activity apparent on PET scanning, we were concerned about the presence of viable tumor and thus referred him to our radiation oncology department for consolidation radiotherapy (30 Gy in 15 fractions).

Six months after completion of the radiotherapy, FDG-PET/CT scanning was repeated. The tumor's size and metabolic activity had decreased (from 7.7×5.2 to 6.2×4.6 cm; maximal SUV, 8.7), and the patient was doing well clinically except for grade 1 sensory neuropathy (minimal paresthesia in fingertips) from the cisplatin chemotherapy. Serum LDH level was 491 U/L.

He was observed closely for another 3 months, and then FDG-PET/CT scanning was performed again (July 15, 2009, 9 months after completion of radiotherapy). Images showed a stable retroperitoneal mass, although its metabolic activity had increased slightly (maximal SUV, 10.9) (Figure 2A, transverse and figure 2B, full-body images). Serum LDH level was 446 U/L.

Because of the residual tumor's continuing hypermetabolic activity, the patient was referred to the urology department. A multidisciplinary conference led to the decision to resect the tumor with diagnostic and therapeutic intent. The patient tolerated surgery well and was

discharged from the hospital a week later (September 2, 2009). Histopathologic analysis of the resected mass revealed extensive necrosis, histiocytes, and giant cell reaction but no evidence of viable tumor.

Three weeks after his surgery, the patient returned with marked abdominal ascites. Weekly paracentesis was begun, which drained up to 9 L weekly. He also began physical therapy to manage his lymphedema, which was causing limited mobility, shortness of breath, and early satiety.

The patient was readmitted to the hospital on November 27, 2009, for a 1-month trial of total parenteral nutrition to help manage the refractory ascites. All of these measures failed to control it, however, and he continued to require weekly paracentesis. His nutritional status deteriorated despite continuing parenteral nutrition, and his mobility was substantially reduced.

In another attempt to control the ascites and improve his quality of life, a retroperitoneal–venous shunt with a pump was placed. After 10 months, his condition had improved, and the shunt was removed on November 9, 2010. When we wrote this report, the patient was still alive and well, more than 5 years after the completion of chemotherapy.

Discussion

Before the widespread use of FDG-PET/CT scanning, investigators relied on the size of the mass to predict the presence of a viable seminoma.^{2,3} Because it was widely believed that tumors larger than 3 cm are much more likely than smaller ones to contain viable cancer, surgical resection was recommended by some investigators for any tumor larger than that.^{2–4} Others simply recommended active surveillance regardless of the tumor's size, saving further therapy until the disease progressed.⁵ After all, tumor size alone does *not* indicate the viability of a mass, and surgical exploration of residual masses is not only invasive, it also may increase the risk of acute morbidity because of desmoplastic reactions that can occur within the treated tumor.⁶

Since the late 1990s, FDG-PET scanning has been used to help improve the prediction of viable tumors. For example, in 1999, Ganjoo and colleagues⁷ prospectively evaluated PET scans of 29 seminoma patients with bulky residual tumors postchemotherapy. Although they found no apparent benefit of using PET in this setting, their study was limited by the small number of patients and the fact that only one patient had a positive scan. Further, PET technology was still evolving at that time.

Subsequently, other researchers conducting similar work have concluded that PET scanning is valuable for ruling out the presence of viable disease in residual masses.^{8,9} In the SEMPET trial, FDG-PET/CT scanning was used in 51 patients who had metastatic pure seminoma with radiographically defined residual masses postchemotherapy.^{10,11} The imaging findings were correlated with either the histologic characteristics of the resected lesion or the clinical outcome, as documented on CT scans, tumor-marker assessments, and/or physical examination during follow-up. The CT-determined size of the residual lesions as 3 cm or smaller or larger than 3 cm was also correlated with the presence or

absence of viable residual tumor. The study investigators found that the specificity, sensitivity, positive predictive value (PPV), and negative predictive value (NPV) of FDG-PET/CT were 100%, 80%, 100%, and 96%, respectively, whereas those respective values were 74%, 70%, 37%, and 92% for CT of the residual tumor by size alone.^{10,11} Thus, with 100% specificity and PPV, the results of the SEMPET trial clearly favored the use of PET over CT alone for predicting viability of postchemotherapy residual tumors in seminoma patients.¹¹

The results of those studies were included in a recent meta-analysis to evaluate the diagnostic accuracy of FDG-PET/CT in predicting viable residual tumors after chemotherapy in patients with metastatic seminoma.¹² PET positivity was compared with data obtained by assessing residual tumor size (<3 or ≥3 cm) with CT scans alone. In this meta-analysis, which included 130 patients in four studies, FDG-PET/CT scanning was superior to CT-determined tumor size alone in predicting tumor viability: specificity (92% vs. 59%), sensitivity (72% vs. 63%), PPV (70% vs. 28%), and NPV (93% vs. 86%).¹² The less-than-100% PPV of PET scanning in this meta-analysis resulted from the inclusion of the data of Ganjoo et al.⁷

FDG-PET/CT is thus currently the best noninvasive modality for predicting the presence of viable residual tumor in patients with postchemotherapy residual masses and for making treatment decisions [observation vs. retroperitoneal lymph node dissection (RPLND) vs. chemotherapy and/or radiotherapy]. The SEMPET trial findings^{10,11} led to the development of the European Germ Cell Cancer Consensus Group guidelines, which support the use of PET in this setting.^{13,14} Further, the current guidelines from the U.S. National Cancer Comprehensive Network recommend the use of PET in the case of residual tumors larger than 3 cm after chemotherapy for pure seminoma.¹⁵

Because of the reported 100% specificity and PPV of PET scanning, the published treatment guidelines that support the use of PET scanning, and the results of our multiple PET scans that suggested tumor viability in the case of our patient, we took the further steps of prescribing postchemotherapy radiotherapy, followed by RPLND and tumor resection. Despite the continually positive FDG-PET/CT scans, however, we learned—only postsurgically—that our patient's residual mass actually did *not* contain any viable tumor cells, and he was thus unnecessarily subjected to surgery and the major postsurgical complications he experienced.

Our patient had the first FDG-PET/CT after 4 weeks of completing of the chemotherapy. This is at the lower bound of the range utilized in the SEMPET trial which is 4–12 weeks.¹¹ However, a longer interval is advisable for clinical practice as there are a proportion of cases showing slow decline of FDG uptake that can generate confusion regarding the need for radiotherapy. We find it interesting that our patient's FDG-PET/CT scanning results were still positive 11 months and 9 months after the completion of chemotherapy and radiotherapy, respectively. It is possible that persistent inflammatory changes, as evidenced by the presence of histiocytes and giant cell reaction within our patient's resected residual mass, account for the false-positive results.

We present this case to raise clinicians' awareness that even when FDG-PET/CT findings indicate viability in residual masses after chemotherapy for seminoma, one may still want to consider those findings to be falsely positive, if the seminoma is indeed a classic seminoma. Conceivably, refractory seminomas may harbor nonseminomatous components¹⁶ that might require additional chemotherapy or surgery, as in the case of teratomas that are not detected on FDG-PET/CT scanning.

Conclusion

To our knowledge, this is the first case of a false positive FDG-PET/CT scan of a residual seminoma after chemotherapy followed by radiotherapy. The decision to undertake salvage radiotherapy (the benefit of which for seminoma that persists after chemotherapy is still somewhat controversial^{17,18}) or surgical exploration in the event of positive FDG-PET/CT scans of a residual seminoma after chemotherapy and/or radiotherapy should depend on a biopsy result that is positive for viability of tumor cells; otherwise, active surveillance would be a valid option for patients with such disease.

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Clinical Practice Points

- Classical seminoma is exquisitely chemosensitive and detecting viable residual disease after chemotherapy is uncommon.
- Up to 80% of patients with retroperitoneal seminoma have residual masses post chemotherapy.
- Currently, FDG-PET/CT scan is the best noninvasive modality for predicting the presence of viable residual tumor in patients with post-chemotherapy residual masses
- Here we describe, to our best knowledge, the first case of a false positive FDGPET/ CT scan of a residual seminoma after chemotherapy followed by radiotherapy.

Figure 1.
CT of the abdomen revealed retroperitoneal mass (arrow).

Figure 2.
FDG-PET/CT scanning revealed a retroperitoneal mass, with maximal SUV of 10.9 (arrow)
(A) transverse image and (B) full-body image.