[¹⁸F]Fluorodeoxyglucose Positron Emission Tomography–Guided Therapy in Metastatic Adrenocortical Carcinoma: An Illustrative Case

Introduction

Adrenocortical carcinoma (ACC) is a rare malignancy with high rates of morbidity and mortality. When feasible, complete surgical resection is the most effective therapy for ACC, which yields the best patient survival rates; however, for the many patients who present with advanced disease, the benefits of major surgical intervention are questionable.¹ Adjuvant chemotherapy is often used after incomplete surgical resection of primary ACC and in patients with metastatic disease. Although little data has been published about the use of neoadjuvant chemotherapy for ACC, some patients may benefit from neoadjuvant systemic therapy that can help control distant metastases, reduce the size of primary tumor, and make surgical resection possible.

[¹⁸F]Fluorodeoxyglucose (FDG) positron emission tomography (PET) is widely used to detect areas of increased glucose uptake, which are associated with malignancy; FDG-PET also provides functional information about glycolytic activity in tumors, including ACC.^{2,3} FDG-PET has been reported to have a higher sensitivity for distant metastases than computed tomography (CT) of the chest, abdomen, and pelvis, although the two forms of imaging may have complementary roles.⁴⁻⁷ To our knowledge, the use of FDG-PET in patients with ACC to monitor responses to chemotherapy or to help in the planning of surgical interventions has not been described. In this article, we report the case of a patient with metastatic ACC who underwent neoadjuvant chemotherapy followed by surgical resection; FDG-PET/CT was instrumental in guiding the treatment plan, including the duration of chemotherapy and the timing and extent of surgery.

Case Report

During the workup for newly diagnosed hypertension, a 38-year-old white man was found to have a mass in the left upper abdominal quadrant on ultrasound imaging. CT of the abdomen confirmed the presence of a 14.7-cm heterogeneous left adrenal mass with a tumor thrombus that extended into the left renal vein, inferior vena cava (IVC), and portal vein, with multiple hepatic metastases, para-aortic lymphadenopathy, and a possible pulmonary metastasis (an axial CT scan of the abdomen, which shows a heterogeneous left adrenal mass [arrow] with a hypodense area in the liver [arrowhead] that were compatible with hepatic metastasis, is presented in Fig 1). Findings from a CT-guided biopsy of the adrenal mass were suggestive of ACC, with a Ki-67 labeling index of 15% (Fig 2; immunohistochemistry staining; original magnification ×200).

The patient was referred to the University of Texas MD Anderson cancer center and reported having stable weight and denied having muscle weakness, striae, palpitations, or other noteworthy complaints. There was no family history of cancer. On physical examination, the blood pressure of the patient was 170/97 mmHg, and his

Fig 1.

heart rate was 90 beats per minute. The patient had mild facial plethora with a subtle cushingoid appearance and, on deep palpation, moderate tenderness without rebound or rigidity in the left upper quadrant of the abdomen. Laboratory testing revealed a serum cortisol concentration of 29 μ g/dL and undetectable adrenocorticotrophic hormone, which were suggestive of autonomous cortisol production. FDG-PET/CT imaging was done for staging purposes and revealed evidence of an increased uptake in the left adrenal mass with vascular extension and distant metastases (Fig 3A, coronal whole-body FDG-PET shows the left adrenal mass [arrow] with hepatic metastases [arrowheads]; Fig 3B, fused axial PET/CT image shows an increased FDG uptake in the left adrenal mass [white arrow], hepatic metastases [arrowhead], and portal vein thrombus [black arrow]). Because of the presence of distant metastases and intravascular thrombus, neoadjuvant systemic therapy

Fig 2.

Fig 3.

was selected as the first-line treatment instead of surgery. The chemotherapy protocol included 28-day cycles of etoposide (100 mg/m² per day on days 5, 6, and 7), doxorubicin (20 mg/m² per day on days 1 and 8), and cisplatin (40 mg/m² per day on days 2 and 9). The patient also

Fig 4.

received concomitant mitotane therapy with a dose that reached 5 g per day and achieved a therapeutic level of 17.4 μ g/mL (target, 14 to 21 μ g/mL).

After five cycles of chemotherapy, repeat CT imaging revealed a partial response to therapy, per Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 (Fig 4; axial CT images postchemotherapy that illustrate the reduced size of the primary adrenal mass [arrow] and liver metastasis [arrowhead]). The primary adrenal mass had decreased from 14.7 to 9.2 cm in the greatest dimension, the para-aortic lymph node had decreased from 5.9 to 1.9 cm and had features that suggested partial calcification, and hepatic metastases were still visible but smaller. PET/CT imaging performed the next day corroborated the CT evidence and also demonstrated metabolic changes in the tumor consistent with a response to therapy. (Fig 5A, coronal view of whole-body FDG-PET that shows the disappearance of uptake in the adrenal mass and hepatic metastasis; Fig 5B, fused axial PET/CT images that show the resolution of FDG uptake in the primary adrenal mass [white arrow], hepatic metastases, and portal vein thrombus [black arrow]).

Before chemotherapy, the standardized uptake value–lean (SUL) peak was 7.1 in the primary tumor and 2.7 in the left para-aortic lymph node; hepatic metastases were more subtle, with SUL peak measurements of 2.1 and 1.9. After therapy, the glucose uptake at all previously identified tumor sites was indistinguishable from background levels, with SUL peak measurements less than two times the mediastinal blood pool activity, which was consistent with a complete metabolic response.

On the basis of CT findings alone, the plan would have been to continue systemic chemotherapy; however, in light of the PET/CT findings, it was decided to proceed with surgery. The patient had a left radical nephrectomy with left radical adrenalectomy, IVC thrombectomy with IVC repair, and retroperitoneal lymph node dissection. The vascular thrombus was adherent to the vascular wall, and a small part (approximately 5%) could not be resected. Resection of the hepatic lesions was not attempted because of the lack of FDG uptake. Pathologic analysis of the surgical specimen revealed a well-circumscribed tumor, which measured 9.5 $\times$ 9.5 $\times$ 5.0 cm and weighed 320 g, that occupied the entire adrenal gland. Grossly, the tumor had necrotic areas with evidence of hemorrhage. Microscopically, there were neoplastic cells present in the primary tumor and renal vein that showed

Fig 5.

extensive necrosis, with less than 1% viable tumor cells (Fig 6A, extensive necrosis of the tumor; original magnification $\times 200$; Fig 6B, area of tumor with preserved architecture, original magnification $\times 400$; hematoxylin and eosin stain). Immunohistochemistry showed tumor cells positive for inhibin, calretinin, and CD10 and negative for ethidium monoazide and S100; these findings were consistent with an adrenocortical origin for the

Fig 6.

mass/ tumor. The Ki-67-labeling index in these areas was less than 1% (Fig 7; Ki-67 staining after chemotherapy; original magnification $\times 400$).

To improve the chance of survival of the patient and because of the incomplete resection of the vascular thrombus, we delivered two

Fig 7.

more cycles of adjuvant chemotherapy and continued mitotane therapy. Twenty-eight months after diagnosis, the patient remained disease-free. Hepatic lesions had resolved on CT imaging, and repeat PET/CT scans were also negative for abnormal uptake at all sites (not shown).

Discussion

ACC is a rare endocrine malignancy with no data or formal recommendations about the use of FDG-PET/CT in patients with ACC for treatment monitoring.

The increasing use of FDG-PET/CT in oncologic practice allows physicians to obtain greater amounts of both anatomic and functional data about malignant tumors. The widely used RECIST to detect a response to systemic therapy depends mainly on cross-sectional body imaging to demonstrate changes in tumor measurements compared with baseline studies.⁸ However, these criteria do not include a functional component in the evaluation, which led to the proposal of new criteria (PET Response Criteria in Solid Tumors [PERCIST]) that combine functional FDG-PET imaging with cross-sectional body imaging.⁹

FDG-PET imaging can provide early indications of a response to anticancer treatments.¹⁰ Moreover, many studies in a variety of tumor types (including lymphoma, breast cancer, and non-small-cell lung cancer) have suggested that metabolic responses on PET imaging are seen earlier than responses on anatomic imaging.¹¹⁻¹³ In patients with gastrointestinal stromal tumors, reliance on CT imaging alone can underestimate the effect of systemic targeted therapy; in one of five patients, FDG-PET imaging detected a response to imatinib mesylate treatment 2 months earlier than CT alone.¹⁴ Similarly, there is a significant correlation between FDG uptake and markers of cell proliferation (ie, Ki-67 index and mitotic activity) in a variety of tumors, including gastrointestinal stromal tumors¹⁵ and non-small-cell lung cancer.¹⁶

In the case presented in this article, PET/CT imaging predicted a greater response to therapy than anatomic imaging had suggested. According to RECIST 1.1, the tumor showed a partial response, with a 51% decrease in the sum of tumor measurements. In contrast, the application of PERCIST determined that the tumor had shown a complete metabolic response. This information indicated the effectiveness of the chemotherapy regimen and prompted an earlier surgical resection than would have been indicated by RECIST alone. Pathologic analysis of the surgical specimen supported the PET/CT impression, with large regions of necrosis, little viable tumor, and minimal cell proliferation. This experience suggested that FDG-PET/CT can assess the effectiveness of systemic chemotherapy for ACC and help surgical planning in patients with ACC. Future studies are needed to validate these observations and determine whether changes in FDG uptake can also predict long-term outcome and survival in patients with ACC as it can in patient with other malignancies.¹⁷

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