

Renal Cell Carcinoma with Paraneoplastic Manifestations: Imaging with CT and F-18 FDG PET/CT

Ba D. Nguyen, M.D., and Michael C. Roarke, M.D.

We present a case of renal cell carcinoma with prominent inflammatory and paraneoplastic manifestations. The initial CT detection of renal malignancy and subsequent post-therapeutic F-18 FDG PET/CT diagnosis of occult osseous metastasis were based on the patient's anemia, thrombocytosis and abnormally increased levels of serum C-reactive protein.

Introduction

Renal cell carcinoma is one of the most common malignant neoplasms of the genitourinary system. It is more frequently detected as an incidental finding during cross-sectional imaging evaluation of unrelated pathology than diagnosed at advanced and disseminated stages of the disease. Awareness of paraneoplastic manifestations such as anemia, thrombocytosis and elevated serum C-reactive protein may prompt clinicians to use various anatomic and functional imaging modalities for diagnosis and post-operative monitoring of renal cell carcinoma.

Case Report

A 67-year-old man presented with unexplained mild

anemia (hemoglobin level: 9.9 g/dl), elevated serum C-reactive protein (57 mg/l), thrombocytosis (platelet count: 533,000/mm³), elevated sedimentation rate (77 mm/h) and low grade fever ranging from 99 to 100 degrees Fahrenheit. Clinical and laboratory evaluation detected no in-

Citation: Nguyen BD, Roarke MC. Renal cell carcinoma with paraneoplastic manifestations: imaging with CT and F-18 FDG PET/CT. *Radiology Case Reports*. [Online] 2007;2:72.

Copyright: © Ba D. Nguyen, M.D. This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs 2.5 License, which permits reproduction and distribution, provided the original work is properly cited. Commercial use and derivative works are not permitted.

Abbreviations: CT, computed tomography; F-18, fluorine-18; FDG, fluorodeoxyglucose; PET, positron emission tomography; RCC, renal cell carcinoma

Ba D. Nguyen, M.D. (Email: nguyen.ba@mayo.edu), Department of Radiology, Mayo Clinic, Scottsdale, AZ, USA.

Michael C. Roarke, M.D., Department of Radiology, Mayo Clinic, Scottsdale, AZ, USA.

Published: August 10, 2007

DOI: 10.2484/rcr.v2i3.72

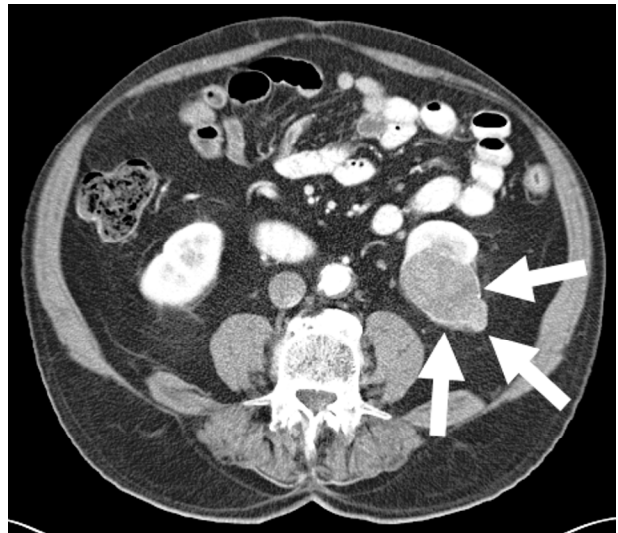


Figure 1. 67-year-old man with renal cell carcinoma with paraneoplastic manifestations. Axial CT image of the abdomen shows a lobulated and heterogeneously enhancing mass arising from the lower aspect of the left kidney (arrows).

Renal Cell Carcinoma with Paraneoplastic Manifestations: Imaging with CT and F-18 FDG PET/CT

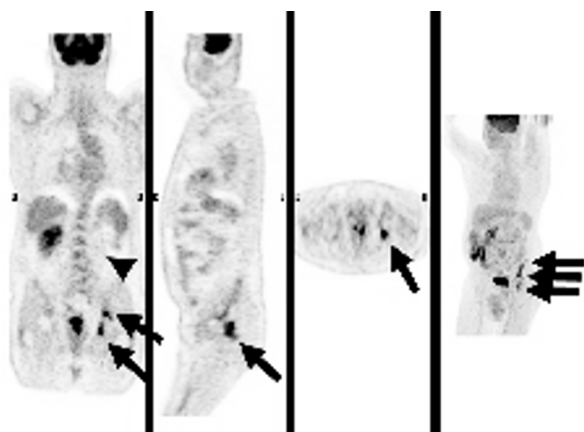


Figure 2. Composite PET image (sequence: coronal, sagittal, axial and volumetric images) shows increased F-18 FDG uptake at the left iliac bone, left acetabulum and left ischium compatible with hypermetabolic osseous lesions (small arrows). The patient is status left nephrectomy with absent activity in the left renal fossa (arrowhead).

fectious etiology. Bone marrow biopsy was unremarkable. A CT scan performed to search for malignancy showed a 5 cm heterogeneously enhancing solid mass in the lower pole of the left kidney compatible with a renal neoplasm (Fig. 1). The patient underwent left laparoscopic radical nephrectomy, which confirmed a renal cell carcinoma (RCC), predominantly of clear cell type, Fuhrman grade 3. The tumor involved the renal capsule but did not extend to the perinephric adipose tissue. There was no tumor invasion of the left renal pelvis or left renal vein. Post-operatively, there was resolution of the anemia and the serum C-reactive protein returned to the normal range (2.99 mg/l). Eight months after the initial surgery, the patient had recurrence of mild anemia (hemoglobin level: 10.5 g/dl) and thrombocytosis (platelet count: 523,000/mm³), re-elevation of serum C-reactive protein (30 mg/l) and new onset of low grade fever up to 100.5 degrees. Serial CT examinations of the chest, abdomen and pelvis were negative for recurrent or metastatic RCC. A month later, there was further increase in the serum C-reactive protein level (94 mg/l). As seen initially, all cultures and serologies were negative for infectious causes. Positron emission tomography (PET) with 2-Deoxy-2-(F-18) fluoro-D-glucose (FDG) was obtained to search for potential CT-occult secondary malignancy. PET showed abnormal radiotracer uptake at the left iliac crest, acetabulum and ischium without corresponding bone lesions on concomitant transmission CT (Fig. 2 & 3). Due to the lack of CT information, PET/CT fusion images were used to guide osseous tissue sampling. The

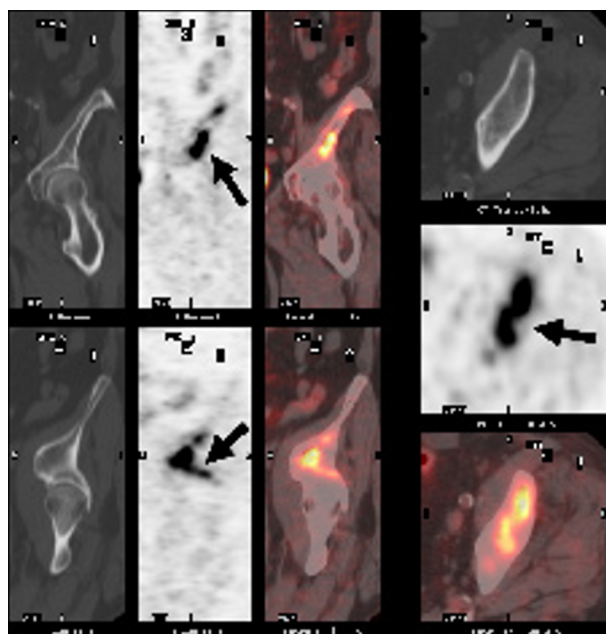


Figure 3. Composite F-18 FDG PET/CT image of the left pelvis (image sequence: CT, PET, and fused PET/CT in coronal, sagittal and axial projections) shows abnormal radiotracer accumulation in the left iliac bone and left acetabulum suggestive of hypermetabolic bone lesions (arrows). The transmission CT of this composite image shows no obvious lesion to match the PET findings.

bone biopsy yielded metastasis from renal cell carcinoma.

Discussion

Renal cell carcinoma (RCC) is the third most common genitourinary malignant tumor and the sixth leading cause of cancer death in the United States [1, 2]. With the advent of rapid and efficient cross-sectional imaging, RCC is frequently diagnosed as a fortuitous finding during assessment of unrelated diseases. Nowadays, the classic triad of gross hematuria, flank pain and flank mass is rarely the initial clinical presentation leading to the detection of this malignancy [1, 2]. During the pre-diagnosis phase of RCC, patients may present with non-specific paraneoplastic manifestations, which represent valuable diagnostic clues for renal malignancy. These paraneoplastic syndromes are probably induced by substances released from the neoplasm itself or the patient's immune system in reaction to the malignancy. Anemia, weight loss and fever are the most commonly encountered paraneoplastic syndromes of RCC in 30-50%, 20-33% and 7-25% of all cases respectively [1, 2]. In addition, thrombocytosis and elevated serum C-

Renal Cell Carcinoma with Paraneoplastic Manifestations: Imaging with CT and F-18 FDG PET/CT

reactive protein (CRP) have been established as prognostic indicators for renal malignancy with good correlation with tumor size, stage and progression [3-5]. CRP, an acute phase reactant encountered in infection, trauma and malignancy, is produced by hepatocytes and other tissues including RCC under the control of serum interleukin 6 (IL-6) [6, 7]. The complex IL-6/CRP has been established as the cause of the paraneoplastic inflammatory syndrome linked to RCC [8]. Awareness of these useful RCC biomarkers along with related paraneoplastic manifestations should prompt clinicians to order imaging studies in the search for renal malignancy.

Multidetector CT is the main imaging modality to evaluate such neoplasms. With negative or doubtful CT results and persistence of un-explained paraneoplastic inflammatory symptoms, functional imaging with F-18 FDG PET may be indicated for whole-body assessment [9-11]. PET imaging is based on the high glucose metabolism of malignant tumors. The radiotracer F-18 FDG, a glucose analog, is incorporated and remains in glucose-avid malignant cells due to improper intra-cellular catabolism providing a high tumor-to-background activity ratio. Even though PET performs poorly compared to CT in the anatomic detection of renal cancer due in part to high physiologic activity of normal renal parenchyma and adjacent collecting system activity, PET is more accurate than CT in the detection of distant and extra-urinary RCC metastases as illustrated in this case [12, 13]. The combined anatomic and functional imaging of PET/CT with image fusion further provides exact localization of hypermetabolic lesions for safe, diagnostic tissue sampling.

This case illustrates the importance paraneoplastic syndromes and C-reactive protein serum levels in prompting the search for clinically occult renal cell carcinoma and its subsequent recurrences and metastases. CT is the main imaging modality for dedicated evaluation of the genitourinary system. In cases of negative or inconclusive CT assessment, F-18 FDG PET/CT may be a valid functional and anatomic imaging modality for detection of hypermetabolic extra-urinary metastases.

References

1. Kim HL, Belldegrün AS, Freitas DG, et al. Paraneoplastic signs and symptoms of renal cell carcinoma: implications for prognosis. *J Urol* 2003; 170:1742-1746 [PubMed]
2. Weiss RH, Lin PY. Kidney cancer: identification of novel targets for therapy. *Kidney Int* 2006; 69:224-232 [PubMed]
3. Mahmoud FA, Rivera NI. The role of C-reactive protein as a prognostic indicator in advanced cancer. *Curr Oncol Rep* 2002; 4:250-255 [PubMed]
4. Casamassima A, Picciariello M, Quaranta M, et al. C-reactive protein: a biomarker of survival in patients with metastatic renal cell carcinoma treated with subcutaneous interleukin-2 based immunotherapy. *J Urol* 2005; 173:52-55 [PubMed]
5. Bensalah K, Leray E, Fergelot P, et al. Prognostic value of thrombocytosis in renal cell carcinoma. *J Urol* 2006; 175:859-863 [PubMed]
6. Costes V, Liautard J, Picot MC, et al. Expression of the interleukin 6 receptor in primary renal cell carcinoma. *J Clin Pathol* 1997; 50:835-840 [PubMed]
7. Jabs WJ, Busse M, Kruger S, Jocham D, Steinhoff J, Doehn C. Expression of C-reactive protein by renal cell carcinomas and unaffected surrounding renal tissue. *Kidney Int* 2005; 68:2103-2110 [PubMed]
8. Blay JY, Rossi JF, Wijdenes J, et al. Role of interleukin-6 in the paraneoplastic inflammatory syndrome associated with renal-cell carcinoma. *Int J Cancer* 1997; 72:424-430 [PubMed]
9. Crotty E, Patz EF Jr. FDG-PET imaging in patients with paraneoplastic syndromes and suspected small cell lung cancer. *J Thorac Imaging* 2001;16:89-93 [PubMed]
10. Younes-Mhenni S, Janier MF, Cinotti L, et al. FDG-PET improves tumour detection in patients with paraneoplastic neurological syndromes. *Brain* 2004;127:2331-2338 [PubMed]
11. Berner U, Menzel C, Rinne D, et al. Paraneoplastic syndromes: detection of malignant tumors using [(18)F]FDG-PET. *Q J Nucl Med* 2003; 47:85-89 [PubMed]
12. Aide N, Cappele O, Bottet P, et al. Efficiency of [(18)F]FDG PET in characterising renal cancer and

Renal Cell Carcinoma with Paraneoplastic Manifestations:
Imaging with CT and F-18 FDG PET/CT

detecting distant metastases: a comparison with CT.
Eur J Nucl Med Mol Imaging 2003; 30:1236-1245
[PubMed]

13. Kumar R, Chauhan A, Lakhani P, Xiu Y, Zhuang H, Alavi A. 2-Deoxy-2-[F-18]fluoro-D-glucose-positron emission tomography in characterization of solid renal masses. Mol Imaging Biol 2005; 7:431-439 [PubMed]