

CASE REPORT

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¹¹C-Choline positive but ¹⁸F-FDG negative pancreatic metastasis from renal cell carcinoma on PET

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ABSTRACT

Choline is a new PET tracer, which uptake may occur via a choline-specific transporter protein and be accelerated during the proliferation of tumor cells. We report a 61-year-old woman with a metastatic pancreatic tumor from renal cell carcinoma, measuring 35×40 mm. PET scans demonstrated accumulation of ¹¹C-choline in the metastatic pancreatic tumor, but no accumulation of ¹⁸F-FDG. Choline PET/CT may play a useful and complementary imaging modality, especially when FDG-PET/CT does not show expected findings or when the evaluation of tumor viability is needed, in patients with renal cell carcinoma.

Key Words: Choline, FDG, PET, Renal cell carcinoma

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Abbreviations & Acronyms:

RCC = renal cell carcinoma

PET/CT = positron emission tomography/computed tomography

¹⁸F-FDG = 2-[¹⁸F]fluoro-2-deoxyd-glucose

CT = computed tomography

RFA = radiofrequency ablation

SUVmax = maximal standardized uptake value

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INTRODUCTION

Metastatic renal cell carcinoma (RCC) is a subtype of urologic cancer with unfavorable prognosis. Approximately one-third of newly diagnosed RCC patients have metastatic disease.¹⁾ Even after nephrectomy of a locally confined disease, 20–30% of patients develop metastases.¹⁾ Effective staging of RCC is therefore crucial for patient management. Improved methods of imaging metastatic RCC would be of value in identifying sites of occult disease and monitoring response to therapy.

Integrated positron emission tomography/computed tomography (PET/CT) using 2-[¹⁸F]fluoro-2-deoxy-D-glucose (¹⁸F-FDG), which exploits the increased utilization and high uptake of glucose by malignant cells, has been widely used as a powerful tool in clinical oncologic imaging for combined metabolic and anatomic evaluation. While ¹⁸F-FDG PET/CT can reliably identify sites of metastatic RCC,²⁾ lesions with indeterminate uptake are still common, and a role for monitoring treatment response has not yet been clearly established.³⁾ A new PET tracer that can reliably image RCC could be of tremendous value.

¹¹C-choline uptake may occur via a choline-specific transporter protein, and could be accelerated during tumor cell proliferation. Here we report a case of pancreatic metastasis from RCC that was negative on ¹⁸F-FDG PET but detected on ¹¹C-choline PET.

CASE REPORT

The policy of Hyogo College of Medicine is that case reports do not require approval from the ethics review board or ethics committee.

A 61-year-old woman underwent right radical nephrectomy and lymphonodectomy for an RCC (pT3bN0M0, clear cell RCC) and left partial nephrectomy for a recurrent left renal tumor, 13 and 5 years ago, respectively. Three years ago, computed tomography (CT) scans revealed new metastatic lesions in the left kidney and pancreas, and she was administered axitinib (INLYTA). Radiofrequency ablation (RFA) for growth of the left renal recurrence was performed 4 months ago. The latest contrast-enhanced CT showed a hypervascular mass measuring 35×40 mm on the body of the pancreas, suggesting growth of the metastatic pancreatic tumor (Figure 1). Whole-body ¹⁸F-FDG PET/CT scan with blood glucose level of 91 mg/dL demonstrated no abnormal ¹⁸F-FDG uptakes anywhere in the body, including the pancreas (Figure 2). Subsequently, whole-body ¹¹C-choline PET/CT showed strong accumulation of ¹¹C-choline in the pancreatic mass, suggesting the presence of a viable metastatic pancreatic tumor (Figure 3). The maximal standardized uptake value (SUVmax) of the pancreatic mass was 12.08. Thus, a viable metastatic pancreatic tumor was strongly suspected from findings of both the contrast-enhanced CT and ¹¹C-choline PET/CT. Because no additional metastatic pancreatic lesion was observed by these diagnostic imaging evaluations, she underwent combined distal pancreatectomy and splenectomy, with subsequent histologic confirmation of pancreatic metastasis from the RCC (Figure 4). The immunohistochemical analysis of tumor cells was negative for glucose transporter 1 (GLUT1).

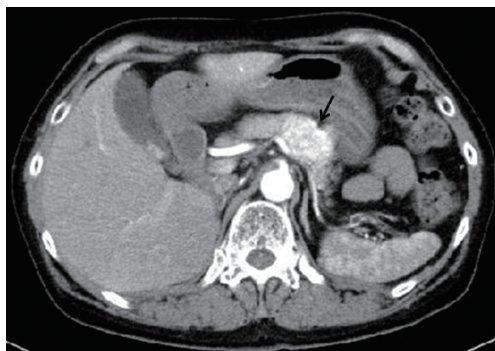


Fig. 1: Arterial phase image of contrast-enhanced dynamic CT shows a well-defined, 35×40 mm, mass with strong enhancement on the pancreatic body (arrow).

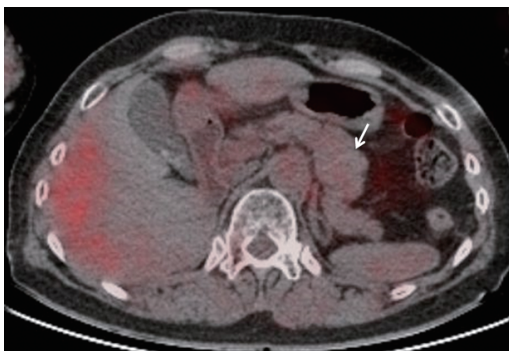


Fig. 2: ^{18}F -FDG PET/CT image shows no accumulation in the pancreatic body mass (arrow).

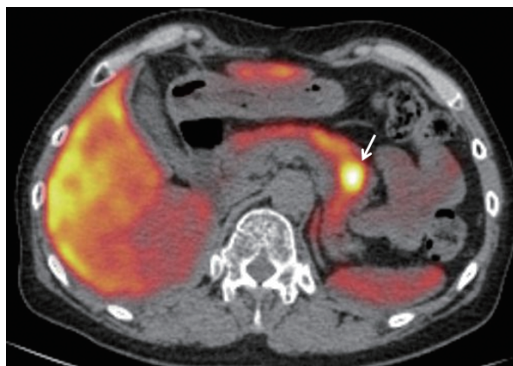


Fig. 3: ^{11}C -choline PET/CT image shows strong accumulation in the pancreatic body mass (arrow). The maximal standardized uptake value (SUVmax) of the lesion was 12.08.

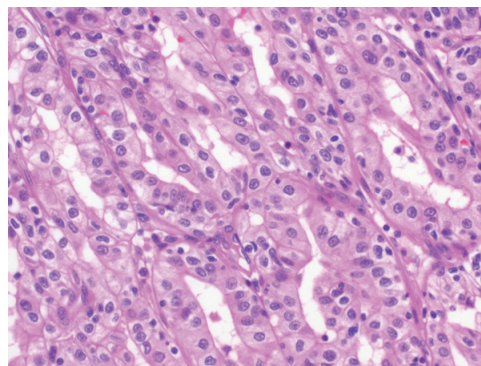


Fig. 4: Microscopic examination of the tumor demonstrated metastatic clear cell carcinoma.

DISCUSSION

^{18}F -FDG PET/CT, although not part of the standard protocol in the staging of RCC, shows promise for restaging and therapy monitoring.²⁾ Many groups have reported its high accuracy for follow-up evaluation of suspected recurrence and/or metastatic lesions in patients with RCC. However, the reported sensitivity of 74–81% is not extremely high.^{4,5)} Nakatani *et al.* demonstrated false negative ^{18}F -FDG PET/CT for restaging RCC metastasis to the lung, mediastinal lymph node, contralateral kidney, brain, pancreas, skin, liver, and thyroid.⁴⁾ The present case showed no FDG uptake in the pancreatic metastasis from RCC, probably due to the lack of GLUT-1 expression. However, Miyakita *et al.* demonstrated no correlation between GLUT-1 immunoreactivity and FDG-PET positivity in 19 RCCs. The mechanism of low FDG uptake by RCC on PET has not yet been clarified.⁶⁾

In Western Europe and North America, ^{11}C - and ^{18}F -choline PET/CT has been successfully used for prostate cancer restaging in patients with biochemical disease recurrence after definitive

therapy.⁷⁾ ¹¹C-choline uptake may occur via a choline-specific transporter protein that is over-expressed in the membranes of prostate cancer cells.⁸⁾ ¹¹C-choline is phosphorylated by choline kinase, which is upregulated and retained within tumor cells for synthesis of phosphatidylcholine.⁸⁾ Phosphatidylcholine is an essential component of cell membranes, being involved in the modulation of transmembrane signaling during carcinogenesis. Therefore, ¹¹C-choline uptake is accelerated during cancer cell proliferation.

Although physiological choline uptake by the kidney and liver may interfere with evaluation of renal and hepatic lesions, whole-body choline PET/CT can be used to evaluate whole-body metastatic lesions in patients with RCC. To our knowledge, there has been only one report that investigated the use of ¹⁸F-choline PET/CT for the purpose of staging and monitoring therapy response in metastatic RCC.⁹⁾ Middendorp *et al.* reported a lesion-based sensitivity of 56% (10/18) in staging two cases, with the false negatives being small pulmonary and retropancreatic lymph node metastases.⁹⁾ Sassa *et al.* demonstrated ¹¹C-cholinePET/CT to be a promising tool for the primary diagnosis and staging of 16 urothelial carcinomas of the upper urinary tract.¹⁰⁾

¹¹C-choline PET/CT is surely more expensive and less available than ¹⁸F-FDG PET/CT; however, it appears useful in RCC patients with suspicion of having distant metastasis, recurrence, or residual tumors based on physical examination, elevated tumour marker levels, abnormal CT and/or magnetic resonance imaging (MRI) findings, and negative or equivocal ¹⁸F-FDG PET/CT findings. Nonetheless, the clinical impact of the use of ¹¹C-choline PET/CT in RCC patients has still to be assessed in larger prospective studies. A cost-effectiveness analysis would be necessary to assess the best diagnostic flowchart in patients with RCC.

In conclusion, choline PET/CT may be a useful and complementary imaging tool in RCC patients, especially when ¹⁸F-FDG PET/CT does not show expected findings or when the evaluation of tumor viability is needed. Staging, restaging, and therapy response monitoring of advanced RCC by choline PET/CT should be investigated further, ideally in comparison with ¹⁸F-FDG PET/CT and CT.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

REFERENCE

- 1) Janzen NK, Kim HL, Figlin RA, Beldegrun AS. Surveillance after radical or partial nephrectomy for localized renal cell carcinoma and management of recurrent disease. *Urol Clin North Am*, 2003; 30: 843–852.
- 2) Kitajima K, Yamamoto S, Fukushima K, Minamimoto R, Kamai T, Jadvar H. Update on advances in molecular PET in urological oncology. *Jpn J Radiol*, 2016; 34: 470–485.
- 3) Calderella C, Muoio B, Isgro`MA, Porfiri E, Treglia G, Giovanella L. The role of fluorine-18-fluorodeoxyglucose positron emission tomography in evaluating the response to tyrosine-kinase inhibitors in patients with metastatic primary renal cell carcinoma. *Radiol Oncol*, 2014; 48: 219–227.
- 4) Nakatani K, Nakamoto Y, Saga T, Higashi T, Togashi K. The potential clinical value of FDG-PET for recurrent renal cell carcinoma. *Eur J Radiol*, 2011; 79: 29–35.
- 5) Alongi P, Picchio M, Zattoni F, Spallino M, Gianolli L, Saladini G, *et al.* Recurrent renal cell carcinoma: clinical and prognostic value of FDG PET/CT. *Eur J Nucl Med Mol Imaging*, 2016; 43: 464–473.
- 6) Miyakita H, Tokunaga M, Onda H, Usui Y, Kinoshita H, Kawamura N, *et al.* Significance of 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) for detection of renal cell carcinoma and immunohistochemical glucose transporter 1 (GLUT-1) expression in the cancer. *Int J Urol*, 2002; 9: 15–18.
- 7) Kitajima K, Murphy RC, Nathan MA, Sugimura K. Update on positron emission tomography for imaging of prostate cancer. *Int J Urol*, 2014; 21: 12–23.

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- 8) Uchida T, Yamashita S. Molecular cloning, characterization, and expression in *Escherichia coli* of a cDNA encoding mammalian choline kinase. *J Biol Chem*, 1992; 267: 10156–10162.
- 9) Middendorp M, Maute L, Sauter B, Vogl TJ, Grünwald F. Initial experience with ¹⁸F-fluoroethylcholine PET/CT in staging and monitoring therapy response of advanced renal cell carcinoma. *Ann Nucl Med*, 2010; 24: 441–446.
- 10) Sassa N, Kato K, Abe S, Iwano S, Ito S, Ikeda M, *et al.* Evaluation of ¹¹C-cholinePET/CT for primary diagnosis and staging of urothelial carcinoma of the upper urinary tract: a pilot study. *Eur J Nucl Med Mol Imaging*, 2014; 41: 2232–2241.