Isolated Hepatic Metastasis of Prostate Cancer with Variable ^{18}F -fluociclovine Uptake by PET/CT Imaging

Endel Sorra¹ · Muhammad U. Aziz¹ · Fangyu Peng^{1,2,3}

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Abstract

A 74-year-old man presented with rapid rising prostate-specific antigen (PSA) 2 years after treatment of prostate cancer with prostatectomy and salvage radiation therapy. PSA increased from 923 to 4349 ng/mL within 2 months. No osseous metastatic lesions of prostate cancer were detected by ^{18}F -sodium fluoride PET/CT imaging at an outside facility. ^{18}F -fluciclovine PET/CT imaging was performed to evaluate local recurrence of prostate cancer at surgical bed of prostatectomy and distant metastasis. One small focus of low-level ^{18}F -fluciclovine radiotracer uptake was noted in the surgical bed of prostatectomy without corresponding soft tissue mass on CT. No fluciclovine-avid lymph nodes or osseous metastatic lesions were detected, but multiple hypodense lesions of variable ^{18}F -fluciclovine radiotracer uptake were noted in the liver, concerning for isolated liver metastasis of prostate cancer. The patient underwent docetaxel chemotherapy for treatment of prostate cancer liver metastasis and showed a favorable response to treatment by significant decreased size of the hypodense lesions in the liver on post treatment abdominal CT, along with dramatic reduction of PSA level and improvement of liver function. The findings from this case highlight the importance of checking hypoattenuating lesions in the liver for the presence of prostate cancer metastatic lesions that might appear similar to other benign hypoattenuating lesions of low fluciclovine uptake relative to physiological ^{18}F -fluciclovine uptake in the normal liver tissues, a potential pitfall at interpretation of ^{18}F -fluociclovine PET/CT imaging.

Keywords Prostate cancer · Liver metastasis · ^{18}F -fluociclovine PET/CT

Introduction

Elevated expression of transmembrane amino acid transporters is a useful biomarker for prostate cancer imaging [1, 2]. ^{18}F -fluociclovine is a radiolabeled synthetic amino acid analogue that has been clinically used for positron emission tomography (PET) imaging of local recurrence and metastasis of prostate cancer in patients presented with rising prostate-specific antigen (PSA) level status post prostatectomy [3, 4]. Knowledge of normal physiologic distribution and variants, as well as typical patterns of prostate cancer spread, is essential

for proper interpretation of ^{18}F -fluociclovine PET imaging [5–7]. Hepatic metastasis of prostate cancer has been increasingly detected with advanced imaging technologies [8–12]. Herein, we report a case of isolated liver metastasis of prostate cancer that presented with multiple hypodense lesions of variable low ^{18}F -fluciclovine uptake, compared with physiological background of ^{18}F -fluociclovine uptake in the liver. Failure in differentiating prostate cancer metastatic lesions with low fluciclovine uptake, relative to physiological ^{18}F -fluciclovine uptake in adjacent normal liver tissue, from other benign hepatic hypodense lesions of low fluciclovine uptake represents a potential pitfall at interpretation of prostate cancer imaging with ^{18}F -fluociclovine PET/CT.

✉ Fangyu Peng
Fangyu.Peng@UTSouthwestern.edu

¹ Department of Radiology, UT Southwestern Medical Center, 5323 Harry Hines Blvd, Dallas, TX 75390-9140, USA

² Advanced Imaging Research Center, UT Southwestern Medical Center, Dallas, TX, USA

³ Harold C. Simmons Comprehensive Cancer Center, UT Southwestern Medical Center, Dallas, TX, USA

Case Report

A 74-year-old man presented for evaluation of prostate cancer metastasis and restaging with ^{18}F -fluciclovine PET/CT imaging due to recent rapid rising of PSA (increase of PSA from 923 to 4349 ng/mL within 2 months), status post

prostatectomy, salvage radiation therapy, and androgen deprivation therapy (ADT). The patient's past medical history was remarkable for hypertension and hypercholesterolemia. The patient was diagnosed with prostate adenocarcinoma (Gleason score 3 + 4 = 7) 13 years ago in an outside facility and was treated with a radical prostatectomy, followed by radiation and ADT using leuprolide acetate (Lupron, 45 mg/6 month IM). Pre-operative PSA level was measured at 6.4 ng/mL which has decreased to 1.2 ng/mL post prostatectomy that declined to undetectable 2 years later post radiation and ADT. ADT was started with leuprolide acetate 45 mg (Lupron) in conjunction with radiation that was switched to histrelin acetate (Vantas implant, 50 mg annually). Three years ago, PSA level was gradually elevated from 0.12 to 0.36 ng/mL measured 8 months ago. The patient was switched from ADT using histrelin acetate (Vantas implant, 50 mg annually) back to ADT with leuprolide acetate 45 mg (Lupron). Two months after change of ADT from histrelin acetate to leuprolide acetate, a dramatic change of PSA level from less than 5 ng/mL to 700 ng/mL was observed in this patient. Bicalutamide (150 mg/day, PO) was added to ADT, without significant improvement of elevated PSA level. The patient underwent CT of the abdomen and pelvis for evaluation of local recurrent malignancy status post prostatectomy. ^{18}F -sodium fluoride (NaF) PET/CT imaging was also performed for the evaluation of osseous metastasis at an outside facility. No mass lesions at surgical bed of prior prostatectomy or enlarged lymphadenopathy was detected, but multiple hypodense lesions were noted in the liver on abdominal CT. No suspicious osseous metastatic lesions were detected on the ^{18}F -sodium fluoride (NaF) PET/CT images.

On the initial visit to the medical oncologist at this hospital, the patient was found to have elevated transaminases (AST 121 u/L and ALT 52 u/L), alkaline phosphatase (168 u/L), and LDH (878 u/L), in addition to elevated PSA levels. The patient underwent ^{18}F -fluciclovine PET/CT imaging for evaluation of local recurrence of prostate cancer and distant metastasis, in a method modified from those previously described [4, 5, 13, 14]. Briefly, PET acquisition was obtained from

mid-thigh to vertex (5 min/bed) using a Siemens Biograph scanner, starting at 3 min post intravenous injection of 397.75 MBq (10.75 mCi) of ^{18}F -fluciclovine. The non-contrast CT scans (200 mAs, 120 kV, 0.5-s rotation time, 5-mm slice, in a caudal-to-cranial direction) were used for attenuation correction and localization. Transaxial, coronal, and sagittal PET images were reviewed in conjunction with fused non-contrast CT. Whole-body biodistribution of radiotracer activity was assessed by visual assessment and semi-quantitative analysis was performed to determine radiotracer concentration (standardized uptake value, SUV), in reference to blood pool radiotracer activity measured from the descending aorta (SUV mean 1.2) and lumbar spine bone marrow radiotracer activity (SUV mean 3.5). Small focus of low-level radiotracer uptake (SUV maximum 3.0) was noted in the surgical bed of prostatectomy, without corresponding mass lesion on CT (Fig. 1a–d). No fluciclovine-avid lymph nodes or osseous metastatic lesions were detected, but multiple hypoattenuating lesions were noted in the liver that showed variable ^{18}F -fluciclovine radiotracer uptake (Fig. 2a–c), compatible with fluciclovine-avid hepatic metastasis of prostate adenocarcinoma. These hypodense metastatic lesions appeared as photopenic areas on the PET images of the liver, compare with adjacent normal liver tissues of more intense physiological ^{18}F -fluciclovine radiotracer activity (Fig. 2b). Semi-quantitative analysis demonstrated variable maximum and mean SUVs (SUVmax/mean) of these hypodense metastatic lesions (SUVmax/mean 6.73/5.38 for hypodense lesion 1, SUVmax/mean 8.42/6.68 for hypodense lesion 2, and SUVmax/mean 8.80/6.86 for hypodense lesion 3). SUVmax/mean of the hypodense metastatic lesions were lower than the SUVmax/mean of physiological ^{18}F -fluciclovine uptake by adjacent normal liver tissues (SUVmax/mean 10.28/9.44 for liver tissue near hypodense lesion 1, SUVmax/mean 9.17/8.04 for liver tissue near hypodense lesion 2, and SUVmax/mean 9.49/8.75 for liver tissue near hypodense lesion 3). On the other hand, SUVmax/mean of these hypodense lesions were higher than SUVmax/mean of bone marrow ^{18}F -fluciclovine uptake measured from the lumbar spine (SUVmax/mean 4.21/

Fig. 1 ^{18}F -fluciclovine PET/CT for evaluation of local recurrence and metastasis of prostate cancer status post prostatectomy. Expected distribution of ^{18}F -fluciclovine in the liver and pancreas was visualized on MIP imaging, with no evidence of fluciclovine-avid lymphadenopathy (a). Small focus of low-level ^{18}F -fluciclovine radiotracer activity was

visualized on the right aspect of the surgical bed of prostatectomy with SUV maximum 3.0 without corresponding soft tissue mass on CT (b–d), equivocal for chronic inflammation or small lesion of recurrent malignancy

Fig. 2 Hypodense lesions of variable ^{18}F -fluociclovine uptake by PET/CT imaging. Numerous hypodense lesions were noted in the liver (a), with variable ^{18}F -fluociclovine radiotracer activity (b, c) that appeared as photopenic area of low intensity of ^{18}F -fluociclovine (L1) or slightly less

intense areas (L2 and L3) compared with physiological background ^{18}F -fluociclovine activity in adjacent liver parenchyma tissue. L1, hypodense lesion 1; L2, hypodense lesion 2; L3, hypodense lesion 3

3.11) or SUVmax/mean of blood pool ^{18}F -fluociclovine uptake measured from the descending aorta in the mediastinum (SUVmax/mean 1.24/1.00).

The patient underwent chemotherapy with docetaxel (75 mg/m^2) for treatment of liver metastasis of aggressive castrate resistant prostate adenocarcinoma, along with standard premedication with dexamethasone and Compazine. The patient responded well to docetaxel chemotherapy, with dramatic decrease of PSA from 4349 to 496.5 ng/mL after the first cycle of chemotherapy. PSA level decreased to 21.51 ng/mL after completion of the 3rd cycle of docetaxel chemotherapy, and further decreased to 5.09 ng/mL after completion of the 4th cycle of docetaxel chemotherapy. Docetaxel chemotherapy was stopped after completion of the 4th cycle due to side effects of toxicities (grade 4 hand-foot syndrome and grade 3 mucositis). The size of the hypodense lesions in the liver has decreased in response to treatment on CT of abdomen and pelvis obtained at 1 month post initiation of docetaxel

chemotherapy (Fig. 3a). There was interval development of cirrhotic changes of the liver and large volume ascites on CT abdomen and pelvis obtained after completion of 4 cycles of docetaxel chemotherapy, at 4 months post initiation of docetaxel chemotherapy (Fig. 3b). The findings of hepatic cirrhotic changes and development of large volume ascites and enlargement of spleen suggested the development of treatment-induced liver pseudocirrhosis and portal hypertension post treatment of extensive liver prostate cancer metastasis [9]. Follow-up CT abdomen and pelvis at 6-month post initiation of docetaxel chemotherapy demonstrated improvement of treatment-induced pseudocirrhosis of liver (Fig. 3c). A few small hypoattenuating foci were noted, representing residua of treated hepatic metastasis, along with reduction of ascites and improvement of splenomegaly. In addition to reduction of PSA levels and reduced size of hepatic hypodense lesions, there were also significant improvement of liver function with a decrease of aspartate aminotransferase (AST) from 121 u/L

CT acquired at 1 month post initiation of Docetaxel chemotherapy

CT acquired at 4 months post initiation of Docetaxel chemotherapy

CT acquired at 6 months post initiation of Docetaxel chemotherapy

Fig. 3 Interval changes of hypodense lesions in the liver by abdominal CT. There was a significantly decreased size of the hypodense lesions in the liver on abdominal CT acquired at 1 month post initiation of docetaxel chemotherapy (a), compared with the lesions seen on pre-treatment abdominal CT (Fig. 2a). Hepatic cirrhotic changes and ascites were

visualized on abdominal CT obtained after completion of 4 cycles of docetaxel chemotherapy (at 4 months post initiation of treatment). Improvement of treatment-induced pseudocirrhosis and reduction of ascites were observed on abdominal CT obtained at 6 months post initiation of docetaxel chemotherapy

prior to chemotherapy to 29 u/L (normal range 10–50 u/L) and decrease of alanine aminotransferase (ALT) from 52 to 20 u/L (normal range 10–50 u/L) post two cycles of docetaxel chemotherapy, along with the reduction of lactate dehydrogenase (LDH) level from 878 to 208 u/L (normal range 135–225 u/L).

Discussion

Most common sites of metastasis from prostate cancer remain the skeletal system and lymph nodes. Prostate cancer metastasis in liver appear as hypodense lesions with heterogeneous peripheral post contrast enhancement [8–11]. Many benign and malignant lesions can appear as hypodense on non-contrast CT images, such as cysts and hemangiomas. Although it might not be difficult to recognize large hypodense lesions of prostate cancer metastasis in this case, it could be challenging to differentiate small hypodense lesion of prostate cancer metastasis from a benign hypodense lesion in the liver. Failure to differentiate isolated prostate cancer liver metastatic lesions with variable ^{18}F -fluciclovine uptake less intense than physiological ^{18}F -fluciclovine activity in the liver tissue from other benign hypodense lesions such as hepatic cysts represents a potential pitfall on interpretation of ^{18}F -Fluciclovine PET/CT imaging.

Small isolated liver metastatic lesion of prostate cancer could be treated with surgical resection. Extensive liver metastatic lesions from prostate cancer have worse outcomes in comparison with metastasis at other sites and often refractory to hormonal therapy [15]. In our case, the patient responded well to docetaxel chemotherapy, with a rapid decrease of PSA level, decreased size of hypodense metastatic lesion, along with normalization of liver functional tests (ALT and AST), and LDH level at 6 months after initiation of docetaxel chemotherapy. The findings from this case report support further study of liver metastasis of prostate cancer and impact of ^{18}F -fluciclovine PET/CT imaging on clinical management of the patients suffered from liver metastasis of prostate cancer [16].

Conclusion

We report a case of isolated liver metastasis with variable ^{18}F -fluciclovine uptake in a patient presented with rapid rising PSA level following prostatectomy and salvage radiation therapy for prostate cancer. It is important to evaluate ^{18}F -fluciclovine uptake by hypodense lesions in the liver for differentiating hypodense metastatic lesions of prostate cancer from benign hypodense lesions of low ^{18}F -fluociclovine uptake. Isolated hypodense metastatic lesions of prostate cancer in the liver represent a potential pitfall on interpretation of ^{18}F -

Fluociclovine PET/CT imaging, in view of physiological distribution of ^{18}F -fluociclovine within the liver.

Compliance with Ethical Standards

Conflict of Interest Endel Sorra, Muhammad U Aziz, and Fangyu Peng declare no conflict of interest.

Ethical Approval All procedures performed in study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent The institutional review board of our institute approved this retrospective study, and the requirement to obtain informed consent was waived.

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