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Case Report

^{11}C-Choline-Avid but ^{18}F-FDG-Nonavid Prostate Cancer with Lymph Node Metastases on Positron Emission Tomography

Kazuhiro Kitajima[a] Kazuhito Fukushima[a] Shingo Yamamoto[b]
Toshiko Yamano[c] Haruyuki Takaki[c] Koichiro Yamakado[c]
Yukako Nakanishi[b] Akihiro Kanematsu[b] Michio Nojima[b]
Shozo Hirota[c]

[a]Department of Radiology, Division of Nuclear Medicine and PET Center, Hyogo College of Medicine, Nishinomiya, Japan; [b]Department of Urology, Hyogo College of Medicine, Nishinomiya, Japan; [c]Department of Radiology, Hyogo College of Medicine, Nishinomiya, Japan

Keywords
Choline · FDG · Positron emission tomography · Prostate cancer

Abstract
Choline is a new positron emission tomography (PET) tracer useful for detection of prostate cancer and metastatic lesions. We report a 70-year-old man with prostate cancer and multiple abdominal, pelvic, and inguinal node metastases. PET scans demonstrated accumulation of ^{11}C-choline in the primary tumor and lymph node metastases but no accumulation of ^{18}F-FDG. Choline PET/computed tomography may be useful for diagnosis of advanced prostate cancer with suspected metastatic lesions and treatment planning.

KARGER

Kazuhiro Kitajima, MD, PhD
Department of Radiology, Division of Nuclear Medicine and PET Center
Hyogo College of Medicine, 1-1 Mukogawa-cho
Nishinomiya, Hyogo 663-8501 (Japan)
E-Mail kazu10041976@yahoo.co.jp

Introduction

Integrated positron emission tomography/computed tomography (PET/CT) with 2-[^{18}F]fluoro-2-deoxy D-glucose (^{18}F-FDG) is a useful tool for combined metabolic and anatomic evaluation of cancers. Although ^{18}F-FDG, an analog of glucose that can visualize metabolic activity, is the most widely used radiotracer for imaging of various malignancies, its application to prostate cancer is limited because of its low sensitivity and specificity [1, 2]. Moreover, urinary excretion of ^{18}F-FDG in the urinary bladder may interfere with evaluation of prostate lesions. Many new tracers have been introduced to overcome these limitations: ^{18}F- or ^{11}C-choline, ^{18}F- or ^{11}C-acetate, 16β-^{18}F-fluoro-5α-dihydrotestosterone, anti-3-^{18}F-fluorocyclobutane-1-carboxylic acid, and prostate-specific membrane antigen are currently under investigation [2].

In Western countries ^{11}C- and ^{18}F-choline PET/CT has been used successfully for restaging of prostate cancer in patients with biochemical disease recurrence after definitive therapy [1–3]. ^{11}C-choline uptake may occur via a choline-specific transporter protein that is overexpressed in the membranes of prostate cancer cells [4]. ^{11}C-choline is phosphorylated by choline kinase, which is upregulated and retained within tumor cells for synthesis of phosphatidylcholine [4]. Phosphatidylcholine is an essential component of cell membranes, being involved in the modulation of transmembrane signaling during carcinogenesis. Therefore, ^{11}C-choline uptake is accelerated during the proliferation of prostate cancer cells.

Here we report a case of advanced prostate cancer with lymph node metastases that was negative on ^{18}F-FDG PET but detected by ^{11}C-choline PET.

Case Report

A 70-year-old man presented with left leg swelling. An initial CT scan of the abdomen and pelvis demonstrated swelling of the para-aortic, pelvic, and inguinal lymph nodes on the left side and swelling and edema of the left leg. Whole-body ^{18}F-FDG PET/CT scan demonstrated these enlarged para-aortic, pelvic, and inguinal nodes, but no abnormal ^{18}F-FDG uptake was evident (Fig. 1a–c). Biopsy of the left inguinal node revealed weakly positive reactivity for prostate-specific antigen (PSA) and prostate-specific antigen phosphatase. The serum PSA level was significantly elevated (5,916 ng/mL), and prostate cancer with lymph node metastases was suspected. Pelvic magnetic resonance imaging (MRI) was undertaken, and abnormal signal intensity was observed in the left transition zone on diffusion-weighted imaging, suggesting prostate cancer (Fig. 2a, b). Diagnostic confirmation of prostate cancer was achieved in the left transition zone by standard transrectal 12-core biopsy (adenocarcinoma, Gleason score 4 + 5). Subsequently, ^{11}C-choline PET/CT showed strong accumulation of ^{11}C-choline in the left transition zone and left-sided para-aortic, pelvic and inguinal lymph nodes (Fig. 3a–c). The maximal standardized uptake value (SUVmax) of the primary lesion and metastatic lymph nodes was 5.03 and 11.20, respectively. Bone metastases were not detected. The clinical stage was T2N1M1. Treatment with bicalutamide and degarelix was started, and the PSA level decreased to 114.7 ng/mL after 3 months of this treatment.

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

Discussion

The use of ^{18}F-FDG for imaging of prostate cancer is limited because: (i) glucose utilization in slow-growing, well-differentiated, and small prostate cancers and metastatic lesions is lower than in other tumor types; (ii) urinary excretion of ^{18}F-FDG leads to high bladder activity that can mask prostate tumors; (iii) there is an overlap in the degree of ^{18}F-FDG uptake between prostate cancer, benign prostatic hyperplasia, and inflammation; and (iv) osteoblastic bony metastasis has a low FDG uptake [1]. In recent years, 2 groups have shown the detection of untreated primary prostate cancer by ^{18}F-FDG PET with a sensitivity of 31% [5] and 44% [6] in patient-based analyses.

There has been some debate about the value of ^{11}C-choline PET/CT for detection of untreated prostate cancer. Studies of ^{11}C-choline PET/CT or PET for the detection of prostate cancer have reported a patient-based sensitivity of 55–100%, a specificity of 43–87%, and an accuracy of 60–84% [3, 5]. Focal choline uptake in the prostate is suggestive of prostate cancer, but nonmalignant conditions such as high-grade prostatic intraepithelial neoplasia, prostatitis, benign prostatic hyperplasia, and normal tissue can also show false-positive focal activity [3].

At some PET centers, ^{11}C- and ^{18}F-choline PET/CT has been used successfully for the restaging of prostate cancer in patients with biochemical recurrence after definitive therapy [3]. Four groups have compared the diagnostic performance of choline and ^{18}F-FDG PET or PET/CT [7–10] for the detection of recurrent lesions in the same prostate cancer patient with PSA failure after definitive therapy, and all groups demonstrated that choline PET or PET/CT was more accurate than ^{18}F-FDG PET or PET/CT. To our knowledge, only one report has compared choline and ^{18}F-FDG PET for the detection of primary untreated prostate cancer [5]. In a study of 43 consecutive patients with suspected prostate cancer (histopathologically confirmed in 26 patients), Watanabe et al. [5] demonstrated that the patient-based sensitivity, specificity, and accuracy of ^{11}C-choline PET was 73, 59, and 67%, whereas the corresponding figures for ^{18}F-FDG PET were 31, 88, and 53%, respectively.

Choline PET/CT has no role in the initial workup for the vast majority of men with newly diagnosed prostate cancer. However, choline PET/CT may be useful in a minority of newly diagnosed patients with a high clinical suspicion of distant metastatic disease (e.g., a serum PSA level higher than 10 ng/mL, a Gleason score of 8–10, and local progression confirmed by palpation and/or MRI) [3, 11, 12]. In this situation, it would be highly desirable to identify men with distant disease before they are exposed to the morbidity of localized therapies that may not be beneficial. Beheshti et al. [11] evaluated ^{18}F-fluorocholine PET/CT for the pretreatment staging of prostate cancer in 130 intermediate- or high-risk patients and demonstrated that patient-based sensitivity and specificity for the detection of metastatic lymph nodes greater than or equal to 5 mm in diameter were 66 and 96%, respectively, 43 bone metastases in 13 patients having been detected. They also estimated that the results of pretreatment ^{18}F-fluorocholine PET/CT would prompt a change of therapy in 15% of patients overall and 20% of high-risk patients. Poulsen et al. [12] evaluated ^{18}F-fluorocholine PET/CT for the pretreatment staging of prostate cancer in 210 intermediate- or high-risk patients and demonstrated a patient-based sensitivity and specificity for the detection of metastatic lymph nodes of 73 and 88%, respectively.

Conclusion

Choline PET/CT may be a powerful tool not only for the restaging of biochemically recurrent prostate cancer but also for the staging of advanced prostate cancer with a high clinical suspicion of distant metastatic disease.

Statement of Ethics

Informed consent was obtained from the patient for the publication of this case report and any accompanying images.

Disclosure Statement

The authors have no conflicts of interest to declare.

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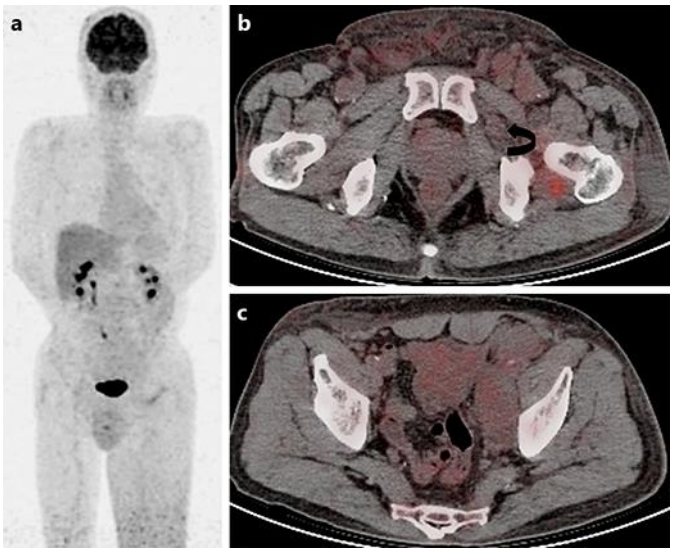

Fig. 1. ^{18}F-FDG PET/CT. **a** Maximum intensity projection of ^{18}F-FDG PET shows no abnormal FDG uptake. The left leg seems to be swollen. **b** The fused ^{18}F-FDG PET and CT image shows no accumulation in the prostate or in the multiple enlarged left inguinal nodes and the node between the obturator internus and externus muscles (curved arrow). The largest inguinal node and the node between the obturator internus and externus muscles measured 35 × 37 and 15 × 18 mm, respectively. **c** The fused ^{18}F-FDG PET and CT image shows no accumulation in the enlarged left obturator and external iliac nodes. The obturator and external iliac nodes measured 35 × 45 and 35 × 35 mm, respectively.

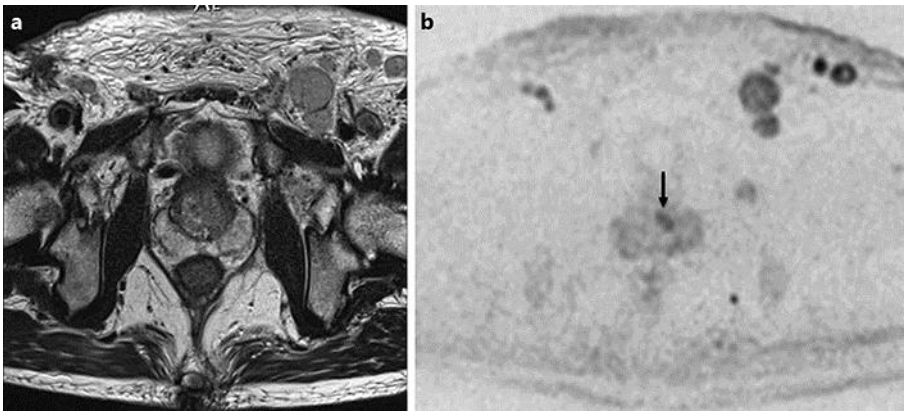

Fig. 2. MRI. **a** Axial T2-weighted image shows multiple enlarged left inguinal nodes. Prostate cancer is not apparent. **b** Axial diffusion-weighted imaging shows abnormal signal intensity in the left transition zone of the prostate (arrow) and multiple enlarged left inguinal nodes, suggesting prostate cancer and lymph node metastases.

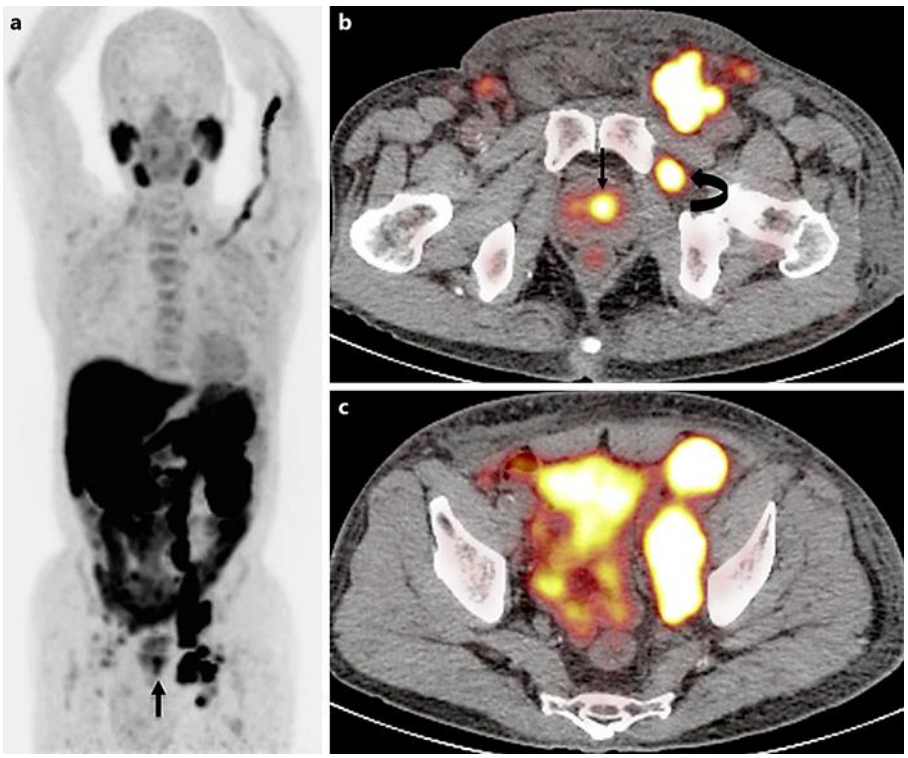

Fig. 3. ^{11}C-choline PET/CT. **a** Maximum intensity projection of ^{11}C-choline PET shows multiple abnormal ^{11}C-choline uptake in the left prostate (arrow) and the left-side abdomen, pelvis, and groin. **b** The fused ^{11}C-choline PET and CT image shows strong accumulation in the left transition zone of the prostate (arrow), multiple enlarged left inguinal nodes, and the node between the obturator internus and externus muscles (curved arrow). The SUVmax of the primary lesion, the node between the obturator internus and externus muscles, and the inguinal node was 5.03, 7.03, and 11.20, respectively. **c** The fused ^{11}C-choline PET and CT image shows strong accumulation in the enlarged left obturator and external iliac nodes. The SUVmax of the enlarged left obturator and external iliac nodes was 9.22 and 9.00, respectively.