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Case Report

Assessment of 68Ga-PSMA-11 PET/CT in Patients with Prostate Cancer

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Abstract

Positron emission tomography (PET)/computed tomography (CT) using Ga-68-labeled prostate specific membrane antigen is utilized for the imaging of biochemical recurrence of prostate cancer. For low PSA values, the recurrence can be diagnosed with PSMA PET/CT through imaging after about one or three hours. In this report, we present intense uptake of Ga-68-PSMA PET/CT in early and late monitoring of a 74-year-old male patient with prostate carcinoma diagnoses. Early Ga68-PSMA-11 PET/CT imaging with 11ng/ml PSA level revealed metastasis involvement lesions while the subsequent scans revealed more metastatic lesions. Furthermore, we present an overview of the future prospects of 68Ga-PSMA PET/CT for therapy and monitoring. 177Lu-PSMA may be useful for treatment in this case.

Introduction and Clinical Findings

Prostate cancer (PCa) is one of the major male malignancies with high morbidity and mortality rates around the world [1]. The two common symptoms (PSA and Gleason Score) for detection of tumor recurrence after radical prostatectomy serve as the most clinical markers in prostate cancer. Conventionally, bone scan, ultrasonography and CT are used as gold standards for imaging recurrences. Many studies on the prepared Glu-NH-CO–NH-Lys-(Ahx)-[68Ga (HBED-CC)] (68Ga-PSMA-11) have shown the ability of this tracer in high contrast detection of PC [2, 3]. 68Ga-PSMA PET-CT has been demonstrated to be capable of localizing recurrence lesions in patients even at low levels of PSA (higher than 2 ng/ml) [4]. 68Ga-PSMA-11 is distinctly superior to the previous radiotracers such as 11C-Choline or 18F-Choline. It is capable of detecting lesions with improved contrast, especially at low PSA levels [2, 5].

In the present study, 68Ga-PSMA-11 was prepared under optimized conditions (pH, temperature, ligand concentration and reaction time), and the appropriate systems for HPLC and RTLC analysis were introduced. Moreover, the brief procedure and SOP were employed for the labeling of PSMA ligands and its quality control. Clinically, 68Ga is derived from a 68Ge-68Ga generator, and due to its long half-life (T1/2=271 days), it allows the generator to operate for several months [4]. In addition, the short half-life of 68Ga (T1/2=68min) allows more elution of the generator in one day. As PSMA is over-expressed in PCa cells, it can be an ideal target for labeling of radio-pharmaceuticals to bind with peripheral membrane cell receptors [6, 7]. PSMA-11 [Fig.1] has been developed for labeling of 68Ga [8]. In many centers the preparation of 68Ga-PSMA-11is conducted in a systematic manner, but pharmaceutical

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purity tests of the final product are highly important for radiopharmacists. Purification tests at the end of synthesis are conducted to remove unbinding 68Ga and 68Ge from the generator. GMP is needed to ensure the production of sterile and safe product for administration in patients. The case was a 74-year-old male patient who had undergone Ga-68 PSMA-HBED-CC PET/CT for restaging of prostate carcinoma. He was diagnosed with prostate adenocarcinoma in 2016 and had been followed up to 2017 using Ga-68 PSMA-11. Additionally, he underwent chemo-radiation therapy using taxotere following the partial cystectomy for high grade invasive prostate carcinoma. After chemotherapy and hormone therapy (Zometa), patient underwent Ga-68 PSMA

PET/CT for the elevation of serum prostate specific antigen levels (early scan). In the early PET/CT scan, the patient had PSA=11ng/ml. For this procedure, 60 MBq of Ga-68 PSMA-11 was administered intravenously via the left antecubital vein. to facilitate the distribution and uptake of radiotracer, the patient rested for 60 minutes in a shielded room. Imaging was performed by an integrated 6-slice PET/CT scanner, which scanned the body from the skull base to the toes. CT scanning was performed without using oral or intravenous contrast materials. In maximum intensity projection and trans-axial fused images, multiple medistinal lymph nodes involvement in supraclavicular, retrosternal, lower paratracheal and left internal mammary lymph nodes were detected [Fig.1]. In addition, lymph node involvement in the para-aortic area (3-4 small-size lymph nodes), right iliac wing and T9 and 11th left ribs were reported. After following up the patient undergoing hormone therapy for three months, PSA level rose from 11 to 36 ng/ml with chemotherapy does not inducing any change in PSA levels. Therefore, Ga-68 PSMA PET/CT was performed again to image recurrent prostate carcinoma progression [1]. To achieve this goal, the same PET/CT protocol was applied. After the analysis of results, we found same scan patterns in the bilateral supaclavicular lymph nodes, 9mm lymph node in the paratracheal region and 15mm lymph node in the retrosternal area, which was consistent with the above-said study.

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Furthermore, 2-3 more lymph nodes in the lower paratracheal and retrosternal stations with increased uptake were observed. The lymph node in AP window, which was 8mm with SUV max=10, grew into 20 mm with SUV max=17.3. Finally, new lymphatic involvements in the left retrocrural and AP window were diagnosed in addition to the previously noted multiple medistinal lymph node involvement in supraclavicular, retrosternal, lower paratracheal and left internal mammary stations. Moreover, lymph nodes involvement in the para-aortic area (3-4 small-sized lymph nodes) as well as new bone lesions in the sternum, left scapula, multiple ribs, T5, multiple lower thoracic and lumbar vertebrae and iliac wings were reported (images C, D). Therefore, following patients diagnosed with prostate cancer using 68Ga-PSMA PET/CT (the same protocols) can be useful for assessing progression and recurrences. Accordingly, many authors have recently focused on developing new radiopharmaceuticals for the early diagnosis of prostate cancer [1]-[5]. In this report, we attempted to share our experience of intense Ga-68 PSMA uptake in a patient with metastatic prostatic cancer.

Primary Objectives

68Ga-PSMA PET/CT is a promising radiotracer for the detection of recurrent prostate cancer after initial therapy in patients with elevated PSA and non-contributory bone scintigraphy, computed tomography (CT) or magnetic resonance imaging (MRI). After intravenous injection of 68Ga-PSMA-11 to the patient, PET/CT imaging was performed after 45-60 minutes. At the end of the study, patients were followed up every 3-6 months for up to one year.

Criteria

1. Histopathologically proven prostate adenocarcinoma.

2. Rising PSA after prostatectomy or radiotherapy. Post radical prostatectomy (RP) - PSA greater than 0.2 ng/mL measured more than 6 weeks after RP.

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3. A history of other malignancies within the last 2 years other than skin basal cell or non-metastasized cutaneous superficial squamous cell

4. Contraindication of furosemide administration including prior allergy or adverse reaction to furosemide or sulfa drugs.

Discussion

This prospective report exhibited that readings are highly reproducible for observers with extensive or limited experience. Moreover, as PSMA expression has been reported in other non-prostate tissues, it is possible that normal and variable PSMA uptake are misinterpreted due to background activity in liver, spleen, small intestine, colon and kidney. About 8-10% of all primary prostate cancers do not exhibit any significant PSMA expressions. This may be due to high tumor-to-background uptake of 68Ga-PSMA -11 and basic understanding of common metastatic pathways. 68Ga-PSMA-11 PET/CT is characterized by specific and high tumor signals. Moreover, the reported sensitivities might be due to overestimations, as it is difficult to identify false-negative lesions, especially in cases of recurrence when histological validation is driven by images. On top of that, lymph node metastases within /outside the pelvis were not separated in our staging system, because this system focused on organs to analyze findings based on their PET/ CT appearance. The cancer staging proposed by American Joint Committee on Cancer concentrates on patient prognosis and thus discriminates between intra and extrapelvic lymphnode metastases. Finally, we did not assessed intra-observer agreement, which might have shed light on reliability and confidence of individual judgments.

Conclusion

68Ga-PSMA-11 PET/CT is not specific for diagnosis of prostate cancer, but it represents the best and most specific tracer available for the imaging of prostate cancer. Understanding the possible uptake conditions in 68Ga-PSMA-11 PET/CT assists nuclear medicine physician to minimize reporting fallacies. Whenever an unusual site of involvement is noted for the 68Ga-PSMA-11 PET/CT, a careful analysis of history and correlative imaging can help resolve the reporting dilemma in most cases. In unsettled cases, and where a management change is expected based on the unusual site of involvement, histopathological confirmation is warranted. 68Ga-PSMA-11 PET/CT is in its early stages and is eventually expected to leave a definitive mark on diagnostic nuclear medicine.

Conflict of Interests: Author hereby declares that there is no conflict of interests.

Fig. 1 Early Ga68-PSMA-11 PET/CT with 11ng/ml PSA level. MIP section and trans-axial metastasis involvement lesions

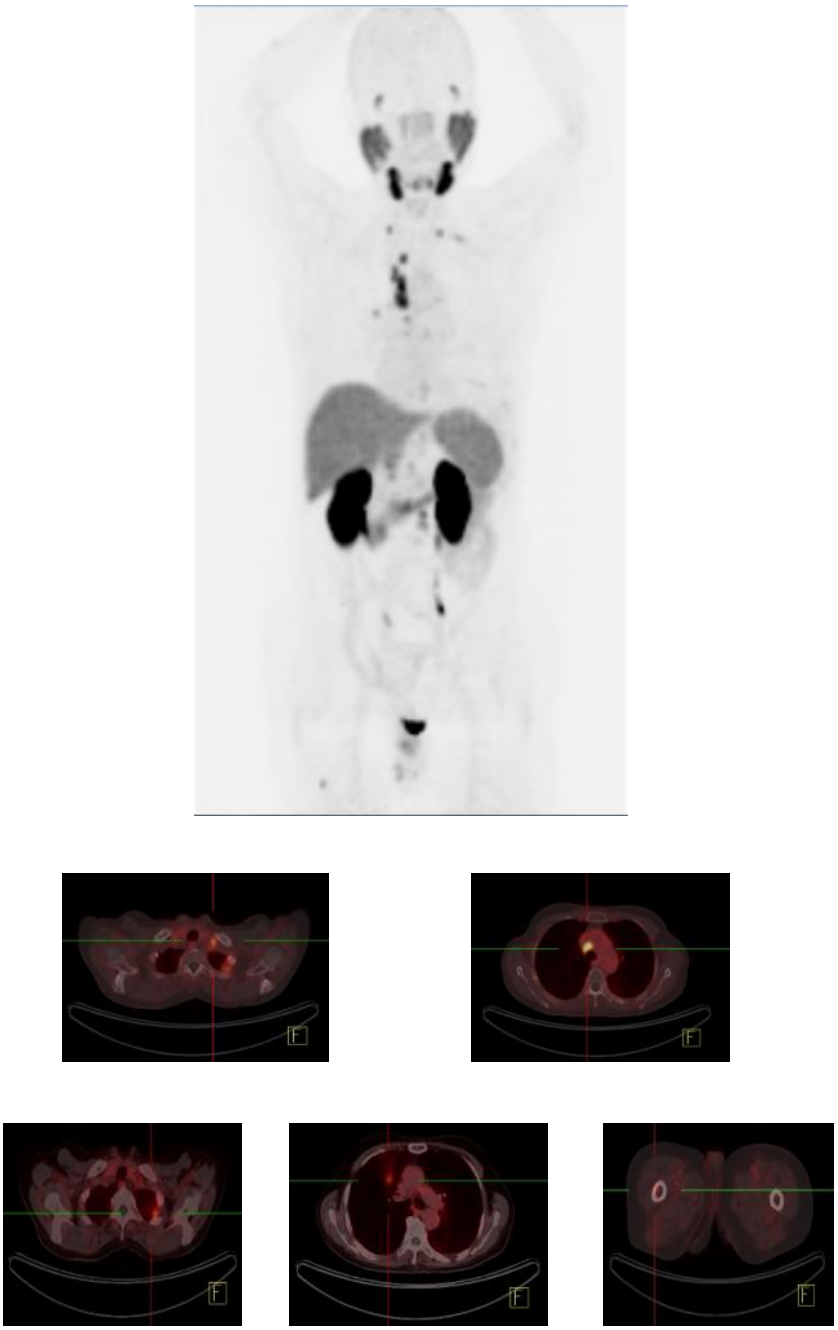

Fig. 2 Following Ga68-PSMA-11 PET/CT with 36ng/ml PSA level. MIP section and trans-axial metastasis involvement lesions