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Clinical note

Value of post-therapy ^{177}Lu PSMA images for accurate interpretation of therapy response with ^{68}Ga-PSMA PET/CT

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ABSTRACT

A 54-year-old man with progressive prostate cancer underwent a ^{68}Ga-PSMA-PET/CT, which showed lymph node and bone metastases. After 2-cycles of ^{177}Lu-PSMA therapy, the repeated ^{68}Ga-PSMA PET/CT showed decreased radiotracer uptake in lymph node and bones metastases, but there were new lesions which may be compatible with progression or tumour sink-effect. A review of ^{177}Lu-PSMA-therapy images revealed that new lesions in the second PET/CT were the metastatic lesions that progressed after the first PET/CT, and subsequently showed a good response. The patient received additional cycles of ^{177}Lu-PSMA therapy, and the disease regressed further, with a PSA of 0.06 ng/mL. Response evaluation of new therapeutic diagnostics (theranostic) agents needs a review of not only diagnostic PET/CT images, but also post-therapy images and laboratory results.

Valor de las imágenes de ^{177}Lu-PSMA post-terapia para una interpretación precisa de la respuesta a la terapia con ^{68}Ga-PSMA PET/TC

Palabras clave:
^{68}Ga-PSMA
^{177}Lu- PSMA
Regresión tumoral
Respuesta a la terapia

RESUMEN

Paciente de 54 años de edad con cáncer de próstata al que se realizó estudio PET/TC con ^{68}Ga-PSMA que mostró afectación linfática y metástasis óseas. Después de 2 ciclos de tratamiento con ^{177}Lu-PSMA, una nueva PET/TC mostró disminución de la captación en los ganglios linfáticos y las lesiones óseas, pero aparecieron nuevas lesiones compatibles con progresión de la enfermedad o efecto llamarada. La revisión de las imágenes de ^{177}Lu-PSMA mostró que las nuevas lesiones de la segunda PET/TC correspondían a lesiones metastásicas que captaban más que en la primera PET/TC y que posteriormente presentaron buena respuesta. El paciente recibió ciclos adicionales de tratamiento con ^{177}Lu-PSMA con regresión de la enfermedad, alcanzando niveles de PSA de 0,06 ng/mL. La evaluación de la respuesta de los nuevos agentes «teragnósticos» precisa realizar una revisión no solo de las imágenes diagnósticas de la PET/TC sino también de las imágenes posterapia y los datos de laboratorio.

Introduction

Prostate cancer is the third leading cause of cancer death in American men, behind lung cancer and colorectal cancer. Although the prognosis of early detected and hormone sensitive prostate cancer is excellent, disease may eventually progress to a more aggressive form, namely metastatic castration-resistant prostate cancer (mCRPC).[1] Although several treatments like abiraterone acetate and enzalutamide were found to increase the survival of these patients, there is a still need for improvement.[2] ^{177}Lu labeled prostate specific membrane antigen (PSMA) is a novel radionuclide therapy and demonstrates favorable safety and high efficacy exceeding those of other third-line systemic therapies in mCRPC patients.[3] Phase II/III studies are also planned to elucidate the survival benefit of this new therapy in patients with mCRPC. Despite an increase in the utilization, optimal dose, timing of cycles and therapy response evaluation with this new therapeutic radiotracer is still under investigation. We present a patient with mCRPC who underwent ^{177}Lu-PSMA therapy and discussed the tricky findings in ^{68}Ga-PSMA PET/CT and post-^{177}Lu therapy images that may guide the therapy plan.

Clinical case

A 54-year-old man with mCRPC had increasing PSA levels (445 ng/mL) despite chemotherapy and androgen deprivation therapy (ADT) referred to our clinic for restaging and evaluation for possible radionuclide therapy. He had underwent ^{68}Ga-PET/CT which revealed supraclavicular lymph node and extensive bone metastases (Fig. 1). Due to high uptake of radiotracer (SUV max: 24) in PET scan, patient received 2 cycles of 7400 MBq ^{177}Lu PSMA therapy. After therapy his PSA decreased to 0.4 ng/mL and post-therapy

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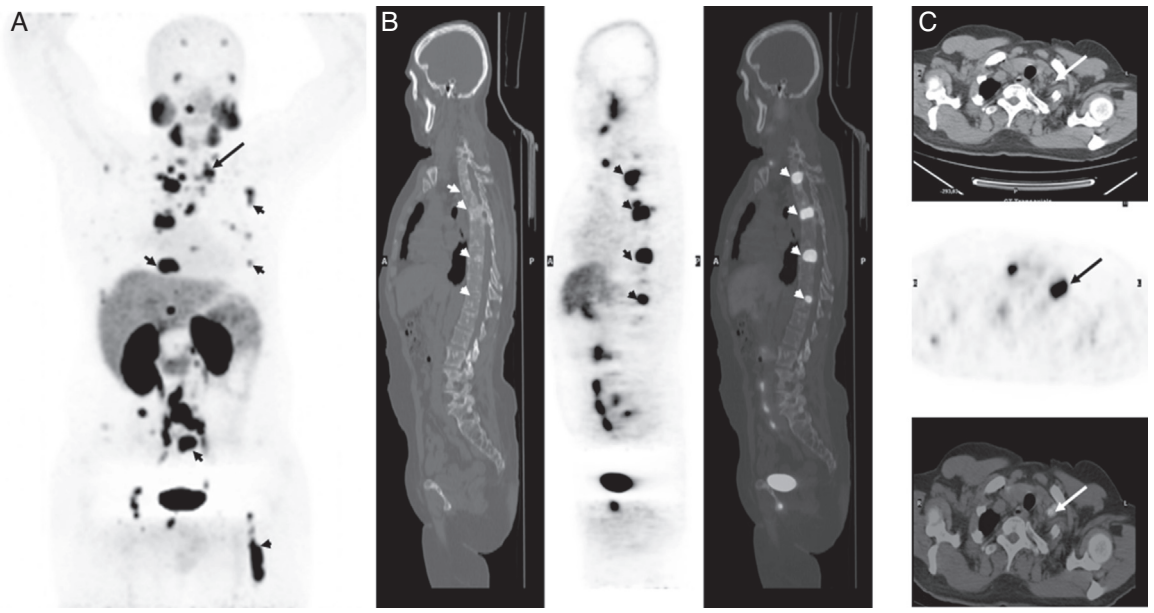

Fig. 1. ^{68}Ga-PSMA PET/CT showed supraclavicular lymph nodes (arrows) and widespread bone metastases (arrow heads) with high radiotracer uptake (SUVmax: 27) in PET maximal intensity projection (MIP), (B and C) sagittal and axial CT, PET and fusion images, respectively.

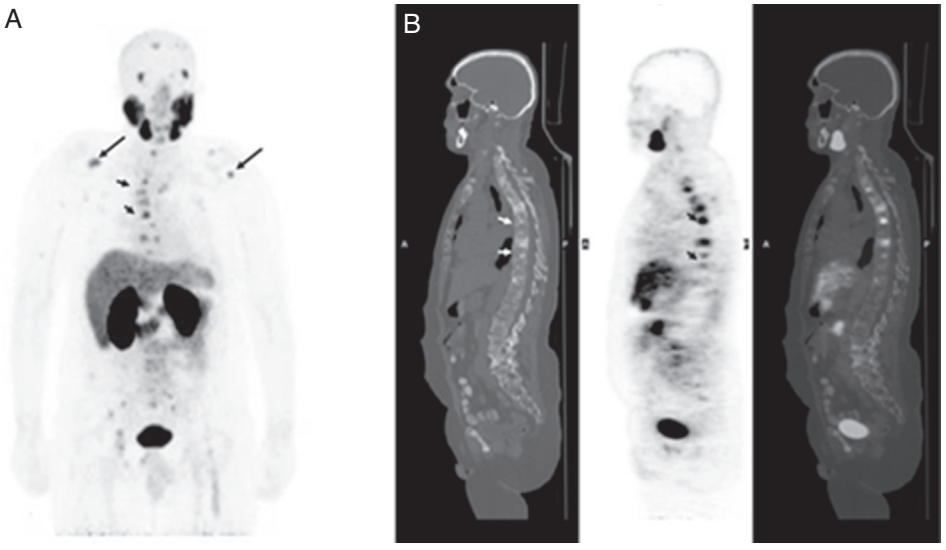

Fig. 2. Post-therapy ^{68}Ga-PSMA PET/CT showed decreased radiotracer uptake in supraclavicular lymph nodes and bones metastases but there were new uptake sites in both humeri (arrows) and vertebral bodies (arrow heads) in PET (MIP) (A) and (B) sagittal CT, PET and fusion images, respectively.

^{68}Ga-PSMA PET/CT showed decreased radiotracer uptake in supraclavicular lymph node and bones metastases. However, there were also new uptake sites in both humeri and in vertebral bodies when compared to pretherapy ^{68}Ga-PSMA PET/CT (Fig. 2). The new lesions were suspicious of disease progression despite therapy. Therefore, post-therapy ^{177}Lu-PSMA images were reviewed for a possible explanation. ^{177}Lu-PSMA images after the first therapy cycle (Fig. 3) showed more extensive bone and lymph node metastases than the first ^{68}Ga-PSMA PET/CT. Normal kidney and liver uptakes were also decreased in post-therapy scans. Comparative evaluation of diagnostic and therapeutic images showed that the disease indeed progressed between the first ^{68}Ga-PSMA PET/CT and the first ^{177}Lu-PSMA therapy (2 months). PSA also increased from 445 to 1532 ng/mL in this interval. The second ^{68}Ga-PSMA PET/CT images (Fig. 2) after 2 cycles showed the regression of the metastatic lesions seen at first in the ^{177}Lu-PSMA post-therapy images. These new lesions detected in the second post-therapy PET scan were accepted as metastatic lesions showing good response to ^{177}Lu PSMA therapy rather than progressive new lesions under therapy. The patient received 2 additional cycles of ^{177}Lu-PSMA and his PSA levels decreased to 0.06 ng/mL with only faint uptakes in vertebra and humerus in post-4th cycle images. Physiological liver and kidney uptakes were also reappeared in the last post-therapy images (Fig. 4).

Discussion

^{177}Lu PSMA is a relatively new radionuclide therapy used for mCRPC. Increased availability of automatic synthesis modules have facilitated the utilization of this therapy. The appropriate timing, dosage and response evaluation are the critical issues that are yet to be optimized. Our patient presents a major diagnostic problem in the therapy response evaluation of theranostic radiotracers. There might be several reasons for the new radiotracer uptake in both

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