Oncology

18-Fluoride-labeled sodium fluoride positron emission tomography is effective for assessing the therapeutic effect of Radium 223; a case report

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Introduction

Recently, 18-Fluoride labeled sodium fluoride positron emission tomography (18F-NaF PET) has been introduced as a new modality aimed at detecting bone metastatic lesions. Bone imaging with NaF PET provides high sensitivity and high resolution compared to bone scintigraphy using 99mTc-methylene diphosphonate (99mTc-MDP). We report a case where NaF PET was useful for evaluating bone metastasis with castration-resistant prostate cancer (CRPC) after treatment with Radium 223 (Ra-223).

Case presentation

An 87-year-old man had undergone prostate needle biopsy after a high prostate specific antigen (PSA) level (6.8 ng/mL) at the age of 73 years. He was diagnosed with adenocarcinoma of the prostate (Gleason score 3 + 4) and was treated with intensity modulated radiation (total 78 Gy), following androgen deprivation therapy (ADT). At 81 years of age, his PSA was found to be elevated again (3.75 ng/mL), and ADT was started. At 85 years of age, PSA recurrence was observed (PSA 8.3 ng/mL, serum testosterone level 13.0 ng/dL), and he was diagnosed with CRPC.

Diffuse osteoblastic lesions were observed on all vertebrae and the pelvic bone with computed tomography (CT) and magnetic resonance imaging (MRI) (Fig. 1 (A) (B)). Lymph node metastasis and visceral metastasis were not observed. No abnormal accumulation was observed in bone scintigraphy (Figure (C)). His serum alkaline phosphatase (ALP) level was 233 U/L (normal range; 115–359 U/L). He was diagnosed as having CRPC with only bone metastasis and we started Ra-223 treatment.

To evaluate bone metastasis quantitatively, NaF PET was performed before and after Ra-223 administration. Abnormal accumulation in the vertebral body, pelvis, femur with NaF PET and elevated standardized uptake value (SUV) were observed. SUV of the left ilium, thoracic vertebra (Th) 1, and Th12 was 7.603, 13.382, 9.616, respectively, suggesting the possibility of active bone metastasis (control SUV in the left forearm was 2.106) (Fig. 2(A)). In NaF PET after 6 courses of Ra-223 administration, corrected SUV by control SUV (1.598) decreased to 5.972 (left ilium), 8.155 (Th12) (Fig. 2 (B)) and it was possible to quantitatively evaluate the therapeutic effect on bone metastasis after Ra-223. Additionally, the ALP was decreased to 125 U/L.

Discussion

NaF was first introduced by Blau et al., in 1962 as a bone imaging formulation; it was approved by the Food and Drug Administration in 1972 and its value was recognized. At the time, however, bone scintigraphy using 99mTc-MDP was more suitable for gamma camera sensitivity. Scintigraphy therefore became popular as a bone imaging modality and imaging with NaF declined. However, since the 1990s, high-sensitivity and high-resolution PET devices have been available and the usefulness of NaF for bone imaging has recently been re-recognized.

The mechanism of accumulation of NaF is thought to be similar to that of 99 mTc-MDP; it accumulates in bone where remodeling is enhanced. NaF was found to be superior to bone scintigraphy in terms of...
short imaging time, high resolution analysis by PET camera, and quantification. A previous study reported that sensitivity and specificity of bone scintigraphy with 99 mTc-MDP were 57% and 57%, respectively, and those of NaF PET were 100% and 62%, respectively. Furthermore, it was reported that NaF PET is superior to bone scintigraphy for visualization of small metastatic lesions, particularly in the vertebrae. In our case, CT and MRI showed diffuse osteoblastic lesions, whereas abnormal accumulation was not observed with bone scintigraphy, which was supposed to detect bone metastasis. The reason for this discrepancy was thought to be that these bone metastatic lesions were very small and had occurred from the bone medulla. Therefore, they were difficult to visualize with the gamma camera because 99 mTc-MDP was insufficiently accumulated into the metastatic lesion. In NaF PET, due to the high uptake rate of 18F-NaF into the metastatic lesion and possible analyzation with the high-resolution PET camera, it was considered that abnormal accumulation could be confirmed using NaF PET even in a small metastatic lesion as in our case.

It has been shown that administration of Ra-223 prolongs the survival time of CRPC patients with only bone metastasis; however, its effect has not been proven on radiographic findings. Using NaF PET, SUV decrease was observed at the metastatic lesion in this case. Due to this, it was possible to quantitatively assess the treatment effect of Ra-223 through radiographic investigation, with a concomitant decrease in serum ALP, which is one of the markers of bone metabolism. For further confirmation of this finding, we are currently conducting a phase II clinical trial (NCT03305224).

Conclusion

NaF PET is superior for visualization of bone metastasis than bone scintigraphy, and it enables quantification of the therapeutic effect of Ra-223.

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Consent

Written informed consent was obtained from the patient for publication of this case report.

Conflicts of interest statement

None.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.eucr.2018.04.005.

Fig. 1. CT (A) and MRI (B) showed diffuse osteoblastic lesions throughout the vertebrae and pelvis (white circle), although bone scintigraphy (C) revealed no abnormal accumulation.

Fig. 2. Standardized uptake value (SUV) and corrected SUV as seen on NaF PET (A; pre-treatment with Ra-223, B; post-treatment with Ra-223) decreased on Th12 and the left ilium after Ra-223 administration.
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