Tc-99m-PSMA-SPECT/CT Is Superior to Tc-99m-MDP-SPECT/CT in the Staging of Prostatic Cancer with Osseous Metastases after External Beam Radiotherapy

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Abstract
Keywords
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In the reported patient with advanced prostate cancer, a bone scan showed a false positive finding in thoracic vertebra bone metastasis after external beam radiotherapy 2 months ago. An additional Tc-99m-prostate-specific membrane antigen scan showed a negative finding, although nonirradiated iliac bone metastasis was concordantly positive in both scans. The decrease in prostate-specific antigen-level from 156.6 ng/mL to 2.3 ng/mL indicates a strong effect of treatment, hence supporting false positivity in bone scan by flare phenomenon.

Introduction
In prostate cancer, existence and number of bone and lymph node metastases substantially influence overall survival.¹ In the last decade, Ga-68-prostate-specific membrane antigen positron emission tomography/computed tomography (PET/CT) has become the gold standard for the diagnosis of prostate cancer prior to primary therapy and when prostate-specific antigen (PSA) relapse occurs.²,³ Unfortunately, the costs for the Ge-68/Ga-68-generator are high and PET/CT systems are not available worldwide. Since Tc-99m-PSMA single-photon emission computed tomography/computed tomography (SPECT/CT) is able to detect extraskeletal and skeletal metastases, it has the potential to replace Tc-99m-methyl diphosphonate (Tc-99m-MDP) bone scan in standard staging, when Ga-68-PSMA PET/CT is not available.

Case Report
A 65-year-old man with PSA level of 154.6 ng/mL had received an initial diagnosis of metastasized prostate cancer cT4 cN0 (Gleason 4 + 5 = 9). A bone scan with Tc-99m-MDP revealed three bone metastases in the left iliac body, right third rib, and thoracic vertebrae (T) 10 to T12 (not published). Systemic treatment with androgen deprivation and local treatment with external beam radiotherapy of T10 with 42.5 Gy and T11-T12 with 50 Gy was performed. The PSA level decreased to 2.3 ng/mL. Restaging was performed with SPECT/CT (GE NM/CT 850ES, GE Healthcare, Dresden, Germany), using 13.9 mCi (515 MBq) Tc-99m-MDP (ROTOP Pharmaka GmbH, Dresden, Germany) and 17.0 mCi (629 MBq) Tc-99m-PSMA (PSMA-Tc-API, Institute of Isotope, Budapest, Hungary).

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Fig. 1  Comparison of scans with Tc-99m-methyl diphosphonate (MDP) and Tc-99m-prostate-specific membrane antigen (PSMA) after external beam radiotherapy of thoracic vertebrae 10 to 12. Within the third month after external beam radiotherapy, whole-body scans with (A) Tc-99m-MDP and (B) Tc-99m-prostate-specific membrane antigen (PSMA) revealed concordant metastatic sites in the (A, B) third rib (blue arrow) and iliac body (pink arrow). Within the radiation field, bone scan (C) was strongly positive, whereas PSMA scan (D) presented in none (T11, green arrow) to slightly (T12, red arrow) increased uptake. MDP uptake extends to the whole T12, (E) whereas PSMA uptake spares the left arcus vertebrae (F). Nonirradiated metastasis of iliac body (G, H) served as internal positive control and had uptake in both scans. SPECT/CT, single-photon emission computed tomography/computed tomography scan.
A Tc-99m-MDP whole-body scan was performed 2 hours post injection, which showed strongly positive findings at the sites of the known metastases in the third rib, iliac body, T11, and T12 (► Fig. 1A). A SPECT/CT (140 kV, 20 mA, 146 mGy/cm) added sclerosis and involvement of T12 including arcus vertebrae (► Fig. 1C, E). A following Tc-99m-PSMA scan with SPECT/CT (140 kV, 30 mA, 337 mGy/cm) revealed concordant positive findings in the third rib and iliac body, prostate cancer, and no lymphatic involvement (► Fig. 1B). The sclerotic lesions in T11 and T12 were negative in the PSMA scan (► Fig. 1D, F). Quantification of uptake (Q.VMI Evolution, GE Healthcare) was performed by comparison of irradiated and nonirradiated lesions. Since the iliac body was not included in the radiation field, it served as an internal positive control. Ratio of T12/iliac body was 1.2 in MDP SPECT/CT in contrast to 0.2 in PSMA SPECT/CT. Normalization of T12 to iliac body indicated a 3.0-fold reduced uptake of T12 in PSMA SPECT/CT.

Discussion

Although androgen deprivation and external beam radiotherapy have led to a remarkable reduction in PSA-level, the uptake of Tc-99m-PSMA and Tc-99m-MDP in nonirradiated sites has remained high. About 2.25 months after external beam radiotherapy, normalized uptake of Tc-99m-PSMA has been reduced by 3.0-fold in comparison to Tc-99m-MDP.

The high uptake of T12 in the bone scan suggests a false positive. The pathophysiological effect is called “flare phenomenon” and is caused by an enhanced turnover of hydroxyapatite as part of the healing process after external beam radiotherapy. Therefore, the tumor-specific binding of Tc-99m-PSMA is able to evaluate the therapeutic effect 2 months after external beam radiotherapy superior to Tc-99m-MDP. Moreover, SPECT/CT with Tc-99m-PSMA is able to reduce the frequency of false positive findings in a bone scan after external beam radiotherapy, presumably after trauma, and in pronounced degenerative changes in the spine. Studies of patients with Tc-99m-PSMA SPECT/CT before and after external beam radiotherapy may show that Tc-99m-PSMA is able to predict responsiveness to external beam radiotherapy, in contrast to Tc-99m-MDP.

Declarations

The authors declare that no funding was applicable. The authors declare that no conflicts of interest/competing interests were applicable. The authors declare that no ethics approval was necessary. The authors declare that no consent to participate was necessary. The authors have consent of publication of their data. The used data and material are available and can be requested. The licenses of used software are available.

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