Evaluating treatment response in breast cancer: a case report on static metastatic disease on bone scans

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ABSTRACT

Background: We report a case of a 54-year-old female patient with carcinoma of the left breast with persistent methylene diphosphonate (MDP) uptake in sclerotic osseous lesions. These lesions were finally declared treated osseous metastatic lesions due to non-avidity on the 18-fluorine-fluorodeoxyglucose positron-emission-tomography/computed tomography [F-18 FDG Positron emission tomography (PET-CT)] scan, normalization of CA-15.3, and resolution of bone pains. To the best of our knowledge, this has not been reported previously.

Case Presentation: A 54-year-old woman with persistent backache was referred for further evaluation by a Tc99m MDP bone scan. A Tc99mmMDP bone scan showed wide-spread skeletal metastatic disease. Magnetic resonance imaging (MRI) showed extensive marrow disease involving the spine and iliac bones. A bone marrow biopsy revealed metastatic carcinoma with a tumor phenotype favoring breast primary. On further workup, the patient was diagnosed with invasive ductal carcinoma of the left breast and was treated with cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitors along with hormone therapy and bisphosphonates, followed by radiation therapy for bone metastasis. The skeletal metastatic disease remains static on three consecutive Tc99m MDP bone scans, despite the clinical improvement and decreased tumor marker levels.

The F-18-FDG-FDG-CT scan done for monitoring treatment response revealed multiple non-avid sclerotic osseous lesions, favoring treatment response. The patient was continued with the same treatment, and a follow-up Tc99m MDP bone scan after 6 months revealed no interval change in the reported lesions compared to the initial scan. However, a synergistically performed F-18 FDG PET-CT scan again showed multiple non-avid sclerotic osseous lesions suggestive of treated metastasis.

Conclusion: This case highlights the importance of 18-F-FDG PET-CT in evaluating the treatment response, especially in patients with symptomatic improvement and falling tumor marker levels with static disease on repeated Tc99m MDP bone scans.

Keywords: Tc99m MDP bone scan, breast carcinoma, F-18-FDG PET-CT, treated metastasis, case report.

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Background

A bone scan detects bone metastases only after an osteoblastic host reaction has begun in response to tumor infiltration [1]. In addition, a lack of anatomical detail, limited sensitivity and specificity, and the confounding effect of the flare phenomenon after therapy make it unsuitable for evaluating the therapy response [2]. Consistent Tc99m Methylene diphosphonate (MDP) uptake in sclerotic lesions without any significant regression of osteoblastic activity even on resolution of underlying malignant/metastatic potential, as evident by non-avidity on the F-18 FDG positron emission tomography (PET-CT) scan, is a rare entity. To the best of our knowledge, this has not often been reported before. It demonstrated the incremental value of F-18 FDG PET-CT in evaluating the response to therapy, especially in patients with static disease, on repeated follow-up Tc99m MDP bone scans. It is necessary to identify these false-positive cases on a bone scan for appropriate management of the patients.

Case Presentation

A 54-year-old woman with a history of backache for 6 months was referred for a Tc99m MDP bone scan in 2021. A Tc99mmMDP bone scan revealed wide-spread skeletal metastasis (Figure 1). In the Magnetic resonance imaging (MRI) of the lumbar spine, extensive marrow disease is seen, with foci of relatively low MR signals occupying almost all vertebral bodies and iliac bones, consistent with marrow disease, with no significant disc disease in the lumbar area. A bone marrow biopsy showed marrow

involvement with metastatic adenocarcinoma, with immunohistochemical staining favoring the breast primary. Mammography showed a 1.5 cm spiculated lesion in the upper outer quadrant of the left breast, which on wide local excision revealed invasive ductal carcinoma, histologic grade 1, estrogen receptor-positive, progesterone receptor-positive, and human epidermal growth factor receptor 2-negative. The serum study showed elevated cancer antigen 15–3 (83 U/ml).

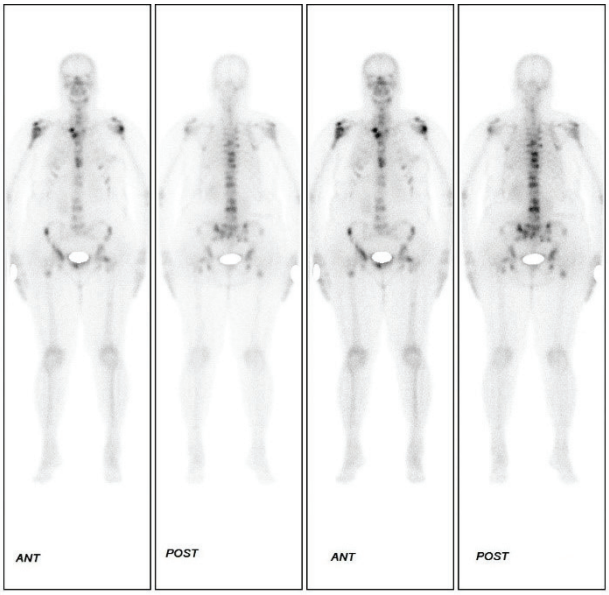

Figure 1. *A Tc99m MDP bone scintigraphy showed multiple areas of abnormally high uptake in the sternum, spine, humerus on both sides, SI joints, pelvic bones, and proximal femori on both sides. This was consistent with the disease spreading to the bones.*

She was put on cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitors along with hormone therapy and bisphosphonates, followed by palliative radiotherapy for spinal and iliac bone metastasis. A bone scan is done at 6 monthly intervals and revealed static disease at two consecutive follow-up scans (Figure 2). However, the cancer antigen 15–3 level has dropped in serum (61 U/ml). The patient's clinical condition is getting better, particularly in relation to bony pains. A synchronized F18 FDG PET/CT scan was done for the evaluation of treatment response. The F-18-FDG PET/CT scan showed several non-avid sclerotic osseous lesions, which was good for treatment response (Figure 3). The patient was continued with the same treatment, and a follow-up Tc99m MDP bone scan after 6 months revealed multiple areas of increased uptake throughout the axial and appendicular skeleton with no significant interval change compared to the initial scan (Figure 4). However, an F-18 FDG PET-CT scan done one week apart showed multiple non-avid sclerotic osseous lesions suggestive of treated metastasis (Figure 5).

Discussion

Cancer metastasis is one of the major causes of morbidity and death in cancer patients. The bone marrow

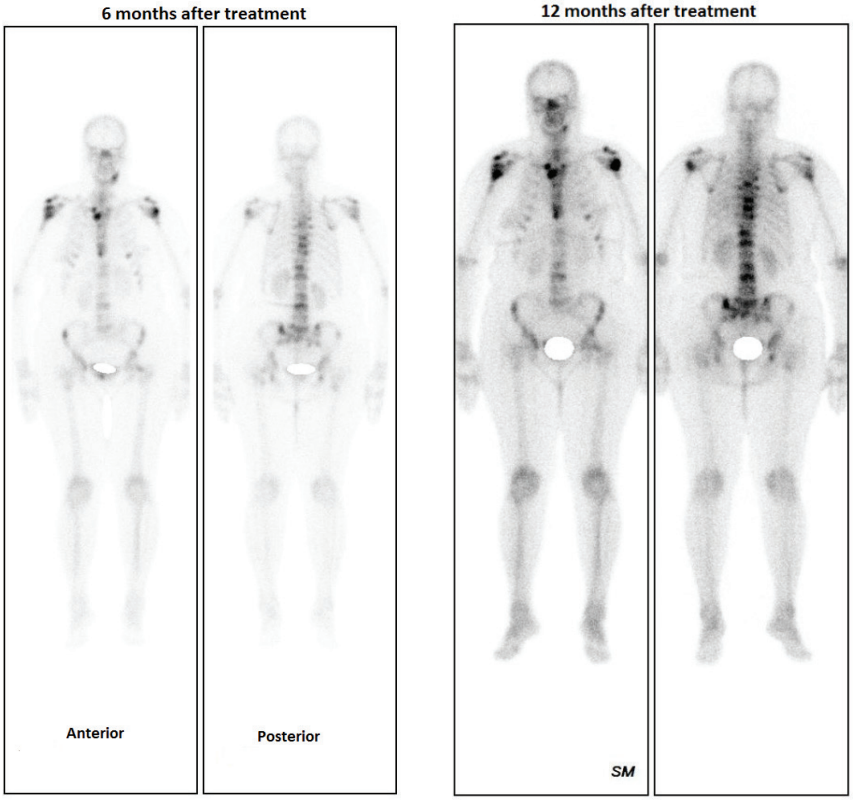

Figure 2. *Tc99m MDP bone scintigraphy done after 6 and 12 months after treatment, showed no significant interval change in metastatic lesions.*

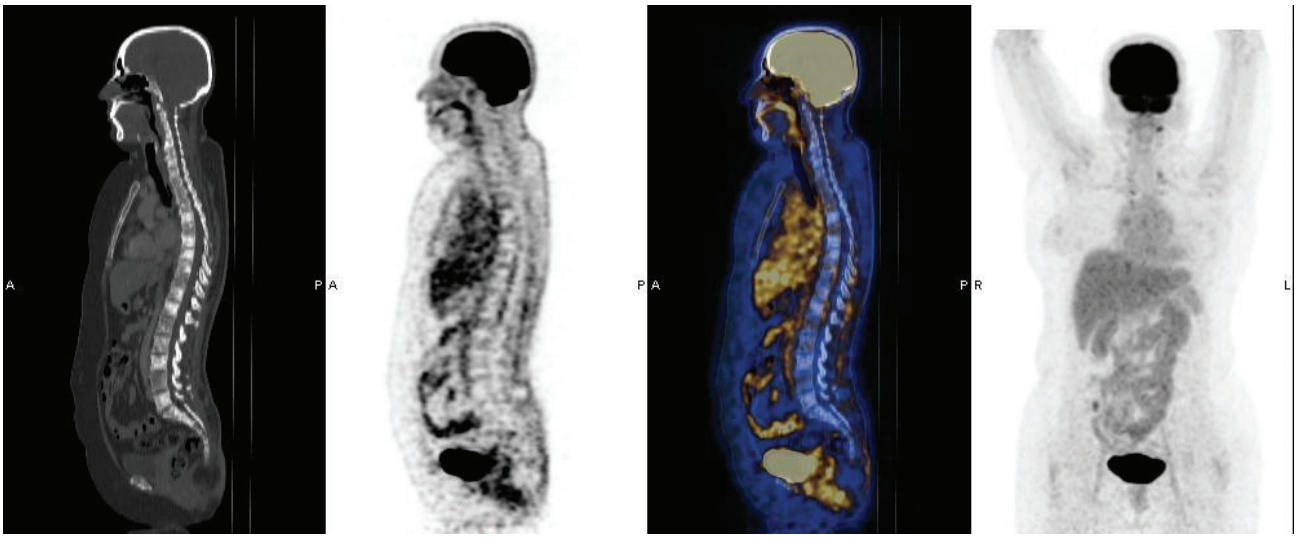

Figure 3. *F-18 FDG PET-CT scan after 1 year of treatment showed multiple sclerotic osseous lesions with no FDG avidity, likely treatment response.*

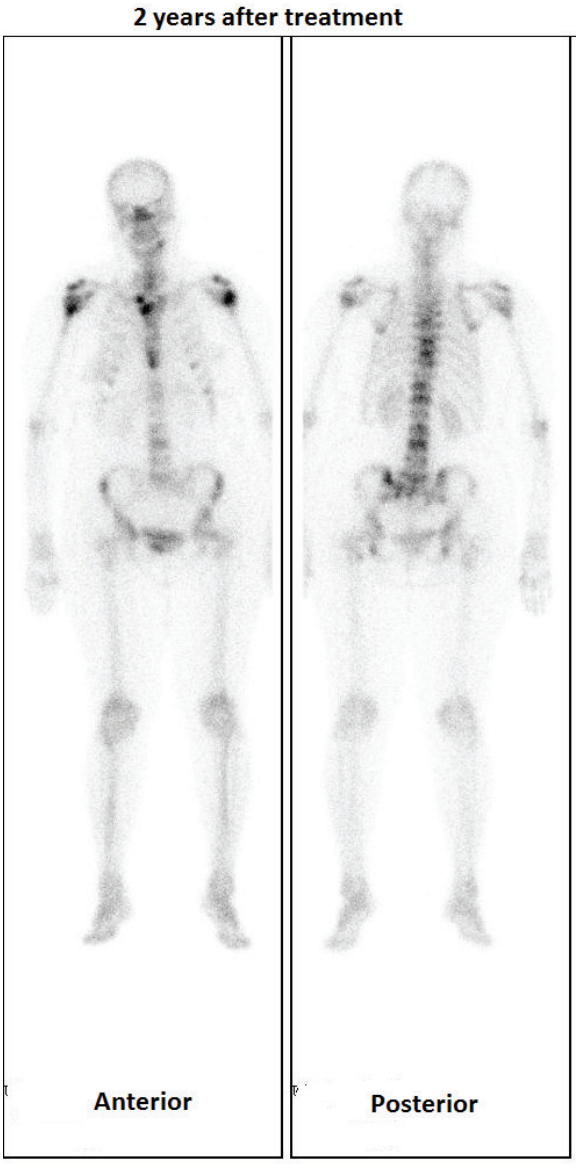

Figure 4. *Tc99m MDP bone scintigraphy done at initial presentation and 2 years after treatment, showed no significant interval change in metastatic lesions.*

and cortex provide a fertile environment with abundant blood flow and growth factors for the growth of metastasis. Once the tumor gets metastasized to the bone marrow, it will trigger complicated interactions regulated by various growth factors released by the tumor, osteoclasts, and osteoblasts, resulting in different types of bone metastasis [3].

Breast cancer guidelines and consensus recommendations [4] indicate that various imaging tests may be used for the evaluation of suspected bone metastasis or in the staging and restaging of patients with breast cancer. Although bone scintigraphy is the most consistently recommended test in guidelines, other investigations have also been recommended for imaging bone metastasis, including plain radiography (X-ray), MRI, CT, PET, single photon emission computed tomography, and related hybrid scans [5].

Molecular imaging provides new clues to explain the regulation of the microenvironment in bone marrow [6,7]. Based on the seed-and-soil theory, the initiation of bone metastasis is not only the result of massive osteotrophic metastatic cancer infiltrating the bone marrow with subsequent increased bone turnover, mapped by bone imaging agents, but also the triggering of serial endocrine systems leading to enhanced glucose metabolism, mapped by molecular imaging agents like FDG. This phenomenon gained importance, especially when we are looking for a response to treatment in which there are continuous reparative phenomena in bones but the mechanism of enhanced glucose metabolism gets slowed down. Previous studies have shown that the sensitivity, specificity, and accuracy for determining skeletal metastatic disease by F18-FDG PET-CT is 97%, 98%, and 98%, respectively, and of bone scans were 83%, 93%, and 98%, respectively [8]. However, 18F-FDG PET/CT has higher sensitivity, specificity,

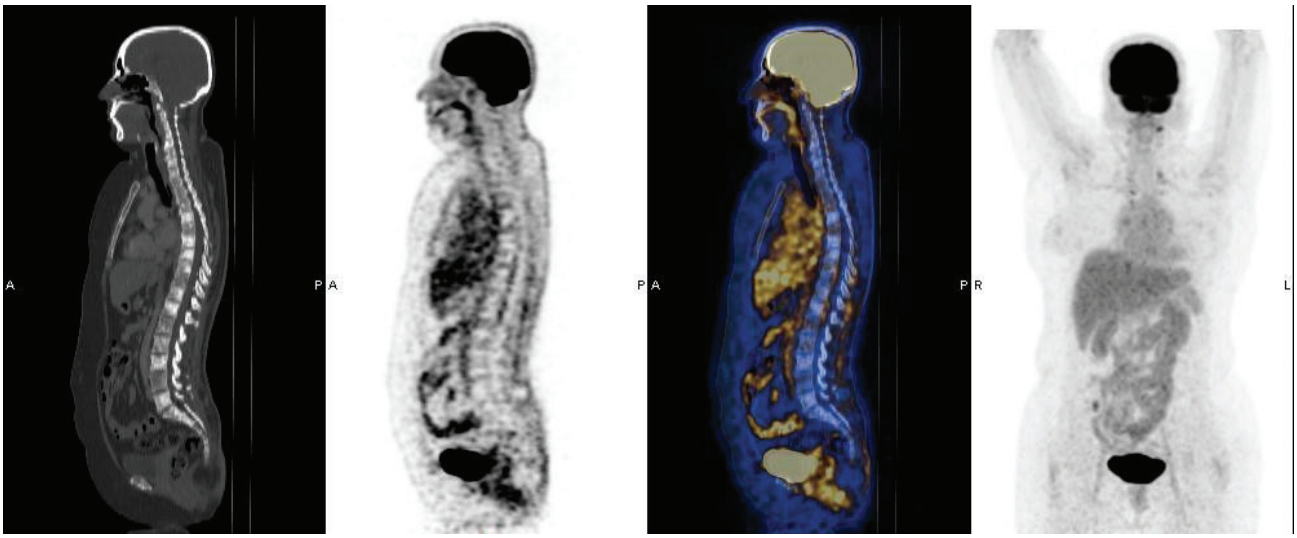

Figure 5. *F-18 FDG PET-CT scan after 2 years of treatment showed no metabolically active bony lesion in the entire imaged skeleton, suggestive of complete treatment response.*

and accuracy in detecting osteolytic bone metastases than 99mTc-MDP whole body bone scan, i.e. e 94.3%, 83.3%, and 94.2%, respectively, compared to 50.2% sensitivity, 50.0% specificity, and 50.2% accuracy of bone scan. [9]

In our patient, we found that even on follow-up, there is continuous uptake of MDP in initially reported sclerotic osseous lesions without any corresponding F18-FDG uptake. The lesions have remained static for the last two and a half years, but the patient has clinically improved with normalization of tumor marker levels, favoring treated osseous metastasis with MDP uptake. Though histopathological evaluation of bony lesions has not been done, the persistence of uptake in these lesions for one and a half years may not favor the phenomena of flare phenomena. The persistent uptake of MDP in these sclerotic osseous lesions indicated an active reparative process due to continued bisphosphonate administration at 3-month intervals. Such false-positive cases may also be avoided by using ancillary tests of osteoclastic activity to bridge the gap between classical tumor markers and imaging techniques while monitoring skeletal metastases.

Conclusion

This case demonstrated the incremental value of F18 FDG PET-CT in evaluating the treatment response, especially in patients with static metastatic disease on repeated follow-up Tc99m MDP bone scans. It is necessary to identify these false-positive cases on a bone scan, especially in the context of falling serum levels of tumor markers and an improved patient's clinical status, thereby leading to appropriate management strategies. It would be an interesting and valuable area of research to establish large-scale clinical correlations based on different cancer entities in the future.

What is new?

The authors report a case of a 54-year-old female patient with carcinoma of the left breast with persistent methylene diphosphonate (MDP) uptake in sclerotic osseous lesions. These lesions were finally declared treated osseous metastatic lesions due to non-avidity on the F18 FDG PET-CT scan, normalization of CA-15.3, and resolution of bone pains. To the best of the authors' knowledge, this has not been reported previously.

List of Abbreviations

CT	Computed tomography
ER	Estrogen receptor
MDP	Methylene diphosphonate
MRI	Magnetic resonance imaging
PET	Positron emission tomography
SPECT	Single photon emission computed tomography

Conflict of interest

The authors declare that they have no conflict of interest regarding the publication of this case report.

Funding

None.

Consent for publication

Informed written consent was obtained from the patient to publish this case in a medical journal, anonymously.

Ethical approval

Ethical approval is not required at our institution for publishing a case report in a medical journal.

Author details

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Summary of the case

1	Patient (gender, age)	54 years old, female
2	Final diagnosis	Carcinoma of left breast with treated metastasis on F18-FDG PET-CT and static on bone scan
3	Symptoms	Backache
4	Medications	cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitors along with hormone therapy
5	Clinical procedure	Tc99m MDP bone scan and F18-FDG PET-CT
6	Specialty	Nuclear medicine