

# The Intricate Diagnostic Journey of a Breast Cancer Patient, Revealing Extensive Hepatic Metastasis Through Extraosseous Uptake in Planar Bone Scintigraphy and SPECT-CT Precision Mapping

<sup>1</sup>Afroza Akhter, <sup>1</sup>Shaila Sharmin, <sup>1</sup>Farhana Rahman, <sup>1</sup>Sabrina Islam, <sup>1</sup>Sadia Hossain, <sup>1</sup>Rawnak Afrin, <sup>1</sup>Tanima Biswas, <sup>1</sup>Rubina Begum, <sup>1</sup>Shankar Kumar Biswas, <sup>1</sup>Jasmine Ara Haque, <sup>2</sup>Mohammad Ashraf-Us-Zaman Mahmud

<sup>1</sup>Institute of Nuclear Medicine & Allied Sciences (INMAS), Dhaka

<sup>2</sup>National Institute of Cancer Research & Hospital (NICRH), Dhaka

**Correspondence Address:** Dr. Afroza Akhter, Senior Medical Officer, INMAS, DMCH Campus, Dhaka, Bangladesh. Phone: +8801816404873  
E-mail: afrozainmas@gmail.com

## ABSTRACT

In breast cancer patients, planar bone scintigraphy is commonly used for detecting osseous metastasis. This case report emphasizes the importance of recognizing unusual extraosseous uptake in bone scintigraphy, even when negative for osteoblastic lesions. A 35-year-old post-treatment breast carcinoma patient exhibited unexpected radiotracer uptake in the upper abdomen. Subsequent SPECT/CT revealed radiotracer-avid calcified hepatic lesions and extensive non-avid metastatic lesions, however no osteoblastic metastasis. Ultrasound-guided core biopsy confirmed extensive hepatic metastases secondary to ductal carcinoma of the breast. This highlights the critical role of SPECT/CT in precisely identifying and characterizing lesions, aiding in advanced breast cancer diagnosis and management planning.

**Keywords:** Breast cancer, Extraosseous Uptake, Planar Bone Scintigraphy, SPECT-CT.

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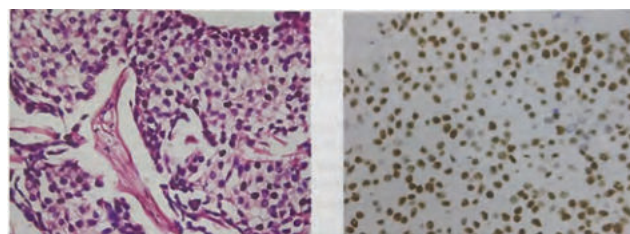
## INTRODUCTION

<sup>99m</sup>Tc-Methylene diphosphonate (MDP) planar bone scintigraphy (PBS) is one of the most common sensitive imaging modalities for the detection of osseous metastasis in breast carcinoma patients. However, sometimes unusual extraosseous uptake in PBS may identify a hidden disease process as a tip of the iceberg and additional single photon emission computed tomography/computed tomography (SPECT/CT) further plays a crucial role in the precise localization and characterization of that lesion, thus informing the referring physician about the advanced stage of the disease, its prognosis, and treatment planning. Here we

reported a case of a breast carcinoma patient having negative planar bone scintigraphy for osteoblastic metastasis with evidence of extraosseous MDP uptake in the upper abdomen, which was further confirmed by SPECT/CT as extensive hepatic metastasis.

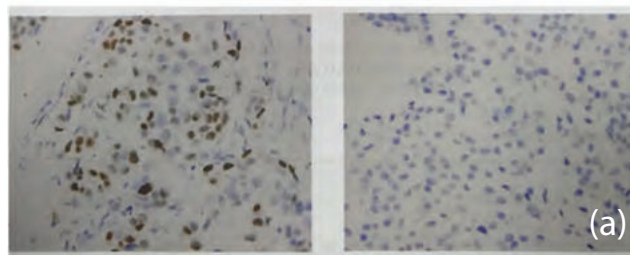
## CASE REPORT

A 35-year-old woman with diagnosed left-sided breast carcinoma (T1N2M0) underwent modified radical mastectomy with axillary clearance in 2015. Histopathology revealed moderately differentiated infiltrating duct cell carcinoma (grade-II) with axillary lymph node metastasis. Immunohistochemistry (IHC) showed estrogen receptor (ER) positivity, progesterone



H&E: Infiltrating ductal carcinoma, NOS, moderately differentiated

Estrogen receptor: Nuclear reactivity, Positive

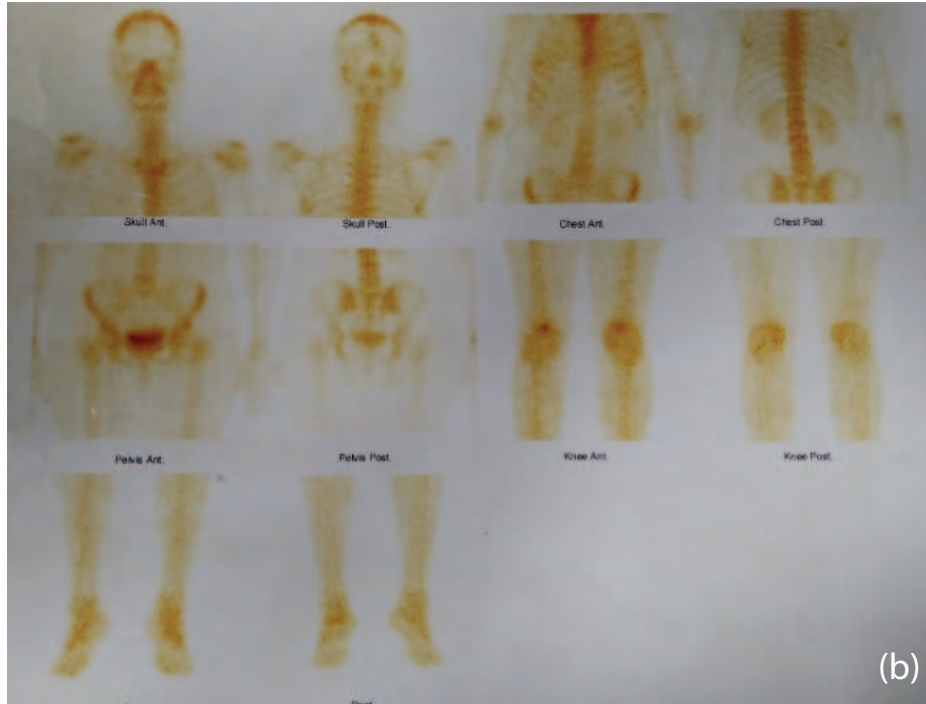


progesterone receptor, Nuclear reactivity, Positive

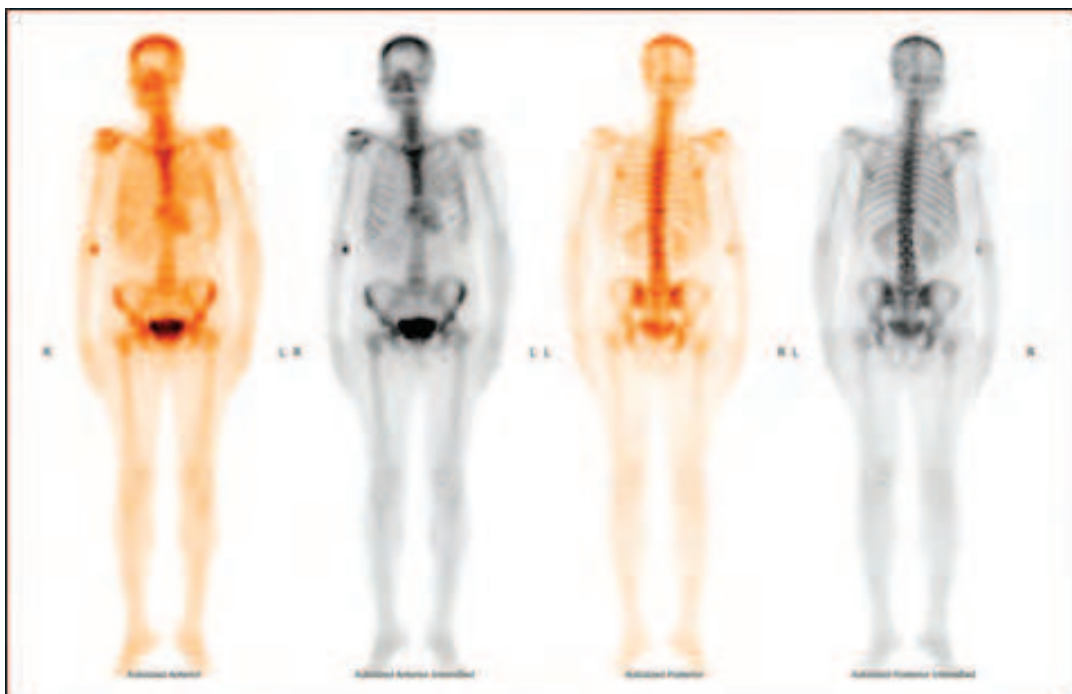
Her2/neu: Membrane reactivity, Negative

receptor (PR) positivity, and human epidermal growth factor receptor 2 (HER2/neu) negativity (Figure 1a). Her baseline <sup>99m</sup>Tc -MDP bone scintigraphy was negative for osteoblastic metastasis (Figure 1b). Following this, she

received six cycles of chemotherapy with 5-fluorouracil, doxorubicin, and cyclophosphamide, along with radiotherapy in 2016. Subsequently, she underwent hormone therapy with tamoxifen for a five-year duration.



**Figure 1:** (a) Immunohistochemistry showing moderately differentiated infiltrating ductal carcinoma (IDCC), ER/PR positive, HER-2 negative status (b) Baseline planar bone scintigraphy: negative for osteoblastic metastasis.

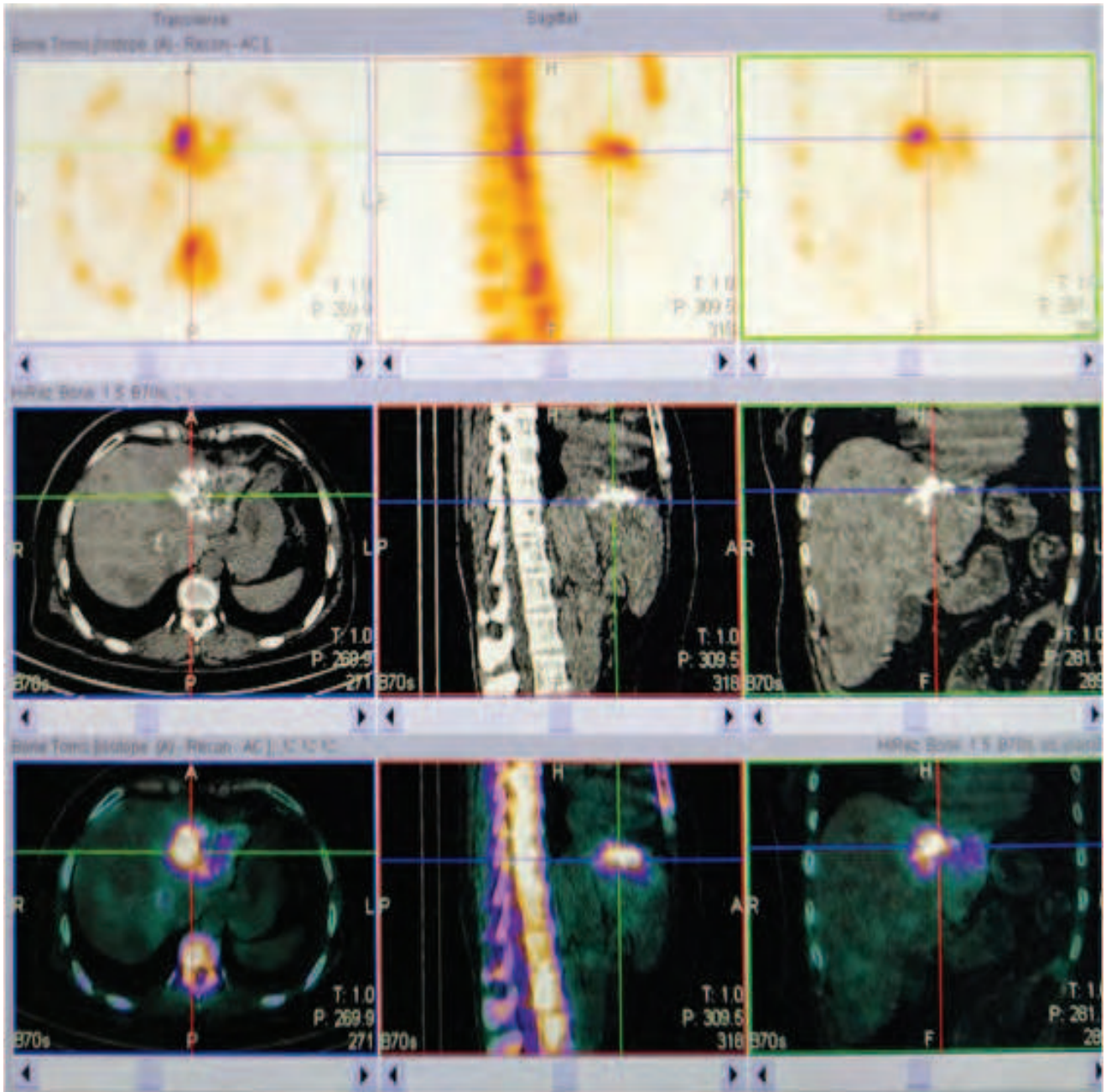


**Figure 2:** <sup>99m</sup>Tc-MDP planar bone scintigraphy showing unusual extraosseous uptake in upper abdomen anterior view (blue arrow), no focally increased radiotracer uptake elsewhere in the skeleton.

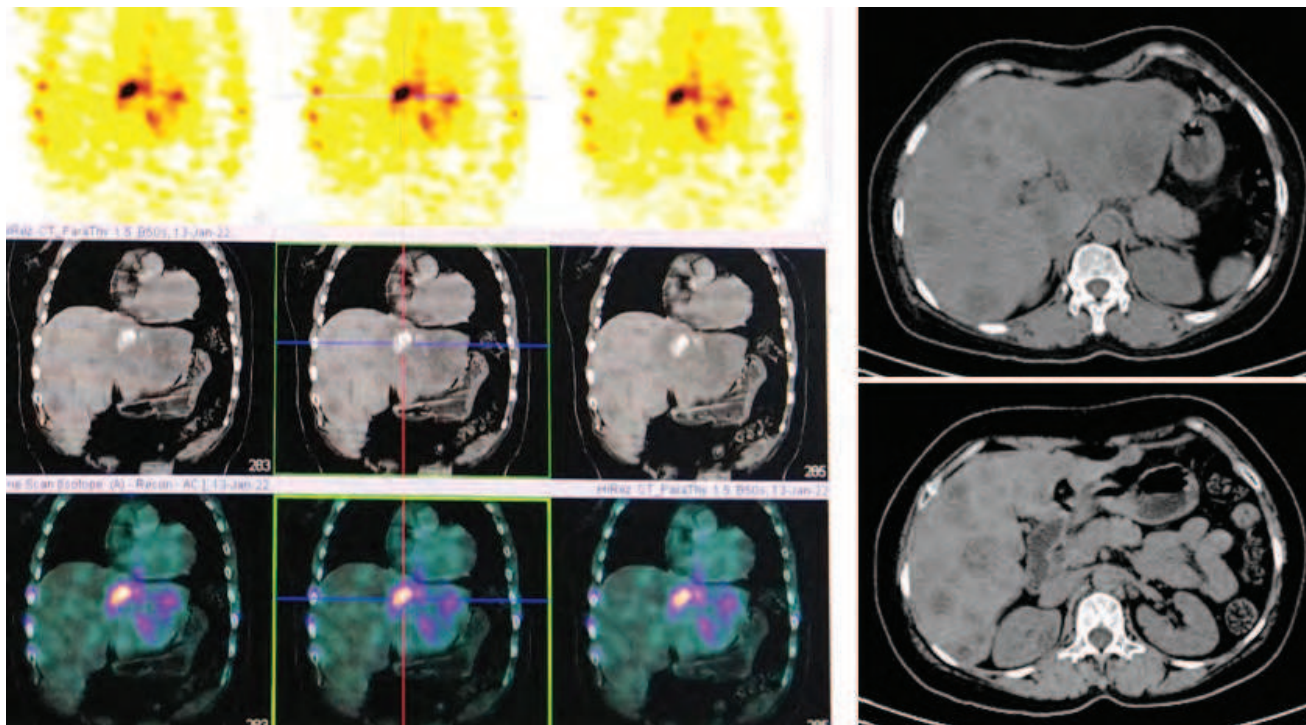
The patient remained asymptomatic until June 2021, with no biochemical or imaging evidence of recurrence during that period. However, she recently reported persistent nausea and loss of appetite over the last three months. Biochemical parameters indicated CA 15-3 levels at 7.80 U/ml, SGPT at

50 U/L, SGOT at 85.0 U/L, and serum bilirubin at 0.29 mg/dl. Referred to the nuclear medicine department for a routine bone scan, her planar bone scintigraphy was negative for osteoblastic metastasis but revealed an incidental unusual radiotracer uptake in the upper abdomen (Figure 2).

Regional SPECT/CT confirmed the tracer activity over calcified hepatic lesions at segment II, III and IV with extensive non-avid hypodense metastatic lesions throughout the hepatic parenchyma; few of them showing central necrosis in CT images (Figure 3, 4).

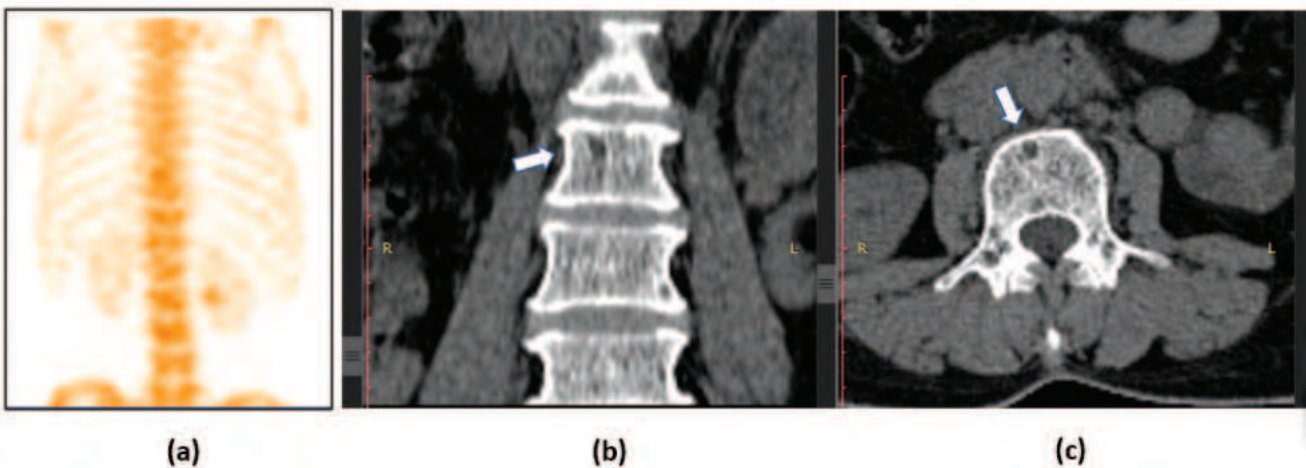


**Figure 3: Regional SPECT-CT of abdomen (upper row SPECT, middle row CT and lower low fused SPECT-CT) in axial, sagittal and coronal views showed intense radiotracer uptake over metastatic calcified hepatic lesions.**



**Figure 4:** SPECT/CT of abdomen (coronal sections, left panel) showing increased 99mTc-MDP uptake in multiple calcified metastatic lesions in hepatic segments II, III and IV. In addition, extensive non-avid hypodense lesions throughout the hepatic parenchyma in axial CT images (right panel).

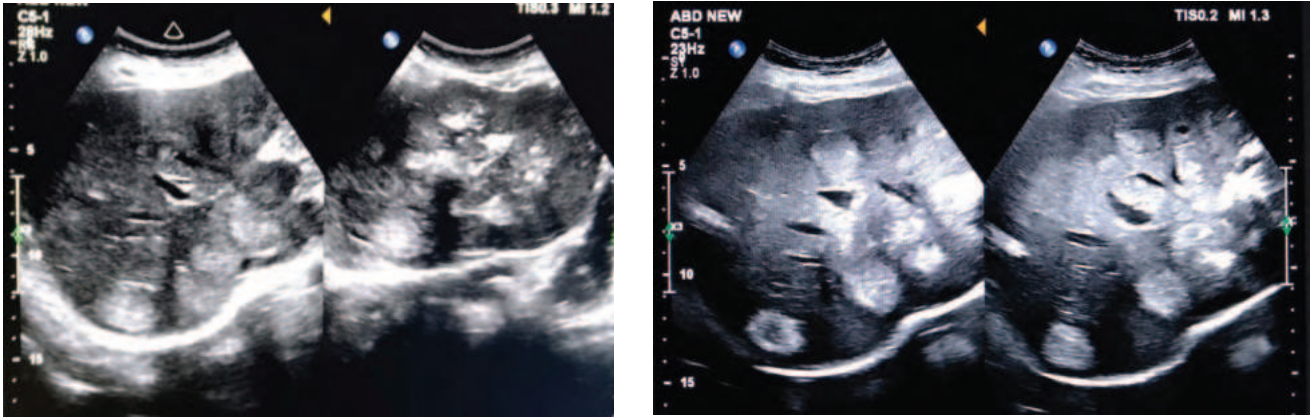
There was minimal osteoporotic change in 3rd lumbar vertebra on CT and no abnormally increased focal osteoblastic activity in SPECT image (Figure 5).



**Figure 5:** (a) Coronal SPECT image of dorso-lumbar vertebrae showed no focal increased osteoblastic activity; (b) Coronal and (c) axial CT images showing minimal osteoporotic changes in 3rd lumbar vertebra.

Ultrasound of abdomen also revealed extensive metastatic lesions in the hepatic parenchyma; multiple irregular areas of calcifications mainly at left lobe and adjacent right lobe (segment II, III & IV) casting posterior acoustic shadow

(Figure 6). Ultrasound guided core biopsy from hepatic lesions revealed metastatic ductal carcinoma. Patient did not perform immunohistochemistry from metastatic hepatic lesions.



**Figure 6: Ultrasound image of abdomen showing multiple solid hypo and hyperechoic lesions of variable sizes throughout the hepatic parenchyma; few lesions having central cystic spaces.**

A new chemotherapy regimen, incorporating injectable docetaxel and oral capecitabine, was initiated for the treatment of visceral metastasis arising from the primary breast carcinoma. Follow-up revealed symptomatic clinical improvement.

## DISCUSSION

Planar bone scintigraphy is a widely available and cost-effective imaging modality for breast carcinoma patients. It serves as both a baseline screening tool and a follow-up method to detect skeletal metastasis in asymptomatic individuals or those at high risk of breast cancer (1). The extraosseous soft tissue uptake of bone-seeking radiopharmaceuticals, such as hepatic MDP uptakes in planar bone scintigraphy, demonstrates clinical significance with various etiologies. The differentiation between benign and pathological conditions is based on the degree and pattern of uptake. Artefactual or faulty preparation of radiopharmaceuticals, such as excess aluminum ion breakthrough in  $^{99m}\text{Tc}$  eluate, misadministration, or extravasation from the injection site, may manifest as mild diffuse hepatic uptake (2, 3). Pathological causes, such as diffuse hepatic necrosis, repeated iron injections, acute hypoxic hepatitis, hypoxia secondary to respiratory failure, amyloidosis associated with plasma cell dyscrasia, and the late stage of multiple myeloma, can exhibit diffuse and intense hepatic MDP uptake. In cases of hepatic metastases, the pattern of MDP uptake typically appears focal and scattered rather than diffuse. This distinction may be attributed to calcifications or cellular necrosis within the metastatic lesions (3, 4). The

similar pattern is observed in our presenting case, and we confirmed it through SPECT/CT. SPECT/CT proves to be effective in accurately localizing and characterizing lesions detected on planar bone scintigraphy (PBS) by directly fusing anatomical and functional information. This fusion enhances the sensitivity and specificity of planar scintigraphy, providing additional diagnostic value (4).

Hepatic metastases can manifest asymptotically, leading to potential misdiagnosis due to vague symptoms such as nausea, loss of appetite, or dull abdominal pain. These symptoms may occur without the presence of jaundice, ascites, hepatomegaly, or even detectable biochemical changes, especially in the advanced stages (5). In our patient's case, she exhibited nonspecific symptoms without significant biochemical changes, and notably, she was on regular hormone therapy. The bone scan played an incidental but crucial role in detecting hepatic metastases. The pattern of distant metastases in breast cancer is influenced by the molecular subtype of the disease. In ER/PR-positive cancers, there is a significantly higher incidence of bone metastases compared to other sites, and this tends to occur more commonly 10-20 years after the initial diagnosis. Conversely, ER/PR-negative cancers have a higher risk of metastatic relapse within the first five years (6). Breast carcinomas expressing HER-2 tend to metastasize to the liver more frequently than ER/PR-positive tumors (7, 8). Hormone receptor-negative/HER-2 positive and triple-negative breast cancers (TNBC) are observed to be more prone to visceral metastases, including those in the brain, liver, and lungs (9, 10). Some studies suggest the

phenomenon of receptor conversion in metastatic breast carcinoma, where there may be changes in ER/PR or HER-2 markers. The reported incidence of this conversion is quite variable and might be related to the intra-tumoral heterogeneity of the primary lesion or the effects of hormonal or targeted therapy (11, 12). Negative conversion generally indicates that the current medication is no longer effective, while positive conversion suggests an opportunity for a new therapeutic approach (13, 14). So, tissue confirmation with IHC is necessary in metastatic lesion or recurrence for clinical outcome prediction and treatment selection. Though the patient had ER/PR-positive and HER-2 negative primary breast lesion, incidental aggressive hepatic metastases were identified at five years of the ongoing hormone therapy and it might be a less frequent presentation. New chemotherapy regimen was designed for hepatic metastases on the basis of SPECT/CT findings and core biopsy report, as IHC of the metastatic hepatic lesions was not performed.

## CONCLUSION

Incidental findings of any unusual extraosseous MDP uptake in planar bone scintigraphy (PBS) represent clinical relevance, often indicating a hidden disease process. This case report highlights the significance of identifying suspicious extraosseous uptake in planar bone scintigraphy, particularly in silent cases of advanced breast cancer patients. Diagnostic precision was achieved through additional SPECT/CT imaging.

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## CONFLICTS OF INTEREST

The authors claim no conflict of interests. Written informed consent was obtained from the patient for publication of this case report and accompanying images.

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