The Pivotal Role of 99mTc-MDP Bone Scintigraphy in Detecting Widespread Extra-Osseous Metastases in Osteogenic Osteosarcoma: A Case Report and Literature Review

Abstract

Background: Osteogenic osteosarcoma is a highly aggressive primary malignant bone tumor with a pronounced propensity for early hematogenous metastasis. While 99mTc-Methylene Diphosphonate (99mTc-MDP) bone scintigraphy is a cornerstone for detecting skeletal metastases, its exceptional utility in identifying metabolically active extra-osseous metastases, a hallmark of osteosarcoma's osteogenic potential, is a critical but less emphasized application.

Case Presentation: We report a compelling case of a 29-year-old male with a history of osteogenic osteosarcoma of the right humerus, initially metastatic to the lungs, treated with radical surgery and adjuvant chemotherapy. A routine follow-up 99mTc-MDP bone scintigraphy revealed not only a focal intense uptake at the right shoulder amputation stump, indicative of local recurrence, but also revealed multiple, unexpected sites of intense extra-skeletal radiotracer uptake. These were localized to the thorax, left lateral chest wall, right iliac fossa, and right thigh. Subsequent diagnostic contrast-enhanced computed tomography (CT) of the chest, abdomen, and pelvis confirmed extensive secondary involvement, including pulmonary, peritoneal, nodal, muscular, and subcutaneous metastases, demonstrating excellent spatial correlation with the scintigraphic findings.

Conclusion: This case underscores the high metastatic potential of osteogenic osteosarcoma, extending beyond bone to soft tissues and viscera. It powerfully illustrates that 99mTc-MDP bone scintigraphy serves as a highly sensitive initial screening tool for detecting both osseous and extra-osseous metastatic disease due to the osteoid-producing nature of these metastases. We further discuss the diagnostic implications and advocate for the integrated use of hybrid imaging, specifically Single-Photon Emission Computed Tomography/Computed Tomography (SPECT/CT), to enhance anatomical localization and diagnostic specificity, thereby refining staging accuracy and guiding optimal therapeutic strategies.

Keywords: Osteogenic Osteosarcoma; Extra-Osseous Metastases; 99mTc-MDP Bone Scintigraphy; SPECT/CT; Soft Tissue Metastases; Case Report.

Introduction

Osteogenic osteosarcoma (OS) is the most common primary malignant bone tumor in children and adolescents, characterized by the direct formation of osteoid or immature bone by malignant proliferating spindle cells [1]. It exhibits aggressive biological behavior with a high propensity for hematogenous dissemination, most commonly to the lungs and other skeletal sites [2]. Accurate staging at diagnosis and during follow-up is paramount, as the presence and extent of metastases are the most critical prognostic factors and dictate treatment strategy [3].

Technetium-99m methylene diphosphonate (99mTc-MDP) bone scintigraphy is a fundamental nuclear medicine imaging modality in oncology. Its mechanism relies on the adsorption of the diphosphonate compound onto hydroxyapatite crystals in areas of increased osteoblastic activity and blood flow [4]. While its primary application in OS is the detection of skeletal metastases (bone-to-bone spread) and assessment of the primary tumor's metabolic activity, it possesses a unique capability to visualize extra-osseous (soft tissue and visceral) metastases. This occurs when these metastases retain the tumor's inherent osteogenic potential, producing microcalcifications or osteoid that avidly bind the radiopharmaceutical [5, 6].

We present a compelling case of a young adult with osteogenic OS that illustrates the exceptional sensitivity of planar 99mTc-MDP bone scintigraphy in uncovering widespread, metabolically active extra-osseous metastatic disease. This case highlights the technique's value as a whole-body screening tool and serves as a springboard to discuss the complementary role of advanced hybrid imaging like Single-Photon Emission Computed Tomography/Computed Tomography (SPECT/CT) in refining diagnosis.

Case Presentation

A 29-year-old male with no significant past medical history presented with a several-month history of progressive pain and swelling in his right proximal humerus. Initial radiographs and subsequent magnetic resonance imaging (MRI) revealed a large, aggressive, osteolytic and osteoblastic lesion involving the metaphysis and diaphysis of the right humerus, with a substantial soft tissue component. A core needle biopsy confirmed the diagnosis of high-grade conventional osteogenic osteosarcoma. Staging computed tomography (CT) of the chest at the time of diagnosis revealed multiple bilateral pulmonary nodules, consistent with synchronous metastatic disease (Stage IV).

The patient underwent a multidisciplinary evaluation and commenced neoadjuvant chemotherapy according to a standard OS protocol (based on regimens containing high-dose methotrexate, doxorubicin, and cisplatin). Following three cycles, he underwent a radical resection of the right humerus with a wide surgical margin, performed via a forequarter amputation (interscapulothoracic amputation). Histopathological examination of the surgical specimen confirmed the diagnosis and showed a poor histologic response to chemotherapy (>90% viable tumor cells). The patient subsequently completed his adjuvant chemotherapy course.

Six months after completing adjuvant therapy, during routine surveillance, the patient remained asymptomatic. However, a follow-up whole-body 99mTc-MDP planar bone scintigraphy was performed. The study revealed two critical findings: an intense, focal area of increased radiotracer uptake at the surgical site of the right shoulder/amputation stump, highly suggestive of local tumor recurrence, and multipleunexpected, and intensely hypermetabolic foci clearly located outside the skeletal system. These included foci in the mid-thorax, the soft tissues of the left lateral chest wall, the right iliac fossa region, and the proximal right thigh (Figure 1).

To further characterize these alarming extra-skeletal findings, a diagnostic contrast-enhanced CT scan of the chest, abdomen, and pelvis was urgently obtained. The CT scan confirmed extensive metastatic progression. It identifiedan increase in size and number of bilateral pulmonary nodules, and multiple discrete metastatic deposits within various muscle groups (e.g., intercostal, iliopsoas, thigh musculature) and subcutaneous tissues.

Retrospective side-by-side analysis demonstrated an excellent spatial correlation between the intense uptake foci on the planar bone scan and the corresponding soft tissue/visceral lesions identified on CT (Figure 2). This confirmed that the scintigraphic findings represented widespread extra-osseous metastatic disease from osteogenic OS.

Given the disseminated nature of the disease, the patient was presented again to the multidisciplinary tumor board. Further curative-intent surgery was not feasible. The decision was made to initiate second-line systemic therapy.

Discussion

This case eloquently demonstrates several key principles in the management and imaging of osteogenic osteosarcoma. First, it underscores the tumor's aggressive and unpredictable biology, with progression occurring despite aggressive multimodal primary therapy. Second, and most centrally, it highlights the indispensable role of 99mTc-MDP bone scintigraphy as a sensitive, whole-body survey tool capable of detecting both skeletal *and* extra-skeletal metastases.

The pathophysiological basis for this lies in the fundamental nature of osteogenic OS. The malignant cells produce osteoid, even at metastatic sites. This ectopic osteoid formation, along with associated microcalcifications and increased vascularity, creates a nidus for 99mTc-MDP adsorption [5, 6]. Consequently, metabolically active extra-osseous metastases can manifest with an intensity equal to or greater than that of normal bone, making them conspicuous on planar imaging, as vividly shown in our patient.

The primary strength of planar bone scintigraphy in this context is its high sensitivity and ability to screen the entire body efficiently and cost-effectively. It can identify unsuspected sites of disease that might be outside the field of view of a routine CT scan, potentially altering disease stage and management, as it did here [7].

However, a significant limitation of planar imaging is its poor anatomical resolution. While it can confirm the *presence* and metabolic activity of a lesion, it cannot precisely *localize* it within soft tissue, distinguish subcutaneous from muscular involvement, or reliably differentiate metastatic uptake from other benign causes of soft tissue calcification (e.g.,

dystrophic calcification, myositis ossificans) [8]. This necessitated the follow-up CT scan in our case for definitive anatomical mapping.

This gap in diagnostic specificity is where hybrid imaging, particularly SPECT/CT, offers a transformative advantage. SPECT/CT seamlessly fuses the high functional sensitivity of scintigraphy with the detailed anatomical roadmap provided by CT in a single session [9]. In a case like ours, SPECT/CT would have likely provided immediate, precise localization of the extra-osseous foci, potentially characterizing them as muscular, nodal, or peritoneal without the need for a separate, delayed CT study. This integration reduces diagnostic uncertainty, minimizes the risk of false-positive interpretations, and accelerates clinical decision-making [10].

The detection of such widespread extra-osseous disease carries profound prognostic implications. It signifies a highly aggressive tumor phenotype and shifts the treatment paradigm from localized strategies (like surgery or radiation for oligometastases) to systemic therapy. Our case, therefore, reinforces that bone scintigraphy remains a crucial component of the surveillance arsenal for OS, not merely for bone but for comprehensive metastatic assessment.

Conclusion

This case report vividly illustrates the high metastatic potential of osteogenic osteosarcoma, which can involve diverse extra-osseous sites. Planar 99mTc-MDP bone scintigraphy proved to be a critical and highly sensitive initial investigation, successfully detecting metabolically active soft tissue and visceral metastases due to their osteogenic nature, which would have otherwise been missed on a skeletal survey alone.

We emphasize that while planar scintigraphy is an excellent screening tool, the inherent lack of anatomical detail is a key limitation. Therefore, based on the learning points from this case, we advocate for the more integrated use of SPECT/CT in the follow-up of high-risk osteosarcoma patients. This advanced hybrid modality can provide a "one-stop-shop" evaluation, offering superior diagnostic accuracy by precisely correlating functional and anatomical information. This leads to more confident staging, better guidance for biopsy or treatment planning, and ultimately, optimized patient management.

List of Abbreviations

OS: Osteosarcoma
99mTc-MDP: Technetium-99m Methylene Diphosphonate
SPECT/CT: Single-Photon Emission Computed Tomography/Computed Tomography
CT: Computed Tomography
MRI: Magnetic Resonance Imaging

Declarations

- **Ethics approval and consent to participate:** Written informed consent was obtained from the patient for publication of this case report and any accompanying images.
- **Consent for publication:** Obtained from the patient (as above).
- **Availability of data and materials:** The datasets used and/or analyzed during the current case are available from the corresponding author on reasonable request.
- **Competing interests:** The authors declare that they have no competing interests.

Funding: No specific funding was received for this case report.

References

[1] Mirabello L, Troisi RJ, Savage SA. Osteosarcoma incidence and survival rates from 1973 to 2004: data from the Surveillance, Epidemiology, and End Results Program. *Cancer*. 2009;115(7):1531-1543.
[2] Bielack SS, Kempf-Bielack B, Delling G, et al. Prognostic factors in high-grade osteosarcoma of the extremities or trunk: an analysis of 1,702 patients treated on neoadjuvant cooperative osteosarcoma study group protocols. *J Clin Oncol*. 2002;20(3):776-790.
[3] Kager L, Zoubek A, Potschger U, et al. Primary metastatic osteosarcoma: presentation and outcome of patients treated on neoadjuvant Cooperative Osteosarcoma Study Group protocols. *J Clin Oncol*. 2003;21(10):2011-2018.
[4] Even-Sapir E. Imaging of malignant bone involvement by morphologic, scintigraphic, and hybrid modalities. *J Nucl Med*. 2005;46(8):1356-1367.
[5] Feldman F, van Heertum R, Saxena C, et al. 18FDG-PET applications for cartilage neoplasms. *Skeletal Radiol*. 2005;34(7):367-374.
[6] Van der Woude HJ, Bloem JL, Verstraete KL, et al. Osteosarcoma and Ewing's sarcoma after neoadjuvant chemotherapy: value of dynamic MR imaging in detecting viable tumor before surgery. *AJR Am J Roentgenol*. 1995;165(3):593-598.
[7] Franzius C, Sciuk J, Daldrup-Link HE, et al. FDG-PET for detection of osseous metastases from malignant primary bone tumours: comparison with bone scintigraphy. *Eur J Nucl Med*. 2000;27(9):1305-1311.
[8] Strobel K, Exner UE, Stumpe KD, et al. The additional value of CT images interpretation in the differential diagnosis of benign vs. malignant primary bone lesions with 99mTc-MDP SPECT. *Eur J Nucl Med Mol Imaging*. 2008;35(11):2000-2008.
[9] Romer W, Nomayr A, Uder M, et al. SPECT-guided CT for evaluating foci of increased bone metabolism classified as indeterminate on SPECT in cancer patients. *J Nucl Med*. 2006;47(7):1102-1106.
[10] Hirschmann MT, Davda K, Rasch H, et al. Clinical value of combined single photon

emission computerized tomography and conventional computer tomography (SPECT/CT) in sports medicine. *Sports Med ArthroscRev*. 2016;24(1):4-9.

Figures

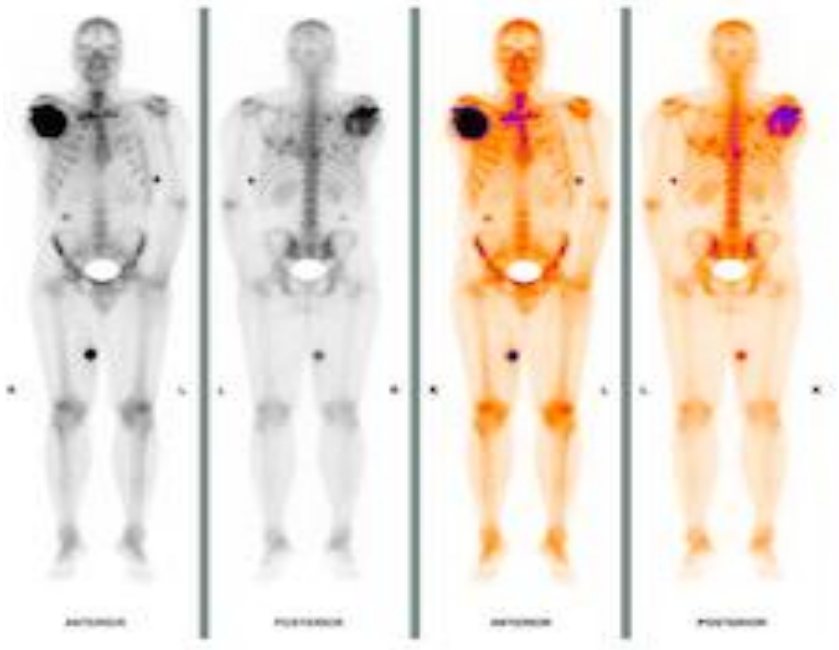

Figure 1: Whole-body Tc-MDP bone scan showing pathological hypermetabolic foci in at the level of the right shoulder amputation stump and extra-osseous foci projecting to the thorax, soft tissues of the left lateral chest wall, right iliac fossa and right thigh

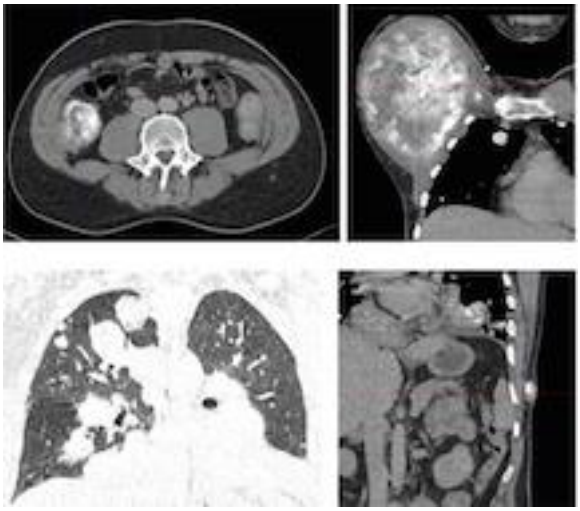

Figure 2:CT scan of the chest, abdomen, and pelvis with axial and coronal CT slices showing secondary pulmonary, lymph node, and subcostal lesions