DEKA IN MEDICINE

Case report

Diagnostic challenges in assessing treatment responds of primary bone lymphoma: A case report

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ABSTRACT

BACKGROUND: Primary Bone Lymphoma (PBL) is quite difficult to assess treatment responses because of limited access to 18F-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT). Therefore, this study intends to highlight one case regarding alternative imaging modalities, such as technetium-99m methylene diphosphonate (99mTc-MDP) and technetium-99m methoxyisobutyl isonitrile (99mTc-MIBI), for activity assessment in tumors as well as their involvement in the marrow.

CASE: A 17-year-old male with persistent pain and swelling in the left knee over one month underwent a bone biopsy that confirmed the diagnosis of Diffuse Large B-Cell Lymphoma (DLBCL) in the tibia. The patient was subjected to chemotherapy using cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP), followed by radiotherapy. PET/CT was unavailable; therefore, metabolic tumor evaluation was performed through 99mTc-MDP and 99mTc-MIBI scintigraphy for tumor activity and bone marrow involvement assessment. Bone scintigraphy with 99mTc-MDP showed increased tracer uptake in the proximal left tibia and distal left femur, indicating ongoing tumor activity. These findings were reinforced by the further assessment with 99mTc-MIBI, which confirmed high metabolic activity in these areas. Subsequently, a bone marrow biopsy evidenced infiltrative lymphoblasts constituting 24.8 percent infiltrating the involved marrow space, thus confirming the bone marrow being infiltrated. Hence, this patient received additional rituximab treatment to enhance treatment outcome.

CONCLUSION: This case portrays the difficulties one faces while evaluating the treatment response in Primary Bone Lymphoma (PBL), as well as the role of 99mTc-MDP and 99mTc-MIBI scintigraphy as alternative metabolic imaging modalities in the absence of PET/CT.

KEYWORDS: Diffuse large b-cell lymphoma; Technetium Tc 99m Medronate; Technetium Tc 99m Sestamibi; bone neoplasms; radionuclide imaging.

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INTRODUCTION

Primary Bone Lymphoma (PBL) is a rare form of non-Hodgkin lymphoma (NHL) that can exclusively affect the bone without involving other lymphoid tissues.[1] PBL accounts for less than 1% of all NHL cases.[2] Diagnosing and evaluating treatment response in PBL often presents clinical challenges due to its nonspecific initial symptoms, such as bone pain and swelling, which can resemble other orthopedic conditions, including osteomyelitis and primary bone tumors like osteosarcoma or Ewing sarcoma.[3] Therefore, histopathological and immunohistochemical examinations are essential to confirm the diagnosis.[4]

Imaging is crucial in diagnosis, staging, and monitoring treatment response in PBL. Conventional imaging modalities such as plain X-rays and magnetic resonance imaging (MRI) are commonly used to assess structural changes in the bone.[1] However, they do not always differentiate between residual active disease and post-treatment reactive changes.[5] 18F-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) is the preferred modality for metabolic tumor evaluation.[6] However, limited access to PET/CT, particularly in developing countries, necessitates using alternative imaging techniques.[7]

Bone scintigraphy using technetium-99m methylene diphosphonate (99mTc-MDP) and technetium-99m methoxyisobutyl isonitrile (99mTc-MIBI) has been proposed as an alternative approach for assessing tumor metabolic activity and detecting bone marrow involvement.[8] Previous studies have shown that 99mTc-MIBI has relatively high sensitivity and specificity in distinguishing malignant from benign lesions and monitoring treatment response.[9] However, interpreting these imaging results remains challenging, particularly in differentiating persistent tumor infiltration from post-treatment reactive changes.[10] This case report aims to illustrate the diagnostic challenges in evaluating treatment response in PBL and to explore the role of 99mTc-MDP and 99mTc-MIBI scintigraphy as alternative metabolic imaging modalities in settings with limited access to PET/CT.

CASE PRESENTATION

A 17-year-old male experienced left knee pain and swelling for one month. A bone biopsy was performed on the lesion, and histopathological and immunohistochemical examinations confirmed the diagnosis of Diffuse Large B-Cell Lymphoma (DLBCL). The patient underwent eight cycles of chemotherapy with the CHOP regimen (cyclophosphamide, doxorubicin, vincristine, and prednisone) over seven months, followed by 21 fractions of radiotherapy for one month and physiotherapy for pain management in the left knee. Throughout the treatment, the patient's response was monitored using various imaging modalities, including plain X-ray, ultrasonography (USG), magnetic resonance imaging (MRI), and radionuclide imaging with Technetium-99m (99mTc). However, 18F-FDG PET/CT was not performed due to limited availability at the hospital where the patient was being treated.

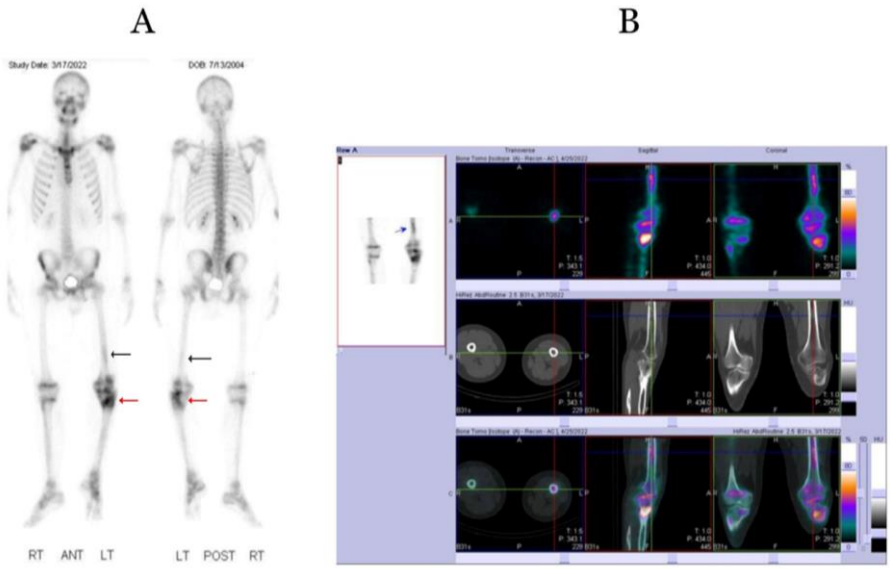

Figure 1. A). Whole-body planar bone scintigraphy showing increased tracer uptake in the medullary region of the distal left femur (black arrows) and proximal left tibia (red arrows). B).

SPECT/CT images of the knee demonstrating focal areas of increased tracer uptake corresponding to the regions seen in the planar scintigraphy, confirming metabolic activity in the distal femur and proximal tibia.

A plain chest X-ray and abdominal USG showed no abnormalities. However, serial plain X-rays of the left lower limb consistently showed an abnormal pattern of malunion fracture in the proximal left tibia throughout and after treatment. MRI revealed a heterogeneous mass with irregular margins in the proximal third of the tibia, infiltrating the surrounding muscles, causing bone destruction and a metaphyseal-diaphyseal tibial fracture. The mass appeared hypointense on T1-weighted images and hyperintense on T2-weighted and T2-weighted Fat-Suppressed (T2FS), with contrast enhancement after contrast administration. 99mTc-MDP showed increased tracer uptake in the proximal left tibia and the medullary region of the distal left femur (Figure 1A), while single photon emission computed tomography/computed tomography (SPECT/CT) of the knee showed areas of increased tracer uptake consistent with bone scintigraphy findings, confirming metabolic activity in the distal femur and proximal tibia (Figure 1B).

Subsequently, 99mTc-MIBI scintigraphy was performed to evaluate bone marrow activity and the tracer uptake previously detected on bone scintigraphy. Planar 99mTc-MIBI scan showed increased tracer uptake in the proximal left tibia (Figure 2A, red arrow), distal left femur, and bone marrow of the bilateral pelvis and left femur (Figure 2A, black arrow). SPECT/CT confirmed persistent tracer uptake over time, indicating residual malignancy and bone marrow involvement (Figure 2B).

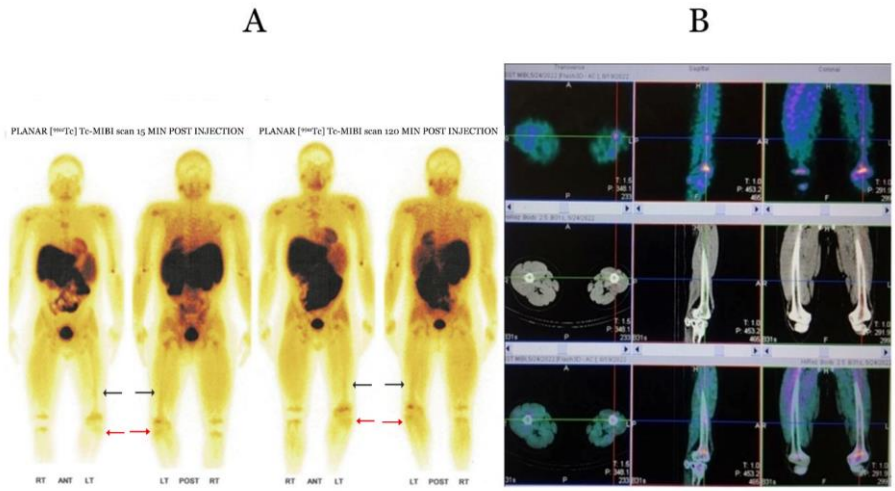

Figure 2. A). Planar 99mTc-MIBI scans at 15 minutes and 120 minutes post-injection demonstrating increased tracer uptake in the proximal left tibia (red arrow), distal left femur, and bone marrow of both the bilateral pelvis and left femur (black arrow). B). SPECT/CT images confirming persistent tracer uptake over time, suggesting residual malignancy and bone marrow involvement.

A bone marrow biopsy from the left iliac crest revealed 24.8% lymphoblast infiltration, confirming DLBCL infiltration in the bone marrow. Based on these findings, the patient was planned to receive additional rituximab therapy alongside the CHOP regimen, considering the advanced stage of the disease and its poor response to initial therapy.

DISCUSSION

DLBCL is the most common subtype of NHL, accounting for approximately 30–40% of adult cases.[11] Primary bone involvement is rare, while secondary bone infiltration is

more common in advanced stages.[3] This case highlights the diagnostic and therapeutic challenges of DLBCL with primary bone involvement.[12] The initial symptoms, such as persistent knee pain and swelling, are often associated with orthopedic conditions like osteomyelitis, osteosarcoma, or Ewing sarcoma.[13] However, biopsy and immunohistochemical analysis confirmed the diagnosis of DLBCL, emphasizing the importance of histopathological evaluation in cases of unexplained bone lesions.[14]

In this case, we utilized imaging studies to evaluate bone marrow activity and tracer uptake. Imaging plays a crucial role in disease evaluation and monitoring.[15] Plain X-ray and MRI provide anatomical details, while 99mTc-MDP bone scintigraphy and 99mTc-MIBI scans help assess metabolic activity and bone marrow involvement.[16] MRI is the standard modality for PBL evaluation due to its high sensitivity and lack of radiation exposure.[17] However, post-treatment signal changes can persist for up to two years, making it difficult to differentiate residual disease from reactive bone marrow changes.[18] The unavailability of 18F-FDG PET/CT in this case—due to limited FDG production in Indonesia and high costs—necessitated the use of alternative radionuclide imaging.[19] Bone scintigraphy has a sensitivity of up to 95% for detecting bone metastases and can identify minimal bone destruction (5–10%) that is undetectable by conventional radiography.[20] However, prolonged tracer uptake in bone scintigraphy can complicate interpretation, as it may result from post-treatment changes or persistent lymphoma infiltration.[21]

In this case, 99mTc-MIBI played a crucial role. Studies have shown that 99mTc-MIBI has a sensitivity of 79.31%, specificity of 86.66%, and a negative predictive value of 81.25% in distinguishing malignant from benign lesions.[22] Abnormal 99mTc-MIBI uptake has been associated with positive bone marrow cytology, while uptake normalization after chemotherapy indicates its potential for monitoring treatment response.[21] In this case, a bone marrow biopsy confirmed bone marrow involvement, which is associated with advanced-stage disease and has significant implications for further treatment decisions.[23] The patient underwent standard chemotherapy with the CHOP regimen, which remains the primary therapy for DLBCL. However, confirmed bone marrow involvement indicated a poorer prognosis.[24] Rituximab was added following current recommendations to improve survival outcomes.[25] Unfortunately, despite intensive therapy, the patient developed B-symptoms and eventually succumbed to disease progression, highlighting the aggressive nature of DLBCL with extensive bone involvement.

This case advocates a multidisciplinary setup for the management of DLBCLs with skeletal disease. Advanced imaging, rapid histopathologic diagnosis, and aggressive multidisciplines are essential in improving patient outcomes. Further studies should focus on developing alternative therapeutic options for patients with refractory or relapsed disease, particularly those in developing regions where access to PET/CT scanning and targeted therapies is limited.

CONCLUSION

This study highlights the importance of 99mTc-MIBI and 99mTc-MDP scintigraphy as valuable alternative imaging modalities for assessing metabolic activity and monitoring tumor response to therapy, especially in the absence of PET/CT, to overcome diagnostic challenges in this case.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Patient consent was waived due to no identification of patients

CONFLICTS OF INTEREST
We have no conflict of interest

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AUTHOR CONTRIBUTION
Idea/concept: BD, BH. Writing—original draft preparation: AA. Writing—review and editing: AA, KP, BD, BH. Control/supervision supervision: KP, BH. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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