Received: 28 May 2020 | Revised: 9 July 2020 | Accepted: 28 July 2020

DOI: 10.1002/ccr3.3267

CASE REPORT

Clinical Case Reports Open Access WILEY

Primary bone lymphoma of the ilium successfully treated without radiation

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Abstract

The addition of radiation therapy to chemotherapy and impact on outcomes in primary bone lymphoma is not clear. Nonetheless, tumor location must be considered as radiation to marrow-rich bone areas can lead to myelosuppression and myelotoxicity.

KEYWORDS

lymphoma, rare tumors, tumors-bone

1 | INTRODUCTION

Primary bone lymphoma (PBL) is a rare malignancy. We present a case of a young man who presented with chronic hip pain and found to have PBL of the ilium that was treated with only chemotherapy. Role of diagnostic imaging and treatment strategies in PBL is discussed. The addition of radiation therapy to chemotherapy and impact on outcomes in primary bone lymphoma is not clear. Nonetheless, tumor location must be considered as radiation to marrow-rich bone areas can lead to myelosuppression and myelotoxicity.

Primary bone lymphoma (PBL) is a rare malignancy that comprises less than 5% of all bone malignancies and about 1%-2% of all lymphomas.[1,2] First identified by Oberling in 1928, PBL is defined by the World Health Organization as lymphoma of a single or multiple skeletal sites that may or may not have regional lymph node involvement.[3] Median age range at the time of diagnosis is between 45 and 60 years old, with a slight male preponderance.[4,5] Common features of

initial presentation include localized bone pain (82%-92%), soft tissue swelling, and pathological fracture.[6] PBL most commonly involves the femur.[6] Here, we report a unique case of PBL involving the ilium that was successfully treated with chemotherapy.

2 | CASE PRESENTATION

A 38-year-old African American man with hypertension initially presented to his primary care clinic in the spring of 2014 with five months of left hip pain that radiated down to the left lower extremity. Pain was worsened by activity and weight bearing which progressively increased in severity over the months. He had no unintentional weight loss, fevers, chills, night sweats, or lymphadenopathy. Patient had a family history notable for esophageal cancer in his father. His initial vital signs were normal including the temperature. On examination, he had point tenderness over the left hip as well as reduced range of motion with external and internal rotation of the left hip due to the pain, but no palpable lymphadenopathy. Complete blood count was unremarkable. Specifically, leukocyte count was 10,000 cells/μL with a normal differential; hemoglobin and platelet count were both normal as well. Lactate dehydrogenase (LDH) was elevated at 236 μ/L. Erythrocyte sedimentation rate was also elevated 88 mm/h The remainder of laboratories such as basic metabolic panel, liver panel, HIV, and HBV serology were otherwise normal. Plain films of the left hip were obtained which revealed sclerosis of the acetabular articular margin (Figure 1A). A magnetic resonance image (MRI) of the pelvis was eventually obtained showing abnormal bone marrow in the entire left hemipelvis and abnormal signal intensity in the surrounding tissues (Figure 1B). Computed tomography (CT) scan of the chest, abdomen, and pelvis was also obtained which demonstrated mixed lytic and sclerotic lesions in the entire left iliac wing, left acetabulum, and left superior and inferior pubic rami; left greater than right pelvic lymphadenopathy and a sclerotic lesion in the thoracic spine (level T8) were also seen. The patient then underwent an image-guided biopsy of the left ilium that showed bone marrow infiltration that was largely replaced by lymphoma (Figure 2). There was a predominant population of B cells which were CD20, PAX5, and BCL6 positive and CD23, CD 30, S-100, cyclin D1, and pancytokeratin negative by immunohistochemistry (Figure 2). B-cell clonality was detected by polymerase chain reaction. Overall, pathology was confirmed to be non-Hodgkin's B-cell lymphoma. A staging positron emission tomography (PET)/CT scan demonstrated intense fluorodeoxyglucose (FDG) uptake in the left iliac crest and surrounding region with a SUV_{max} of 15.3 (Figure 1C). Moderate uptake in the left pelvic lymph nodes (SUV_{max} 4.7-5.0) and mild uptake in the axillary lymph nodes (SUV_{max} 2.5-2.9, interpreted as nonspecific) was also noted. A bone marrow biopsy and aspiration were done which demonstrated a normal reactive marrow without malignancy. In order to better subtype the lymphoma, more bone tissue was needed. Given the anatomic location and risk of pathologic bone fracture, the risks and benefits of repeating the biopsy were discussed with the patient, after which he declined the procedure. It was decided to pursue an alternative route and biopsy a more accessible lymph node that was seen on PET/CT. Since moderate to intense FDG uptake was also observed in the cervical lymph nodes (SUV_{max} 8.3), fine-needle aspiration of the right cervical lymph node was performed. However, the pathology only showed a reactive lymph node. A diagnosis of primary bone lymphoma was favored

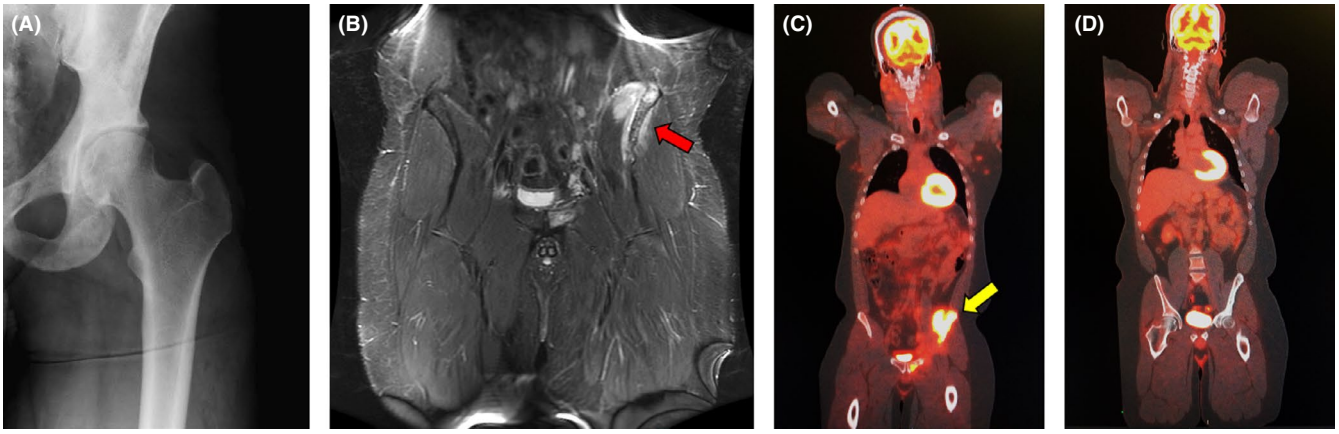

FIGURE 1 A, Plain film X-ray of the left hip revealing sclerotic acetabular margins. B, Magnetic resonance imaging (MRI) of the pelvis showing abnormal bone marrow in the left hemipelvis as well as abnormal signal intensity in the surrounding soft tissues (red arrow). C, FDG PET/CT sacn of the body at diagnosis showing intense FDG uptake in the iliac crest and surrounding region (yellow arrow, SUV_{max} 15.3). Variable FDG uptake in cervical, axillary and iliac lymph nodes was also noted. Fine needle aspiration of right cervical lymph node only showed a reactive lymph node (pathology not shown). D, Repeat FDG PET/CT scan 5 y after chemotherapy showing complete metabolic remission

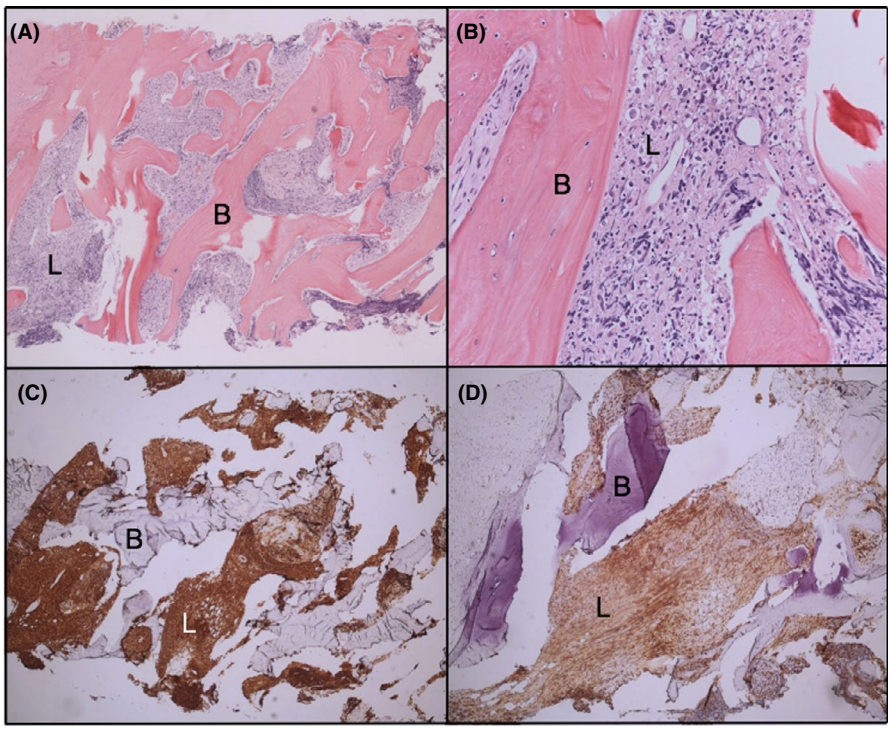

FIGURE 2 A, The bone biopsy demonstrates that the normal marrow is replaced by lymphoma (L), surrounded by bony trabeculae (B). B, High-power view of the lymphoma demonstrates that the infiltrate consists of large atypical cells with hyperchromasia and high nuclear-cytoplasmic ratio. C, By immunohistochemistry, the lymphoma infiltrate is positive for CD20 (brown). D, Lymphoma infiltrate is positive for BCL6 (brown). (A, hematoxylin and eosin, 100×; B, hematoxylin and eosin, 200×; C, immunoperoxidse, 100×, D, immunoperoxidse, 200×)

over disseminated lymphoma. Based on the likely involvement of regional pelvic lymph nodes, he was found to have Stage IIE disease with a revised International Prognostic Index (R-IPI) score of one due to the elevated LDH. Patient received six cycles of chemotherapy with R-CHOP, which was well tolerated. Follow-up PET/CT scan following completion of chemotherapy showed complete metabolic response. Consolidative radiation therapy was considered, but the patient declined. Repeat staging scans one year and five years after chemotherapy showed that the patient had remained in complete remission (Figure 1D).

3 | DISCUSSION

The diagnosis of PBL can be challenging as the initial musculoskeletal symptoms can be nonspecific. Laboratory results in PBL are typically unremarkable and relatively unhelpful in diagnosis.[2] Additionally, it can be difficult to differentiate PBL from other primary bone tumors such as osteosarcoma, chondrosarcoma, or Ewing's sarcoma based on radiographic imaging alone. Nonetheless, plain X-ray films are the initial diagnostic test of choice and frequently reveal osteolytic and/or osteoblastic lesions involving the cortex.[7] CT and MRI can aid in diagnosis, staging, and follow-up of PBL due to more precise delineation of cortical destruction.[8] In addition, FDG PET/CT imaging is considered a standard tool for initial evaluation, staging, and assessment of treatment response; studies have demonstrated that PET/CT is both more sensitive and specific than bone scintigraphy in identifying osseous infiltration of lymphoma.[9] Local soft tissue extension, as seen in our case, may be seen on imaging and is associated with poor prognosis.[10] Bone biopsy is also recommended in order to characterize pathology but must be balanced with the risk of pathological fracture as in our patient.[2]

Given the rare incidence of PBL, management has been largely driven by retrospective data from case reports and case series. The majority of PBL cases are due to diffuse large B-cell lymphoma (DLBCL), so treatment has typically involved CHOP-based chemotherapy, with R-CHOP demonstrating a higher 3-year progression-free survival (88%) compared to CHOP (52%).[11] Evidence regarding the addition of radiation therapy and impact on overall survival (OS) in PBL is mixed. One study found that combined chemotherapy and radiation were associated with a higher 5-year OS rate than either modality alone.[12] Similarly, a small retrospective analysis showed a statistically significant improvement in OS with combined modalities regardless of the use of rituximab.[13] However, the use of both chemotherapy and radiation therapy had a worse 10-year OS in patients with advanced disease.[11] Patients with DLBCL subtypes who received consolidative radiation after chemotherapy were not observed to have improved OS compared with patients who only received chemotherapy.[14] Particular attention to tumor location should be made as radiation therapy to bones with high marrow concentrations, such as the pelvis in our patient, can lead to myelotoxicity and myelosuppression.[2] Here, we describe our unique experience with treating a patient with an untypeable PBL using chemotherapy alone who achieved a durable complete response five years after treatment.

Although rare, PBL can present in the ambulatory setting disguised as common musculoskeletal symptoms which may or may not be accompanied by constitutional symptoms. Our case highlights a multimodal diagnostic approach using various imaging techniques along with pathologic confirmation. The role of consolidative radiation therapy following chemotherapy is unclear and should be further investigated in future studies.

ACKNOWLEDGEMENTS

Published with written consent of the patient.

CONFLICT OF INTEREST

The authors have no potential conflicts of interest to disclose.

AUTHOR CONTRIBUTIONS

CBN and ML: wrote the manuscript. GV and US: acquired the images used in the figures. CS, QH, GR, and SVY: revised and gave final approval of the manuscript prior to submission.

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How to cite this article: Nguyen CB, Li M, Verstovsek G, et al. Primary bone lymphoma of the ilium successfully treated without radiation. *Clin Case Rep*. 2020;8:3129–3132. https://doi.org/10.1002/ccr3.3267