

Primary Bone Lymphoma: A Retrospective Analysis of 15 Patients Treated in a Single Tertiary Center

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ABSTRACT

Objective: Primary bone lymphoma is a rare type of lymphoma that originates in bone tissue without systemic involvement. This study aimed to evaluate the clinical characteristics, treatment approaches, and outcomes of patients diagnosed with primary bone lymphoma at a single tertiary care center.

Methods: Fifteen patients diagnosed between 2013 and 2020 were retrospectively reviewed. Data including patient demographics, tumor localization, histological subtype, disease stage, treatment modalities, and response rates were analyzed using descriptive methods.

Results: The median age was 53 years (range: 30-73), with 7 male and 8 female patients. Most patients presented with localized disease and diffuse large B-cell histology. The pelvic and axial skeletons were the most frequently involved areas. All patients received systemic chemotherapy, and 80 percent also underwent radiotherapy. Complete remission was achieved in 87 percent of cases. After a median follow-up of five years, 87 percent of patients were alive and 80 percent remained in long-term remission. One patient with widespread bone involvement experienced disease progression and died.

Conclusion: Primary bone lymphoma can be successfully treated with systemic chemotherapy and radiotherapy. This study confirms that patients with localized disease in particular may achieve long-term survival with appropriate combined treatment.

Keywords: Primary bone lymphoma, diffuse large B-cell lymphoma, chemoradiotherapy, retrospective analysis

INTRODUCTION

Primary bone lymphoma (PBL) is an uncommon malignancy, accounting for a small fraction of all lymphomas and bone tumors. Recent estimates indicate that PBL comprises approximately 3-7% of primary bone tumors and under 2% of all lymphomas in adults.¹ In other words, fewer than 5% of extranodal non-Hodgkin lymphomas arise in bone. PBL most often presents as diffuse large B-cell lymphoma (DLBCL) confined to the skeletal system, without distant nodal or visceral involvement. It can occur at any age but is typically

diagnosed in mid-adulthood; the median age at presentation ranges from the mid-40s to 60 years in most series. There is a slight male predominance (reported male:female ratios around 1.2-1.8:1).² Clinical presentation usually includes localized bone pain, swelling, or pathologic fracture, and systemic "B" symptoms (fever, night sweats, weight loss) are present in a subset of patients.

The majority of PBL cases are histologically DLBCL, though rare cases of T-cell lymphoma (such as anaplastic large cell lymphoma) and other subtypes have been reported.³ The most



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frequently involved sites are the long bones –notably the femur, humerus, and tibia– followed by axial skeleton sites like the spine and pelvis. Imaging often reveals lytic bone lesions, and diagnosis is confirmed by biopsy with histopathological and immunophenotypic analysis.

Optimal management of PBL typically involves a combination of systemic chemotherapy and localized radiotherapy (RT). The introduction of anthracycline-based chemo-immunotherapy [e.g., rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone (R-CHOP) regimen for B-cell PBL] has significantly improved outcomes. RT to the involved bone provides excellent local control; however, RT alone is associated with high rates of systemic failure. Combined modality therapy has been shown to yield superior overall survival (OS) and lower relapse rates than single-modality treatment. Prior studies have demonstrated 5-year survival rates around 80-90% for PBL patients, especially when treated with chemo, RT.⁴ Nonetheless, data are limited due to the rarity of this entity, and most published evidence comes from retrospective series.

In this context, we report a retrospective analysis of 15 patients with PBL treated at a single tertiary center. We describe their clinical characteristics, treatment approaches, and outcomes, and compare these findings with the existing literature. By sharing our single-institution experience, we aim to contribute to the understanding of this rare lymphoma and to highlight factors relevant to its prognosis and management.

MATERIAL AND METHODS

Study Design and Setting

This study is a retrospective case series of patients diagnosed with PBL at our tertiary care academic hospital. We reviewed records from all patients treated at our center with a diagnosis of PBL over a defined period (2013-2020). The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of the University of Health Sciences Türkiye Kartal Dr. Lütfi Kırdar Training and Research Hospital (approval no.: 2020/514/177/31, date: 13.05.2020). Our hospital is a tertiary referral center that provides oncology services, and all included patients had both, diagnosis and treatment at this institution.

MAIN POINTS

- Primary bone lymphoma is a rare but highly treatable malignancy when diagnosed early and managed with combined chemo-radiotherapy.
- This study confirms excellent remission and survival outcomes, particularly in patients with localized disease.
- Diffuse large B-cell lymphoma was the most common histological subtype, and the pelvic, and axial skeleton were the most frequently affected anatomical sites.
- A multidisciplinary treatment approach involving chemotherapy, radiotherapy, and surgical stabilization (when needed) can result in long-term disease control and functional recovery.

Inclusion Criteria

Patients were included if they had a pathological diagnosis of lymphoma originating in bone, with disease confined to the skeletal system (with or without regional lymph node involvement) at presentation, consistent with the definition of PBL. Patients with secondary bone involvement from systemic lymphoma were excluded. We identified 15 patients who met these criteria during the study period.

Data Collection

After Institutional Review Board approval of Kartal Dr. Lütfi Kırdar Training and Research Hospital we collected data from medical charts and electronic records. The data abstracted included patient demographics (age at diagnosis, sex), presenting symptoms and duration, diagnostic workup findings, histopathological subtype of lymphoma, anatomic site of the primary bone lesion(s), staging information (Ann Arbor stage, presence of B symptoms), treatment modalities used (chemotherapy regimen, number of cycles, use of RT with dose), treatment response, and follow-up outcomes. Radiological and pathology reports were reviewed to confirm the extent of disease and bone sites involved. Treatment response was assessed using standard response criteria for lymphoma [complete response (CR), partial response (PR), stable disease, progressive disease] based on imaging and clinical evaluation after therapy.

Statistical Analysis

Given the small sample size, analysis was primarily descriptive. Continuous variables (e.g., age, follow-up time) are presented as median and range. Categorical variables (e.g., sex, histological subtype, response rates) are summarized as counts and percentages. No formal hypothesis testing was performed. Survival outcomes such as OS and progression-free survival were estimated descriptively based on available follow-up data, without Kaplan-Meier analysis due to the limited number of events. Data analysis was conducted using basic statistics functions.

RESULTS

Demographics and Clinical Presentation

A total of 15 patients with PBL were analyzed. The median age at diagnosis was 53 years (range: 30-73 years). The cohort included 7 male and 8 female patients, corresponding to a male-to-female ratio of approximately 1:1.14.

All patients had localized bone-related symptoms, most commonly bone pain at the affected site (in 13 patients, approximately 86%), sometimes accompanied by swelling. Four patients (26.8%) sustained a pathological fracture through the lymphoma-infiltrated bone (humerus, distal femur, iliac wing). The median duration of symptoms prior to diagnosis was 6 months. Systemic B symptoms (fever, night sweats, weight loss) were documented in 2 patients (13%). In several cases, the initial differential diagnosis included osteomyelitis or other bone tumors (e.g., multiple myeloma). Definitive diagnosis was established by bone biopsy and histopathology in all cases.

Anatomical Sites and Staging

The anatomical distribution of primary sites is summarized in Table 1. Long bones were frequently affected, however, the pelvic and axial skeleton, including the vertebrae, represented the most common sites overall. Femoral involvement was present in 2 patients (13%), tibial (\pm fibula) in 1 patient (7%), and humeral in 1 patient (7%). Other sites included the glenoid, distal tibia, proximal humerus, distal clavicle, and sternum (one patient each). Eight patients (53%) had pelvic and axial skeleton involvement, including vertebrae. No cases of skull, mandible, or rib involvement were observed. According to Ann Arbor staging, 12 patients (80%) had early-stage disease (Stage I-II), limited to a single bone or one bone with its regional lymph nodes. Three patients (20%) presented with multifocal bone involvement without other organ spread, which was classified as Stage IV disease, as multiple bone lesions are considered disseminated in lymphoma staging.

Table 1. Distribution of Primary Bone Sites in 15 PBL Patients

Anatomic site	No of patients	Percentage of total (%)
Pelvic and axial skeleton (incl. spine)	8	53%
Femur	2	13%
Glenoid	1	7%
Distal tibia	1	7%
Proximal humerus	1	7%
Distal clavicle	1	7%
Sternum	1	7%
Total	15	100%

Distribution of primary bone lymphoma sites in the study cohort. The pelvic and axial skeleton was the most commonly affected region. PBL, primary bone lymphoma.

Histopathology

Most cases (14 of 15, 93%) were diagnosed as DLBCL. Immunohistochemistry in these cases was positive for B-cell markers (CD20, etc.). One patient (7%) was diagnosed with anaplastic large cell lymphoma (ALCL, a T-cell subtype). This aligns with expectations that most PBLs are of B-cell origin, 5 with an occasional T-cell lymphoma case. All diagnoses were confirmed by expert hematopathological review. In two DLBCL cases, high-grade morphological features were noted, but they were still classified as DLBCL. No cases of Hodgkin lymphoma or low-grade lymphoma were detected.

Treatment Administered

All patients received systemic chemotherapy as first-line treatment. Most B-cell lymphoma patients received R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone). The median number of chemotherapy cycles was 6 (most patients received 6-8). The T-cell ALCL case was treated with CHOP (rituximab was not administered, as it was CD30⁺ + ALCL). In addition to chemotherapy, 12 patients (80%) received local radiotherapy to the primary bone lesion (30-45 Gy). Patients with Stage I or II disease were more likely to receive combined modality treatment (chemotherapy + radiotherapy), whereas Stage IV patients were treated with chemotherapy alone.

Surgical interventions were performed in selected cases for local control and structural stabilization. Tumor resection prostheses were applied in two patients with distal femoral involvement and one patient with proximal humerus involvement. Clavicle resection was performed in the patient with distal clavicle involvement; the Harrington procedure was applied in the patient with an iliac wing-acetabular fracture (Figure 1); and posterior instrumentation was performed in the patient with T11 vertebral involvement (Figure 2). These procedures were

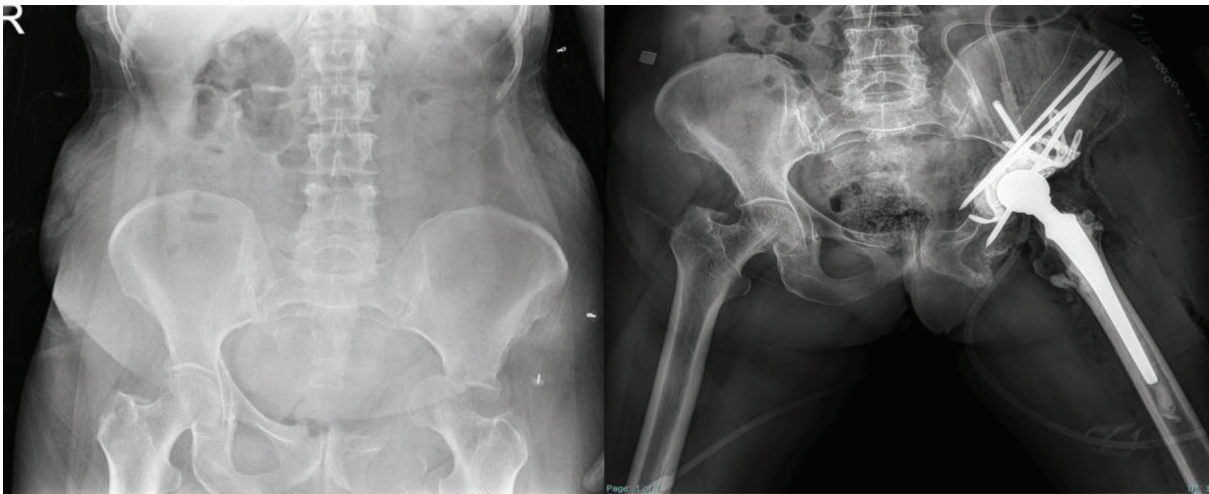


Figure 1. Preoperative and postoperative imaging-Harrington procedure. Preoperative (left) and postoperative (right) pelvic radiographs of a patient with primary bone lymphoma involving the iliac wing and acetabulum. Preoperative imaging shows bone destruction and loss of structural integrity in the left hemipelvis. The patient underwent Harrington reconstruction with total hip arthroplasty, Steinmann pins, plate fixation, and screws, providing structural stabilization and enabling functional restoration after oncologic treatment.

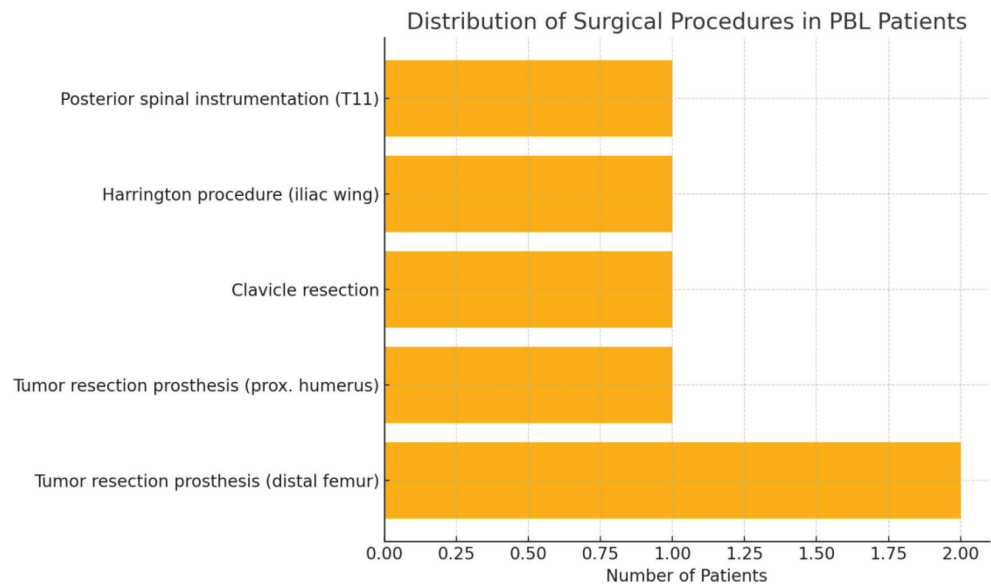


Figure 2. Distribution of surgical procedures in PBL patients. Distribution of surgical procedures in patients with primary bone lymphoma. Tumor resection prostheses were the most frequent, particularly for distal femur and proximal humerus involvement. Other procedures included clavicle resection, Harrington procedure for iliac wing fracture, and posterior spinal instrumentation for vertebral involvement.

PBL, primary bone lymphoma.

performed in conjunction with systemic therapy. Combined chemoradiotherapy, supplemented by surgery when necessary, reflects the current multidisciplinary approach. This approach aims to maximize local control and eradicate systemic disease.⁶

Response and Survival Outcomes

Treatment response was evaluated after completion of first-line therapy (chemo ± RT). A CR, defined as the absence of detectable disease on imaging and resolution of symptoms, was achieved in 13 patients (87%). All patients who received combined modality therapy achieved complete remission (CR), and post-treatment imaging (most commonly positron emission tomography (PET)/computed tomography confirmed complete metabolic remission. Two patients (13%) achieved only a partial remission (PR), defined as either residual lesion activity or size reduction without complete clearance. Both PR cases were observed in patients with multifocal bone disease. These patients were closely monitored, and one subsequently received salvage chemotherapy with radiotherapy to the remaining active lesion. No cases of primary refractory disease (progression during therapy) were observed in this series.

The median follow-up was 37 months (range: 18-66 months), and survival outcomes were encouraging. At the last follow-up, 13 patients (87%) were alive, including 12 (80%) in continuous complete remission. One patient who had initially shown a PR relapsed 18 months after treatment and died of progressive lymphoma despite salvage therapies. Another patient died of a cardiac cause at 30 months, while in remission. The 3-year OS rate was approximately 87% and the disease-free survival rate was similar among patients with localized disease. Due to the small sample size, formal survival curves were not plotted; however, the results are consistent with the high survival rates

reported in larger studies.⁷ Notably, all early-stage (I/II) patients who received combined chemo-radiotherapy remained in remission, underscoring the efficacy of this approach in localized PBL. Lymphoma-related mortality occurred only in a patient with initially advanced (multifocal) disease.

During follow-up, no major skeletal complications or significant postoperative problems were observed. Functional outcomes were satisfactory in all surviving patients, with adequate mobility. Surgical interventions such as tumor resection, prostheses, clavicle resection, the Harrington procedure, and spinal instrumentation were well tolerated. In the patient with a humeral fracture, bone healing was satisfactory following tumor resection and prosthetic reconstruction. These findings indicate that, in addition to effective lymphoma treatment, appropriately selected surgical interventions can help maintain skeletal integrity and support functional recovery.

DISCUSSION

In this retrospective analysis of 15 patients with PBL treated at a single tertiary center, we observed treatment outcomes consistent with prior literature, reaffirming the favorable prognosis of this rare disease when appropriately managed. The majority of patients (87%) achieved complete response following combination therapy, with estimated 3-year overall survival of approximately 87%.

Nearly all patients in our series had DLBCL histology and presented with localized skeletal disease, which aligns with previous reports that describe DLBCL as the predominant subtype of PBL.⁸ The median age of our cohort was 53 years (range: 30-73), slightly younger than the typical 5th to 6th-decadepeak typically seen in the 5th to 6th decades in larger Western series.^{7,9} This difference may reflect the inclusion of

a broader age spectrum and the small sample size. Our cohort had a near-equal sex distribution (7 males, 8 females), differing from the mild male predominance reported in some studies.⁷ In contemporary series, elevated serum lactate dehydrogenase (LDH) levels and higher International Prognostic Index (IPI) scores have been consistently associated with inferior outcomes, while achieving a complete metabolic response on end-of-treatment PET is one of the strongest predictors of favorable survival. In our cohort, LDH and IPI data were limited, but all patients who achieved PET-CR have remained in remission.^{5,10}

Unlike prior series where long bones —particularly the femur— were most commonly involved, our distribution showed more frequent axial skeleton and pelvic bone involvement. The femur was involved in only 2 patients (13%), the tibia (± fibula) in 1 patient (7%), and the humerus in 1 patient (7%). Other isolated sites included the glenoid, distal tibia, proximal humerus, distal clavicle, and sternum. Importantly, 8 patients (53%) had axial or pelvic involvement, including vertebral disease, which is relatively high compared to some Western cohorts, but similar to certain Japanese or multiethnic series, where axial PBL predominates and higher-stage disease is more common.¹¹ Our cohort’s relatively higher rate of axial/pelvic involvement aligns with findings from recent large adult PBL series (Liang et al.¹², Li et al.¹³), which also report that spinal/axial bone involvement is associated with a distinct clinical course and may contribute to increased need for stabilization and symptom-driven interventions.^{12,13}

Despite this variation in anatomical distribution, 80% of our patients had Ann Arbor stage I-II disease at presentation, consistent with the general trend that PBL remains localized in most cases at diagnosis.¹⁴ All patients were treated with curative intent, utilizing anthracycline-based chemotherapy (typically R-CHOP) with involved-field radiotherapy in localized cases (Table 2). According to recent multi-institutional data, in limited-stage PB-DLBCL, excellent outcomes can be achieved with systemic therapy alone; routine consolidative radiotherapy may not provide additional benefit after PET-documented complete remission, whereas radiotherapy remains reasonable for partial responders or symptomatic sites. In multifocal disease, RT is typically reserved for palliation or focal control.^{15,16} This combined modality treatment is well-established as the standard of care and has shown improved outcomes over single modality approaches.⁷

Beyond fracture stabilization, surgery in PBL may be indicated for mechanical instability threatening functional

integrity, intractable pain unresponsive to systemic therapy or radiotherapy, or neural compromise in vertebral disease. In selected pelvic cases, reconstructive approaches such as the Harrington procedure can restore load transfer and mobility.⁵ The complete response rate of 87% and the sustained remission observed in our patients support the effectiveness of this approach. Previous studies, including those by Beal et al.¹, have shown 5-year overall survival rates of 80-90% in similarly treated cohorts. Our findings are in line with these data, and notably, all stage I-II patients treated with combination therapy remain disease-free to date.

The only relapse in our series occurred in a patient with multifocal bone involvement, echoing the known poorer prognosis in disseminated PBL.¹⁰ Nonetheless, even this patient initially responded to treatment, underlining the chemosensitivity of PBL.

Study Limitations

This study has limitations due to its retrospective design and small sample size. The absence of standardized reporting on prognostic markers such as LDH and IPI scores restricts further risk stratification. Moreover, variations in follow-up duration limit long-term outcome analysis, especially regarding late complications or secondary malignancies.

Still, our study adds valuable real-world evidence, demonstrating that effective treatment of PBL is achievable even in single-center settings. For clinicians, the key message remains: early biopsy of suspicious bone lesions, appropriate histopathologic confirmation, and multidisciplinary management are essential. Our findings reinforce that with modern chemoimmunotherapy and site-directed radiotherapy, PBL —though rare— is a highly curable lymphoma, particularly when diagnosed in its localized stage.

Clinical Implications

For clinicians, our findings reinforce the importance of treating PBL with curative intent using combination chemo-immunotherapy and site-directed radiotherapy, particularly in patients with localized disease. The high response and survival rates observed in our series —despite a notable proportion of patients having axial or pelvic involvement— highlight the disease’s sensitivity to modern therapeutic strategies.

Early and accurate diagnosis remains a critical challenge. Several patients were initially misdiagnosed with benign conditions such as osteomyelitis or other non-neoplastic bone lesions,

Table 2. Treatment Modalities and Outcomes in 15 PBL Patients

Stage	Treatment given	No of patients	Response (CR/PR)
Stage I/II	R-CHOP + RT	12	12 CR / 0 PR
Stage IV	Chemotherapy alone	3	1 CR / 2 PR
Total		15	13 CR / 2 PR

Treatment modalities and therapeutic responses in 15 patients with primary bone lymphoma. All patients with localized disease (Ann Arbor Stage I/II) received combined chemo-immunotherapy (R-CHOP) and involved-field radiotherapy, achieving complete remission (CR). Among three patients with advanced-stage disease (Stage IV), chemotherapy alone yielded one complete remission and two partial responses (PR), demonstrating lower efficacy compared to combined modality treatment. RT, radiotherapy.

consistent with the known diagnostic difficulty of PBL due to its rarity and nonspecific clinical presentation. Increased clinical awareness and prompt biopsy of suspicious bone lesions are essential to avoid delays in treatment initiation.

Optimal management requires a multidisciplinary approach involving hematology/oncology, radiation oncology, and orthopedic surgery, especially when structural compromise or pathological fractures are present. Timely coordination between specialties ensures comprehensive care and enhances the likelihood of long-term remission.

CONCLUSION

In summary, our single-center retrospective analysis of 15 patients with primary bone lymphoma demonstrates excellent treatment outcomes with modern combined modality therapy. Most patients had DLBCL and presented with localized disease; however, our cohort had a relatively high rate of axial and pelvic involvement, highlighting potential variations in disease presentation across different populations.

All patients received systemic therapy, typically R-CHOP, with radiotherapy applied in localized cases. The complete response rate was high, and the only relapse occurred in a patient with multifocal disease, consistent with literature indicating that disseminated PBL may have a higher risk of recurrence.

While limited by small sample size and retrospective design, our findings contribute real-world evidence supporting current treatment standards. Future studies should focus on multi-institutional collaboration to refine prognostic factors (e.g., PET response, molecular subtypes) and further optimize therapeutic strategies.

Given the rarity of PBL, sharing institutional experiences remains essential. Our results affirm that, despite diagnostic challenges, primary bone lymphoma is a highly curable malignancy when diagnosed promptly and managed with a multidisciplinary, evidence-based approach.

Ethics

Ethics Committee Approval: Approved by the University of Health Sciences Türkiye, Kartal Dr. Lütfi Kırdar Training and Research Hospital Hospital Ethics Committee (approval no.: 2020/514/177/31, date:13.05.2020)

Informed Consent: Retrospective study.

Footnotes

Author Contributions

Concept Design – M.S.A.; Data Collection and/or Processing – M.S.A., Ö.F.S.; Analysis or Interpretation – M.S.A., E.B.; Literature Review – Ö.F.S., S.A.G.; Writing, Reviewing and Editing – E.B., S.A.G.

Declaration of Interests: The authors declare no conflict of interest.

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