

Primary Bone Lymphoma: A series from a Cancer Institute in Pakistan

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Abstract

Primary bone lymphoma (PBL) is an uncommon tumour. Numerous studies have been reported from Western countries, but none from Southeast Asia. We reviewed a series of seven consecutive patients diagnosed and treated with PBL at our hospital between March 2002 and January 2007. All patients underwent chemotherapy with half receiving radiotherapy as their initial treatment. Six (84%) patients were male and 1 (16%) female with a median age of 33 (range: 23-85). All had diffuse large B-cell lymphoma (DLBCL) of bone except one (85 - M) who had chest wall cutaneous T-cell lymphoma with iliac blade involvement. The femur was the most frequently involved site (43%). Except for three patients that involved the lymph nodes, all patients had disease limited to bone. The 5-year overall survival rate was 43%. Although the number of patients was small, the data presented here revealed several characteristics of PBL.

Introduction

Primary bone lymphoma (PBL) is a rare disease; its incidence is 7% of all malignant bone tumours, 4-5% of all extranodal non-Hodgkin lymphoma (NHL) and less than 1% of all malignant lymphomas.¹ Previous reports showed its particular tendency to affect older adults although PBL can occur at any age. There is also a male predominance. The femur-bone has been reported to be the most commonly involved location as a single site.

Many PBL patients have had early clinical stage diseases²⁻⁶ and the most important prognostic factor has been the disease stage.^{4,7} Histopathologically, the majority of PBL cases have been diffuse large B-cell lymphoma (DLBCL) according to the World Health Organization (WHO) classification.

There are several problems with previous PBL reports. Small sample size, heterogenous definitions of PBL and the response criteria for PBL are some of the limitations in the described. Most case-series include patients with early stage disease and that too from Western countries. There are no patient reports or PBL from Asian countries.

We report the results of clinicopathological analyses conducted on 7 consecutive patients with PBL who received their treatment at our hospital during the past 5 years.

Patients and Methods

We reviewed the case notes of seven consecutive patients who were diagnosed with Primary bone lymphoma (PBL) and received treatment at Shaukat Khanum Memorial Cancer Hospital and research Center, Pakistan between March 2002 and January 2007. The histopathological diagnoses were made according to the World Health Organization (WHO) classification. According to the WHO classification, lymphoma involving bone can be classified into four groups.³ Clinical Staging was determined according to the revised American Joint Committee on Cancer (AJCC) staging system for lymphoid neoplasms. The clinical variables were recorded from the clinical notes. These include age, gender, B symptoms, serum lactate dehydrogenase (LDH) level, clinical stage (CS), primary bone site, number of bone lesions, other involved sites with lymph-node lesions or extranodal lesions (except for the bone), treatment, response to initial treatment and the histopathological subtype.

All patients underwent chest X-ray; computed tomography (CT) scans of the neck, chest, abdomen and pelvis; magnetic resonance image (MRI) of bone lesions; histological examination of clot obtained by bone marrow aspiration or bone marrow biopsy; total body scintigraphy; upper gastrointestinal tract endoscopy; blood smears; and physical examinations. Stage IIE disease was defined as lymph-node involvement adjacent to the bone lesion according to the AJCC staging system.

For assessment of response, we used response criteria based on the International Workshop Response Criteria (IWRC) combined with the MRI and total body scintigraphy findings. It included complete response (CR), partial response (PR) or stable disease (SD) as determined by either an FDG-PET or gallium scan.

The bone biopsy is expected to get either small round blue cell tumour or definitive evidence for lymphoma. In case of small round blue cell tumour, different stains for differentiation of various tumours were used, like MIC 2 for - Ewing's sarcoma, LCA for Lymphoma, Desmin + Myogenin for Rhabdomyosarcoma and NCE for Neuroblastoma.

If definitive evidence of lymphoma was found in specimen, we confirmed it with LCA only and if this was

positive, CD20 (B cell marker) was done.

The overall survival (OS) was defined as the interval between the dates of diagnosis and last follow-up. All statistical analyses were performed using SPSS version 13.0 (SPSS I3 for Windows). Descriptive analysis was done on all the variables.

Results

During the study period, a total of 1426 patients with lymphoma were evaluated. The demographic and clinical characteristics of the 7 patients with primary bone lymphoma are summarized in Table.

Table: Patient demographic and clinical characteristics.

Median age: 33 years (23-85 years)
Time to diagnosis: 3.7 months (1-7 years)
Male gender: 6
B Symptoms: 3 patients
Presentation: Pain = 3 - Fracture = 2 Swelling = 3
LDH elevation (normal < 460 u/L) 5/7
Bone involvement: Mono-ostotic = 6 Polyostotic = 1-
Radiological pattern: Lysis = 3 Sclerosis = 2 Soft tissue spread = Nil
Permeative = 2
Clinical Stage I - 4 patients
II - 2 patients
III - 1 patients
WHO Group 1 or 2- 6 patients
Group 3- 1 patients
Lymph node involvement- 3 patients
Extranodal lesions- 1 patient
Initial Chemo: CHOP regimen- 6 patients
Survival: 5 years = 43%

Among the primary involved sites of the bone, the extremities were the most frequently involved site (5 patients; 71%). The femur was the commonest involved bone. Five patients presented with a solitary lesion, while 2 patients had multifocal bone lesions. Three males were classified as WHO Group 1, three males again as Group 2, one female was classified as Group 3.

Three (43%) patients presented with stage IE disease, four (43%) with stage IIE, and one patient (14%) with stage III. One of two patients with a solitary bone lesion had a distant lymph node (cervical) metastasis. None of the patients had bone marrow involvement at their initial diagnosis, but one patient had the extranodal disease. DLBCL was the most common histopathological PBL subtype (6 of 7 patients; 86%).

Six patients underwent chemotherapy with CHOP regimen (cyclophosphamide [CPA], doxorubicin [DOX], vincristine [VCR] and prednisolone [PSL]). Four (66%) of the 6 patients received combined modality treatment of sequential chemotherapy and radiotherapy. One achieved complete remission and 6 patients achieved partial

remission. All patients were alive at the time of the last follow-up and remained in remission, except for one patient who has a progressive disease. The 5-year overall survival rate was 43%.

Discussion

The incidence of Primary bone lymphoma (PBL) is so rare that many aspects of the disease remain unsolved.

There were a number of interesting findings in our series. First, it is very rare in our population; study of 1426 cases of lymphoma revealed only 7 cases of PBL a prevalence rate of 0.5%. Second, there was a predominance of DLBCL in histopathological subtypes. Third, the femur was the most commonly involved site, as was found in the majority of previous reports from Western countries.^{2-4,6,7} Fourth, there were no PBL patients with bone marrow involvement at the time of their initial diagnosis.

Our study also revealed male preponderance, like previous reports.^{2-5,7,8} The clinical presentation is nonspecific. Bone pain is the most common symptom, reported by most of patients, followed by local swelling, with 50% of cases.⁹ In another study, the most common rheumatic manifestations at presentation were arthralgia, spinal cord compression, and bone/joint swelling.¹⁰ Histopathologically, the previous studies reported that the majority of patients with PBL were DLBCL.² Our results are consistent with these findings.

Chemotherapy followed by radiation therapy is used in localized forms of PLB. More extensive lesions (stages III and IV) are usually treated with chemotherapy alone. CHOP and ACVBP are the most widely used chemotherapy regimens. A combination of chemotherapy and radiotherapy was the best treatment for patients with PBL.⁵ A retrospective analysis of 52 patients with PBL revealed CR rates for patients treated by radiotherapy alone and chemotherapy with or without radiotherapy was 64% and 85%, respectively. The relapse rates between the two groups were 57% and 6%, respectively.⁴ These previous reports confirmed the superiority of chemotherapy to radiotherapy alone as the initial treatment for PBL patients. PBL patients treated with a combination of chemotherapy and radiotherapy were found to have a significantly better survival than the patients treated with single modality therapy.⁶ Number of patients in our study was relatively small, further studies are needed to clarify the characteristics of PBL and its optimal treatment strategy.

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