

Leukemia -Lymphoma and Myeloma

Primary Bone Lymphoma: An Experience of a Regional Cancer Center from India

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South Asian J Cancer 2021;9:227–229.

Abstract



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Background Primary bone lymphoma (PBL) is a rare disease, representing <5% of all extranodal non-Hodgkin's lymphomas (NHLs). The optimal treatment strategy is still unclear. Here, we report our institutional outcome analysis of patients diagnosed with PBL.

Materials and Methods From 2007 to 2014, the medical records of 22 patients with PBL were reviewed. Analysis was done for symptom-, patient-, disease-, and treatment-related characteristics. All patients were treated with chemotherapy with or without radiotherapy. Treatment response and impact of different prognostic factors on clinical outcome were analyzed.

Results The median age of presentation was 44 years (range: 18–70 years). A total of 19 (86.4%) patients were ≤60 years of age and 3 (13.6%) patients were >60 years. Out of all, 18 were males and 4 were females. Ann Arbor clinical staging at diagnosis was Stage I in 13 (59.1%), Stage II in 3 (13.6%), Stage III in 2 (9.1%), and Stage IV in 4 (18.2%) patients. Spine was the most common site of involvement seen in 12 (54.5%) patients. Diffuse large B cell lymphoma histology was seen in 8 (36.4%) patients and 8 (36.4%) had high-grade NHL. Chemotherapy with cyclophosphamide, doxorubicin, vincristine, and prednisolone was given to 20 (90.9%) patients, whereas 2 (9.1%) patients received cyclophosphamide, doxorubicin, vincristine, prednisone, and rituximab. Radiotherapy (30–40 Gy) was delivered to 19 (86.4%) patients. The median follow-up period was 40 months (range: 8–105 months). The overall response rate was 86.3% with complete response (CR) in 15 (68.1%) and partial response in 4 (18.2%) patients. Relapses were seen in three (13.5%) patients: two nodal, and one in the bone. Disease-free survival (DFS) and overall survival (OS) at 5 years were 56.6 and 72.7%, respectively. CR after initial treatment was associated with a significant better OS, 80 and 25%, respectively ($p < 0.0001$). Age, sex, stage, International Prognostic Index, histologic subtype, and number of sites had no significant influence on OS. Combining radiation therapy with chemotherapy (with or without rituximab) also did not improve the OS or DFS of patients.

Conclusion In spite of small number of patients reported in this study, conventional chemotherapy remains an effective treatment option for patients with PBL. OS was found to be affected by the initial response to treatment.

Keywords

- ▶ India
- ▶ NHL
- ▶ primary bone lymphoma

DOI <https://doi.org/10.1055/s-0040-1721173> ISSN 2278-330X.

How to cite this article: Mahajan R, Yadav B. S., Sharma S. C., Gupta A, Kumar S. Primary Bone Lymphoma: An Experience of a Regional Cancer Center from India. South Asian J Cancer 2021;9(4):227–229.

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Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

Introduction

Primary bone lymphoma (PBL) is a rare disease, representing <5% of all extranodal non-Hodgkin's lymphomas (NHLs) and <2% of all lymphomas in adults.¹ The most common histopathological subtype of PBL is diffuse large B cell lymphoma (DLBCL).² Standard treatment regimens have not yet been established because of the low incidence rates of PBL. PBL was initially treated with radiation therapy (RT) or surgery. After the introduction of cytotoxic agents as treatment options for PBL, several studies have established that chemotherapy combined with RT is better than RT alone.^{1,3} Many studies have shown that the addition of rituximab to chemotherapy regimens improves outcomes in patients with aggressive nonosseous NHL, whereas others have not shown additional benefits of supplementing chemotherapy with either rituximab or RT.^{4,5} Thus, optimal treatment strategy is still unclear. Here, we report our institutional outcome analysis of patients diagnosed with PBL.

Materials and Methods

From 2007 to 2014, the medical records of 22 patients with PBL (biopsy proven) were reviewed. A complete history was recorded and physical examination including local examination of disease. Baseline investigations such as complete blood count, blood biochemistry, chest X-rays, and bone marrow biopsy with histopathological examination were done. All patients underwent neck, chest, abdominal, and pelvic computed tomography (CT) scans or positron emission tomography (PET) scan. Staging was done with CT/PET scans. All patients were treated with chemotherapy with or without RT. Clinical features, treatment response, and impact of different prognostic factors on clinical outcome were analyzed.

Assessment of response to treatment was defined according to the international workshop criteria.⁶ Complete response (CR) was defined as disappearance of all detectable clinical and radiographic evidence of disease, excluding abnormalities attributed to bone remodeling. Partial response (PR) was defined as a $\geq 50\%$ reduction in all measurable tumors. Progressive disease (PD) was defined as a $\geq 50\%$ increase in the size of previously involved sites or the appearance of new lesions despite treatment. Stable disease was defined as a response lesser than PR, but not fulfilling the PD criteria.

Results

The median age of presentation was 44 years (range: 18–70 years). A total of 19 (86.4%) patients were ≤ 60 years of age and three (13.6%) patients were of >60 years of age. Out of all, 18 were males and 4 were females. Ann Arbor clinical staging at diagnosis was Stage I in 13 (59.1%), Stage II in 3 (13.6%), Stage III in 2 (9.1%), and Stage IV in 4 (18.2%) patients (–Table 1). Spine was the most common site of involvement seen in 12 (54.5%) patients (–Table 2). DLBCL histology was seen in eight (36.4%) patients and eight (36.4%) patients had high-grade NHL. Chemotherapy with cyclophosphamide, doxorubicin,

Table 1 Patient characteristics

Characteristics		Number of patients	Percentage
Age	<60	19	86.4
	>60	3	13.6
Sex	Male	18	81.8
	Female	4	18.2
B symptoms	No	70	94.6
	Yes	4	5.4
IPI	Low	7	31.8
	Low intermediate	1	4.5
	Not defined	14	63.6
Stages	I	13	59.1
	II	3	13.6
	III	2	9.1
	IV	4	18.2
Number of sites	Solitary	17	77.3
	Multiple	5	22.7
Histology	NHL—high grade	8	36.4
	NHL	5	22.7
	DLBCL	8	36.4
	Burkitt's lymphoma	1	4.5
Treatment	CCT	3	13.6
	CCT+RT	19	86.4
Chemotherapy	CHOP	20	90.9
	R-CHOP	2	9.1

Abbreviations: CCT+RT, computed chemotherapy + radiotherapy; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisolone; DLBCL, diffuse large B cell lymphoma; IPI, International Prognostic Index; NHL, non-Hodgkin's lymphoma; R-CHOP, cyclophosphamide, doxorubicin, vincristine, prednisone, and Rituxan.

Table 2 Bone sites

Bone sites	Number of patients	Percentage
Spine	12	54.5
Femur	2	9.1
Pelvic bone	2	9.1
Ribs	2	9.1
Humerus	1	4.5
Tibia	1	4.5
Skull	1	4.5
Sternum	1	4.5

vincristine, and prednisolone was given to 20 (90.9%) patients, whereas 2 (9.1%) patients received cyclophosphamide, doxorubicin, vincristine, prednisone, and Rituxan, RT (30–40 Gy) was delivered to 19 (86.4%) patients. Only two patients had Grade 3 hematological toxicity during chemotherapy, whereas in the rest, both chemotherapy and radiation treatment were tolerated well. The median follow-up period was 40 months (range: 8–105 months). The overall response rate was 86.3% with CR in 15 (68.1%) and PR in 4 (18.2%) patients. Relapses were seen in three

(13.5%) patients: two nodal, and one in the bone. Disease-free survival (DFS) and overall survival (OS) at 5 years were 56.6 and 72.7%, respectively. CR after initial treatment was associated with a significantly better OS, 80% versus 25%, respectively ($p < 0.0001$). Age, sex, stage, International Prognostic Index (IPI), histologic subtype, and number of sites had no significant influence on OS. Combining RT with chemotherapy (with or without rituximab) also did not improve the OS or DFS of patients.

Discussion

PBL is a rare disease, and thus, conducting prospective studies is challenging and experience in the literature comes from small retrospective case series. In our series, DLBCL and high-grade NHL were the most common histopathologic subtypes in accordance with other series.⁷ NHL histology with grade not mentioned was also seen in five patients in our study.

Interestingly, the sites of occurrence differ among the various studies: in our study, predominance of axial involvement was seen; this was also seen in the Surveillance, Epidemiology, and End Results (SEER) database study, which reported a predominance of axial involvement among 1,500 PBL patients.^{8,9} Pelvis was the most common site seen in two series of Japanese patients,^{10,11} whereas in studies by Heyning et al and Zinzani et al, the most common sites of disease were the long bones.^{12,13} Another study of 131 patients of the British Columbia Cancer Agency reported equal frequency between axial and extremity involvement.⁵

Combination chemotherapy results in durable responses, but no prospective randomized studies have been performed to optimize treatment strategies. Some studies have shown improved response and OS results in patients who received chemotherapy with RT.^{13,14} However, the study of the British Columbia Cancer Agency reported conflicting results.⁵ More recently, the introduction of the anti-CD20 monoclonal antibody rituximab has transformed the treatment of NHLs. In our study, combining RT with chemotherapy (with or without rituximab) also did not improve the OS or DFS of patients. A large number of small retrospective studies have reported conflicting results, as a result of which we are unable to conclude the effect of rituximab in the OS of PBL patients.^{4,5,15,16} In our study, the 5-year survival rate was 72.7%, and we found that it was significantly affected by the initial response after first-line treatment ($p < 0.0001$). The reported 5-year survival rates vary greatly, from 60% for the patients diagnosed after 1996 in the SEER database study up to 95.2% in a series published by Pellegrini et al in 2011.^{8,16} Various studies have reported different prognostic factors, such as age,^{8,9} sex,¹⁵ stage,⁵ lactate dehydrogenase levels,¹⁴ IPI,⁵ histologic subtype,¹⁰ and number of bones involved,⁴ but in our study, none of these mentioned factors had any significant influence on OS. Retrospective nature and small number of patients in our study are the main limitations of our study. In view of cost constraints, only two (9.2%) patients received rituximab.

Conclusion

In spite of small number of patients reported in this study, conventional chemotherapy with radiation remains an effective treatment option for patients with PBL. OS was found to be affected by the initial response to treatment. However, prospective studies are needed that will help clarify many aspects of the disease.

Funding

None.

Conflicts of Interest

There are no conflicts of interest.

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