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Primary Bone lymphoma: Histopathological diagnosis and orthopedic management

SAJJAD FAKHIR NASIR ABUALEISE[1],

1 Department of Orthopedic, Al-Basrah Teaching Hospital, Basrah Health Directorate, Ministry of Health/ Environment, Basrah, Iraq

SURA ALI MOHSIN AL NAMIL[2*]

2 Department of Histopathology, Al-Sadder Teaching Hospital, Basrah Health Directorate, Ministry of Health/ Environment, Basrah, Iraq

*Corresponding
SuraAlnamil
61001
Basrah, Iraq
Ahmedsalihdr2008@yahoo.com

Abstract

Primary localized bone lymphoma (PBL) is a rare affection prevalent in humans. It often involves long bones. The diagnosis is based on the histopathological studies with immunohistochemical studies of biopsies. In the present study, aims are to examine the clinicopathologic characteristics of PBL, and determine the management. A retrospective study conducted in our clinics for patients who had received a diagnosis of primary bone lymphoma during the period 2019. We identified 21 patients. In all the cases there was pathological confirmation of the diagnosis. Data collected regarding the patients' age, sex, site of lesion, symptoms, stage, and histologic subtype. Staging was performed according to the Ann Arbor system. The mean age at diagnosis of the cohort was 56.5±11.73 years. Of the 21 patients, there were 8 males (38.1%) and 13 females (61.9%). Grade II histology made up the majority of lymphoma reported (11, 52.4%). The diffuse large B cell type was the most frequent histological entity observed (16, 76.2%). The most commonly presented site was the lower limb 6(28.5%). Eight cases for stage IE, and IIE (38.1%) were recorded. Almost always 17(81%) cases were presented as single lesion. Pain was the most documented complaint (90.5%). Resection was performed in 5 cases. Of the cohort, 42.9% were initially treated with radiotherapy alone, 14.3% with chemotherapy alone, and 81% with a CCRT. Primary localized bone lymphoma is a rare disorder prevalent in human. It often involves long bone. The diagnosis is based on the anatomo-pathological and immuno-histochemical studies of a bone biopsy.

Keywords: Primary bone lymphoma; Chemotherapy; Radiotherapy; Biopsy

Introduction

The World Health Organization (WHO) defined primary bone lymphoma as a single bone lesion with or without regional lymph node involvement or multiple bone injuries without distant visceral or lymph node involvement [1]. It is a rare condition, represented 1-3% of Non-Hodgkin's lymphomas, 5% of extra- Non-Hodgkin's lymphomas and 3% of primary bone tumors [2,3]. Primary bone lymphoma (PBL) is discovered for the first time in 1939 by Parker and Jackson [4]. PBL is accounting for 3% of all primary malignant bone tumors [3], 2% of all lymphomas [5] and less than 5% of all extra-nodal NHL [6]. Patients aged between 50–70 and there is a male predominance. The most common histologic subtype is diffuse large B-cell lymphoma (DLBCL). The treatment ranged from monotherapy with radiotherapy to combination chemotherapy or combined modality therapy and more recently to immune-chemotherapy with the addition

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of the anti-CD20 monoclonal antibody rituximab [5, 6]. PBL may be complicated at presentation by pathological fracture or spinal cord compression [7]. WHO classifies PBL into four groups [8] ; Group A: lymphoma involving a single bone site with or without regional lymph node involvement. Group B: lymphoma involving multiple bones but with no evidence of other disease sites. Group C: lymphoma involving a bone site at the presence of disseminated lymph node or visceral disease. Group D: lymphoma involving any part of the body, diagnosed by bone biopsy performed to rule out possible involvement.
In the present study, aims are to examine the clinicopathologic characteristics of PBL, and determine the outcome of orthopedic management.

Methods

A retrospective study conducted in our clinics for patients who had received a diagnosis of primary bone lymphoma during the period 2019. We identified 21 patients. In all the cases there was pathological confirmation of the diagnosis. Data collected regarding the patients' age, sex, site of lesion, symptoms, stage, and histologic subtype. Staging was performed according to the Ann Arbor system. Patients with disease involving a single bone site were categorized as stage IE (WHO Group A). In case of regional lymph node involvement, called stage IIE. Finally, stage IVE included patients with multiple bone involvement without evidence of distant nodal or visceral disease (WHO Group B). Stage IIIE patients, defined as those with distant nodal disease were excluded from the definition of PBL [9, 10]. All statistical analyses were performed with SPSS (version 24.0; SPSS, Chicago, Ill., USA). All variables were tested for normal distribution of the data. Normally distributed data were expressed as means ± SD. All significance tests were 2 tailed and conducted at the 5% significance level.

Ann Arbor stage	Definition
IE	Single bone lesion
IIE	Single bone lesion with contiguous lymph node involvement
III	Bone injury with distant lymph node involvement
IV	Multiple bone lesions or a diffuse bone lesion of a long bone

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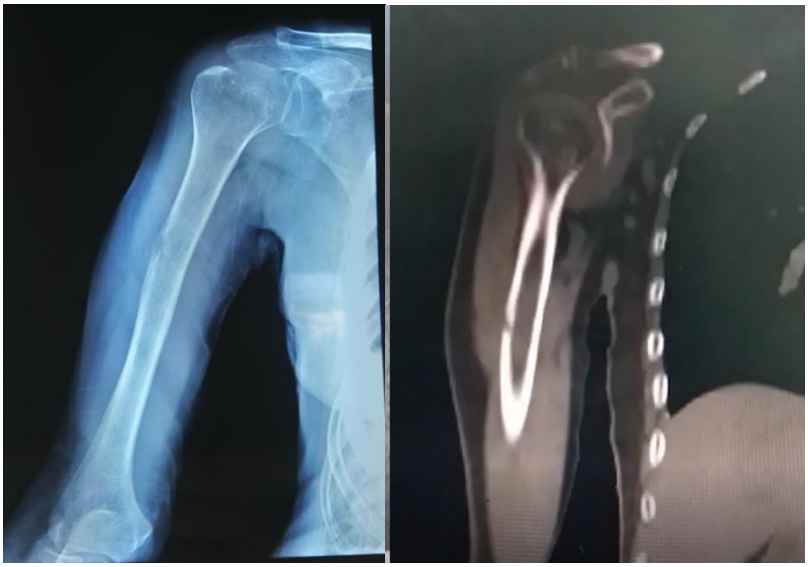

Figure 1. 48-years–old female, right humerus showed a small lytic lesion of the external cortex of shaft without a periosteal reaction. The CT revealed the same lesion with no soft tissue extension and a bone biopsy, the IHC results in favor of diffuse large B cell lymphoma.

Results

The mean age at diagnosis of the cohort was 56.5±11.73 years (range, 25-80). Of the 21 patients described in this work, there were 8 males (38.1%) and 13 females (61.9%). Grade II histology made up the majority of lymphoma reported (11, 52.4%) while grade I found in (10, 47.6%). The diffuse large B cell type was the most frequent histological entity observed (16, 76.2%). There were 3 of 21 cases which were the follicular type. Immunocytochemistry showed that most of samples that were interpreted were of B cell origin. The most commonly presented site was the lower limb 6(28.5%), and the femur was the most frequently involved bone. Eight cases for stage IE, and IIE (38.1%) were recorded. Almost always 17(81%) cases were presented as single lesion whereas 4(19%) cases were multifocal bone involvement. Pain was the most documented complaint (90.5%). Other presentations were mass or soft tissue swelling (33.3%), and pathological fractures (9.5%). Resection was performed in 5 cases. Of the cohort, 42.9% were initially treated with radiotherapy alone, 14.3% with chemotherapy alone, and 81% with a CCRT.

Table . Primary bone lymphoma variables (n=21).

Variables		No.	%
Age	56.5±11.73 (25-80)		
Sex	Male	8	38.1
	Female	13	61.9
Grade	I	10	47.6
	II	11	52.4
Histology	Diffuse B cell	16	76.2
	Follicular	3	14.3
	Unspecified	2	9.5
Stage	IE	8	38.1
	IIE	8	38.1
	III	4	19

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	IV	1	4.8
Site	Upperlimb	4	19
	Lowerlimb	6	28.5
	Hip	5	23.9
	Thorax	2	9.5
	Spine	3	14.3
	Skull	1	4.8
Site number	Oligo	17	81
	Multi	4	19
Symptoms	Pain	19	90.5
	Pathological fracture	2	9.5
	Swelling	7	33.3
	Mixed	12	57.1
Management	Surgery	5	23.9
	Chemotherapy	3	14.3
	Radiotherapy	9	42.9
	Combined	17	81

Discussion

Primary bone lymphomas are defined by the primary location of a malignant lymphoma in the bone, with a negative extension assessment within 6 months of the positive diagnosis. Another inclusion criterion is unique bone localization, but some authors integrate multifocal bone lymphomas into primary bone lymphomas [11]. The most frequent anatomical sites are bones with significant hematopoietic activity (long bones, vertebrae, and pelvis) [12]. Sometimes, mandibular involvement represents 2-17% of published cases, the clavicle is reached 4% of cases [2, 8].

Bone pain is the most frequently reported symptom (60-100%). Local swelling is found only in 50% of cases [13]. A pathological fracture rarely reveal the disease (10-17% of cases) [2]. Spinal cord compression is a symptom revealing of certain vertebral localizations [2, 11, 13]. B symptoms are rarely seen [5].

The diagnosis is based on a bone biopsy with an anatomo-pathological and immune-histochemical studies [5, 7].

Radiotherapy was the standard curative treatment for primary bone lymphoma localized pattern. Currently, chemotherapy followed by radiotherapy has demonstrated its interest in overall survival without relapse, and constitutes the reference treatment regimen [6, 14, 15]. CHOP chemotherapy is the standard first line treatment [15].

Currently, the roles of surgery in the management of primary bone lymphomas is limited. The aims of surgery are to get biopsy allows the diagnosis, to the treatment of pathological fractures and threatening lesions of fracture or spinal instability [3-5].

Conclusion

Primary localized bone lymphoma is a rare disorder prevalent in human. It often involves long bone. The diagnosis is based on the anatomo-pathological and immuno-histochemical studies of a bone biopsy.

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