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AN EPIDEMIOLOGICAL, CLINICAL AND PATHOLOGICAL STUDY OF LYMPHOMAS OF THE BONE AND MUSCULOSKELETAL SYSTEM AMONG POPULATION FROM THE SOUTH OF IRAQ

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Abstract

Lymphomas of the bone and musculoskeletal tissue are uncommon. Yet, they constitute a certain frequency that they merit certain consideration. A study was conducted to clarify the behavior of such type of lymphomas in the South of Iraq, epidemiologically, clinically, pathologically, biochemically and immunologically. Results show that they form minority among total lymphoma cases, but they were the third common type among extranodal lymphomas with male gender, adult age and urban residency predominance.

There was a predominance of low performance status, absence of B symptoms, neurological and musculo-skeletal manifestations, secondary bone, especially the spine, involvement. Non-Hodgkin lymphoma (NHL) was the most predominant, mainly the intermediate grade, with diffuse large cell lymphoma (DLCL) and Burkitt lymphoma (BL) as the main histological types encountered. Hematologically, there was mild anemia, rapid ESR (> 50 mm), normal platelets count in the majority, leucocytosis in < half and monocytopenia predominance. Biochemically they were characterized by normal liver function tests with the exception of high serum alkaline phosphatase, normal total serum proteins, hypoalbuminemia, normal serum urea, creatinine & uric acid, hypercalcemia, with serum LDH and B2MG elevation in the majority. Serum anti EB virus antibodies were seen in 1/4th of cases and the majority were of the higher IPI scores (both high intermediate & high). Those results were comparable to some and contradicting to other studies elsewhere.

Introduction

Lymphomas constitute a heterogeneous group of clonal lymphoid system neoplasms arising as a result of a one or more of somatic mutations in a lymphocyte progenitor[1]). They include distinct disorders defined by their clinical, histological, immunological, molecular, and genetic characteristics. Each one of these represents a clonal expansion of a normal precursor cell[2]. They rank as the 6th in incidence and mortality among malignancies at global level[3]. However, in Basra City, they occupied the 3rd rank among malignancies in males and the 2nd in females and represent 8.2% of all new malignant cases registered over the years 2005-2008[4].

Primary bone lymphomas (PBL), (defined as lymphoma localized to the bone without evidence of lymph nodes or other tissues at presentation: a modification of the initial Coley criteria in 1950 of 'Lymphoma presenting in an osseous site with no evidence of disease elsewhere for at least six months after diagnosis')[5,6] are uncommon among extranodal lymphomas. They accounts for <5% of all bone malignancies and are mostly are NHL. Secondary bone involvement in nodal NHL is uncommon, too, and typically is

restricted to aggressive types where the lesions are usually lytic[7]. For staging purposes, involvement of bone only is regarded as stage I, while involvement of bone along with other sites, or secondary to nodal disease is considered as stage IV, which differs entirely in prognosis. Diffuse large B-cell lymphoma is the most common type in both primary and secondary lymphomas. Primary bone NHL lymphomas usually arise from the appendicular skeleton or from flat bones of the axial skeleton, while secondary bone lymphomas usually involve the axial skeleton (skull, spine, ribs, and pelvis). Primary HL of the bone is very rare, whereas secondary involvement is found in 10%–25% of patients[8]. The imaging findings of bone lymphoma at conventional radiography, CT, and MR imaging are nonspecific, and usually reflect an aggressive pattern of bone destruction. It had been proved that FDG PET is more specific and sensitive than conventional bone radiology in identifying bone involvement by malignant lymphoma[8,9].

Aims of the study

The study aims to clarify the incidence, epidemiology, clinical presentations, staging, classification, pathological types and hematological, biochemical, immunological alterations of lymphomas of the bone and musculoskeletal tissue (both primary and secondary) among patients from the south of Iraq.

Materials and methods

During the period of June 2008-February 2012, 669 newly diagnosed lymphoma patients, from Basra, Missan, Thi Qar, Muthanna, Babylon and Wasit Governorates, were studied. Of them, 347 cases had extranodal lymphomas, out of which, bone and musculoskeletal lymphomas (both primary and secondary) were 43 cases. Most of the workup had been done in the Laboratory Departments of both Basra General Hospital and Basra Children Specialty Hospital. Some of the work had been accomplished in the researcher's Private Laboratory.

All cases were subjected to a thorough clinical study including: age, gender, residency of origin (the site they were living for the last 20 years). Those from Basra, were categorized into 5 regions: City Center, North, South, and East and West (Table I).

Table I: Geographical divisions of Basra Governorate adopted

Territory	Included Areas
Center	All districts and avenues within the official boundaries of City Centre.
North	Garma, Hartha, Daer, Qurna, Midaena, Talha.
East	Shatt-Al-Arab, Nashwa.
west	Shiaeba, Safwan.
South	Zubair, Um Qasir, Fao, Abul-Khaseeb.

Patients were segregated into rural or urban in origin depending on whether they at live, for the last 5 years, in rural or urban areas. The smoking habit, the duration of smoking and the number of cigarettes consumed per day were asked for. The drinking habit was asked for, too.

A history of a possible exposure to radiation (a direct exposure to a blast or war explosion, the presence of suspected war remnants in the vicinity of residence for > 5 years, or, the direct exposure to radiation in the form of therapy for another disease) was asked for.

A positive family history of any malignant disease (affecting the 1stdegree relatives) and the type of the tumor was ascertained too.

The chief complaint and duration of illness (in months) were inquired for. The presence of "B" symptoms: an increase in body temperature >37.3 °C for >10 days

(matched with measuring body temperature by examination), any drenching sweating especially at night, and loss of >10 % of body weight over a period of 3 months, were asked for[10]. The same was done for the presence of intense itching, any change in bowel habit and any history of a bleeding tendency. The general status of the patient was assessed, according to the Eastern Cooperative Oncology Group Performance Status (Table II)[11].

Table II: The Eastern Cooperative Oncology Group Performance Status (11).

Grade	Description
0	Fully active, able to carry on all pre-disease performance without restriction.
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature (eg, light housework, office work).
2	Ambulatory and capable of all self-care but unable to carry out any work activities, up and about more than 50% of waking hours.
3	Capable of only limited self-care, confined to bed or chair more than 50% of waking hours.
4	Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair.
5	Dead.

Patients were examined thoroughly for the presence of fever (by measuring the core temperature of the patient at the time of initial presentation), pallor, jaundice, hepatomegaly, splenomegaly (the last two were matched with the findings on abdominal ultrasound examination), neurological and cutaneous manifestations, ecchymotic patches anywhere or any evidence of a bleeding tendency, the presence of palpable lymphadenopathy and their sites. An enlargement of any two or more groups of the non-contiguous groups above was considered to be "generalized"[12].

All the patients were subjected to chest radiographs and abdominal ultrasound examinations and then were staged using the Ann Arbor Classification System[13] into 4 stages: I, II, III and IV.

All patients were subjected to hematological investigations, including full blood count, using the Beckman-Coulter 5 differential hematology analyzer which was properly calibrated according to the manufacturer's instructions with quality controls included between batches[14], erythrocyte sedimentation rate (ESR) (Westergren method)[15], peripheral blood smear examination to find the presence of abnormal lymphoid/leukemic peripheral blood cells, bone marrow aspiration, touch imprint and trephine biopsy (Figure I). Both direct and indirect antigolobulin tests (DAT & IAT) were done, too[16]. Normal results used were those adopted by the International Council of the Standardization in Hematology (ICSH) and the British Committee for Standardization in Haematology (BCSH)[17,18].

For those with palpable, accessible lymph nodes, fine needle aspiration was performed, stained with haematoxylin stain[19] and examined. Hodgkin lymphomas were classified according to the original Rye classification since it is popular among both pathologists and clinicians for its simplicity, ease of use, the association of individual types with prognostic differences when treated with current therapy and because of the lack of immunophenotypic studies[20], while the non-Hodgkin's lymphomas were classified using the International Working Formulation because of the lack of cytogenetic, immunological and molecular studies[21,22].

Patients were subjected to a battery of biochemical tests including: liver function

and renal function tests, serum uric acid, calcium, lactate dehydrogenase (LDH), beta-2-microglobulin[23-33] and serological tests including the anti gliadin antibodies (AGA), anti tissue transglutaminase (ATTA), anti Epstien-Barr virus (EBV) antibodies and anti Helicobacter pylori antibodies[34-37].

Cases were, after that, categorized according to the International Prognostic Index scoring system (Table-3)[38]. Data were fed and analyzed using the SPSS (Statistical Package for Social Sciences) version-17[39].

Table III: The International Prognostic Index for Non-Hodgkin Lymphoma[39]

Risk Factors		
Age		<60 / ≥60 years
Serum LDH		Normal / elevated (> twice normal)
Performance status		0-1 / ≥2
Stage		I,II / III,IV
Extranodal involvement		0-1 / ≥2
Risk category	Low	0-1
	Low intermediate	2
	High intermediate	3
	High	4-5

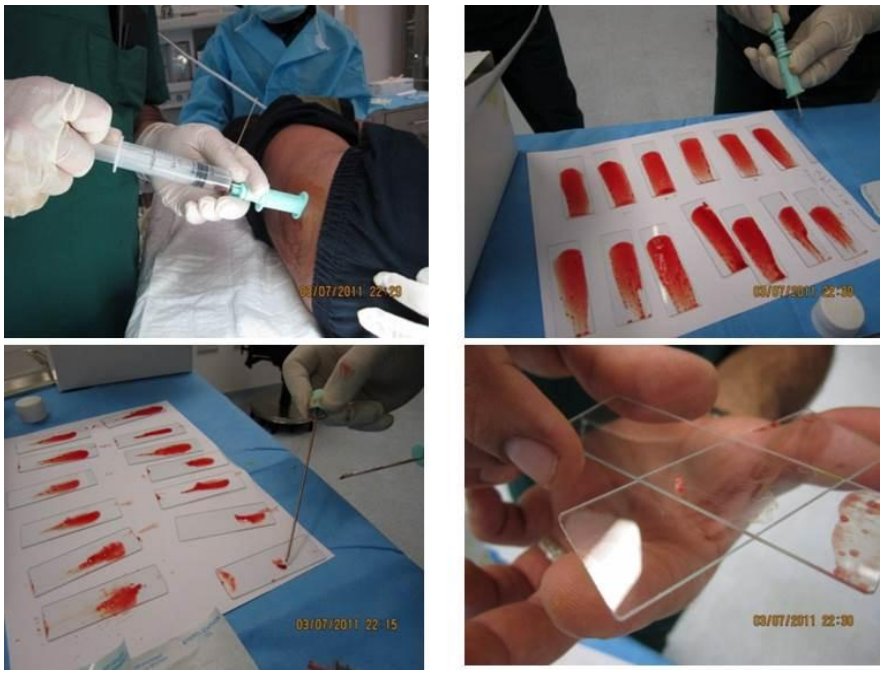


Fig. 1: Bone marrow aspiration and trephine biopsy procedures to one of the study cases, showing the way how to spread marrow smears and how to make marrow touch imprint from the biopsy piece.

Results

Lymphomas of the bone and musculo-skeletal system represented a minority among total lymphoma cases (6.4 %) and the third most common group (12.4%) of extranodal lymphomas (ENL). Patients ranged between 1.0-79.0 years of age, with a mean of 39.98 years (Table-IV). Adults were much more affected than children (79.1 vs 20.9%) and the most frequent age interval was between 40.1-50.0 years (16.2%). Males formed 62.8% of them. More than half of patients were from Basra Governorate (55.8%) and in

those from Basra, City Center was the greater source of cases (58.3%) and 65.1% of cases were urban in origin. Smoking habit was seen among 34.9% of patients, most of them (73.3%) smoked for >20 years and 53.3% were smoking <20 cigarettes /day. Only 2.3% of them were alcohol-consumers. Those who gave a positive history of exposure to chemicals and radiation hazards constituted 9.3% and 18.6%, respectively. No case with a positive family history of a malignant disease was encountered (Table-V).

Table IV: Mini., maxi. & mean of variables among bone lymphoma cases of study

Variable	Minimum	Maximum	Mean	SD
Age (year)	1.0	79.0	39.98	23.42
Duration of illness (month)	0.5	12.0	4.46	2.77
Hb (g/dl)	4.70	13.40	10.70	1.77
PCV (%)	16.00	43.20	33.44	5.61
ESR (mm/hr)	10	130	82.74	25.52
WBC (x109/L)	2.80	107.00	12.48	16.47
N (%)	2	87	60.79	16.04
L (%)	10	57	30.00	9.12
M (%)	1	10	2.74	2.51
E (%)	0	25	3.05	3.87
Platelets (x 109/L)	21	618	259.35	116.54
T.S. Bilirubin	0.4	5.4	1.01	0.75
SGOT	13	213	33.02	30.66
SGPT	14	234	37.56	34.34
ALP	34	287	138.79	65.08
T. Proteins	54	89	70.33	7.98
Albumin	20	52	32.51	6.86
Globulins	22	55	37.84	6.42
Urea	20.4	66.0	37.85	10.02
Creatinine	0.70	1.30	1.02	.14
Uric acid	2.3	8.9	5.01	1.66
Ca	7.9	13.9	11.21	1.51
LDH	187.00	657.00	396.95	138.99
B2MG	3.11	10.40	4.31	1.22

Clinically, 79.1% had a short duration of illness (≤6 mo). The most prevalent performance status was 4 (58.1%), followed by 3 (34.9%), while status 2 formed the least (7.3%) and none presented with status 1. Less than half of patients (41.9%) presented with fever, while weight loss and sweating were seen among 30.2% and 55.8% of them, respectively (B symptoms). The most prevalent presenting features were neurological and musculoskeletal manifestations (90.7% for each), followed by lymphadenopathy (LAP) (48.8%), splenomegaly (41.9%), pallor (37.2%), respiratory manifestations (20.9%), and hepatomegaly (16.3%). Other manifestations were less in frequency. More than half of patients (51.2%), presented without, while of those with LAP, patients with 2 groups of lymph nodes enlarged were the commonest (23.3%), followed by generalized LAP (16.2%). Cervical and Weldyer ring LN involvement were the most common (52.4% and 47.6%, respectively). Involvement of the bone alone represented 20.9% of cases while the involvement of other organs/tissues in addition to the bone constituted 79.1% of cases. The commonest sites of bone involvement are the spine, which constituted 37.2% of cases, followed by involvement of maxillary sinus (18.6%), mandible (7.0%). Involvement of both the humerus and femur were seen in 4.7% of cases, equally (Table-6) (Figure II).

Table V: Demographic characteristics of bone lymphomas in south part of Iraq

Variable		N	%
Age	Adults	34	79.1
	Children	9	20.9
Age intervals	≤ 10	6	14.0
	10.1-20.0	6	14.0
	20.1-30.0	2	4.6
	30.1-40.0	6	14.0
	40.1-50.0	7	16.2
	50.1-60.0	5	11.6
	60.1-70.0	6	14.0
	70.1-80.0	5	11.6
	>80.0	0	0
Gender	Male	27	62.8
	Female	16	37.2
Residency	Basra	24	55.8
	Missan	7	16.3
	Thi Qar	10	23.3
	Wasit	1	2.3
	Babylon	1	2.3
Geographical distribution of Basra Patients (N=24)	Center	14	58.3
	North	3	12.5
	South	4	16.7
	West	0	0
	East	3	12.5
Urban		28	65.1
Rural		15	34.9
Smokers		15	34.9
Duration of smoking (Yrs)	<20	4	26.7
	>20	11	73.3
No. of cigarettes/day	<20	8	53.3
	>20	7	46.7
Drinking habit		1	2.3
Exposure to chemicals		4	9.3
Exposure to radiation		8	18.6
Positive family history of malignancy in 1st degree relatives		0	0
Total		43	100

Histopathologically, positive fine needle aspiration (FNA) was seen in 90.0% of cases to whom the test was done (10 cases). Non-Hodgkin lymphoma constituted the majority of cases compared to HL (86.0% vs 14.0%) and 66.6% of HL cases were of lymphocytic depletion (LD) and 16.7% were both mixed cellularity (MC) and nodular sclerosis (NS), equally. The most frequent histological type of NHL was the diffuse large cell lymphoma (DLCL) (37.9%) followed by Burkitt lymphoma (BL) (13.5%) and follicular mixed cell lymphoma (FMCL) (10.8%). Most of NHL cases were of the intermediate and high grades (59.5% and 21.6%, respectively) (Table-VII).

Table VI: Clinical study of bone & musculoskeletal lymphomas in south of Iraq.

Variable		N	%
Duration of illness (month)	≤ 6	34	79.1
	>6	9	20.9
Performance status	1	0	0
	2	3	7.0
	3	15	34.9
	4	25	58.1
Fever		18	41.9
Weight loss		13	30.2
Sweating		24	55.8
Pallor		16	37.2
Change in bowel habit		4	9.3
Cutaneous manifestations		7	16.3
Neurological manifestations		39	90.7
Pruritus		8	18.6
Pleural effusion		0	0
Ascitis		0	0
Respiratory manifestations		9	20.9
Bleeding tendency		1	2.3
Hepatomegaly		7	16.3
Splenomegaly		18	41.9
Musculoskeletal manifestations		39	90.7
Jaundice		1	2.3
Lymphadenopathy		21	48.8
Groups of LN involvement	0	22	51.2
	1	4	9.3
	2	10	23.3
	Generalized	7	16.2
Sites of LN involvement (N=21)	Cervical	11	52.4
	Axillary	5	23.8
	Inguinal	6	28.6
	Supraclavicular	4	19.0
	Submandibular	6	28.6
	Postauricular	6	28.6
	Weldyer ring	10	47.6
	Mesenteric	1	4.8
	Other LNs	3	14.3
	Mediastinal	3	14.3
	Paraaortic	4	19.0
Types of Extranodal involvement	Bone alone	9	20.9
	Bone/muscles +	34	79.1
Bones involved*	Maxillary sinus	8	18.6
	Humerus	2	4.7
	Spine	16	37.2
	Mandible	3	7.0
	Orbital	1	2.3
	Temporal	1	2.3
	Pareital	1	2.3
	Tibia	1	2.3
	Ribs	1	2.3
	Femur	2	4.7
Total		43	100

*More than one bone may be involved in one patient.

Table VII: Histopath. study of bone & musculoskeletal lymphomas in south Iraq.

Variable		N	%
FNA Positivity (N=10)		9	90
Types of Lymphoma	HL	6	14.0
	NHL	37	86.0
Histological types of HL (N=6)	LD	4	66.6
	MC	1	16.7
	NS	1	16.7
Histological types of NHL (N=37)	BL	5	13.5
	DLCL	14	37.9
	DMCL	2	5.4
	DSCL	2	5.4
	FLCL	4	10.8
	FMCL	4	10.8
	FSCL	3	8.1
	IL	2	5.4
	LL	1	2.7
IWF Grades (N=37)	LG	7	18.9
	IG	22	59.5
	HG	8	21.6
	Msc	0	0
Total		43	100

Hematologically, the hemoglobin concentration ranged between 4.70-13.40 g/dl with a mean of 10.72 g/dl. The majority were anemic (82.4%), with mild-moderate anemia predominating on the severe (60.5%, 18.6% and 2.3%, respectively). Hematocrit ranged between 16.00-43.20% with a mean of 33.44% and the majority, (88.4%), was below 40%. Red cell sedimentation (ESR) ranged between 10-130 mm/hr with a mean of 82.74mm and the majority (90.7%) had >50 mm, of them, 20.9% had >100 mm sedimentation. The total WBCs count ranged between 2.80-107.00 x 109/L, with a mean of 12.48 x 109/L. Less than half (43.5%) of cases had leucocytosis, mostly (44.2%), below 50.00 x 109/L. Neutrophil differential count ranged between 2-87%, with a mean of 60.79% and the majority (93.0%) of them had normal counts. Differential lymphocytes count ranged between 10-57% with a mean of 30.00% and 20.9%, 72.1% and 7.0% of cases had below normal, normal and above normal counts, respectively. Differential monocytes counts ranged between 1-10%, with a mean of 2.74% and 60.5% of them had below, and 39.5% had normal counts. Differential eosinophils count ranged between 0-25%, with a mean of 3.05% and 51.2% of them had below normal, 44.1% had normal and 4.7% of them had high counts. Platelets counts ranged between 21.0-618.0 x 109/L, with a mean of 259.35 x 109/L and the majority, (93.0%), had normal counts while only 7.0% had thrombocytopenia. Malignant lymphoid cells were seen in the peripheral blood of 7.0% of cases and 4.7% presented with leukemic phase. Prolonged PT and PTT were seen in 2.3% of cases while positive Coombs' tests (both DAT and IAT) were seen 7.0 % and 9.3% of cases, respectively (Table-VIII). Biochemically, total serum bilirubin ranged between 0.4-5.4 mg/dl, with a mean of 1.01 mg/dl and 69.8% of them had normal and 30.2% presented with above normal levels. Serum AST and ALT ranged between 13-213 and 14-234 IU/L, with their means 33.02 and 37.56 IU/L, respectively and the majority of patients, (81.4% and 79.1%), had normal levels of both . Serum alkaline phosphatase ranged between 34-287 IU/L,

Table VIII: Hematological alterations among bone and musculoskeletal lymphoma cases in the South of Iraq.

Variable		N	%
Hb (g/dl)	< 6.0	1	2.3
	6.0-9.0	8	18.6
	9.01-12.50	26	60.5
	>12.50	8	18.6
PCV (%)	< 20	1	2.3
	20.0-30.0	7	16.3
	30.1-40.0	30	69.8
	> 40.0	5	11.6
ESR (mm/hr)	≤ 25	3	7.0
	26-50	1	2.3
	51-75	8	18.6
	76-100	22	51.2
	> 100	9	20.9
T WBCs (x109/L)	< 4.00	2	4.7
	4.00-10.00	20	46.5
	10.01-50.00	19	44.2
	50.00-100.00	1	2.3
	> 100.00	1	2.3
Neutrophils (%)	< 40	2	4.7
	40-80	40	93.0
	> 80	1	2.3
Lymphocytes (%)	< 20	9	20.9
	20-40	31	72.1
	> 40	3	7.0
Monocytes (%)	< 2	26	60.5
	2-10	17	39.5
	> 10	0	0
Eosinophils (%)	< 2	22	51.2
	2-6	19	44.1
	> 6	2	4.7
Platelets (x109/L)	< 20	0	0
	20-50	1	2.3
	51-149	2	4.7
	> 150	40	93.0
Malignant lymphoid cells in PB		3	7.0
Leukemic phase (> 20 % malignant lymphoid cells in PB)		2	4.7
Prolonged PT		1	2.3
Prolonged PTT		1	2.3
Positive DAT		3	7.0
Positive IAT		4	9.3
Total		43	100

with a mean of 138.79 IU/L and 74.4% of cases had elevated, while 25.6% of them had normal levels. Total serum proteins ranged between 54-89 g/L with a mean of 70.33 g/L and 76.7% presented with normal level, while 14.0% of them had hypoproteinemia. Serum albumin, ranged between 20-52 g/L, with a mean of 32.51 g/L> and 81.4%, of cases presented with hypoalbuminemia. Serum globulins ranged between 22-55 g/L with a mean of 37.84 g/L and 46.5% and 51.2% of them had normal and elevated serum levels, respectively. Serum urea ranged between 20.4-66.0 mg/dl with a mean of 37.85 mg/dl and serum creatinine ranged between 0.70-1.30 mg/dl with a mean of 1.02 mg/dl and the majority (81.4% and 97.7%), had normal levels of both. Serum uric acid ranged between 2.3-8.9 mg/dl, with a mean of 5.01mg/dl and 76.7% of cases had normal levels. Serum calcium

ranged between 7.9-13.9 mg/dl with a mean of 11.21 mg/dl and 65.1% of cases had hypercalcemia. Serum LDH ranged between 187.00-657.00 IU/L with a mean of 396.95 IU/L and the majority (93.0%) of cases had elevated and 48.8% of them had more than double the normal levels of this enzyme. Serum B2 microglobulin ranged between 3.11-10.40 u/ml with a mean of 4.31 U/ ml and all cases (100.0%) had elevated level (Table-IX).

Table IX: Bioch. Alter. among bone and musculoskeletal lymphoma in south Iraq

Variable		N	%
T.S. bilirubin (mg/dl)	< 0.3	0	0
	0.3-1.0	30	69.8
	> 1.0	13	30.2
SGOT (IU/L)	< 15	2	4.7
	15-45	35	81.4
	> 45	6	14.0
SGPT (IU/L)	< 15	1	2.3
	15-45	34	79.1
	> 45	8	18.6
ALP (IU/L)	< 30	0	0
	30-85	11	25.6
	> 85	32	74.4
TS Proteins (g/L)	< 62	6	14.0
	62-82	33	76.7
	> 82	4	9.3
S. Albumin (g/L)	< 35	35	81.4
	35-52	8	18.6
	> 52	0	0
Globulins (g/L)	<25	1	2.3
	25-37	20	46.5
	> 37	22	51.2
B Urea (mg/dl)	< 20	0	0
	20-45	35	81.4
	> 45	8	18.6
S Creatinine (mg/dl)	< 0.7	1	2.3
	0.7-1.4	42	97.7
	> 1.4	0	0
Uric acid (mg/dl)	< 3.0	3	7.0
	3.0-7.0	33	76.7
	> 7.0	7	16.3
S Calcium (mg/dl)	< 8.0	1	2.3
	8.0-10.5	14	32.6
	> 10.5	28	65.1
S LDH (IU/L)	80-190	3	7.0
	191-380	19	44.2
	> 380	21	48.8
S B2MG (mg/L)	0.0-3.0	0	0
	> 3.0	43	100
		43	100

Immunologically, 2.3% of cases had positive both antigliadin and anti-tissue transglutaminase antibodies. No case registered to have positive anti H. pylori antibodies while 25.6% of them had positive anti EB viral antibodies.

Most cases (95.4%) had higher IPI scores (65.2% for the high and 30.2% for the high intermediate), while the low scores (both low and low intermediate) constituted 4.6%, collectively (Table-X).

Table X: Serological study and IPI distribution among bone and musculoskeletal lymphoma cases in the South of Iraq.

Variable		N	%
Immunological study	Positive anti gliadin Abs	1	2.3
	Positive anti TTG Abs	1	2.3
	Positive Anti H pylori Abs	0	0
	Positive anti EBV Abs	11	25.6
IPI	Low	1	2.3
	Low intermediate	1	2.3
	High intermediate	13	30.2
	High	28	65.2
Total cases		43	100

Discussion

The frequency of lymphomas of the bone and musculoskeletal tissues in this study (6.4% of the total lymphoma cases, 12.4% of extranodal lymphomas (ENL) with age ranging between 1.0-79.0 years and a mean of 39.98 years), seems higher than that reported by Ludwig, 2002 and Aboulafia et al 1998, who stated that primary lymphomas of bone (PBL), are one of the rarest primary bone malignancies, accounting for less than 5% of all primary bone tumors, 3-5% of all bone tumors and 5% of all primary extranodal NHL[40,41], while secondary involvement of bone and marrow, as stated by Baar et al 1999, is seen in 5-15% of patients with HL and 30-53% of patients with NHL[42]. It is still higher than that reported by Fletcher, et al 2002[43] who reported that bone lymphoma (both primary and secondary) comprises 8.8% of ENL, while Maruyama et al 2006 stated that the incidence of PBL is 7% of all malignant bone tumors, 4–5% of all extranodal NHL and less than 1% of all malign. lymphomas[44]. However, Suresh et al stated that primary lymphomatous involvement of skeletal muscle is seen in only 0.3% of HL and 1.5% of NHL[45].

The higher incidence of bone lymphomas among adults & male sex is comparable to the findings of Mathur and Gellman 2011 who reported a male predominance (male: female ratio 1.8:1), and main affection in the fifth to seventh decade of life[46]. It is also comparable to Jawad et al, 2010 who reported a male predominance (53.9%) with the main age affected was > 60 years (55.7%)[47]. The predominance of low performance status (status 4) and B symptoms is higher than that reported by Mathur and Gellman, 2011[46], where systemic (B) symptoms, were seen in fewer than 10% of patients in true stage IE lymphoma of bone. This difference is attributed to the fact that in this study, cases were both of primary and secondary bone lymphomas. The higher frequency of neurological manifestations in the study is attributed to the higher frequency of spinal involvement, a thing compatible with the finding of Peng et al 2009 where neurological manifestations due to spinal cord compression were seen in 81.3% of cases presented with lymphoma of the spine[48].

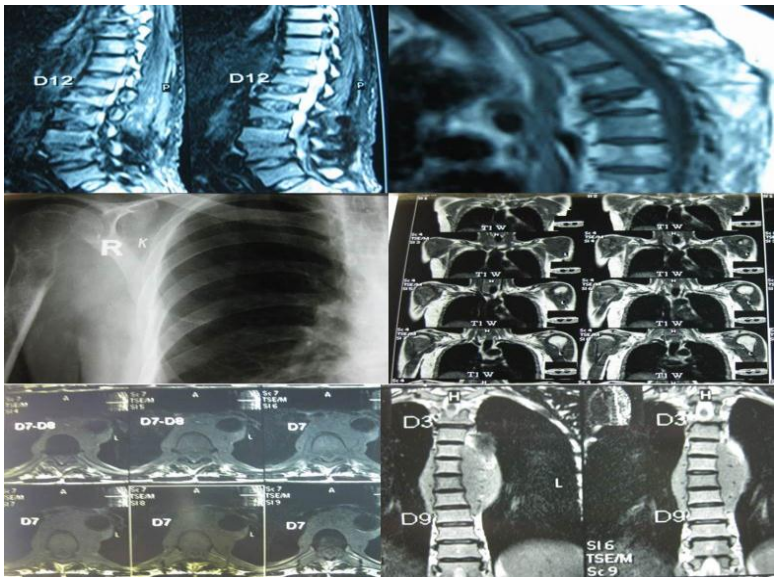
The type of bone involvement in this study is somewhat compatible with those reported by Jawad et al 2010, where the axial skeleton (vertebra, ribs, sternum, clavicle and associated joints, bones of the skull and face, associated joints, and the mandible) formed 62. 5% of cases, while the appendicular skeleton formed the rest[47].Yet, it contradicts with that reported by Salter et al 1989, where the femur is the most common site of predilection, forming (29%) of cases, followed by (in descending order of frequency): pelvis (19%), humerus (13%), skull (11%) and tibia (10%)[49]. Histopathological types of bone and musculo-skeletal lymphomas in this study are comparable to those reported by Ludwig 2002[40] and Kitsoulis et al 2006[50], where most of PBL are of NHL type while HL is extremely rare (the majority of which are nodal and of NS

type). Histological subtype distribution of NHL in this study is comparable to that of Mathur and Gellman, 2011[46], Kitsoulis et al 2006[50] and Chan et al 1991[51], who stated that in adults, diffuse large B-cell lymphoma is the most common subtype, accounting for (60-90% of cases). It is also comparable to that reported by Jawad et al 2010[47], where DLBCL was the most predominant, accounting for 66.3% of cases and the high grade was markedly predominating (97%). However, Krishnan et al 2003 and Ueda, et al 1989, stated that 75% of all classifiable PBL were intermediate grade (diffuse mixed small and large cell or large cell lesions) in the Working formulation. On the basis of the current WHO classification, the majority of cases were classified as diffuse large B-cell lymphomas[52,53]. The majority of cases in this study, (90.7%), had > 50 mm ESR, of them, 20.9% had > 100 mm sedimentation, is compatible to Mathur and Gellman, 2011 who stated that the ESR is frequently elevated, especially when there is systemic disease involvement[46]. Hypercalcemia in about 2/3rd, (65.1%) of cases is contradicting to Mathur and Gellman 2011[46], who stated that hypercalcemia is seen in some pediatric patients and has been associated with a poorer prognosis, and to Bhagavathi and Fu 2009 and Desai et al, 1991, too, who reported that rarely, symptoms of hypercalcemia (eg, lethargy, constipation, and somnolence) are present[54,55]. The predominance of serum LDH elevation in the majority (93.0%) of cases (48.8% of them show > double the normal level), is also compatible with that reported by Mathur and Gellman 2011[46] who stated that most patients have elevated (LDH) levels, which is directly proportionate to the disease load and also to, but higher than, Ahmad et al 2009 where LDH was elevated among 71.4% of cases of PBL[56].

Conclusions and recommendations

We conclude, from this study, that bone and musculoskeletal lymphomas, though are uncommon among population from the Sothern Part of Iraq, they seem more common than reported elsewhere with more severe and aggressive features at presentation. Thus a detailed study of them and the co-operation between orthpeditians, hematologists and histopathologists is necessary to clarify the detailed behavior of such tumors among them. This necessitates the need of the use of the revised WHO classification which needs the introduction of immunophenotyping and molecular and genetic study of cases.

Fig. 2: Bone involvement by lymphoma: a and b: Destruction of lumbar spine by lymphomatous lesions, c and d: involvement of right humeral head, e and f: involvement of dorsal spine and paravertebral soft tissue.



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