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THE PATTERN OF OSTEOSARCOMA IN SOUTHERN PART OF IRAQ

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Abstract

Osteosarcoma is a malignant tumor of mesenchymal cells characterized by the direct formation of bone or osteoid tissue by the proliferating malignant tumor cells. Grading of tumor is a good prognostic indicator. It constitutes a basic factor of the current Enneking osteosarcoma staging system. The detection and identification of markers able to differentiate a high from a low malignant osteosarcoma which would substantially help the diagnosis, the prognosis and consequently the therapeutic approach of these tumors.

This study is aimed to determine: The contribution of osteosarcoma to the total number of the malignant bone tumors registered in Basrah during the period of the study. The various histological subtypes and grades of osteosarcoma.

A total number of thirty-seven cases of osteosarcoma diagnosed during the period 2000-2004 inclusive were collected from private and governmental hospital histopathological labrotaries in Basrah province. Clinical data concerning the age, sex, clinical presentations, radiological features and gross appearance of affected bone were evaluated. Histological sections of 25 out of 37 cases, were collected, re-evaluated and grades. Osteosarcoma was the most common primary malignant tumor of bone classified according to the tumor matrix into histological subtypes and analyzed for histological accounting for 35.92% of the primary malignant and 20.55% of the total malignant bone tumors. Of these 37 osteosarcoma cases, 35 (94.59%) were intramedullary and 2 (5.40%) were parosteal surface osteosarcoma. The male to female ratio was 1.1:1. The second decade was the most common age group of occurrence accounting for 23 out of 37 cases (62.2%). The main presenting clinical features were painless swelling recorded in 51.4%.The distal end femur, proximal end tibia and proximal end humerus were the most common sites of affection accounting for 27.02%, 32.43%, 16.21% respectively. The most common subtypes of osteosarcoma was osteoblastic (52%) followed by fibroblastic (Osteosarcoma 24%) and chondroblastic (20%); while telangiectatic subtypes was rare (4%). Parosteal osteosarcoma was a rare variant in our locality and other variants were not diagnosed during the period of the study. The majority of osteosarcoma cases (76%) were of grade III, followed by grade II (16%) and grade I (8%).

Introduction

Osteosarcoma is the most common primary malignant bone tumor, accounting for approximately 20% of all primary bone sarcomas[1]. Its annual incidence in the United States was 1.7 cases/million/year[2], while in Iraq it forms 43.4% of primary malignant bone tumors[3]. Although treatment modalities have been improved over the past decades, it is still a tumor with a high mortality rate in children and young adults. The peak incidence is registered in the second decade of life[1]. Most osteosarcomas are highly malignant arising within the metaphyseal area of long bones. According to the main histological component central osteosarcomas are subdivided into various histological subtypes (which are conventional osteosarcoma, small cell,

telangeictatic, anaplastic, well differentiated, fibrohistiocytic, giant cell osteosarcomas). Surface osteosarcoma mainly parosteal and periosteal as well as, well differentiated intramedullary osteosarcomas behave like low grade malignant tumors[4]. Grading is a good indicator for the outcome in patients with osteosarcoma[5].The determination of malignancy grade is of major significant. It constitutes a basic factor of the current Enneking osteosarcoma staging system; it is therefore evident that the detection and identification of markers able to reliably differentiate a high from a low malignancy osteosarcoma which would substantially help the diagnosis, the prognosis and consequently the therapeutic approach of these tumors[6].

Materials and Methods

This study was done to analyze the pattern of osteosarcoma in Basrah province. A total number of thirty seven cases of osteosarcoma diagnosed during the period 2000-2004 inclusive were collected from private and governmental hospital histopathological labrotaries in Basrah province. Clinical data concerning the age, sex, clinical presentations, radiological features as well as gross appearance of affected bone were evaluated. Histological sections and slides of twenty- five (25) cases stained with hematoxylin and eosin were collected. The available collected histopathological slides of twenty-five cases (out of 37) were re-evaluated and classified according to the tumor matrix into histological subtypes (osteoblastic, fibroblastic, chondroblastic, telangeictatic). Analyzed for histological grading. Histological variables including amount of tumor matrix, tumor cell density, tumor cell pleomorphism, number of mitoses, tumor necrosis and tumor growth into the vessels or tumor cells within the vessels. Tumor grade were scored subjectively according to the method used by Kirpensteijn et al[5]; as in (table I).

Results

During the period from (2000-2004) a total of 180 cases of malignant bone tumors were diagnosed. Of these tumor cases 103 were diagnosed as primary malignant tumors and 77 cases as secondary. Osteosarcoma was diagnosed in thirty seven cases which represent (20.55%) from the total number of malignant bone tumors and (35.92%) of the primary malignant bone tumors. Of these 37 osteosarcoma cases 35 (94.59%) were intramedullary and 2 cases(5.40%) were parosteal surface osteosarcomas.

Age Sex Distribution: Of the 37 osteosarcoma cases, 20 were males (54%) and 17 were females (45.94%). The age range from 8-52 years with a median of 19.5 years. The male to female ratio was 1.1: 1 The second decade was the most common age group of occurrence account for 23 out of 37 cases (62.2%), Clinical Features: The main presenting clinical features were painless swelling recorded in 19 cases, followed by painful swelling in 9 cases, while only pain in 6 cases, pathological fractures in 2 cases, and 1 case with limitation of joint movement The Anatomic Distribution of Osteosarcoma: The femur was the most frequent site of affection, seen in 13 cases (35.13%). Of these 13 cases, 10 cases affect the distal end femur, 2 cases affect the proximal end femur, and 1 case affects the shaft. The tibia comes next to the femur in the order of incidence of affection, 12 cases (32.43%) are recorded and all of them in proximal end tibia. The above results show that 22 cases (59.45%) occurred around the knee joint. Six cases affect the humerus, all of them seen in proximal end. Two cases affected the distal end radius, while one case was record-

ed for each of the rib, nasal bone, maxilla and dorsal vertebra).

The histological Subtypes of Osteosarcoma: Of the 37 cases the slides and paraffin blocks were available for only 25 cases for histopathological evaluation. All the 25 cases were intramedullary osteosarcoma. The predominant histological subtypes was osteoblastic osteosarcoma (figure-1) account for 13 cases (52%), Fibroblastic (figure 2) and chondroblastic (fig.3) subtypes had an intermediate position. while the telangeictatic subtypes (fig.4) was the least common account for 1 case (4%), (Table II) The Histological Grades of Oateosarcoma*:* Histologically grading of osteosarcoma depend on tumor matrix, tumor cell density, necrosis (fig.5), pleomorphism (fig.6) and mitoses (fig.7) The majority of cases were grade III, seen in 19 cases (76%), in 12 out of 19 cases, the initial grade was II but with vascular invasion (figure-8) change to grade III. Of the remaining 6 cases, 4 had grade II (16%) and 2 had grade I (8%), as shown in Table III and Table IV.

Figure 1

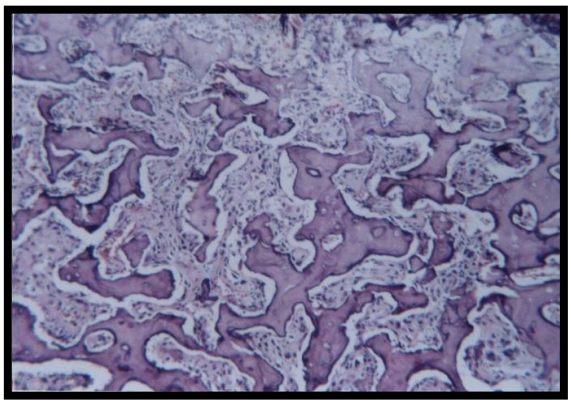


Figure 2

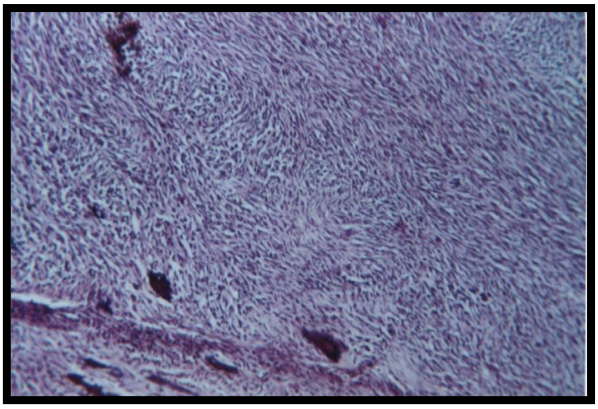


Figure 3

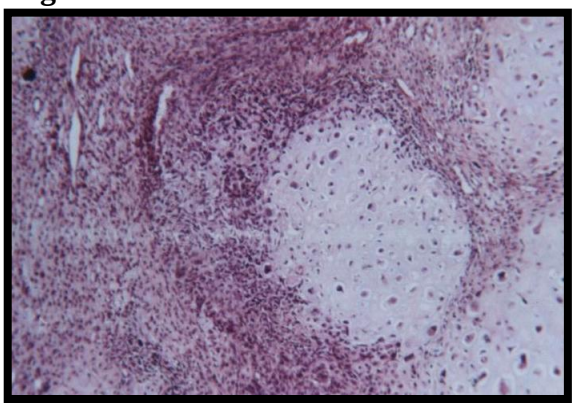


Figure 4

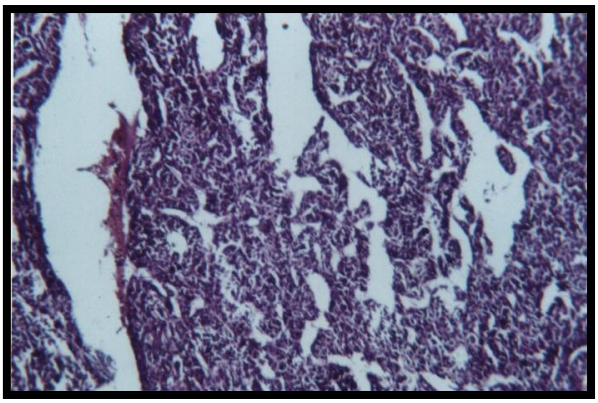


Figure 5

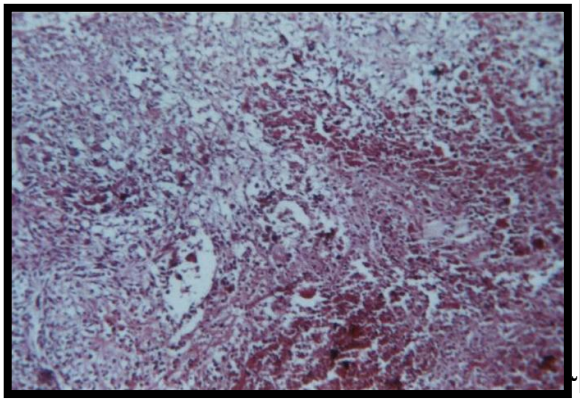


Figure 6

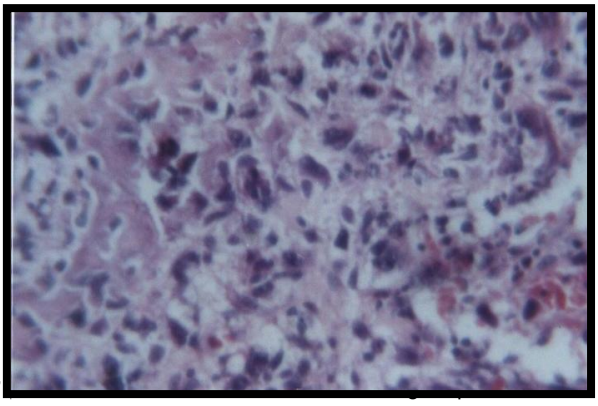


Figure 7

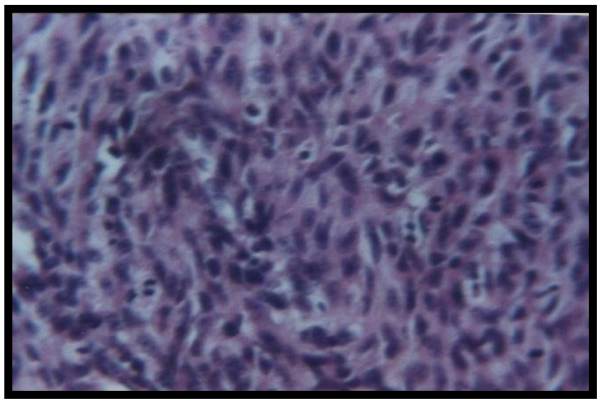
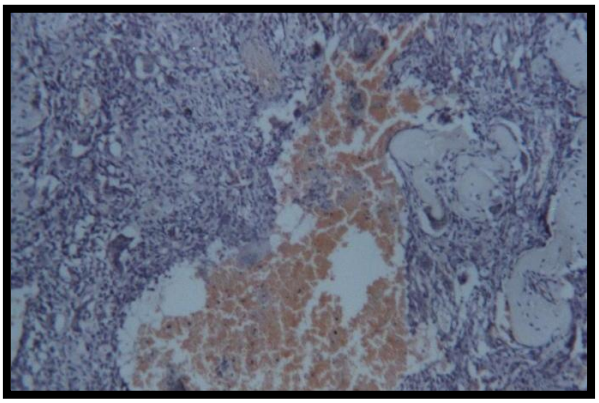


Figure 8



Discussion

In the present study, osteosarcoma was the most common primary malignant tumor of bone accounting for (35.92%) of the primary malignant and (20.55%) of the total malignant bone tumors. An observation similar to Hamdan study in the south part of Iraq that showed osteosarcoma being the most common primary malignant bone tumor in the period 1980-1999 accounting for (26%) of the total registered primary malignant bone tumors[7]. Iraqi Cancer Registry during the period 1995-1997 found that osteosarcoma was the most common primary malignant bone tumor accounting for (43.2%)[3].

A study done in Northern part of Iraq found that osteosarcoma was the commonest primary malignant tumor (45%) in the period 1980-1990(8). However, 10 years later Ewing's sarcoma was reported to be the leading primary malignant bone tumor accounting for (31.3%), followed by osteosarcoma (28%) as reported by the same worker[8,9]. Ewing's sarcoma was also reported as the most common primary malignant bone tumor by Katchy et al in Kuwait[10].

Osteosarcoma was also reported as the most common primary malignant bone tumor in Iran[11], India[12], Northern part of Pakistan[13], Nigeria[14], Cameroon[15], New York[16], and Mexico[17]. The sex ratio is nearly equal in this study. In Twaij study in 1994-1996 in Basrah male to female ratio was 1.5:1[18].A male to female ratios of 1.2:1 and 1.8:1 were reported by AL-Jumaily et al in each of his two studies conducted in Northern part of Iraq[8,9]. However, Ahmed et al reported a sex ratio of 3.3:1 in Northern Pakistan in 1994[13]. The second decade was the peak incidence of osteosarcoma observed in this study, a finding similar to the observations of Al-Jumaily and Twaij in Iraq[8,9,18], Ahmed et al in Pakistan[13]. Painless swelling was the most common presenting feature in our patients (51.4%); while in Twaij study in Basrah painful tender swelling was the leading presenting feature[18]. In the present study the distal femoral and proximal tibial ends were the most common sites of affection followed by proximal end humerus. Similar observations were reported by Twaij study in Basrah Province[18] and Northern Iraq[8,9]. The most common subtypes of osteosarcoma in this study was osteoblastic (52%) of the total, followed by fibroblastic and chondroblastic (24%, 20% respectively); while telangiectatic subtypes was rare (4%).

Larsson et al[19], Conventary et al[20] both were in agreement that osteoblastic osteosarcoma was the most common

subtype and that telangectatic subtype was absent ; while chondroblastic and fibroblastic subtypes fall in between. Matsuno et al[21] reported that telangiectatic subtype contributes 2.5% of the total of his studied cases while Huvos et al[22] found that 11% of his studied cases were telangiectatic.

No other similar study in our locality is reported to compare our histological results with them. In this study, the majority of osteosarcoma cases (76%) were of grade III, followed by grade II (16%) and grade I (8%). In canine osteosarcoma and using a similar histological grading system Kirpensteijn et al[5] found that grade III is the most common histological grade (75.3%), grade I is the least common (4.2%), while grade II falls in between (20.5%). In human but using another histological grading system (Broders grading system) Coventry et al[20] found that the majority of cases were of grade III (54.4%), followed by grade IV and grade II (26.7%, 17.2% respectively); while grade I was (1.6%) only.

Conclusions

1. Osteosarcoma is a common primary malignant bone tumor accounts for 35.92%.
2. The peak incidence was in the second decade of life. Sex ratio was nearly equal.
3. Metaphyseal ends of long bones were the most common sites of affection with 59.45% of the cases occurred around the knee.
4. Painless swelling was the most common presenting features, while limitation of joint movement was the least common.
5. Osteoblastic osteosarcoma was the commonest subtypes.
6. Most cases were of high grade tumors (G III).
7. Parosteal osteosarcoma was a rare variant in our locality.
8. No small cell osteosarcoma, fibrohistiocytic or giant cell- rich variants were diagnosed during the period of the study.

Table I: classification for osteosarcoma grades determination using kirpensteijin et. al histological scores.

*Tumor grade	tumor matrix		tumor cell density		necrosis		pleomorphism		Mitoses/3HPF		** vascular invasion
	score	%	score	%	score	%	score	%	score	NO.	
Grade I	1	>50 %	1	<25 %	0-1	<25 %	0-1	<25 %	1	<10	-ve
Grade II	2	25-50%	2	25-50%	2	25-50%	2	25-50%	2	10-20	-ve
Grade III	3	<25 %	3-4	>50 %	3-4	>50 %	3-4	>50 %	3	>21	+ve

(*) Tumor grade was determined according to the classification schedule (table IV)
Cases that collecting score equal or less than 5 were considered grade I.
Cases that collecting score from 6-10 were considered grade II.
Cases that collecting score more than 10 were considered grade III.
(**) Osteosarcoma was scored grade III if sign of tumor growth into the vessels or tumor cells within the vessels were present.

Table II: The histological subtypes of osteosarcoma

Histological subtypes	No. of cases	Percent
Osteoblastic	13	52
Fibroblastic	6	24
Chondroblastic	5	20
Telangeictatic	1	4
Total	25	100.0

Table III: The histological grades of osteosarcoma.

Grade	No. of cases	Percent
I	2	8
II	4	16
III	19	76
Total	25	100.0

Table IV:

Case No.	Histological subtypes	Histological Variables						Scores	Initial grade	Final grade
		Vascular invasion	Tumor matrix	cell density	Tumor necrosis	Pleomo-rphism	Mitosis			
1	Chondroblastic	+ve	2	3	0	3	2	10	GII+v*	GIII
2	Chondroblastic	-ve	2	2	0	3	1	8	GII	GII
3	Osteoblastic	+ve	3	3	1	4	1	12	GIII+v	GIII
4	Osteoblastic	-ve	1	1	0	1	2	5	GI	GI
5	Osteoblastic	+ve	2	3	2	3	1	11	GIII+v	GIII
6	Osteoblastic	-ve	2	2	0	3	2	9	GII	GII
7	Fibroblastic	+ve	1	2	0	4	1	8	GII+v	GIII
8	Fibroblastic	+ve	3	4	1	3	1	12	GIII+v	GIII
9	Fibroblastic	+ve	3	3	0	2	1	9	GII+v	GIII
10	Osteoblastic	-ve	2	3	0	3	1	9	GII	GII
11	Fibroblastic	+ve	3	4	1	1	1	10	GII+v	GIII
12	Osteoblastic	+ve	2	3	0	3	1	9	GII+v	GIII
13	Osteoblastic	+ve	1	2	0	3	1	7	GII+v	GIII
14	Chondroblastic	+ve	1	2	0	3	1	7	GII+v	GIII
15	Telangiectatic	+ve	3	4	0	2	1	10	GII+v	GIII
16	Osteoblastic	-ve	3	3	0	3	2	11	GIII	GIII
17	Osteoblastic	+ve	2	2	0	3	1	8	GII+v	GIII
18	Osteoblastic	+ve	3	3	0	2	1	9	GII+v	GIII
19	Fibroblastic	+ve	3	3	0	3	2	11	GIII+v	GIII
20	Osteoblastic	+ve	2	3	0	3	2	10	GII+v	GIII
21	Osteoblastic	-ve	2	3	0	3	3	11	GIII	GIII
22	Osteoblastic	+ve	3	3	0	3	2	11	GIII+v	GIII
23	Fibroblastic	-ve	2	3	0	3	1	9	GII	GII
24	Chondroblastic	+ve	1	2	0	2	1	6	GII+v	GIII
25	Chondroblastic	-ve	1	2	0	1	1	5	GI	GI

NOTE: * v: indicate vascular invasion.

The above table show that nineteen cases (19) were with grade III. Seventeen cases (17) (out of 19) had vascular invasion. Twelve cases (12) (out of 19) had an initial grade II, but with vascular invasion they had a higher grade level (GIII).

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