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LIPOSARCOMA : THE COMMONEST SOFT TISSUE SARCOMA

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Abstract

Liposarcoma is the most common soft tissue sarcoma of adult life. In our locality liposarcoma constituted 42% of soft tissue sarcomas admitted to Mansoura Oncology Unit (Surgery and Radiation Oncology and Nuclear Medicine) within 2 years. Thirty six cases of liposarcoma were studied with a peak incidence between 15-67 years with median age 38.4 years. The incidence in females exceeds that in males by about 1.7:1 . Fifty percent of cases were in the lower extremities and 38.8% in the trunk. Well differentiated and myxoid variety (grade 1) constituted 61% of liposarcoma cases. Local failure occurred in only 6 patients (16.6%). Eleven patients develop remote metastases (30.6%) and the most common site of metastases was the lung followed by the liver and bone. DFI was Longest in patients receiving postoperative radiotherapy (22.8 ± 4.6 months).

Introduction

Soft tissue sarcoma are an exceedingly rare entity, the management of which has undergone rapid evolution over the past 30 years. These changes have been driven by improve understanding of the natural biology of this disease cluster. As recently as 1950, soft tissue sarcoma was a purely surgical illness treated by radical amputation, this approach has been superseded by management that includes radiotherapy and chemotherapy administered prior to surgery or postoperatively (Pollock, 1992) liposarcoma are malignant lesions of adipose tissue (Spittle etal., 1971).

Four subtypes of liposarcomas are generally recognized: well differentiated myxoid, lipoblast, round cell and pleomorphic. Well differentiated liposarcomas can exhibit aggressive local invasion, though they tend not to metastasize only later in their course. Round cells are comprised of uniform round cells with a highly vascular meshwork of capillaries. These are highly malignant lesions and like the pleomorphic liposarcoma have only a 20-30% 5 years survival in most reported series (Rosenberg et al., 1992).

Preoperative radiotherapy doses are usually less than those needed postoperatively to achieve comparable tumour control 45 to 50 Gy preoperativly versus 60 to 65 Gy postoperatively due to relatively more hypoxic environment of postoperative scar tissue (Nielsen et al., 1991).

Balanced against the preoperative radiotherapy advantages (regression of tumour after radiotherapy may make resection easier and decrease shedding of viable tumour cells at the time of resection) are the delay in surgical resection (5 weeks of radiotherapy followed by 5 weeks of post irradiation tissue healing) and the 30% incidence of significant wound healing problems induced by preoperative radiotherapy (Skibber et al., 1987). In light of these considerations, postoperative radiotherapy is generally reserved for previ-

ously unradiated recurrent lesions, Brennar et al., 1991, in examining their earlier soft tissue sarcoma experience they identified prognostic factor that correlated with recurrence and survival, these parameters including tumour site, histopathology, size, grade and adequacy of resection and radiotherapy received.

Numerous adjuvant chemotherapy trials conducted thus for have failed to demonstrate unequivocal survival advantages for systematically treated patient (Delaney et al., 1991). Most chemotherapy regimens capable of causing tumour regression have moderate to severe complications and only a 40% to 50% overall response rate (Rosenberg et al., 1992).

Patients and Methods

Within the last 2 years from January 1990 to January 1992, 36 patients with liposarcoma were referred to Mansoura Oncology Unit (Surgery and Radiation Oncology and NuclearMedicine Department). All patients were subjected to physical examination to determine the approximate size of the lesion attachment to the deep or superficial structure, relationship of the tumour to prior biopsy, functional status of the affected part and presence of prior injury or concurrent medical diseases.

The radiologic evaluation of the patients with soft tissue sarcomas include:

1- Soft tissue radiograph of the affected part.
2- C.T, MRI through the affected region.
3- Chest Tomogram or C.T.
4- Arteriogram in certain instance for identification of the position and state of major vessels, local extent of the disease, displacement of the vessels and for venous phase for venous drainage to prevent major tumour embolization at start of surgery.

Truecut needle biopsies play a major role in the diagnosis because of easy manoeuver and no tendency for haematoma formation which lead to spread of the tumour beyond the site of natural tumour invasion in incisional biopsy. The diagnostic accuracy of truecut needle biopsy about 87% success and the other tumours need incisional or excisional biopsies. The biopsy site must be removed in any definitive resection, care should be taken to place the biopsy site at such a location not to compromise subsequent definitive surgical excision.

Pathologically liposarcoma classified as :

grade I : well differentiated liposarcoma, myxoid liposarcoma.
grade II : round cell liposarcoma.
grade III : pleomorphic liposarcoma.
(According to Costa et al., 1984).

Lasty after clinical examination and investigation staging was done using the TNM staging of soft tissue sarcoma (Russel et al., 1977). The rational for treatment of operable liposarcoma was combining surgery followed by post operative radiotherapy.

Surgical treatment of liposarcom

The use of radical surgical procedures such as radical local resection or amputation is the first treatment for better local control which reach to 84% of cases (30/36).

The radical local resection require better tumour localization with an acceptable wide safety margin of normal tissues which can be obtained between the edge of the tumour and the adjacent critical and non resectable structures, such as major vessels (although 2 cases of liposarcoma of the thigh with femoral artery invasion or implication within the tumor were excised with the tumour, with great saphenous vein graft for arterial reconstruction), nerves and bone, such as the groin, knee, popliteal space, most portions of the leg, many sites of the head and neck area, axilla, elbow region.

Because of this limitation, 7 cases were subjected for amputation and this amputation above the level of the proximal joint above the tumour and one of these cases showed also local failure 1.5 year later and need more proximal amputation for control of local recurrence.

In performing radical local resection of liposarcoma wide excision of all normal tissue in the tumour area for several centimeters including the skin and subcutaneous tissues near the tumour also excision include the previous scar or biopsy site as well as any area that may have contained haematoma from pervious biopsies. Venous outflow ligation must be performed initially at the first surgical procedure. The compartment of muscle including the tumour must be excised en toto with the tumour from the origin to the insertion.

In retroperitoneal liposarcoma the adjacent adherent normal structures as kidney or intestine must also removed. Lastly tumour spilling must be avoided to prevent local failure. Salvage treatment of patients with local failure need aggressive treatment unless there is concomitant distant metastases because usually is of high grade. Salvage treatment was done for 6 patients two of them underwent amputation.

3 cases undergone lymphadenectomy 2 cases were subjected for inguinal lymphadenectomy and one case for axillary lymphadenectomy. Radiation therapy for these patients is planned during the immediate postoperative period, but is not started until the wound has healing, finding of both the gross and microscopic pathologic examination are integrated with the description of the surgical procedure to aid in design of the optimal treatment plan.

The radiation treatment volume encompasses all tissues suspected of involvement by tumour plus those handled in the surgical procedure (Because of the large treatment volume, treatment plan must exclude uninvolved tissues to the maximum extent possible). Using a telecobalt unit at 80 S. S. D. All patients were irradiated postoperatively (except in case of grade I, less than 5 cm, well differentiated liposarcoma and amputation) with a dose range between 60 to 65 Gy for 6-6.5 weeks, we must first define the target volume in three dimension by physical examintion and radiographic (C. T). The initial treated volume covers the tissue involved by both gross and microscopic tumor which is comparable to that would be removed by radical surgical procedure with a dose 50 Gy /5 weeks during this component a bolus is placed over the scar (if there is suspicious of

involvement), the treatment volume is then reduced to cover only the site of the initial tumour with a dose of 10-15 Gy for 1-1.5 week.

In this study the use of effective systemic chemotherapy in the form of CYVADIC protocol only in the presence of metastases as chest and liver:

CY Cyclophosphamide 500 mg/m2 day 2 I.V
V Vincristine 1.4 mg /m^2 day 1 , 8, 15 I.V.
A Adriamycin 50 mg / m^2 day 2 I.V.
DIC Dacarlazine 250 mg / m^2 day 5 I.V.
(Repeated every 3 weeks)

Results

Thirty six cases of. liposarcoma were studied with a peak incidence between 26 and 51 years, in the study group age range between 15-67 years with median age of 38.4 year. The average age depends on some extent on the anatomical distribution of the tumour thus individuals with liposarcoma in the retroperitoneum are on the average 10 years older than those with tumours in the extremities, presumably because liposarcoma of the peritoneum are detected and treated at a later stage of the disease.

In this study, liposarcoma predominately in female with incidence 64% and 36% in males (1.7:1). Table 2.

Liposarcoma most often presents as asymptomatic soft tissue mass because these lesions arise in a compressible soft tissue are often far from vital organs until reach a considerable size. Pain, tenderness or functional disability occur in 16% of cases, retroperitoneal liposarcoma presents with weight loss, renal displacement which lead to hydronephrosis and pyelonephritis.

Pyrexia had occurred in 6 cases (16%) from renal affection or tumour necrosis. The clinical behaviuor of liposarcorma closely reflects the variable microscopic appearance, other clinical manifestations were concomitant with liposarcoma, cancer breast was observed in 2 cases as a second primary tumour, also one case with intestinal polyposis. Also 16% a second liposarcoma were found and one of these 6 cases develop liposarcoma firstly in the thigh, in the retroperitoneal and then cancer breast.

Fifty percent of cases of liposarcoma were in the lower extremities and 38.8% in the trunk as shown in table (3). Liposarcoma of the thigh are usually deep seated and found mainly in the quadriceps muscles and popliteal fossa, also the right side more common than the left side. Most of cases are of pathological grading I and II liposarcoma as in table (4).

Table (5) represents the stage of the liposarcoma 61.8% of patients were stage I (a = 3 patients, b = 19 patients) but only 5 patients 13.1% were stage IV a. The Disease Free Interval (DFI) was largest (22.8 ± 4.6 months) in patients receiving postoperative radiotherapy following radical surgery while it is nearly similar in patients subjected for radical surgery or amuptation. This difference is statistically significant (P =< 0.05) Also there is a statistically significant correlation between grading and DFI (table 7).

Eleven patients develop remote metastasis (30.6%) and most develop metastases in the

first 1 and 1/2 year. Seven patients develop metastases in the first 18 months and 11 patients develop metastasis within 30 months. The most common site of metastasis had occurred in the lung followed by liver and bone, a surperising case which develop multiple scattered skin metastasis all over the body (table 8).

Local failure had observed in 6 cases (table 9), four of them in the thigh and were excised in three cases and one case subjected for hip disarticulation and two cases of retroperitoneal liposarcoma and were explored again for more radical excision including the kindey and loops of intestine. The surgical salvage was done for cases without metastases.

The metastatic potential of high grade liposarcoma is responsible for most of local failure and remote secondaries. Also trunkal sarcoma is worse than he exlremities and responsible for rising of incidence of metastases. Also the distal extremities is of good prognosis than that of the proximal one.

Surprising data about the second liposarcoma which develop in 6 patients and these tumours managed primarily by surgery, chemotherapy and radiotherapy. Most of these cases develop after 2 years of the first liposarcoma and only one develops 6 months after management of the primary liposarcoma.

Those patients who develop other primary liposarcoma are of grade I and only one of grade II and this data indicate the multicentricitiy of liposarcoma and these cases are prognostically better except one case develop cancer breast, retroperitoneal sarcoma and died lastly of brain metastases.

Discussion

The comprehensive treatment of patients with liposarcoma mandates a team approach. The collaborative efforts of invasive radiologist working with pathologists have resulted in accurate tissue biopsy for diagnosis and staging.

Radical surgical approach with the development of adjuvant systemic approaches with radiotherapy offers the promise of better targeted therapy that more effectively controls tumour dissemination and local failure. Liposarcoma is the most common soft tissue sarcoma of adult life its incidence ranged from 16-18% in most of the literature (Russel etal., 1977).

In this study liposarcoma constituted 42% of soft tissue sarcoma admitted to Mansoura Oncology Unit (surgery and radiotherapy) within 2 years, beside its high incidence among sarcomas, liposarcoma is remarkable because of its frequent large size, which is probably unsurpassed among tumour in general, and its variable histological picture.

In the present series that incidence in females exceeds that in males by (1.7:1) while in most studies the incidince in males exceeds that in females by (1.5:1) (Romsdah et al., 1983) and (Rosenberg et al., 1992), this high incidence may be due to small number of patients in this series.

In this study well differentiated and myxoid variety (grade I) were 61% in patients with liposarcoma while pleomophic variety (grade

III) was 22.4%. This is in agreement with that obtained by (Costa et al., 1984). In the present study 61% of patients were stage (I a and b) (a - 3 patients and b - 19 patients) while only 5 patients (13.1% years) were stage (IV a) this result confirm that reported by Brennan et al., (1991).

The DFI was longest in patients receiving postoperative radiotherapy (22.8 ± 4.6 months) these similar to that reported by Nielsen et al., (1991) Patients with grade I liposarcoma had longer DFI than that of grade II and III this result confirms that obtained by Brennan et al., (1991.

Seven patients developed metastases in the first $1\frac{1}{2}$ years, the most common site of metastases was the lung followed by the liver and bone, local failure occurred in only 6 patients (16.6%) this results are in agreement with that reported by (Rosenberg et al., 1992).

Summary And Conclusion

The treatment of patients with liposarcoma mandates a team work included radiologist and pathologist for accurate diagnosis and staging, radical surgical approach and postoperative radiotherapy. This team work approach has improved the outcome of liposarcoma with more effectively control of tim-out dissemination and local failure.

Table1: Schema for Staging Soft Tissue Sarcomas by TNMG.

T	Primary tumor
	T1 Tumor less than 5 cm
	T2 Tumor 5 cm or greater
	T3 Tumor that grossly invades bone, major vessel,or major nerve
N	Regional Lymph nodes
	N0 No histologically verified metastases to regional lymp nodes
	N1 Histoligically verified metastases to regional lymp nodes
M	Distant metastasis
	Mo No distant metastasis
	M1 Distant metastasis
G	Histologic grade of malignancy
	G1 Low
	G2 Mderate
	G3 High
Stage I	Grade 1 tumor less than 5 cm in diameter with no regional
Stage Ia	lymph nodes or distant metastses .
G1T1 N0 M0	
Stage Ib	Grade1 tumor 5 cm or greater in diameter with no regional
G1 T2 N0 M0	lymph nodes or distant metastses.
Stage II	Grade 2 tumor less than 5 cm in diameter with no regional
G2 T2 N0 M0	lymph nodes or distant metastses.
Stage IIb	Grade 2 tumor 5 cm or greater in diameter with no regional
G2 T2 N0 M0	lymph nodes or distant metastses.
Stage III	Grade 3 tumor less than 5 cm in diameter with no regional
Stage III	lymph nodes or distant metastses.
G3 T1 N0 M0	
Stage IIIb	Grade 3 tumor 5 cm or greater in diameter with no regional
G3 T2 N0 M0	lymph nodes or distant metastses.
Stage IIIc	Tumor of any grade or size (no invasion) with regional
G1-3T1-N2M0	lymph nodes, but no distant metastses.
Stage Iv	Tumor of any grade that grossly invades bone, major
Stage Iva	vessel, or major nerve with or without regional lymph node
G1-3T3N0-M0	metastases but without distant metastases.
Stage Ivb	Clinically diagnosed distant metastases
G1-3T1-3N0M1	

(Russell WO, cohen J, Enzinger F et al : A clinical and pathological staging system for soft tissue sarcomas. Cancer 40 : 1562 - 1570, 1977)

Table 2: Sex distribution in 36 patients with liposorcoma

Sex	NO	%	Ratio
Female	23	63.9 %	1.7
Male	13	36.1%	1
Total	36		

Table 3: Site distribution.

Anatomical location	No of cases	%
Lower extremities	18	50.0 %
thigh	13	36.1
buttock	4	11.1
lower leg	1	2.8
Upper extremities	2	5.6
Trunk	16	44.4%
retroperitoneal	8	22.2
inguinal region	3	8.3
back	2	5.6
chest wall	1	2.8
Head & Neck	2	5.6
Total	36	100.0

Table 4: Patholgical grading of 36 patients with liposorcoma

Grade	NO	%
Well differnetiated I	16	44.4
Myxoid variety	6	16.6
Round cell II	6	16.6
Pleomorphic variety III	8	22.4
Total	36	100%

P = < 0.05

Table 5: Stages of liposarcoma.

Stage of the disease	No of patients	%
Stage Ia (less than 5 cm & G1)	3	8.3
Stage Ib (>5 cm& G1)	19	52.7
Stage IIb (>5 cm & G2)	6	16.6
Stage IIIb any size, G3 &+ ve L.N	3 2 inguinal 1 axillary	8.3
Stage IVa any grade tumor invade bone major vessles or nerve .	5	13.1

Table 6 : Disease free intervals (DFI) in 36 patients with liposorcoma by treatment modality.

Treatment Modality	No of patients	DFI (in months)
radical surgery + Postoperative radiotherpy	26	22 :8 ± 4.6
radical surgery	3	15.3 ± 3.7
amputation	7	12.2 ± 3.3
Total	36	

P = < 0.05

Table 7: Disease Free intervals by grading.

Grade	No of patientstients	DFI (months)
Grade I	22	18.3 ± 3.7
Grade II	6	14.3 ± 2.7
Grade III	8	11.2 ± 2.3
Total	36	

P = < 0.05

Table 8: site of distant metastases (11/36).

Site of 1st metastases	No	No
lung	5	14%
liver	2	5.6 %
bone	2	5.6 %
brain	1	2.8 %
skin	1	2.8 %
total	11	30.6 %

Table 9: Local failure and grade

Grade	No	%
I	0	0
II	2	33.3
III	4	66.6
Total	6	

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الملخص العربى

الورم الدهنى الخبيث أكثر أنواع الأورام الخبيثة للأنسجة الرخوة

د. ناظم شمس د. إيناس عبدالحليم

قسم جراحة الأورام ، قسم علاج الأورام بالإشعاع والطب النووى - كلية الطب - جامعة المنصورة

إن الورم الدهنى الخبيث هو اكثر انواع الاورام الخبيثة للانسجة الرخوة فى سن البلوغ . فى منطقتنا وجد أن هذا المرض يمثل ٤٢ ٪ من اورام الانسجة الرخوة الخبيثة التى تتردد على اقسام جراحة الاورام وعلاج الاورام بالاشعاع والطب النووى بمستشفى المنصورة الجامعى خلال سنتين.

وجدد ان ٣٦ ٪ من الحالات كان قمة حدوثة بين ١٥ - ٦٧ سنة مع متوسط فترة عمر ٣٨.٤ سنة ووجد أن حدوث هذا المرض في السيدات اكثر من الرجال بنسبة ١:١.٧ ، وأن ٥٠٪ من الحالات كانت في الاطراف السفلي ، ٣٨.٨ ٪ فى الجزع، ١٦.٦ ٪ من المرضى حدث لهم ارتداد موضعى واحدى عشر مريض ظهر عندهم ثانويات بنسبة ٣٠.٦ ٪ وكان اكثر الاماكن عرضة الرئة يليها الكبد والعظام ، ووجد ان فترة شفاء المرضى كان اطول فى المرضى الذين اخذوا علاج اشعاعى بعد الجراحة (٢٢ر٨ + ٤ر٦ شهر)