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Malignant Lymphoma of the Spinal Extradural Space

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Abstract

The natural history, treatment and results of 30 cases with NHL in the spinal extradural space were analyzed. It was found that the spinal cord compression caused by extradural NHL is generally a late manifestation of the disease, although early involvements are occasionally encountered. The dorsal spinal cord is the most frequently involved segment and pain, weakness, and paraesthesia are cardinal symptoms. In our study intermediate grade of NHL is the most frequent variety followed by high and low grade histopathology. Radiation treatment delivered in the early phase of the compression is commonly successful in reversing the neurologic symptoms. The immediate response rate following treatment was 59% including 45.5% complete respomse and 13.5% partial response. the median survival showed significant difference between low grade and intermediate and high grade tumours ($p > 0.01$) as well as between stage 1. II patients versus stage - LLL, IV cases.

Introduction

THE first case of malignant lymphoma involving spinal cord was described by Welch in 1910 [1] and the first series of cases with emphasis on the relative frequency of neurologic manifestations was reported by Ginsberg in 1927 [2]. Malignant lymphoms account for 11% of the tumours associatad with spinal cord compression [3]. Hodgkin's disease and diffuse, 'histiocytic' lymphoma are the most common histologic types [4]. For

many years, surgery and post-operative radiotherapy hasve been the accepted treatment for primary, Extradural NHL. yet neither the optimal required rodiotherapy treatment fields and doses are clearly defined, nor the role, if any, chemotherapy is precisely defined.

In an attempt to resolve some of these issues, we reviewed retrospectively the kasr El-Eini centre of radiation oncology and nuclear medicine (NEMROCK) experience with patients treated for NHL of the spinal extradural space between 1980 and 1988 inclusive. We report here the results of this study including clinical features, histologic subtypes and response to treatment. This may help to formulate guide lines for better management of these cases.

Patients and Methods

During the peroid of 1980-1988, 628 cases of non-Hodgkins lymphomas were investigated, treated and followed at Kasr El-Aini Center of Radiation Oncology and Nuclear Medicine (NEMROCK). Of whom thirty cases had spinal Extra-dural NHL localisation. Eight patients were primary spinal NHL, where in 22 cases the spinal cord was affected secondary to other sites. Eight out of the 22 secondary tumors, were originally nodal where 14 cases were originally extranodal in their sites.

All cases had histologic diagnosis of NHL. The diagnosis of spinal cord compression was based on myelographic studies, and / or obvious meurologic manifestations. In 17 patients (57%), myelogram was done, and in 13 patients (43%), extradural NHL was found at laminectomy.

Apart from 2 cases, who did not attend treatment, all patients had recevied treatments for their disease either in the form of radiotherapy, chemotherapy or both.

Histopathlogy was described according to International working formulation [5]. Cases were staged according to Ann-Arbor system [6].

Treatment

Radiotherapy was the main treatment employed for 28 patients. Therteen had laminectomy before radiotherapy. Radiation treatments were directed to the involved spinal cord segment through a single posterior field with liberal margins. Planned tumour doses of 40 Gy were aimed at 200 CGY daily tumor dose, 5 treatments per week. Mean tissue dose was calculated at depth of 4-6 cm according to site of spine irradiated. The radiation therapy was given using cobalt. 60. In all patients who received doses below 40 Gy, tretment was intrerrupted due to rapid deterioration of patients clinical status. The radiotherapy treatment was followed by combination chemotherapy. In 15 patients C.V.P (cyclophosphamide, Oncoven and prednisone); was given while in patients attending after 1985 (13 patients) CHOP (cyclophosphamide, adriam-

ycin, procarbazine and prednisone) regimens were given.

Response of meurologic deficit to treatment was assessed according to criteria of Friedman el al [4]:

A. Complete response, patient returned to normal function or experienced only slight neurologic dysfunction post treatment. B. Partial response, a moderate degree of meurologic impairment persisted after treatment.

C. Poor response, pain relieved but initial neurologic deficit persisted.

Follow up was done monthly by clinical evaluation, haemogram, blood chemistry including liver, renal functions and skeletal survey when indicated.

Neurologic dificits in the present study were categorized into two groups:

1. Group I: Neurologic deficit signifies paraparesis sensory deficit and/or visceral dysfunction (loss of sphincter control).

2. Group II: Neurologic deficit including complete motor paralysis of extremities.

Results

A total of 30 cases (4.77%) of spinal extradural NHL were encountered among 624 patients suffering from non-Hodgkin's lymphoma at (NEMROCK)during the period of 1980-1988. Eight (1.27%) were primary and 22 (3.5%) were secondary.

When frequency by age was reviewed, it showed three patients in the 0-19 year age group, 17 in the 20-39 year age group, 9 in the 40-69 year age bracket, and only one patient over 60 years, with male to female ratio of 5:1.

The duration of symptoms at the time of presentation ranged from one month to 9 months with mean duration of 3.8 ± 2.6 months.

Analysis of clinical data of this group of patients showed that; pain was the most common symptom, it occurred in 12 cases (40%) either alone or in association

Table (1): Presenting Complaints and frequency of Spinal Cord Levels Involved in 30 Patients with Spinal Extradural NHL (NEMROCK) 1980-1988.

Symptom	Pain	Weakness & Parasethesia	Compplete Paralysis	Sphincteric troubles
No.& %	12 (40%)	9 (30%)	7 (23.3%)	2 (6.7%)
Level	Cervical	Dorsal	Dorso lumbar	Lumbar
No. & %	3 (10%)	16 (53.3%)	2 (6.7%)	9 (30%)

with,other symptoms, followed by weakness and paraesthhesia, 9 cases (30%). Complete paralysis was reccorded in 7 cases (23.3%), and impairment of sphincteric function in 2 cases (Table 1).

The frequency distribution of spinal cord levels involved is shown in Table 1. Of the 30 cases received, 3 were in the cervical area, 16 in the dorsal area, 2 in the dorsolumbar region, and 9 cases in the lumbar area.

Cases with sufficient histopathological data were classified according to the International Working Formualtion (IWF), [5] and cases lacking data were considered as unclassified. Five cases only had low grade histology (16.7%), 19 cases had intermediate and high grades (63.3%), while 6 cases were unclassified 20% (table 2).

A comparison of clinical characteristics of primary and secondary spinal NHL is shown in Table (3).

Table (2):Histopathology of 30 Patients with Spinal Extradural NHL according to the Working International Formulation.

Histopathologic Subtypes	No.	%
Low grade	5	16.7
Intermediate grade	14	46.6
High grade	5	16.7
Unclassified	6	20
Total	30	100

Table (3):Clinical Characteristics of Primary and secondary NHL.

	Primary spinal NHL		2ndy Spinal NHL	
No. of cases	8		22	
Age range	13-49 years		12-75 years	
(mean)	31.75 ± 4.5		38.3 ± 3.8	
M / F ratio	7 : 1		4.5 : 1	
Histopathology:		%		%
- low grade	4	50%	1	4.54%
- intermediate grade	3	37.5%	1	50 %
- high grade	1	12.5%	4	18.18%
- unclassified	0	0	6	27.28%

In twenty-three cases, the minimal requirements for clinical staging were fulfilled. Fifteen cases were found in stages III & IV i.e. (65.7%) (table 4).

Patients with stage IV (9 cases), showed liver affection in 7 cases and 2 cases with bone marrow disease.

Treatment Results:

Out of the 26 patients evaluable for immediate response, 15 cases (57.7%) achieved complete response while 9 cases (34.6%) showed no response. Twenty two patients were evaluable for more than 12 months follow-up or died from the disease during this period. Ten out of the 15 (66.6%) remained in complete remission with a median survival of 21.6 ± 12.9 months versuus 18.6 ± 16.9 and 6.6 ± 5.27 months for partial and non responders respectively (table 5), comparison of response between primary and secondary types is shown in table (6).

Table (4):Clinical Staging in 23 Patients with Spinal Extradural (NEMROCK - 1980 - 1988)

Clinical Stages	No.	%
Stage I	6	26.1
Stage II	2	8.67
Stage III	6	26.13
Stage IV	9	39.13
Total	23	100

* In 7 Cases, the minimal requirements for Proper Staging were not adopted.

Impact of treatment on nearologic deficit:

In the present study, initial examination disclosed 16 (53.3%) patients in group I with neurologic deficit and 14 (46.7%) patients in group II.

Good response was recorded in 75% of cases in group I meurlogic deficit compared to 21% in group II (table 7).

Various risk factors were tested for their prognostic effect on 22 evaluble cases. Histopathology and clinical stages were the statistically significant prognostic factors (table 8).

The influence of different treatment regimens on the disease free survival is shown in Table 9. Four out of 8 patients (50%) who received radiation therapy only showed more than 12 months disease free survival. the corresponding figure of combined radiation and chemotherapy was 14.2% (2/14). The difference between the two groups was not statistically significant ($p < 0.05$). The four patients who received radiation therapy only were clinically stage I and all of them had low grade histopathology (table 9).

Table (5): Median Survival According to Treatment Results in 26 Evaluable Cases (NEMROCK - 1980 - 1988)

Treatment results	No. of cases	Median survival	Ranges
Complete remission	15	21.6 ± 12.9	9-67
Partial remission	2	18.6 ± 16.9	2-40
No Response	9	6.6 ± 5.27	1-14

Table (6):Comparison of Response Between Primarry and Secondary Spinal NHL.

Primary spinal NHL (8 cases)			2nd spianl NHL (22 cases)		P-valvue
Treatment Response (during 1st 12 months)					
- Complete remission	4/8	50%	6/22	27.3%	N.S
- Partial remission	2/8	25%	1/22	4.5%	N.S
- No response	0/8	0%	9/22	40.5%	
- Lost follow up	2/8	25%	6/22	27.5%	

Table (7):Impact of treatment on Neurologic Deficit According to the Degree of Dysfunion.

Neurological deficit	Response	No Respone	Total
Group I	12/16	4/16	16
	75%	25%	
Group I I	3/14	11/14	14
	21.4%-	78.6%	

$P > 0.01$

Table (8): Prognostic Factors in the 22 Evaluable Spinal Extrdural NHL cases (NEMROCK 1980 - 1988).

Prognostic factors	No. of cases	Median survival months	D. F. survival > 12 months	%	*p* Value of Median survival
Age					
< 15	20	13.75 ± 14.9	6	30	N.S.
> 15	2	9.5 ± 3.5	-	-	
Sex					
Males	19	13.6 ± 15.4	5	26.3	N.S.
Females	3	10.3 ± 6.3	1	33.3	
Clincal Stages					
I & II	8	20.6 ± 18.5	5	62.5	$p > 0.01$
III & IV	14	8.9 ± 9.4	I	7.14	
Histopathology grade:					
Low grade	4	29 ± 22.3	3	75	$p > 0.01$
Int & highgrade	15	11.2 ± 8.9	3	20	
Unclassified	3	8 ± 4.3	-	-	

Table (9): Effect of Treatment Regimens on DFS in the 22 Evaluable Spinal Extradural NHL cases (NEMROCK - 1980 - 1988)

Type of treatment	No. of cases	D. F survival cases	%	*p* - value
Radiotherapy	8	4	50	< 0.05
Radioth. and chemothorapy	14	2	14.2	

Discussion

Non hodgkin lymphoma of spinal extradural region accounts for 2-3% of non-Hodgkin's lymphoma as reported by Friedman et al [4] and Reddy et al [7]. A nearly similar incidence of this disease (4.77%) was reported in the present work.

Of the 30 patients of spinal cord compression presented, 18 (60%) occurred in the dorsal and lumbar spine, a finding similar to that of others, Torma [8] and Friedman et al [4].

Intermediate and high grades varieties were the commonest histopathological subtypes in the present work (63.3%). A figure less than reported by Reddy et al [7] who reported 83% of the same subtypes. This may be explained by the fact that 20% of the cases in the present work were considered histopathologically unclassified. Only 5 of the 24 cases calssified according to the International working formulation [5] were of low grade. From this point of view, our patients tend to fall into a relatively unfavourable prognostic category. This finding is in agreement with Jones et al [9] and Levitt et al. [10].

Thoracic localization is the most common site involved in the present series. The same finding was reported by Torma [8] and Friedman et al [4]. There is no definite reason for this localization, although, there is suggestion that risk venous plexus and intercommunicating vessels between retroperitoneal and spinal vessels can explain this particular site selection. However, this hypothesis can not explain this particular localization in primary cases.

The clinical presentation of the study group appeared logistic. It was either pain or weakeness and occasionally complete paralysis. These results are similar to data reported by Mullins et al [11].

Friedman et al [4] indicated that spinal cord compression from malignant lymphoma usually occurs with advanced stages of tumour. In this study 65.2% of cases fulfilling the minimal requirements for proper clinical staging were found in advanced stages.

When spinal cord compression is diagnosed early and treated promptly, the outcome of treatment may give a good figure, of response. In the present study 75% of good response was achieved in minor neurological deficit group. Such figure is similar to what was reported by Friedman et al [4].

While the histopathology and the clinical stages were the statistically significant prognostic factors, other facts, as age and different treatment regimens may also influence the prognosis. Freeman et al [12] and Pollack et al. [13], proved that the addition of chemotherapy to irradiation significantly enhanced the duration of survival. In the present work the value of chemotherapy was not statistically signifi-

cant. However, this may be explained by the finding that all cases who received chemotherapy were of advanced stages and unfavourable pathology. Furthermore, the two groups of comparison were not treated in a prospective randomised way as regards same histopathology grade and stage.

Conclusion:

When diagnosed early, spinal cord compression due to malignant non-Hodgkin's lymphoma can be treated successfully. Cord compression may be the first clinical evidence of the disease. In patients with malignant lymphoma the symptom of pain with or without neurologic deficit should initiate an immediate investigation of extradural space even in the presence of disease in vertebral bones or retroperitoneal, pleural or mediastinal tissues.

Radiation therapy is an important treatment modality that can be used alone in patients with minor neurologic deficits. Laminectomy is indicated when there is a rapid increase in neurologic deficit. In any event, laminectomy should always be accompanied by irradiation.

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