

Surgeon's role in the management of lymphomas

Yogendra Singh¹
Geeta Sayami²
Mahesh Khakurel³

Abstract

A retrospective analysis of the lymphomas treated at the Department of Surgery, T.U. Teaching Hospital, Kathmandu between 1995 to 1999 was carried out in an attempt to clarify the role of surgeons in the management of such cases. Sixty patients with the diagnosis of lymphoma mainly NHL (52 cases), were admitted during the past 5 years. The average age was 41 ± 17 years ranging from 7 to 70 years. The female to male ratio was 1:1.5. The majority of NHL patients (80%) presented with superficial lymphadenopathy, most commonly in the cervical lymph nodes, where almost 50% of cases were diagnosed by FNAC. The rest - 20% (9 cases) presented with abdominal lump where laparotomy was performed in 7 cases and USG guided FNAC was done in 2 cases to confirm the diagnosis of lymphoma. Six cases (11.5%) of NHL were of extra-nodal origin (4 stomach and 2 colon). All 6 cases were subjected to radical surgery for carcinoma. According to the Ann Arbor staging system, most of the lymphoma cases were in stage III or IV and 25% of the cases presented with B symptoms. Serum LDH correlated with therapeutic response in 80% of nodal lymphomas (8 out of 10 cases). Almost all the patients received chemotherapy with most commonly used regimens - CHOP, BACOP or MOPP. However, 20% of the patients failed to complete the course of chemotherapy. There was 3 mortality (5%) during therapeutic course because of the progressive recurrent disease. Although the follow-up records were available for half of the cases, major morbidity included recurrence of the disease in two cases, CNS involvement in two cases and second malignancy in one case following the treatment of lymphomas. Therefore, in our set up, a surgeon has a sole responsibility for putting tissue diagnosis, relieving the complication of the disease or treatment, chemotherapy of the lymphomas, especially NHL.

Keywords: Lymphomas; biopsy; extra-nodal disease; surgical excision; chemotherapy.

Introduction

Lymphomas are a heterogeneous group of lymphoid malignancies which constitute only about 4% of all other cancers.¹ They respond well to chemotherapy and/or radiation therapy, and only a small number of patients with localized disease may benefit from surgical excision. However, the surgeon is asked to see the lymphoma patients to perform a diagnostic biopsy, to establish vascular access for chemotherapy, or to treat complications of therapy or disease.² A cytological diagnosis of lymphomas by fine needle aspiration cytology (FNAC), sometimes, may be sufficient to allow therapeutic intervention, but more often a biopsy is required before embarking on a major treatment. The objective of this study was to clarify the role of a surgeon in the management of lymphomas especially in a set up where there is a lack of specific oncological service.

Patients and methods

Case records of all 60 patients admitted to the Department of Surgery, Tribhuvan University Teaching Hospital, Kathmandu, Nepal between 1995 and 1999 with histo-and/or cyto-pathologically diagnosed lymphomas were retrieved from the surgical record file. Patients' age, clinical presentation, histocytological features, therapeutic modalities and follow-up details were available for analysis. We carried out a retrospective analysis of the lymphomas mainly non-Hodgkin's lymphoma (NHL) treated at our hospital in an attempt to define the natural history and treatment outcome.

Results

There were sixty patients with lymphoma: 8 cases with Hodgkin's disease (HD) and 52 cases with NHL; all were treated during the past 5 years. The average age was 41 ± 17 years ranging from 7 to 70 years. HD was common in younger age group. The male patients were 36 & females were 24; the female to male ratio was 1:1.5 (Table I). The most common presentation of the nodular NHL was superficial lymphadenopathy (36 out of 45 cases), where FNAC diagnosis was sufficient for initiation of treatment in 50% of the cases. Nine cases were presented with deep group of lymph node involvement, where laparotomy was done in 7 cases and USG guided FNAC was done in 2 cases to confirm the diagnosis of lymphoma. Six cases of extranodal NHL included 4 cases of gastric and 2 cases of colonic origin (Table II). All 6 cases were operated (definite procedures like gastrectomy or colectomy) upon for carcinoma, the postoperative biopsy revealing the diagnosis of NHL. One case was presented with massive ascites (Fig. 1) and cytological analysis of the ascitic fluid

confirmed the diagnosis. Moreover, 20% of the cases had received anti tubercular treatment for some period before presenting to our institute. According to Ann Arbor staging system, most of the NHL cases (92%) were presented with stage III or IV out of 26 cases, and one-fourth of the cases presented with B symptoms (Fig. 2). The histocytological grading was available in 40 cases of NHL; 10, 15 and 15 cases were low, intermediate and high grade NHL, respectively. Raised erythrocyte sedimentation rate (ESR) and serum lactate dehydrogenase (LDH) are important diagnostic value in 10 out of 15 cases. Serum LDH also correlated with therapeutic response of nodal lymphomas in 8 out of 10 cases.

Table I: Age and Sex Incidence of the Lymphomas

<i>Age groups (yrs)</i>	<i>No. (%)</i>	<i>Male/Female</i>
<20	5 (8.3)	3/2
20-29	13 (21.6)	12/1
30-39	10 (16.7)	8/2
40-49	12 (20)	6/6
50-59	10 (16.7)	4/6
≥ 60	10 (16.7)	3/7
Total	60 (100)	36/24

Table II: Presentations and Methods of Diagnosis for NHLs

<i>Presentation</i>	<i>No.</i>	<i>Methods of Diagnosis</i>
<u>Nodal:</u>	<u>46</u>	
Superficial	36	FNAC-18
Cervical	35	Biopsy-18
Inguinal	30	
Axillary	10	
Multiple	5	
Deep	9	Laparotomy-7
Abdominal	8	US guided FNAC-2
Ascites	1	Fluid cytology-1
<u>Extranodal:</u>	<u>6</u>	
Stomach	4	Gastrectomy-4

Colon		Colectomy-2
	2	

Almost all the patients with lymphomas received multiple-drug chemotherapy regimens: CHOP (37 cases), BACOP (17 cases), and MOPP (6 cases). The second line of drugs was used in one case and intrathecal methotrexate was used in another case. 20% of the cases failed to complete the whole cycle of chemotherapy due to various reasons. Only 50% of the post therapeutic follow-up records were available for analysis. There were 3 mortality (5%), 2 with progressive recurrent disease and one with post operative (gastric lymphoma) multiple organ failure. The major morbidity was recurrence of the disease-2, CNS involvement-2, and second malignancy (after HD)-1, respectively.

Fig. 1: Abdominal NHL with gross Ascites

Fig. 2: Ann Arbor Staging of 26 cases of NHL

Fig. 3a: FNAC diagnosis of HD

Fig. 3b: FNAC diagnosis of NHL

Discussion

NHLs are more than 5 times as common as HD.³ The median age of occurrence appears to range from the late 40s to early 50s, but the disease occurs in all age groups. They are more common in males than in females.⁴ Although our present series is small, the findings are consistent. There is also evidence of male predominance, primarily for diffuse lymphoma. Compared with HD, NHLs are clinically diverse. In accordance to our data, Rosenberg, *et al.*⁵ found that the majority of NHLs presented with painless, peripheral lymphadenopathy. The primary site of involvement was cervical node, inguinal, axillary and/ or multiple nodal sites, respectively. NHLs are known to arise from extra-nodal sites in 10 (30%) case,⁶⁻⁸ The gastrointestinal tract is the site most frequently affected accounting for 4-18% of all extra-nodal forms of NHL.⁹⁻¹⁰

When lymphoma is suspected, proper tissue diagnosis and classification are crucial for the initiation of treatments.¹¹ While taking lymphnode biopsy, efforts should be made to avoid traction or cautery, because preservation of architecture is essential.¹² If multiple lymphnodes are enlarged, biopsy of the cervical area is preferred to axillary node, which in turn is superior to inguinal node. In case of matted nodes or suspected extra-nodal disease, sufficient amount of tissue should be taken out.

FNAC is a simple and primary investigation performed in most of the centres. This technique is very useful in diagnosing metastatic carcinoma. However, the accuracy rate of diagnosing lymphomas especially high-grade lesions is 50% to 75%.^{13,14} FNAC is also useful for the selection of a representative node for biopsy, for the diagnosis of recurrent lymphoma, for staging the extent of the disease and for monitoring treatment.¹⁵ In the present series, FNAC diagnosis was sufficient to initiate a definite treatment in 33% of the lymphoma cases, because cytological gradings were available (Fig. 3).

Various prognostic factors have been associated with the survival of lymphoma patients, such as age at diagnosis, performance status, serum LDH, number of nodal and extra-nodal sites of disease, and tumour bulk.¹⁶ Elevated erythrocyte sedimentation rate (ESR) or LDH levels may provide hints of relapse. Therapeutic approaches to the lymphoma patients are based on the stage of the disease, physiologic status of the patient and histologic differentiation.¹⁷ NHLs have a monoclonal proliferation of lymphocytes with a majority of B cell derivation. Histological grading is done on the basis of diffuse versus follicular (nodular) pattern of lymph node involvement, small versus large cell type and cleaved versus noncleaved nuclear morphology.

Treatment of lymphomas is predominantly non operative, relying on chemotherapy and/or radiation therapy. In HD, the role of the surgeon was once large involving staging laparotomy. At present, chemotherapy is the predominant modality of treatment in all ages and therapeutic distinctions centered on the histology of laparotomy specimens no longer exist.¹⁸ Cyclophosphamide (C), Vincristine or Oncovin (O) and Prednisone (P) are generally part of most combination regimens. Other drugs that have been useful include Hydroxyrubicin (H), Bleomycin (B), CCNU (carmustine), Nitrogen mustard (mustine), Procarbazine (P) and Methotrexate (M) in high doses with citrovorum factor rescue. There are chemotherapeutic regimens in various combination for lymphomas, CHOP is the standard therapy for intermediate- to low-grade lymphomas.¹⁹ In our series also, CHOP was the most commonly used chemotherapy regimen. There is an important area where the surgeon can help the lymphoma patients by keeping long-term venous access for chemotherapy.²⁰ But somehow, institution of long-term venous access was not practised here at our hospital.

There is a definite role of the surgeon in extra nodal lymphomas especially gastrointestinal ones. As in our study, surgical resection and subsequent histopathological examination of the whole tumour is more accurate in making a diagnosis. Because, endoscopic biopsy may contain non-representative areas of the lymphomas or biopsy specimens maybe too small for definite diagnosis. Moreover, surgery offers the chance to remove the main tumour bulk while preventing severe gastrointestinal complications that could be caused by the tumour itself or by chemotherapy and radiotherapy.²¹ While the early stage of gastrointestinal lymphoma maybe cured by resection, advanced disease requires adjuvant chemoradiotherapy.

Despite all advances in diagnostic facility, the majority of the patients with intraabdominal mass, undergo laparotomy to confirm the diagnosis of lymphoma. A few patients may require an emergency operation because of gastrointestinal complications like haemorrhage, perforation and obstruction.

With the increasingly intensive chemotherapy regimens used in the treatment of patients with advanced lymphoma, patients are at a higher risk

of suffering from the toxicities of the treatment.²² Prolonged pancytopenia is likely to be encountered, so adequate supportive care even with granulocyte stimulating factor (GSF) becomes an essential part of therapy. Opportunistic infections are not uncommon and prevention of bleeding is necessary to minimize morbidity and mortality.²³ Late chemotherapeutic toxicity has become an alarming problems as more and more patients with lymphoma are being cured of the disease. Sterility is related to chemotherapy regimens, especially those containing alkylating agents. The sex and age of patients are additional factors which affect fertility following chemotherapy. Sperm storage has to be considered in younger adult male patients and should be advised on contraception as pregnancy is still possible while receiving chemotherapy.

Second malignancies, especially leukemia and other solid tumours are associated with the use of chemotherapy regimens, especially those containing alkylating agents.²⁴ The risk is increased further by the concomitant use of radiotherapy.

Patients with lymphoma face a difficulty in the developing country like ours. They face unpleasant side effects and because of long-term therapy undergo considerable psychological and social stress as well as financial problems. Sympathetic support from the management team and specific oncological service centre are of utmost importance.

Conclusion

Some lymphomas especially NHLs are first seen in the abdomen and mediastinum as a fast-growing diffused tumour and they require surgical attention. A small number of patients with localized disease may benefit from attempt at tumour extirpation. A surgeon also treats the complications of the disease or treatment. In general, the surgeon most often encounters the patient with lymphoma for biopsy for tissue diagnosis. In a few occasions, a surgeon is also involved for institution for long-term venous access for chemotherapy.

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