

The Retrospective Analysis of Malignant Lymphoma in Srinagarind Hospital

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มะเร็งต่อมน้ำเหลืองในโรงพยาบาลศรีนครินทร์

ดวงทิพย์ วงศ์แสงนาค

ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น

ได้ทำการวิเคราะห์ย้อนหลังผู้ป่วยโรคมะเร็งต่อมน้ำเหลืองที่มารับการตรวจและรักษาในโรงพยาบาลศรีนครินทร์ มหาวิทยาลัยขอนแก่น ตั้งแต่ปี พ.ศ.2527-2529 มีผู้ป่วยทั้งสิ้นจำนวน 194 ราย เป็นผู้ป่วย Hodgkin's Disease 19% และ Non-Hodgkin's lymphoma 81% ในกลุ่ม Hodgkin's Disease ชนิดที่พบมากที่สุดคือ Mixed cellularity (22%) และ Nodular sclerosis (19%) กลุ่ม Non-Hodgkin's lymphoma ชนิดที่พบมากที่สุดคือ Diffuse histiocytic (27%) และ Diffuse poorly differentiated lymphocytic lymphoma (22%) ผู้ป่วยโรคมะเร็งต่อมน้ำเหลือง พบในเพศชายมากกว่าเพศหญิง อายุเฉลี่ย 40-50 ปี ประมาณ 75-80% ของผู้ป่วยมาพบแพทย์ในระยะที่ III และ IV อาการสำคัญที่นำผู้ป่วยมาพบแพทย์ คือ กล้ามเนื้ออ่อนแรง โดยเฉพาะต่อมน้ำเหลืองที่คอโต และประมาณ 50% มีการลุกลามนอกกระบอกต่อมน้ำเหลือง ตำแหน่งที่พบบ่อย คือ ไชกระดูกและระบบทางเดินอาหาร ผู้รายงานสามารถติดตามผู้ป่วยได้ 152 ราย อัตราการรอดชีวิตของผู้ป่วยโรคมะเร็งต่อมน้ำเหลืองทั้งสองชนิดไม่แตกต่างกันอย่างมีนัยสำคัญทางสถิติ แต่กลุ่มที่ได้รับการรักษาด้วยอัตราการรอดชีวิตเฉลี่ยดีกว่ากลุ่มที่ไม่ได้รับการรักษาอย่างชัดเจน โดยที่เมื่อครบ 12 เดือน หลังจากให้การวินิจฉัย ผู้ป่วยที่ได้รับการรักษาที่ยังมีชีวิตอยู่มีประมาณ 65% ในขณะที่กลุ่มที่ไม่ได้รับการรักษาเหลืออยู่เพียงประมาณ 25%

INTRODUCTION

Malignant lymphoma (ML) is one of the most serious disease in almost every part of the world^(1,2) including Thailand^(3,4), especially in the north-east. Statistical data from tumor registry of National Cancer Institute, the incidence of ML is 1% and 1.3% in the year 1980 and 1981, respectively^(5,6). The exact incidence of this disease in north-east Thailand has not yet been determined. However figure from

tumor registry of Cancer Unit Srinagarind Hospital, Khon Kaen University showed that the incidence in all sexes were 1.8%, 4.0% and 3.8% from the year 1984 - 1986^(7,8,9), respectively.

We have done retrospectively reviewed of ML cases seen at Srinagarind Hospital, Khon Kaen University by several considerations ie : age, sex distribution, pathological grading, clinical manifestation, clinical staging including survival. —X—

MATERIALS AND METHODS

A three years retrospective study of lymphoma cases in the view of clinical and pathological aspect was done among the patients age 15 years old or older seen at Srinagarind Hospital Khon Kaen University between 1984-1986.

The data was collected from hospital medical records, pathological reports and records from tumor registry of cancer unit in this hospital.

The cases-studied were divided into two groups as Hodgkin's disease (HD) and Non-Hodgkin's lymphoma (NHL). In this study HD was classified according to Rye modification of the Lukes and Butler classification^(10,11) and that of NHL based on Rappaport⁽¹²⁾ with some modifications.

The total available data obtained were 194 cases, 169 of which tissue diagnosis originally done at Srinagarind Hospital and 25 cases were referred from other hospitals which have already had tissue diagnosis.

A comprehensive review was made of the hospital records of these patients with special attention paid to original and eventual sites of disease involvement.

The completeness of clinical staging varies for patients seen during the period. Non-invasive studies such as complete history taking, physical examination, routine blood studies (complete blood count, alkaline phosphatase, uric acid, liver and renal function test), chest radiography were performed in the majority of the patients. Other special investigations such as ultrasonography, lymphangiography, barium meal and CAT scan were studied in some indicated patients.

Bone marrow aspirations were performed in 108 patients at the time of initial presentation and bone marrow biopsies were done only in about one-third of those cases.

The staging was retrospectively determined for all patients according to the Ann Arbor (1970) international staging classifications⁽¹³⁾.

Survival follow-up information was available for 152 patients and survival curves were constructed according to the method of Kaplan and Meier⁽¹⁴⁾. We also compared survival of the treatment group and non-treatment group. Criteria of treatment group included the patients whom received chemotherapy more than 6 courses or radiotherapy or combination of the treatment.

RESULTS

Histological types

Clinical and histopathologic review were performed in 194 patients, of these 37 cases were HD (19%) and 157 cases were NHL (81%) (table 1). The distribution of histological type is shown in table 2 and 3. For HD, the most common histologic subtype found is mixed-cellularity (22%) and nodular sclerosis ranked second (19%).

In NHL, majority of the cases (107 patients) were classified as diffuse histologic type, while only 4 patients were nodular type. Interestingly all of these 4 patients were nodular lymphocytic poorly differentiated lymphoma. Concerning diffuse histologic pattern, the most frequent subtype was diffuse histiocytic lymphoma (27%), and diffuse lymphocytic poorly differentiated came second (22%). There were still some undetermined group (17%) in which most of them were referred to receive treatment.

Table 1 Histologic type of Malignant lymphoma

Type	Cases	%
Hodgkin's disease	37	19
Non Hodgkin's Lymphoma	157	81
	194	100

Table 2 Histologic type of Hodgkin's disease

Hodgkin's disease	Cases	%
Lymphocytic predominant	3	8
Nodular Sclerosis	7	19
Mixed cellularity	8	22
Lymphocytic depletion	5	13
Unknown	14	38
	37	100

Table 3 Histologic type of Non-Hodgkin's lymphoma

Non Hodgkin's Lymphoma	Cases	%
Diffuse well differentiated lymphocytic	15	10
Nodular poorly differentiated lymphocytic	4	3
Diffuse poorly differentiated lymphocytic	34	22
Diffused mixed lymphocytic-Histiocytic	16	10
Diffuse histiocytic	42	27
Lymphoblastic	5	3
Diffuse undifferentiated	11	7
Mycosis fungoides	2	1
Unknown	28	17
Total	157	100

Table 4 Clinical staging of Malignant lymphoma

Staging	Hodgkin's Disease	%	Non Hodgkin's Lymphoma	%
I	4	10.8	11	7
I _E	1	2.7	2	1.3
II	3	8.1	15	9.6
III	6	16.2	26	16.6
IV	17	46	93	59.2
Unknown	6	16.2	10	6.3
Total	37	100	157	100
B Symptoms	9		28	

Geographic distribution

All of the patients in this study came from different provinces but in North-east Thailand only.

Age and Sex

Age and sex distribution are illustrated in figure 1 and 2. It is found that male was more common than female, by the sex ratio of 1.3 : 1 in HD and 2.7 : 1 in NHL. Age ranged from 15 to 87 years. Mean age in NHL was 48.3 and in HD was 40 years old.

Staging and Survival

About 20% of HD and 25% of NHL were presented as stage I and II. Up to 24% of HD and 18% of NHL had B symptoms, among these 80% were in advanced stage.

The initial manifestation and some important laboratory findings are listed in table 5. Positive results from bone marrow study were 29/108 as shown in table 6. Extranodal involvement commonly found in bone marrow, gastro-intestinal tract and bony skeleton (table 7).

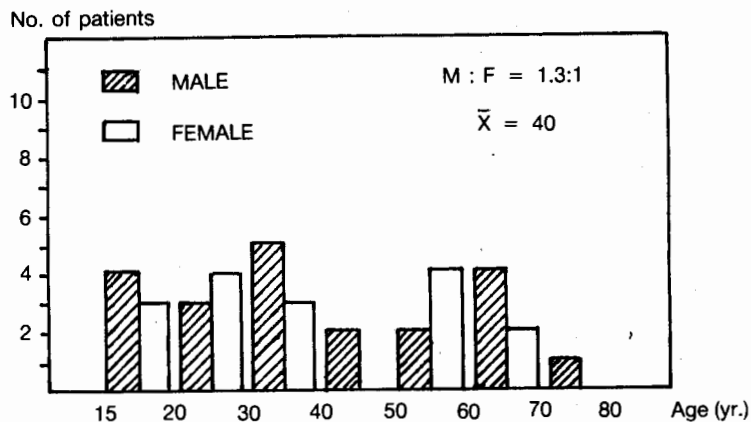


Fig. 1 Age and sex incidence of 37 cases of Hodgkin's Disease

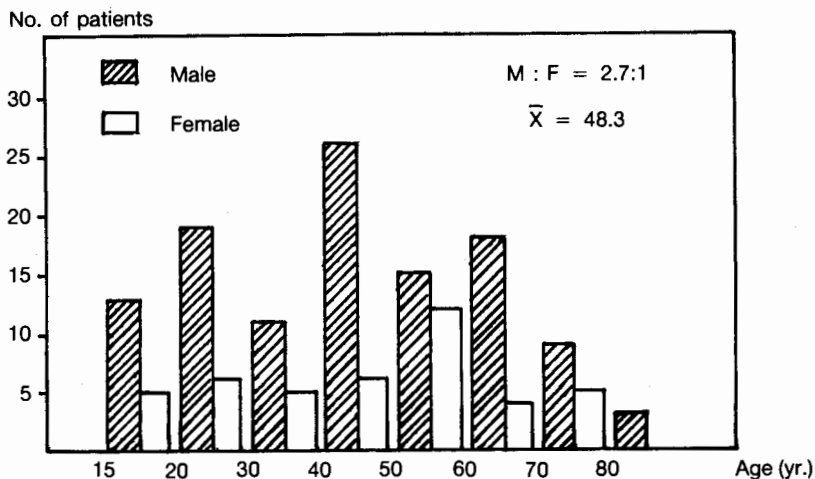


Table 5 Clinical manifestation of 37 cases of Hodgkin's and 157 cases of Non-Hodgkin's lymphoma

Manifestation	Hodgkin's disease Percent	Non-Hodgkin's Lymphoma Percent
1. Mass	(25/37) 68	(126/157) 80
Cervical Lymphadenopathy	(23/25) 92	(76/126) 60
Lymphadenopathy-Other groups	(20/25) 80	(99/126) 79
Abdominal Mass	(8/25) 32	(33/126) 26
2. Extranodal Involvement	(17/37) 46	(89/157) 57
3. Fever	(6/37) 16	(18/157) 11
4. Hepatomegaly	(9/37) 24	(42/157) 27
5. Splenomegaly	(5/37) 14	(25/157) 16
6. Superior Vena Caval Syndrome	(2/37) 5	(6/157) 4
7. Mediastinal Mass	(1/37) 3	(10/157) 6
8. Hemoglobin < 10 g%	(6/23) 26	(28/129) 22
9. Uric Acid > 6 mg%	(7/24) 29	(31/88) 35
10. Alkaline Phosphatase > 3 Unit	(5/28) 18	(21/114) 18

Table 6 Result of bone marrow study

Examination	Case	Positive result
Aspiration	74	21
Biopsy	14	4
Aspiration + Biopsy	20	4*
Total	108	29

* 2 cases positive both aspiration and biopsy
and the other 2 cases positive only biopsy.

Table 7 Extranodal Involvement found in Hodgkin's disease and Non-Hodgkin's lymphoma

Site	Hodgkin's Disease	Non Hodgkin's Lymphoma
Bone Marrow	4	25
Gastro-Intestinal	3	15
Osseous	2	10
Neurological	2	7
Skin	-	5
Pleural Effusion	-	13
Other	6	14
Total	17	89

Survival data was available for 152 patients, 60 of whom were still alive at the time of the last follow-up (fig. 3). Median survival for HD is 10 months and that of NHL is 7 months. There is no statistical difference in survival between the two ($\chi^2 = 0.1$). Over all survival of stage III and IV lymphoma are nearly the same (fig 4). Fig 5 demonstrates survival of the patients according to treatment and non-treatment group.

DISCUSSION

Several studies of ML in Thailand have been reported from different centers^(1,2, 15-17), mostly by university hospitals in Bangkok. The majority of those cases were the people living in the central part of the country. Reported from Maharaj Nakorn Chiang Mai Hospital⁽¹⁷⁾ seemed to be the only study which surveyed spectrum of this disease in the north.

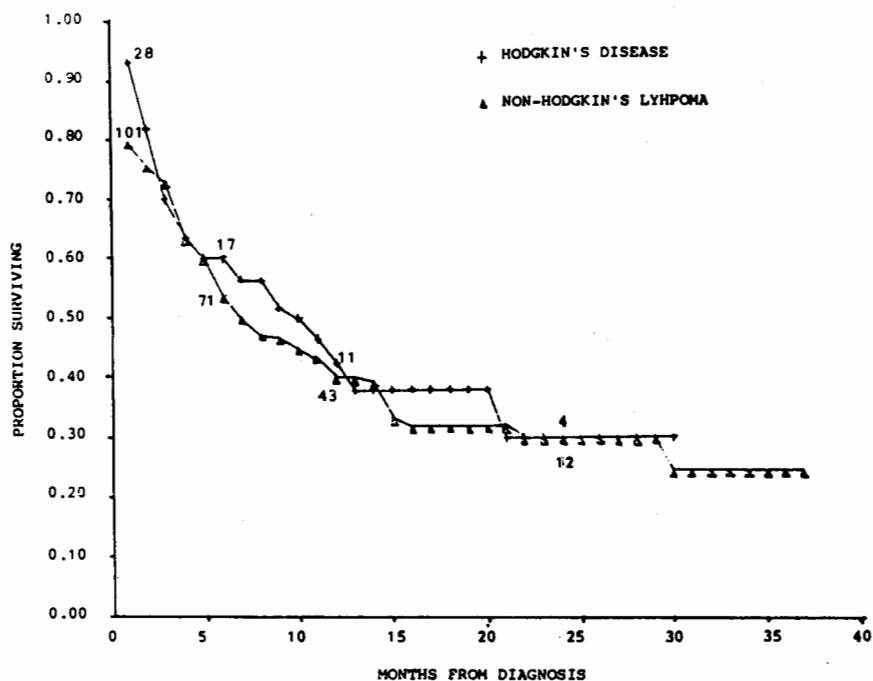


Fig.3 SURVIVAL OF HODGKIN'S AND NON-HODGKIN'S LYMPHOMA PATIENTS FROM MONTHS OF DIAGNOSIS

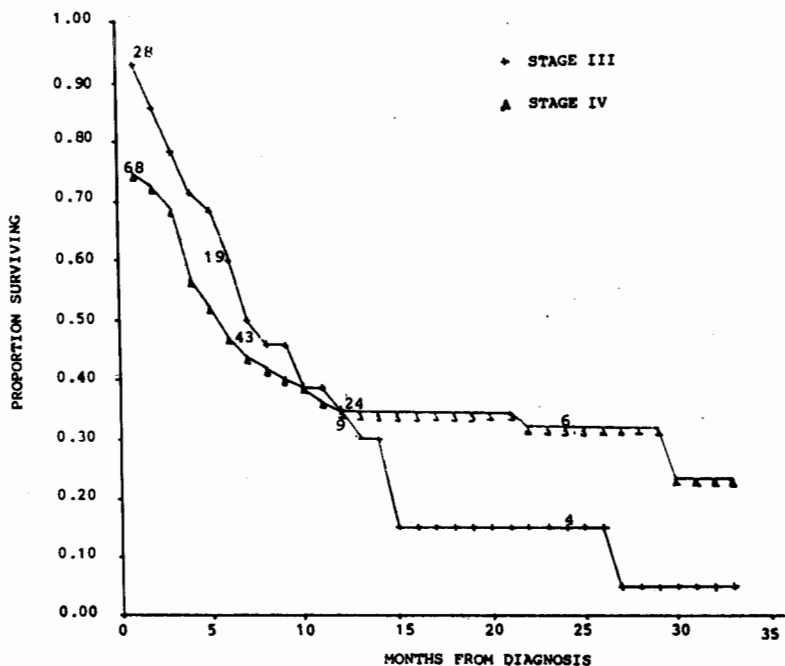


Fig.4 SURVIVAL OF STAGE III, IV LYMPHOMA PATIENTS FROM MONTHS OF DIAGNOSIS

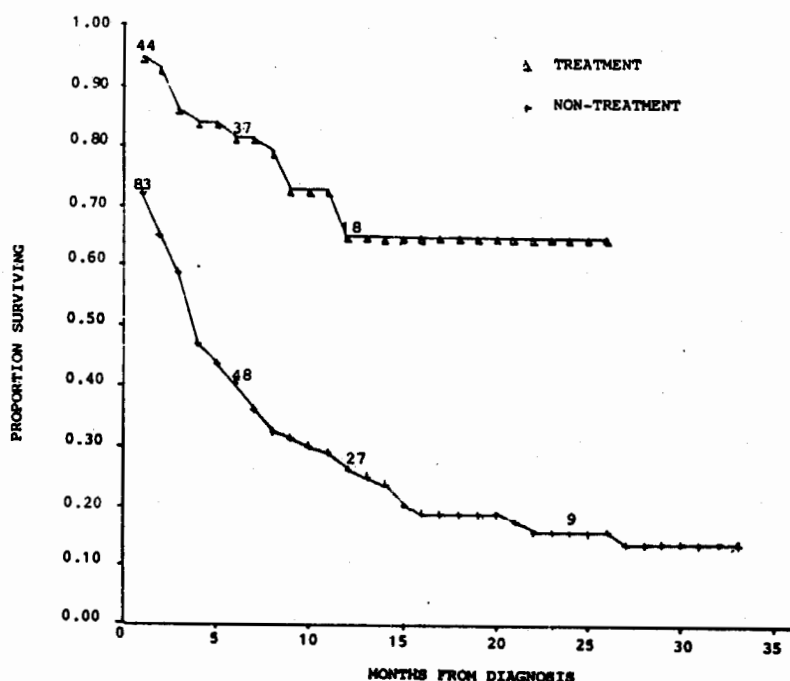


Fig.5 SURVIVAL OF LYMPHOMA PATIENTS ACCORDING TO TREATMENT AND NON-TREATMENT GROUP FROM MONTHS OF DIAGNOSIS

Piankijagum A, et al⁽²⁾ had presented the largest series of ML in Thailand (1,095 cases) which collectively reviewed during 1957-1971. From that study 15.8% of the cases (135/1095) were the northeastern patients.

Studies from many centers including Pramongkutklo Hospital⁽¹⁵⁾, Maharaj Nakorn Chiang-Mai Hospital⁽¹⁷⁾ and ours have the same findings that NHL is 4-5 times more common than HD, and average male to female ratio is about 2 : 1. Mean age of NHL is higher than that of HD, this feature is not much different from other reports^(2,15,18).

For this study, the great majority of the patients first seeked medical attention because they have noticed an unusual mass, particularly cervical lymph nodes. More than 50% of NHL presented with concomitant extranodal involvement right from

the beginning, which means far advance of the disease. The proportion of the patients with systemic symptoms increases both with stage and unfavorable histologic subtype. About 80% of stage IV of both HD and NHL in this report had B-symptoms. Our finding is quite similar to the reports from other countries in the East ie Singapore, India, Middle East etc.^(1,2,18-24)

concerning histologic subgroup of HD, we found that mixed cellularity was higher than nodular sclerosis, the finding is different from those found in the west^(25,26)

For NHL, it is of interest that, there is only a few number of nodular type (3%) in our report, the finding is quite contrast to 20-50% incidence commonly found in the Western Countries^(4,18,21-23,25-27). This could be explained by late presentation of our patients and possible progression of the nodular to the diffuse form.

There are also the preference of extranodal involvement in particular histologic subtypes in NHL as noted in this and some previous reports^(3,28,29). Bone marrow involvement is mostly found in lymphocytic cell type both in well differentiated and poorly differentiated form. For gastrointestinal involvement, the predominant subtypes commonly found are diffuse histiocytic and diffuse lymphocytic poorly differentiated lymphoma, which is similar to other studies^(1,3,15,30-33). There is no any case of primary gastrointestinal lymphoma in this report.

There have been major advances in the treatment of ML during the past two decades (34-38), due to extensive studies of clinical trials by various combination effective chemotherapy. In our experience there is no difference in overall survival of both HD and NHL. But if we compared between the treatment and non-treatment group, up to 3 years follow up, there is a definite significant better prognosis of the treatment group than the other one.

In conclusion we present the pattern of ML of Northeastern patients including clinical feature, histologic type, staging and its survival studied in 3 years. Among 194 cases, 81% were NHL and 19% were HD. Mixed cellularity and nodular sclerosis were the common histologic subtype found in HD but for NHL, diffuse histiocytic and diffuse poorly differentiated lymphocytic were the predominant subtypes. In both HD and NHL male were more common than female with average age about 40-50 years old. About 20% of HD were presented as stage I and II, while 75% of NHL were in stage III and IV. Cervical node enlargement were the common leading symptom and half of the patients had evidence of extranodal involvement. There is no difference in overall survival of both HD and NHL but significant difference between treatment and non-treatment group.

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