Original Article

Clinical Features and Treatment Outcome of Patients with non-Hodgkin Lymphoma in Sawanpracharak Hospital

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Objective: *To study the clinical manifestations and treatment outcome of patients with non-Hodgkin lymphoma (NHL) treated at Sawanpracharak Hospital.* ***Materials and Methods:*** *A retrospective analysis of 113 patients with newly diagnosed NHL treated from January 2005 to December 2009 was performed.* ***Results:*** *The mean age was 56.3 ± 13.6 years (range, 20-86), male:female ratio was 1:1.1. The most common histologic subtype was diffuse large cell lymphoma (66.4%), followed by follicular lymphoma (5.3%), and peripheral T-cell lymphoma (4.4%). Immunophenotypic data showed 89.2% of B cell and 9.9% of T cell lymphoma. Three patients (2.7%) had HIV infection. According to the International Prognostic Index (IPI), distribution of 91 patients with aggressive lymphoma were 29.6%, 22.0%, 25.3%, and 23.1% in low, low intermediate, high intermediate and high risk groups, respectively. Primary extranodal lymphomas comprised 36.3% of all patients and the most common site was gastrointestinal tract (39.0%). Most of the patients (77.9%) were treated with CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone). Of the 98 evaluable patients, 52.0% achieved complete remission and 19.4% died during treatment. The 3-year overall survival rate was 37.6% (95%CI: 27.7-47.4) with a median followed-up time of 1.4 years (range, 26 days-6.7 years). According to IPI, the 3-year survival rate was significantly better in low/low intermediate risk group than in high intermediate/high risk group, (61.3% vs.15.3%, p < 0.001).* ***Conclusion:*** *Patients with NHL in the present study were comparable to published Thai data. The inferior survival particularly in high risk patients warranted improvement of supportive care and better access to evidence-based treatments with superior outcomes.*

Key Words : ● *non-Hodgkin lymphoma* ● *Clinical features* ● *Treatment outcome* ● *Survival*

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Non-Hodgkin lymphoma (NHL) is a common hematologic malignancy. The estimated age-standardized incidence rate in Thailand in male and female were 5.0 and 3.2 per 100,000 respectively.[1] The most common histologic subtype was diffuse large B cell lymphoma[2,3] and the 4-year overall survival rate of NHL from multicenter study in Thailand was 40%.[2] Most of the nationwide data are collected from university hospitals. Sawanpracharak is a regional hospital located in Nakhonsawan. Majority of the patients are from five provinces: Nakhonsawan, Kamphaengphet, Uthaithani, Chainat, and Phichit. The hospital has participated in Leukemia and Lymphoma Disease Management Program launched by the National Health Security Office, the Ministry of Public Health of Thailand since 2006. The review of clinical profile and treatment outcomes of NHL patients in our hospital is of crucial importance for the improvement of patient quality care. The present study objective was to analyze

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the clinical manifestations and treatment outcome of patients with NHL treated at Sawanpracharak Hospital.

Materials and Methods

The retrospective analysis of the patients with biopsy-proven newly diagnosed NHL, age ≥ 15 years, treated with chemotherapy at Sawanpracharak hospital from January 2005 to December 2009 was performed. Baseline patient evaluations included clinical examinations, blood tests, chest radiograph and/or computerized tomography (CT) of the chest, CT or ultrasonogram of the whole abdomen, imaging procedures or special investigations of the relevant parts, and bone marrow aspiration and biopsy. The clinical data obtained from medical records included age at diagnosis, sex, ECOG (Eastern Cooperative Oncology Group) performance status[4], Ann Arbor stage[5], B symptoms[6], sites of disease at presentation[7], bulky disease (largest tumor size ≥ 10 cm), serum lactate dehydrogenase (LDH), creatinine, bilirubin, human immunodeficiency virus (HIV) antibody, International Prognostic Index (IPI)[6], and initial chemotherapeutic regimen. The criteria for diagnosing primary extranodal lymphoma were as follows: 1) the patient presented with signs and symptoms related to the extranodal site, 2) a tissue diagnosis of lymphoma at the extranodal site was required; and 3) the lesion was the presenting focus of disease, necessitating the direction of treatment primarily to that site[7]

Outcome assessments were response to initial chemotherapy and overall survival (OS) rate. Response definitions were 1) complete response (CR): disappearance of all measurable lesions observed at diagnosis for at least 4 weeks 2) partial response (PR): regression of all measurable lesions at least 50% and no new site of disease 3) progressive disease (PD): ≥ 25% increased over the size at the entry or previously maximum regression or appearance of any new lesion. 4) stable disease (SD): response was less than PR but not a progression and 5) death. The survival duration was calculated from the date of diagnosis until death or last follow-up. The data was presented in frequency, percentage, mean and standard deviation. If the data was not in normal distribution, it was presented with median and range. The probability of survival was estimated using the Kaplan-Meier method and the log-rank test was used to compare the OS rates between risk groups with 95% confidential interval (CI). A significant level of 0.05 was used. All statistical analyses were performed with Stata 10.1 software.

Results

From January 2005 to December 2009, 151 newly diagnosed NHL patients were diagnosed at Sawanpracharak Hospital. Thirty eight patients were excluded for not receiving chemotherapy in 31 cases, and for referring patients to the other hospitals in 7 cases. A total of 113 patients were analyzed. The mean age was 56.3 ± 13.6 years (range, 20-86), 46% of the patients aged between 41 and 60 years and 42.5% aged greater than 60 years old. Male to female ratio was 1:1.1. The most common histologic subtype was diffuse large B cell lymphoma (DLBCL) (66.4%), followed by follicular lymphoma (5.3%), peripheral T cell lymphoma (4.4%) and other subtypes (23.9%). Immunophenotypic data in 111 patients showed B cell, T cell lymphoma and undetermined subtype in 99 (89.2%), 11 (9.9%) and 1 (0.9%) respectively. The patient and clinical characteristics at diagnosis were detailed in Table 1. Nearly half (46.9%) of the patients had ECOG performance status ≥ 2, 59.3% had stage III-IV disease, 49.6% had B symptoms and 69.7% had elevated serum LDH. Three patients (2.7%) had HIV infection. The percentage of distribution in IPI risk group for 91 patients with aggressive lymphomas were 29.6%, 22.0%, 25.3%, and 23.1% in low, low intermediate, high intermediate and high risk groups, respectively. Most of the patients had normal renal and liver functions and normal serum albumin level. (data not shown). Forty-one patients (36.3%) presented with primary extranodal disease and the three leading sites were gastrointestinal tract (39.0%), Waldeyer's ring (17.1%) and soft tissue (12.2%). (Table 2)

Initial chemotherapeutic regimens of 113 patients

Table 1. Patient and clinical characteristics

Charcteristics	n (%)
Total patients	113 (100)
Age (year)	
20-40	13 (11.5)
41-60	52 (46.0)
> 60	48 (42.5)
Male:Female = 1:1.1	
ECOG performance status ≥ 2	53 (46.9)
Ann Arbor stage III-IV	67 (59.3)
B symptoms	56 (49.6)
Bulky disease (n = 106)	29 (27.4)
Elevated serum LDH (n = 109)	76 (69.7)
HIV infection	3 (2.7)
Primary extranodal disease	41 (36.3)
IPI (aggressive NHL, n = 91)	
Low/ low intermediate	47 (51.6)
High/ high intermediate	44 (48.4)
Histopathology	
Diffuse large cell lymphoma	75 (66.4)
Follicular lymphoma	6 (5.3)
Peripheral T cell lymphoma	5 (4.4)
Mantle cell lymphoma	4 (3.5)
CLL/SLL*	3 (2.7)
Others	8 (7.1)
Unclassifiable	12 (10.6)

**Chronic lymphocytic leukemia/Small lymphocytic lymphoma*

Table 2. Sites of primary extranodal lymphoma (n = 41)

Site	n (%)
Gastrointestinal	16 (39.0)
Waldeyer's ring	7 (17.1)
Soft tissue	5 (12.2)
Bone marrow	3 (7.3)
Testis/ovary	3 (7.3)
Sinonasal	2 (4.9)
Brain	2 (4.9)
others	3 (7.3)

were CHOP (77.9%), cyclophosphamide, vincristine, and prednisone (CVP) (8.8%), rituximab-CHOP/CVP (6.2%) and others (7.1%). In 98 evaluable patients, 52.0% achieved CR, 18.4% had PR while 3.1% and 7.1% were in SD and PD, respectively. Deaths during treatment were reported in 19 patients (19.4%), of which 10 patients died from infection during treatment. With a median follow-up time of 1.4 years (range, 26 days-6.7 years), the median survival time of all 113 patients was 1.9 years and the 3-year OS rate was 37.6% (95%CI: 27.7-47.4). The 3-year OS rate of the patients in low/low intermediate IPI risk group was 61.3% (95%CI: 44.6-74.3) compared with 15.3% (95%CI: 5.5-24.9) of the patients in high intermediate/ high IPI risk group ($p < 0.001$), (Fig 1A, B).

Discussion

In the present study, the majority of patients were aggressive lymphoma and diffuse large B cell lymphoma was the most common histologic subtype comparable to the previous reports.[2,3] There was a lower number of T cell lymphoma (9.9%) compared with previous reports from Thai (16-25%)[2,3,6] and Asian countries (15-30%).[8-11] This might be explained by small population size and the number of patients excluded.

Gastrointestinal tract was the leading site of extranodal presentation comparable to the previous reports,[6] accounted for one-third of primary extranodal cases in the present study.

Primary isolated bone marrow lymphoma, the uncommon extranodal presentation[12], was found in three patients. All of them were diffuse large B cell lymphoma, two patients presented with pancytopenia, and one presented with autoimmune hemolytic anemia. (data not shown)

The patient characteristics, distribution of aggressive lymphomas in IPI risk groups were comparable to previous Thai study[2]. The majority of patients were treated with doxorubicin-based regimens as previous reported but the outcomes were different. The 3-year OS rate in the present study was 37.6% compared with

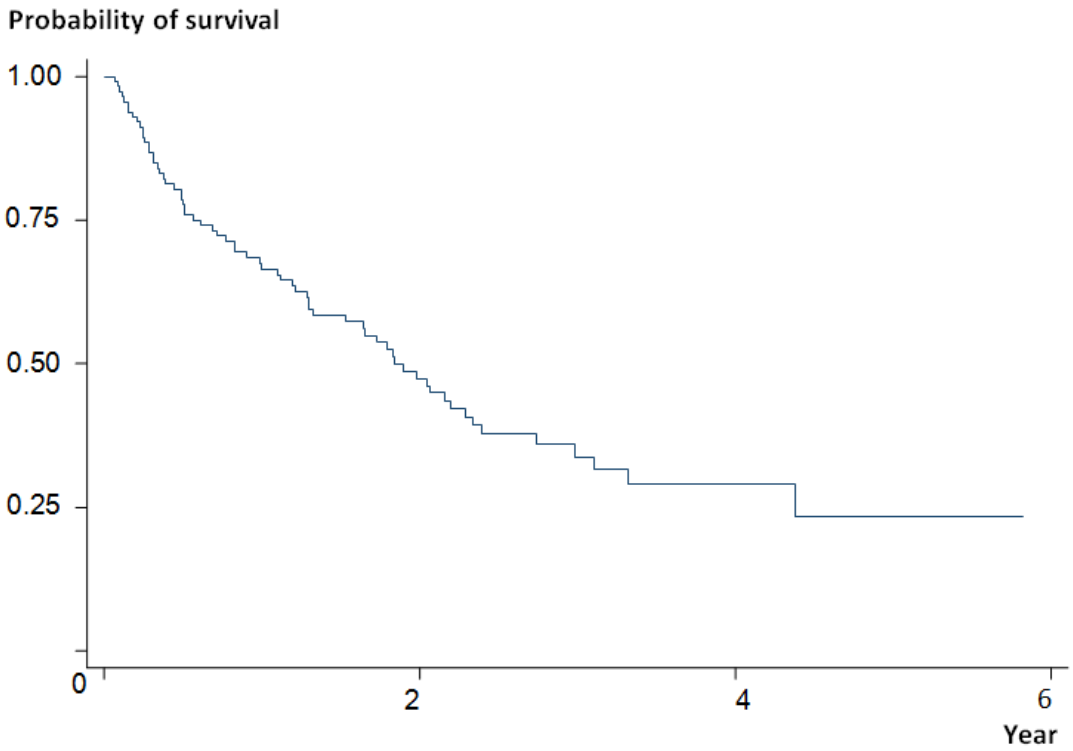

Fig. 1A Overall survival of all 113 patients with malignant lymphoma

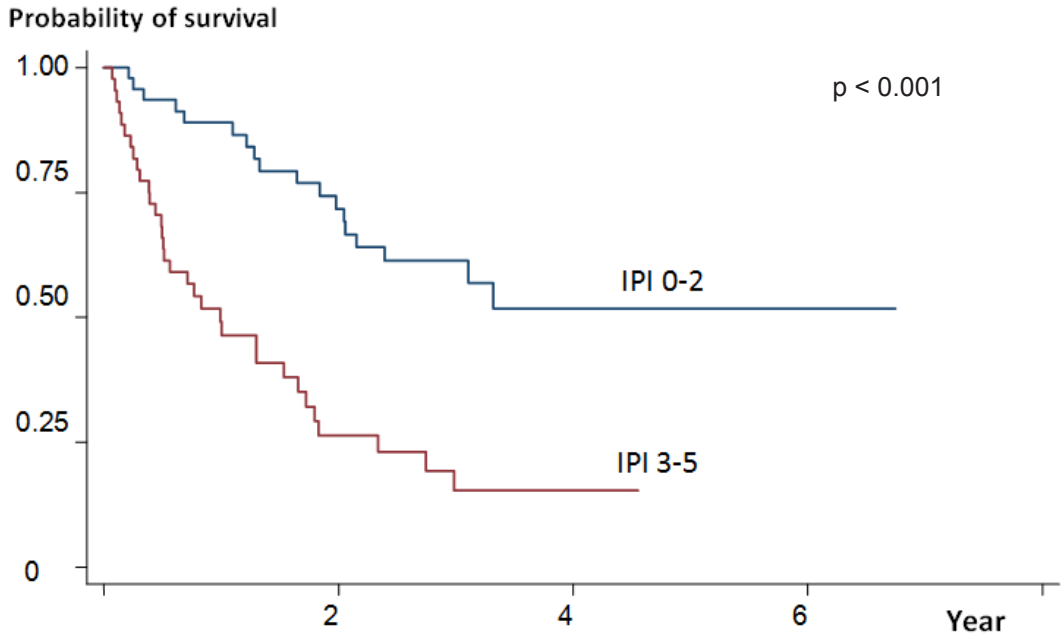

Fig. 1B Overall survival according to IPI risk groups

4-year OS rate of 40% in large scale Thai data[2]. In Western population, the 5-year relative survival of 66.8% was reported in the US patients with NHL diagnosed between 2002 and 2004.[13]

The inferior outcome could be from differences in care. In the present study, there was high early death rate (19.4%) and about half were due to complications, reflected the inadequacy of supportive care. Subgroup analysis of patients according to IPI showed that the patients in high intermediate/high risk group had worse prognosis. The CR rate of this group was 25% (data not shown) and the 3-year OS rate was only 15.3%.

Apart from improvement of supportive care, the poor outcome warranted the more effective treatment strategies. The addition of rituximab to CHOP regimen was shown to improve outcomes for patients with DLBCL and other B-cell lymphoma subtypes.[14-16] Current situation, only small number of patients could access to high-price rituximab and the drug is not covered under the universal coverage payment scheme. Hematopoietic stem cell transplantation was shown to provide better outcome for relapsed/refractory lymphoma.[17-19] For Sawanpracharak hospital, this procedure needs a referral to the university hospital and could be provided to a minority of patients with relapsed/ refractory lymphoma in the present study. (data not shown).

In conclusion, our study elaborated on NHL patients treated at a regional hospital in the lower northern/ upper central part of Thailand. The inferior survival compared with previous reports especially in high risk patients warranted the improvement of supportive care and better access to evidence-based treatments with superior outcome.

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ลักษณะทางคลินิกและผลการรักษาผู้ป่วยมะเร็งต่อมน้ำเหลือง non-Hodgkin ในโรงพยาบาลสวรรค์ประชารักษ์

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วัตถุประสงค์ *เพื่อศึกษาลักษณะทางคลินิกและผลการรักษามะเร็งต่อมน้ำเหลืองชนิด non-Hodgkin (NHL) ที่โรงพยาบาลสวรรค์ประชารักษ์* ***วัสดุและวิธีการ*** *ศึกษาย้อนหลังผู้ป่วย NHL รายใหม่อายุ 15 ปีขึ้นไปที่รักษาด้วยยาเคมีบำบัดในช่วงเดือนมกราคม 2548-ธันวาคม 2552* ***ผลการศึกษา*** *ผู้ป่วยทั้งหมด 113 ราย อายุเฉลี่ย 56.3 ± 13.6 ปี (พิสัย 20-86) อัตราส่วนชาย:หญิงเท่ากับ 1:1.1 ชนิดของ NHL ที่พบบ่อย 3 ลำดับแรกคือ diffuse large cell lymphoma (ร้อยละ 66.4) follicular lymphoma (ร้อยละ 5.3) และ peripheral T cell lymphoma (ร้อยละ 4.4) ผลตรวจ immunophenotype เป็น B cell ร้อยละ 89.2 และ T cell ร้อยละ 9.9 พบผู้ป่วยติดเชื้อเอชไอวี ร้อยละ 2.7 ผู้ป่วย aggressive lymphoma 91 รายแบ่งตาม International Prognostic Index (IPI) ร้อยละ 29.6, 22.0, 25.3 และ 23.1 อยู่ในกลุ่ม low, low intermediate, high intermediate และ high risk ตามลำดับ ผู้ป่วยร้อยละ 36.3 มีอาการนำของโรคที่อวัยวะนอกต่อมน้ำเหลืองซึ่งอวัยวะที่พบบ่อยที่สุดคือทางเดินอาหาร (ร้อยละ 39.0) เคมีบำบัดสูตรแรกที่ผู้ป่วยส่วนใหญ่ได้รับคือ CHOP (ร้อยละ 77.9) ในผู้ป่วยที่ประเมินผลการรักษาได้ 98 ราย ร้อยละ 52 เข้าสู่ภาวะโรคสงบ (complete remission) ร้อยละ 19.4 เสียชีวิตในช่วงที่ได้รับเคมีบำบัด ค่ามัธยฐานของระยะเวลาที่ติดตามผู้ป่วยเท่ากับ 1.4 ปี (พิสัย 26 วัน - 6.7 ปี) อัตราการรอดชีวิตรวมที่ 3 ปีร้อยละ 37.6 (95%CI: 27.7-47.4) อัตราการรอดชีวิตที่ 3 ปีของผู้ป่วยกลุ่ม low/low intermediate ดีกว่ากลุ่ม high/high intermediate IPI อย่างมีนัยสำคัญ (ร้อยละ 61.3 เทียบกับร้อยละ 15.3) ($p < 0.001$)* ***สรุป*** *ลักษณะทางคลินิกของผู้ป่วย NHL ที่โรงพยาบาลสวรรค์ประชารักษ์ใกล้เคียงกับการศึกษาที่ผ่านมาของไทย ผลการรักษาด้วยเคมีบำบัดมีอัตราการเข้าสู่ภาวะโรคสงบและอัตรารอดชีวิตรวมที่ 3 ปี อยู่ในเกณฑ์ต่ำกว่าโดยเฉพาะในกลุ่มเสี่ยง ควรปรับปรุงแก้ไขการรักษาประคับประคอง และพิจารณาการรักษาที่มีหลักฐานยืนยันว่ามีประสิทธิภาพมากขึ้น*

Key Words : ● *มะเร็งต่อมน้ำเหลือง* ● *ลักษณะทางคลินิก* ● *ผลการรักษา* ● *อัตราการรอดชีวิต*
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