RESEARCH ARTICLE

Adult Non Hodgkin's Lymphoma Patients: Experience from a Tertiary Care Cancer Centre in North East India

Munlima Hazarika[1]*, Asif Iqbal[1], Manigreeva Krishnatreya[2], Jagannath Dev Sharma[3], Chidananda Bhuyan[1], Bhargab Jyoti Saikia[1], Partha Sarathi Roy[1], Rashmi Das[1], Pintu Nandy[2], Amal Chandra Kataki[4]

Abstract

There is paucity of data on non Hodgkin's lymphoma (NHL) from our population in North-East India. In this retrospective study, patients were consecutively followed-up to see the clinic-pathological pattern of NHL, various responses, and pattern of relapses to first line treatment with chemotherapy. All patients in the present study received standard regimen of cyclophosphamde, doxorubicin, vincristine, prednisolone (CHOP) with or without rituximab (R-CHOP) as per our institutional protocol as first line therapy. Our study has shown that, in our adult population, the majority of NHL cases present with stage II and stage III disease and extra nodal involvement, B-cell lymphomas and diffuse large cell lymphomas being the most common subtypes. International prognostic index was a significant factor for varied responses to treatment. The majority of relapses after complete remission occurred in the first year.

Keywords: Non Hodgkin's lymphoma - adult - responses to treatment - first line chemotherapy

Asian Pac J Cancer Prev, **16 (7)**, 2879-2881

Introduction

Non-Hodgkin's lymphomas (NHL) are the most varied in terms of pathology, clinical aggressiveness, response to treatment and relapse. There is marked variation in these parameters in patients from different geographic regions (Anderson et al., 1998; Smedby, 2006; Dominik et al., 2007; Bofetta, 2011; Zelenetz et al., 2011). These variations were magnified due to the lack of standard protocol for treatment for most part of the last century. Although now, a routine treatment regimen has been adopted on the basis of histologic and molecular subtypes, chromosomal abnormalities, and risk stratifications (Sengar et al, 2011), such cutting edge facilities are not available in most centers, and treatment heterogeneity still persists. NHL is not a common cancer in this part of the world however; it has been seen to be a common cancer in a hospital based study adjacent to North East India (Hussain et al., 2012). There is paucity of both prospective and retrospective studies on Non Hodgkin's lymphoma from North-eastern part of India, it deserves proper approach. To address these issues, we have tried a retrospective study on patient population from the North-Eastern India.

Materials and Methods

Records of all consecutive NHL patients that registered in our hospital from April 2008 to March 2011 were reviewed for this study. For the study, we considered patients who were above 20 years of age because histologic subtypes of NHL below this age group are different and most of them behave differently (Sengar et al., 2011). Only newly diagnosed and immunohistochemistry (IHC) confirmed cases who were treatment naïve were selected for evaluation. Hospital records were retrospectively reviewed for inclusion and exclusion criteria and then evaluated for stage; grades, prognostic index, histology, IHC, treatment regimen, and follow up information. Patients were assigned to one of the four prognostic scores according to the international prognostic index (IPI). Patients were staged according to the modified Ann Arbor Staging system. Histopathological diagnosis in all cases were reviewed and reported by the expert hemato-pathologist as per WHO 2008 classification for hemato-lymphoid neoplasms.

All patients received standard regimen of cyclophosphamde, doxorubicin, vincristine, prednisolone (CHOP) with or without rituximab (R-CHOP) as per institutional protocol as first line therapy. Patients were evaluated after completion of 3 cycles and 6 cycles of chemotherapy. Those who achieved remission were followed up every 3monthly during first year, 6 monthly during 2nd and 3rd year and then once yearly. Follow-up included detailed history, physical examination, complete blood count, serum lactate dehydrogenase, chest

*[1]Department of Medical Oncology, [2]Department of Cancer Epidemiology and Biostatistics, [3]Department of Pathology, [4]Department of Gynecologic Oncology, Dr. B Borooah Cancer Institute, Guwahati, India *For correspondence: drmunlimahazarika@yahoo.com*

radiography and abdominal ultra sonography. Computed Tomogram (CT) scan of the chest, abdomen and pelvis were advised annually or if otherwise indicated for confirmation of relapse. Responses following first line treatment were one of the following complete remission (CR), partial remission (PR), stable disease (SD), and progressive disease (PD). The criteria followed were based on response evaluation criteria for solid tumors as outlined by Eisenhauer et al (2009).

Statistical analysis

Descriptive statistics up-to single decimal place was used and test of independence was done by Chi square test. $p<0.05$ was considered as significant.

Results

Of the 111 patients analyzed, 73 were male and 38 female with a male: female was 1.9. Age of patients ranged 20-88 years, and the median and mean age were 54 and 51.9 years respectively. The age group distribution is shown on Figure 1.

Most of the patients presented with stage II disease 42 (37.8%) followed by 28 (25.2%) patients in stage III and 22 (19.8%) patients had stage IV disease (Table 1). 41(36.9%) patients presented with only nodal disease, and 70 (63.1%) patients with both nodal and extra nodal as shown in table 1. Of 70 patients who had extra-nodal disease at presentation includes spleen in 21.4% (15), tonsil in 15.7% (11), stomach in 5.7% (4), and others were in the orbit, ileum, large bowel, thyroid, nasopharynx, testis bone marrow, bone, uterus, maxilla and lung.

Ninety patients had B-cell lymphoma (81.1%) and 21 had T-cell (18.9%) lymphoma. Diffuse large cell lymphoma (DLCL) was the most common subtype in 62 (55.8%) patients, followed by follicular lymphoma in 11(9.9%), anaplastic large cell lymphoma 10 (9.0%), Peripheral T- cell lymphoma 8 (7.2%), small lymphocytic lymphoma 8 (7.2%) and marginal zone B-cell lymphomas including MALT lymphomas in 5(4.5%) patients. Thirty six (32.4%) tumor were high grade, 45 (40.5%) intermediate and 30 (27.0%) were low grade tumors (Table 1). Thirty five (31.3%) patients had low International Prognostic Index (IPI), 37(33.3%) had low intermediate IPI, 22(19.8%) had high intermediate IPI and 17(15.3%) had high IPI (Table 1).

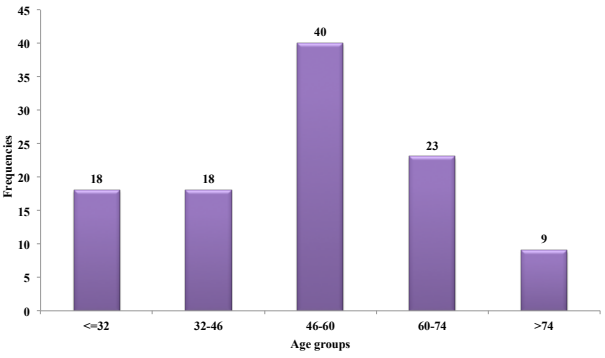

Figure 1. It Shows the age Group Distribution of Adult NHL Patients in Our Population

Out of the 111 patients, 43 patients achieved complete remission (38.7%), 43 patients partial remission (38.7%), 7 patients had disease progression (6.3%), 15 patients stable disease (13.5%). One patient expired after 1st line chemo therapy and 2 patients could not complete 1st line chemo therapy. So, the responses to first line treatment with CHOP with or without rituximab were available in 108 patients. The association of T/B cell and grade with responses to first line treatment was p=0.87 and p=0.732 respectively and that with IPI was p=0.005 (Table 2).

Pattern of relapses

Out of the 43 patients who achieved complete remission, there were relapses in 20 (46.5%) of patients till the time of analysis. Thirteen (65%) patients relapsed within first year, three (15%) during 2nd year and four patients (20%) during 3rd year. Out of the 20 patients relapsed after achieving complete remission following

Table 1. Clinical and Pathological Characteristics of Patients with NHL

Variables	#(%)
Stage	
I	19 (17.1)
II	42 (37.8)
III	28 (25.2)
IV	22 (19.8)
Presentation	
Only nodal	41(36.9)
Nodal and extra nodal	70 (63.1)
Cell type	
B Cell	90(81.1)
T cell	21 (18.9)
Grade	
High	36(32.4)
Intermediate	45 (40.5)
Low	30 (27.0)
International Prognostic Index	
High	17 (15.3)
High Intermediate	22 (19.8)
Low Intermediate	37 (33.3)
Low	35 (31.5)

Table 2. Variables and Different Responses to First Line Chemotherapy

Variables	CR	PD	PR	SD	p value
T/B Cell					
B	36	5	34	12	0.871
T	7	2	9	3	
Grade					
H	11	3	15	7	0.732
I	20	3	15	5	
L	12	1	13	3	
IPI					
High	2	2	9	2	0.005*
High Intermediate	4	2	11	4	
Low Intermediate	14	0	17	6	
Low	23	3	6	3	
Gender					
Male	30	2	27	13	0.052
Female	13	5	16	2	

*CR=Complete response, PD=Progressive disease, PR=partial response, SD=stable disease

1st line CT, 1 had local relapse, 9 had systemic relapse, 8 patients relapsed with bone marrow involvement and 2 patients presented with nodal relapse but in a separate site.

Discussion

Non Hodgkin's lymphoma show considerable variation clinically, biologically and epidemiologically worldwide (Bofetta, 2011). Case-control study from India has shown the risk of NHL to be high in smokers, mutton consumption, and in individuals with exposure to pesticides (Balasubramanium et al., 2013). Recent meta-analyses have shown the association of red meat and processed meat with NHL and a weak association with certain genetic polymorphism (Zhou et al., 2014). In our population most of the cases were seen at 46-60 years age group and males were almost twice affected. Analytic epidemiological studies on NHL will be required to establish additional risk factors for our population. Of primary extra nodal NHL, central nervous system followed by gastrointestinal were common (Padhi et al., 2012). In our present study, spleen followed by stomach was common extra nodal sites of NHL. The distribution of NHL subtypes in India shows important differences with those from the rest of the world. Follicular lymphoma and mantle cell lymphoma are less common in India compared to Europe and the USA. Peripheral T-cell lymphomas and T/NK-cell lymphomas of nasal and nasal types, which are common in many other Asian countries, are also less prevalent. T-cell lymphoblastic lymphoma and anaplastic large T/null cell lymphoma are more prevalent in India (Naresh et al., 2000). In our observation B-cell lymphomas formed 81 % of the NHLs, whereas T-cell lymphomas formed 19 % of the total. This finding is similar to one by Sader-Ghorra et al (2014). DLCL was the most common subtype followed by follicular lymphoma, anaplastic large cell lymphoma, peripheral T- cell lymphoma, and small lymphocytic lymphoma. Low IPI NHL had a favorable prognosis in one recent study (Mersoytlu et al., 2014). In the present study IPI was significant factor in the initial response to first line chemotherapy ($p<0.05$), whereas the stage at presentation and grade had no significant impact in the various outcomes ($p>0.05$).

With the advent of newer therapeutic protocol the outcome of aggressive NHL has improved during the last few decades with 60-80% complete remission; 20-40% relapses which are most commonly occurred during the 2nd -3rd years after completion of treatment (Salles et al., 1994). In our observation 38.7% of the total patients achieved complete remission of which 46.5% subsequently relapsed within 3 years. In our study most of the relapses were detected in sites where lymphoma was diagnosed initially (90%). In a study Elis et al. (2002) observed that 63% relapse occurred in both primary and new nodal sites simultaneously, whereas 23% relapses occurred only at a new site. 65% of relapses occurred within the first year in our study population.

In conclusion, in adult NHL of our population, majority presents at stage II and stage III disease, and with extra nodal presentation, B-cell lymphomas and diffuse large cell lymphoma were the common subtypes. International prognostic index was a significant factor for varied responses to treatment. Majority of relapses after CR occurred at the first year.

References

Anderson JR, Armitage JO, Weisenburger DD (1998). Epidemiology of the non-Hodgkin's lymphomas: distributions of the major subtypes differ by geographic locations. *Ann Oncol*, **9**, 717-20.

Balasubramanium G, Saoba S, Sarade M, Pinjare S (2013). Case-control study of risk factors for non-Hodgkin lymphoma in Mumbai, India. *Asian Pac J Cancer Prev*, **14**, 775-80.

Bofetta P (2011). Epidemiology of adult non-Hodgkin lymphoma. *Ann Oncol*, **22**, 27-31.

Dominik D. Alexander, Pamela J, et al (2007). The non-Hodgkin lymphomas: a review of the epidemiologic literature. *Int J Cancer*, **120**, 1-39.

Elis A, Blickstein B, Klein O, et al (2002). Detection of relapse in non- Hodgkin's lymphoma : role of routine follow up studies. *Am J Hematol*, **69**, 41-4.

Eisenhauer EA, Therasse P, Bogaerts J, et al (2009). New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). *Eur J Cancer*, **45**, 228-47.

Hussain MA, Pati S, Swain S , et al (2012). Pattern and trends of cancer in Odisha, India: a retrospective study. *Asian Pac J Cancer Prev*, **13**, 6333-36.

Mertsoylu H, Muallaoglu S, Besen AA, et al (2014). Primary extranodal non-Hodgkin's lymphoma: clinicopathological features, survival and treatment outcome in two cancer centers of southern Turkey. *Asian Pac J Cancer Prev*, **15**, 7207-11.

Naresh KN, Srinivas V, Soman CS (2000). Distribution of various subtypes of non-Hodgkin's lymphoma in India: astudy of 2773 lymphomas using REAL and WHO Classifications. *Ann Oncol*, **11**, 63-7.

Padhi S, Paul TR, Challa S, et al (2012). Primary extra nodal non Hodgkin lymphoma: a 5 year retrospective analysis. *Asian Pac J Cancer Prev*, **13**, 4889-95.

Sader-Ghorra C, Rassy M, Naderi S, Kourie HR, Kattan J (2014). Type distribution of lymphomas in Lebanon: five-year single institution experience. *Asian Pac J Cancer Prev*, **15**, 5825-8.

SallesG,Shipp MA, Coiffier B (1994). Chemotherapy of non-Hodgkin's aggressive lymphomza. *Semi Hematol*, **31**, 46-69.

Schuetz JM, Daley D, Leach S, et al (2013). Non-Hodgkin lymphoma risk and variants in genes controlling lymphocyte development. *PLoS One*, **8**, 75170.

Sengar M, Akhade A, Nair R, et al (2011). A retrospective audit of clinicopathological attributes and treatment outcomes of adolescent and young adult non-Hodgkin lymphomas from a tertiary care center. *Indian J Med Paediatr Oncol*, **32**, 197-203

Smedby KE (2006). Epidemiology and etiology of non-Hodgkin lymphoma a review. *Acta Oncol*, **45**, 258-71

Zelenetz AD, Abramson JS, Advani RJ et al (2011). Non Hodgkin's lymphomas. *J Natl Compr Canc Netw*, **9**, 484-560

Zhou JY, He LW, Liu J, et al (2014). Comprehensive assessment of associations between ercc2 lys751gln/asp312asn polymorphisms and risk of non-Hodgkin lymphoma. *Asian Pac J Cancer Prev*, **15**, 9347-53.