ORIGINAL ARTICLE

Korean J Intern Med 2014;29:352-360
http://dx.doi.org/10.3904/kjim.2014.29.3.352

KJIM

Clinical characteristics, pathological distribution, and prognostic factors in non-Hodgkin lymphoma of Waldeyer's ring: nationwide Korean study

Seong Jun Lee[1], Cheol Won Suh[2], Soon Il Lee[3], Won Seog Kim[4], Won Sik Lee[5], Hyo Jung Kim[6], Chul Won Choi[7], Jin Seok Kim[8], Ho-Jin Shin[1], and The Consortium for Improving Survival of Lymphoma

[1]Division of Hematology-Oncology, Department of Internal Medicine, Medical Research Institute, Pusan National University Hospital, Pusan National University School of Medicine, Busan; [2]Department of Internal Medicine, Asan Medical Center, Seoul; [3]Department of Internal Medicine, Dankook University Hospital, Cheonan; [4]Department of Internal Medicine, Samsung Medical Center, Seoul; [5]Department of Internal Medicine, Inje University Busan Paik Hospital, Busan; [6]Department of Internal Medicine, Hallym University Sacred Heart Hospital, Seoul; [7]Department of Internal Medicine, Korea University Guro Hospital, Seoul; [8]Department of Internal Medicine, Severance Hospital, Seoul, Korea

Received: June 9, 2013
Revised : July 22, 2013
Accepted: October 4, 2013

Correspondence to
Ho-Jin Shin, M.D.
Division of Hematology-Oncology, Department of Internal Medicine, Medical Research Institute, Pusan National University Hospital, Pusan National University School of Medicine,
179 Gudeok-ro, Seo-gu, Busan 602-739, Korea
Tel: +82-51-240-7839
Fax: +82-51-254-0192
E-mail: hojinja@hanmail.net

Background/Aims: In Asia, the incidence of non-Hodgkin lymphoma (NHL) has increased in recent decades. Waldeyer's ring (WR) is the most common site of NHL involving the head and neck. In this study, the pathological distribution of WR-NHL and its clinical features were analyzed retrospectively.

Methods: From January 2000 through December 2010, we analyzed the medical records of 328 patients from nine Korean institutions who were diagnosed with WR-NHL.

Results: The study group comprised 197 male and 131 female patients with a median age of 58 years (range, 14 to 89). The rate of localized disease (stage I/II) was 64.9%, and that of low-risk disease (low/low-intermediate, as defined by the International Prognostic Index) was 76.8%. Diffuse large B-cell lymphoma (DLBCL; 240 patients, 73.2%) was the most common pathologic subtype, followed by peripheral T-cell lymphoma (14 patients, 4.3%) and nasal NK/T-cell lymphoma (14 patients, 4.3%). WR-NHL occurred most frequently in the tonsils (199 patients, 60.6%). Extranodal involvement was greater with the T-cell subtype (20 patients, 42.5%) compared with the B-cell subtype (69 patients, 24.5%). Multivariate analyses showed that age ≥ 62 years, T-cell subtype, and failure to achieve complete remission were significant risk factors for overall survival.

Conclusions: DLBCL was found to have a higher incidence in Korea than those incidences reported by other WR-NHL studies. T-cell lymphoma occurred more frequently than did follicular lymphoma. T-cell subtype, age ≥ 62 years, and complete remission failure after first-line treatment were significant poor prognostic factors for overall survival according to the multivariate analysis.

Keywords: Head and neck; Non-Hodgkin lymphoma; Diffuse large B-cell lymphoma; T-cell lymphoma

pISSN 1226-3303
eISSN 2005-6648
http://www.kjim.org

INTRODUCTION

The prevalence of non-Hodgkin lymphoma (NHL) has increased in the last decade [1]. Immune-suppression, genetics, and exposure to chemical agents have contributed to the increasing incidence of NHL [2-4]. NHL is not limited to lymph node progression; in contrast to Hodgkin lymphoma, it may arise from or involve extranodal organs in approximately one-third of cases. Waldeyer's ring (WR) is the most popular site of involvement among NHLs presenting in the head and neck. WR originates from lymphoid tissues surrounding the digestive and respiratory systems, including those around the Eustachian tube, upper palatine tonsils, nasopharynx, oropharynx, salivary glands, and sublingual sites. In Asia, NHL involving WR (WR-NHL) has increased recently [5-10].

The increased understanding of the pathology and physiology of lymphoma has led to changes in its classification. The World Health Organization (WHO) classification of lymphomas was revised in 2001 and again in 2008 [11,12]. However, recent studies of lymphomas involving WR were performed in few lymphoma subtypes and under limited circumstances. Therefore, those studies were limited in their ability to determine the overall characteristics of WR-NHL. In this study, the clinical characteristics and pathological distribution of WR-NHL in Korea were analyzed retrospectively according to the 2001 and 2008 WHO lymphoma classifications.

METHODS

From January 2000 through December 2010, 328 Korean patients pathologically confirmed as WR-NHL from nine independent institutions were reviewed retrospectively. Pathologic diagnosis was determined according to the 2001 and 2008 WHO classifications of lymphomas [11,12]. Patients were classified by the Ann Arbor staging system according to the results of computed tomography (CT) scans, positron emission tomography (PET)-CT, bone marrow biopsy, and cerebrospinal fluid analysis if necessary. Clinical and laboratory parameters including age, sex, Eastern Cooperative Oncology Group (ECOG) performance status, and biochemical laboratory results were evaluated. The disease stage and extranodal involvement were also investigated.

Patients with localized disease were classified into five groups according to their treatment: 1) supportive care; 2) chemotherapy alone; 3) chemotherapy plus radiotherapy; 4) radiotherapy alone; and 5) surgical resection. The surgical resection group included patients who underwent chemotherapy or radiotherapy after surgery. We evaluated the treatment results and survival of each group using serial CT scans.

Progression-free survival (PFS), disease-free survival (DFS), and overall survival (OS) were analyzed using the Kaplan-Meier and the Cox proportional regression methods. PFS was calculated as the period from the first day of treatment to the date of disease progression or death from any cause. DFS was calculated as the period from the date of complete remission (CR) to that of relapse or death while in CR. OS was calculated as the period from the first day of treatment to the date of death from any cause. The results were expressed as means with 95% confidence intervals (CIs) where appropriate, and $p < 0.05$ was considered indicative of statistical significance. Statistical analysis was performed using the PASW version 18.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Patients

The median patient age was 58 years (range, 14 to 89). The male:female ratio of the 328 patients was 1.5:1. More than half of the patients (64.9%) presented with localized disease (Ann Arbor stage I or II). In particular, the majority of B-cell lineage NHL cases presented as localized disease (71.1%). T-cell lineage NHL cases more frequently showed disseminated disease (57%) compared with other NHLs. Most patients were in the low/low-intermediate risk group (252/328 patients, 76.8%) according to the International Prognostic Index (IPI) and had good performance status (ECOG 0; 311/328 patients, 94.8%). Serum lactate dehydrogenase (LDH) levels were primarily in the normal range (280/328 patients, 85.4%). B symptoms (> 10% weight loss in 3 months, night sweats, and fever) were seen in

Table 1. Baseline characteristics of Waldeyer's ring non-Hodgkin lymphoma patients

Characteristic	No. (%)
Total	328
Age, median (range), yr	58 (14–89)
Sex	
Male	197 (60.1)
Female	131 (39.9)
PS (ECOG)	
≤ 1	311 (94.8)
> 1	17 (5.2)
IPA	
Low/low-intermediate	252 (76.8)
High-intermediate/high	71 (21.6)
Unknown	5 (1.6)
Serum LDH level	
Normal	280 (85.4)
Elevated	41 (12.5)
Unknown	7 (2.1)
Ann Arbor stage	
I/II	213 (64.9)
III/ IV	112 (34.1)
Unknown	3 (1.0)
B symptoms	
Absent	279 (85.1)
Present	46 (14.0)
Unknown	3 (0.9)
Bone marrow involvement	
Absent	298 (90.9)
Present	30 (9.1)

PS, performance status; ECOG, Eastern Cooperative Oncology Group performance status; IPI, International Prognostic Index; LDH, lactate dehydrogenase.

14% of the patients (Table 1).

Pathologic distribution

The tonsils (60.6%) were the most common site of involvement in WR-NHL, followed by the nasopharynx (6.4%), oropharynx (5.4%), sublingual site (4.8%), and salivary glands (1.8%). Of the cases with tonsillar involvement, 15% (30 cases) also had involvement of the nasopharynx or oropharynx (Table 2).

B-cell lineage NHL (281 patients, 85.6%), compared with T-cell lineage NHL, was predominant among WR-NHL cases. Diffuse large B-cell lymphoma (DLBCL; 241/281 patients, 85.8%) was the most commonly observed subtype of B-cell lineage lymphoma. Peripheral T-cell lymphoma (14 patients, 4.3%), and NK/T-cell lymphoma (14 patients, 4.3%) were the most common subtypes of T-cell lineage WR-NHL. Other subtypes included extranodal marginal zone B-cell lymphoma (11 patients, 3.4%), mantle cell lymphoma (nine patients, 2.7%), and follicular lymphoma (four patients, 1.2%). Other subtypes of NHL, excluding DLBCL, showed low prevalence (< 5%).

Extranodal NHL

Extranodal NHL was observed in 89 patients (27.1%). Bone marrow was the most common site of involvement (n = 30), followed by the gastrointestinal tract (n = 24); lung, pleura, and mediastinum (n = 16); bone (n = 10); and liver (n = 6). A small number of cases also involved the kidneys, ovaries, testis, cerebrospinal fluid, skin, nasal cavity, brain parenchyma, eyelid, conjunctiva, trachea, glottis or the thyroid gland. A total of 48 patients (14.6%) had one extranodal site of involvement, while 41 patients (12.5%) had more than one (Tables 3 and 4). Of the 281 patients with B-cell lineage lymphoma, extranodal involvement was observed in 69 patients (24.5%). Of the 47 patients with T-cell lineage lymphoma, extranodal involvement was observed in 20 patients (42.5%); furthermore, a higher incidence was found in patients with nasopharyngeal involvement. In patients with DLBCL, the most common site of involvement was the gastrointestinal tract. Of the nine patients with mantle cell lymphoma, six had involvement of the bone marrow.

Treatment outcomes and survival analyses

Patients with WR-NHL showed distinct differences in OS according to stage or IPI (Fig. 1). There were 227 patients in the chemotherapy alone group (69.2%), 63 patients in the chemotherapy plus radiotherapy group (19.2%), 16 patients in the radiotherapy alone group (4.9%), 17 patients in the surgical resection group (5.2%), and five patients in the supportive care group (1.5%). Most of the patients in the surgical resection group had DLBCL, and all received tonsillectomy. Of the surgical resection group, nine patients received chemotherapy, two received radiation therapy, and five

http://dx.doi.org/10.3904/kjim.2014.29.3.352

Table 2. Pathologic distribution of Waldeyer's ring non-Hodgkin lymphoma cases

Lymphoma subtype	No. (%)	Tonsil	Nasopharynx	Oropharynx	Base of tongue	Salivary gland	Oral cavity	Unknown
Diffuse large B-cell lymphoma	241 (73.5)	152	11	12	13	3	2	48
Mantle cell lymphoma	9 (2.7)	6	0	0	0	1	0	2
Follicular lymphoma	4 (1.2)	3	1	0	0	0	0	0
Small lymphocytic lymphoma	3 (0.9)	1	1	0	0	0	0	1
Burkitt lymphoma	5 (1.5)	4	0	1	0	0	0	0
Extranodal marginal zone lymphoma of MALT	11 (3.4)	4	2	1	1	0	0	3
T-cell-rich B-cell lymphoma	3 (0.9)	0	0	0	0	1	0	2
Lymphoblastic lymphoma	2 (0.6)	2	0	0	0	0	0	0
Nodal marginal zone lymphoma	6 (1.8)	6	0	0	0	0	0	0
Peripheral T-cell lymphoma	14 (4.3)	6	4	1	1	1	0	1
Nasal NK/T-cell lymphoma	14 (4.3)	7	0	2	1	0	0	4
Angioimmunoblastic T-cell lymphoma	9 (2.7)	5	1	0	0	0	0	3
Anaplastic large T-cell lymphoma	3 (0.9)	2	0	0	0	0	0	1
Other T-cell lymphomas	5 (1.5)	1	1	1	0	0	1	1
Total	328	199	21	18	16	6	3	65

MALT, mucosa-associated lymphoid tissue.

Table 3. Extranodal site distribution of Waldeyer's ring non-Hodgkin lymphoma (n = 328)

Variable	No. (%)
No. of involved extranodal sites	
0	239 (72.9)
1	48 (14.6)
≥ 2	41 (12.5)
Involved extranodal sites	
Bone marrow	30 (9.1)
Gastrointestinal tract (stomach/ileum/colon/rectum)	24 (7.3)
Lung/pleura/pericaridium	16 (4.8)
Bone	10 (3.0)
Liver	6 (1.8)
Others[a]	37 (11.2)

[a]Others: kidney, breast, parotid gland, cerebrospinal fluid, brain, ovary, testis, skin, nasal cavity, lacrimal duct, conjunctiva, eye lid, trachea, glottis, thyroid gland, and thyroid cartilage.

received combined chemoradiotherapy after tonsillectomy. One patient did not receive any additional treatment after tonsillectomy (Table 5).

The median follow-up duration was 24.2 months (range, 0.2 to 106.1 months). The surgical resection group tended to have marginally better DFS compared with the chemotherapy alone group (2-year DFS rate, 100% vs. 84.6% ± 4.8%; $p = 0.097$) or chemotherapy plus radiotherapy group (2-year DFS rate, 100% vs. 92.1% ± 3.8%; $p = 0.088$). The surgical resection group also showed improved OS compared with the chemotherapy alone group (2-year OS rate, 100% vs. 83.1% ± 4.2%; $p = 0.036$) or the chemotherapy plus radiotherapy group (2-year OS rate, 100% vs. 82.9% ± 5.0%; $p = 0.025$) (Fig. 2).

Prognostic factors

In this study, patients aged ≥ 62 years were found to

Table 4. Extranodal site of involvement according to involvement of Waldeyer's ring

Extranodal site	Bone marrow	Gastrointestinal tract	Bone	Lung/pleura/ pericardium	Liver	Others[a]
Base of tongue	1	0	0	1	0	1
Tonsil	17	18	6	6	2	17
Oral cavity	0	0	0	0	0	0
Salivary gland	2	1	0	1	1	6
Oropharynx	1	2	1	0	2	3
Hypopharynx	0	0	0	0	0	0
Nasopharynx	1	0	0	1	0	3
Location of WR not specified	8	3	3	7	1	7
Total	30	24	10	16	6	37

WR, Waldeyer's ring.
[a]Others: kidney, breast, parotid gland, cerebrospinal fluid, brain, ovary, testis, skin, nasal cavity, lacrimal duct, conjunctiva, eye lid, trachea, glottis, thyroid gland, and thyroid cartilage.

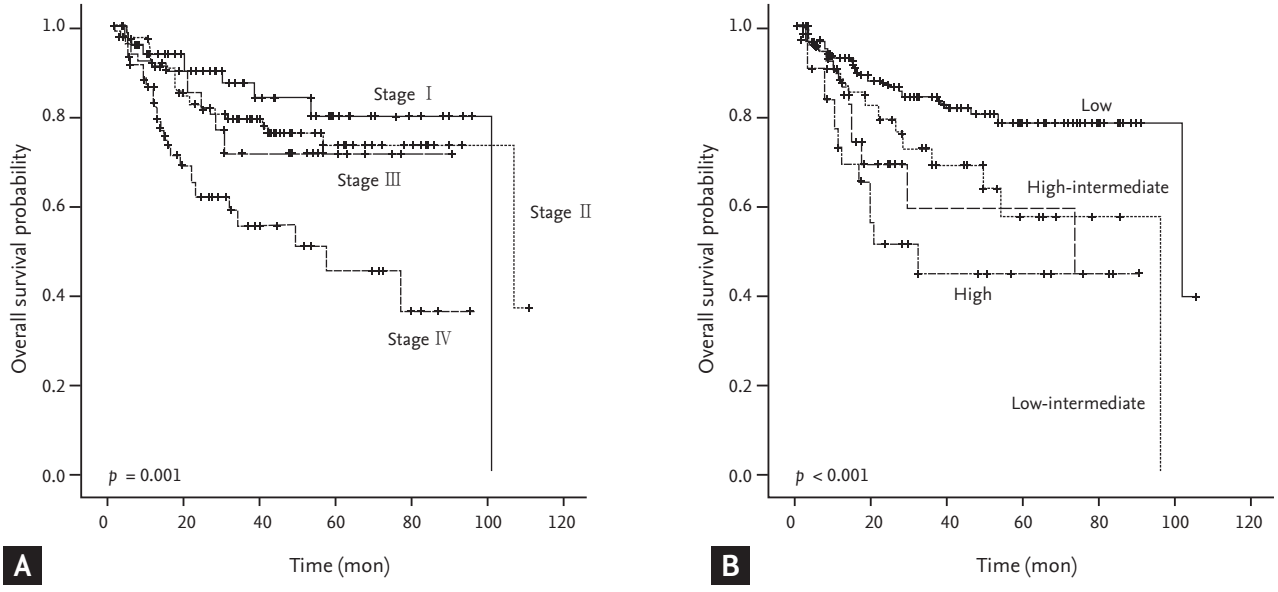

Figure 1. Overall survival of Waldeyer's ring non-Hodgkin lymphoma according to stage (A) and International Prognostic Index (B).

have a lower OS rate. In addition, poor performance status (ECOG > 1), B symptoms, elevated serum LDH level, HBsAg (+), hepatitis C virus (HCV) Ab (+), Epstein-Barr virus (EBV) (+), extranodal site number > 1, T-cell subtype, high-intermediate/high risk IPI, advanced stage (Ann Arbor stage III/IV), and no CR after first-line treatment were found to be significantly poor prognostic factors by univariate analysis (Table 6). Among these factors, age ≥ 62 years, T-cell subtype, and no CR after first-line treatment were verified to be significantly poor prognostic factors by multivariate analysis (Table 7).

DISCUSSION

Pathological distributions and baseline characteristics of WR-NHL patients in Korea were analyzed. Similar

http://dx.doi.org/10.3904/kjim.2014.29.3.352

to previous studies, the most frequent pathological subtype was DLBCL [9,13,14]. While in general the DLBCL subtype involves the bone marrow in 10% to 15% of cases, the DLBCL subtype involving the bone marrow comprises only 3.3% of WR-NHL cases; furthermore, relatively few of these cases have any extranodal involvement [5,7,9].

NK/T-cell lymphoma and peripheral T-cell lymphoma occurred more frequently in this study than has been reported from Western nations. Our data showed a low incidence of follicular lymphoma (1.2%); however, it is the second most common lymphoma subtype of WR-NHL in Western populations [15]. Our results were similar to those reported in Japanese and Chinese studies [7,15-17]. The distribution of histological subtypes depends on regional and racial differences;

Table 5. Treatment according to Waldeyer's ring non-Hodgkin lymphoma subtype

Lymphoma subtype	No. (%)	CTx	RTx	CTx + RTx	SR	Supportive care
Diffuse large B-cell lymphoma	241 (73.4)	170	6	50	13	2
Mantle cell lymphoma	9 (2.7)	9	0	0	0	0
Follicular lymphoma	4 (1.2)	2	0	2	0	0
Small lymphocytic lymphoma	3 (0.9)	1	2	0	0	0
Burkitt lymphoma	5 (1.5)	5	0	0	0	0
Extranodal marginal zone lymphoma of MALT	11 (3.4)	1	7	0	1	2
T-cell-rich B-cell lymphoma	3 (0.9)	3	0	0	0	0
Lymphoblastic lymphoma	2 (0.6)	2	0	0	0	0
Nodal marginal zone lymphoma	6 (1.8)	2	1	0	2	1
Peripheral T-cell lymphoma	14 (4.3)	11	0	3	0	0
Nasal NK/T-cell lymphoma	14 (4.3)	7	0	6	1	0
Angioimmunoblastic T-cell lymphoma	9 (2.7)	9	0	0	0	0
Anaplastic large T-cell lymphoma	3 (0.9)	3	0	0	0	0
Other T-cell lymphomas	4 (1.2)	2	0	2	0	0
Total	328	227	16	63	17	5

CTx, chemotherapy; RTx, radiotherapy; SR, surgical resection; MALT, mucosa-associated lymphoid tissue.

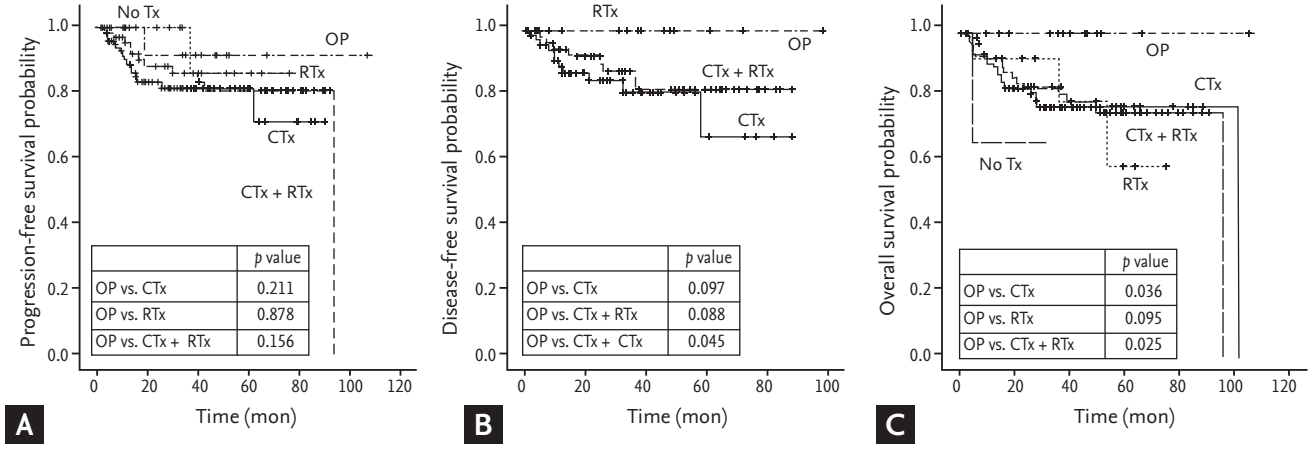

Figure 2. Progression-free survival (A), disease-free survival (B), and overall survival (C) of Waldeyer's ring non-Hodgkin lymphoma with localized disease according to treatment. CTx, chemotherapy; RTx, radiotherapy; OP, surgical resection +/- chemotherapy or radiotherapy.

therefore, this distribution might be related to susceptibility of the host to the EBV and human T-cell leukemia virus [13,18-20]. We also performed serum immunological studies of EBV infection in some patients (n = 79). Of 17 patients positive for EBV antibodies, five had T-cell lineage WR-NHL. EBV infection did not affect the survival outcomes; however, further evaluation to confirm the relationship between EBV infection and T-cell lineage WR-NHL may be helpful to determine the etiology of WR-NHL.

DLBCL has a heterogeneous nature, and it varies in its response to treatment as well as in its prognosis [15,21-23]. While it was reported that the germinal center B-cell-like (GCB) type has a better response to treatment, DLBCL with BCL2 rearrangement showed a poor response to treatment [24-27]. In this study, tis-

Table 6. Univariate analysis of prognostic factors for patients with Waldeyer's ring non-Hodgkin lymphoma

Parameter	3-Year PFS		3-Year DFS		3-Year OS	
	%	*p* value	%	*p* value	%	*p* value
Age ≥ 62 yr	72.3 vs. 85.9	0.030	70.1 vs. 88.6	0.004	61.0 vs. 83.4	< 0.001
ECOG > 1	36.6 vs. 82.6	0.015	57.1 vs. 82.6	0.327	30.1 vs. 76.2	< 0.001
B symptom (+)	79.1 vs. 80.7	0.907	75.5 vs. 82.5	0.285	60.9 vs. 76.4	0.019
Elevated serum LDH	66.1 vs. 83.1	< 0.001	62.9 vs. 84.1	0.022	61.7 vs. 76.9	0.002
HBsAg (+)	78.5 vs. 83.3	0.323	83.1 vs. 84.4	0.660	68.8 vs. 75.5	0.013
HCV Ab (+)	37.5 vs. 85.1	0.015	0 vs. 83.4	0.502	0 vs. 71.2	< 0.001
EBV (+)	75.3 vs. 87.0	0.030	80.8 vs. 84.2	0.430	55.1 vs. 74.3	0.005
Extranodal site > 1	79.0 vs. 80.7	0.563	76.7 vs. 82.3	0.345	55.7 vs. 76.7	0.011
T-cell subtype	57.0 vs. 84.3	< 0.001	76.0 vs. 82.3	0.159	50.7 vs. 78.0	< 0.001
High-intermediate or high IPI	67.0 vs. 84.0	0.017	64.9 vs. 86.1	0.005	51.9 vs. 80.6	< 0.001
Advanced stage	72.8 vs. 84.2	0.043	73.8 vs. 85.8	0.069	60.6 vs. 80.8	0.001
No CR	48.1 vs. 90.3	< 0.001	34.9 vs. 87.1	< 0.001	57.2 vs. 82.9	< 0.001

PFS, progression-free survival; DFS, disease-free survival; OS, overall survival; ECOG, Eastern Cooperative Oncology Group; LDH, lactate dehydrogenase; HCV, hepatitis C virus; EBV, Epstein-Barr virus; IPI, International Prognostic Index; CR, complete remission.

Table 7. Multivariate analysis of prognostic factors for overall survival in patients with Waldeyer's ring non-Hodgkin lymphoma

Parameter	HR (95% CI)	*p* value
Age ≥ 62 yr	2.645 (1.427–4.904)	0.001
ECOG > 1	0.903 (0.306–2.856)	0.906
B symptom (+)	0.983 (0.464–2.086)	0.800
Elevated serum LDH level	1.017 (0.788–1.312)	0.644
HBsAg (+)	1.089 (0.409–2.901)	0.294
Anti-HCV Ab (+)	6.380 (0.777–52.415)	0.081
EBV (+)	2.592 (0.897–7.483)	0.078
Extranodal site > 1	1.214 (0.517–2.847)	0.711
T-cell subtype	2.944 (1.410–6.147)	< 0.001
High-intermediate or high IPI	1.140 (0.770–1.688)	0.466
Advanced stage	1.333 (0.563–3.154)	0.637
No CR	1.536 (1.270–1.856)	< 0.001

HR, hazard ratio; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; LDH, lactate dehydrogenase; HCV, hepatitis C virus; EBV, Epstein-Barr virus; IPI, International Prognostic Index; CR, complete remission.

http://dx.doi.org/10.3904/kjim.2014.29.3.352

sues from the WR of 56 patients were subjected to immunohistochemical evaluation of markers such as CD10, BCL6 and MUM1. These patients were divided into GCB and non-GCB groups according to the Han's criteria [27], and the differences in survival between the two groups were determined. There was no statistically significant difference between the groups, which could be due to evaluation of an insufficient number of patients to confirm the immunohistochemical staining results.

In the current study, among those with localized disease, the surgical resection group showed improved survival compared with the chemotherapy or chemotherapy plus radiotherapy group. Almost all patients in the surgical resection group had the DLBCL subtype and underwent tonsillectomy for confirmation of the pathological diagnosis. Therefore, it is possible that the surgical resection group had better survival, because tonsillar involvement itself may be a favorable prognostic factor compared with involvement of other sites. Mohammadianpanah et al. [28] reported that tonsillar lymphoma tended to be localized and to have a good outcome. They showed that combined chemotherapy and radiation therapy was highly effective and probably curative for the majority of patients with stage I, nonbulky disease [28]. Our data also showed relatively good outcomes in the chemotherapy and the chemotherapy plus radiotherapy group. However, all patients in the surgical resection group survived, and all but one received chemotherapy or chemoradiotherapy after surgery. Although a small number of patients were analyzed in our study, it is speculated that in patients with localized DLBCL, surgical resection followed by chemotherapy or chemoradiotherapy might be a better treatment than other modalities.

Prognostic factors related to survival were subjected to univariate and multivariate analyses. The T-cell lineage of WR-NHL was a significant poor prognostic factor. These findings could be related to the greater extranodal involvement, especially in the bone marrow and liver, at the time of diagnosis in these patients, compared with those with the B-cell subtype. Involvement of remote lymph nodes or extranodal involvement was found in the majority of T-cell lineage NHL cases. Conversely, most B-cell lineage NHL cases presented with spreading to adjacent lymph nodes [9,17]. The IPI and Ann Arbor stage are commonly used to assess prognosis in WR-NHL. Age ≥ 62 years, elevated LDH levels, and advanced stages were significant poor prognostic factors for survival [5,14,17]. Failure to achieve CR after first-line treatment was also a significant poor prognostic factor according to the multivariate analysis.

In conclusion, DLBCL was found to be more frequent in Korea than reported in WR-NHL studies from other nations. And T-cell lineage NHL was found to occur more frequently than follicular lymphoma. T-cell lineage NHL, age ≥ 62 years, and failure to achieve CR after first-line treatment were all significant poor prognostic factors for overall survival according to the multivariate analysis.

KEY MESSAGE

1. Diffuse large B-cell lymphoma was found to be more frequent in Korea than Western countries.
2. T-cell lineage non-Hodgkin lymphoma, age ≥ 62 years, and failure to achieve complete remission after first-line treatment were all significant poor prognostic factors for overall survival.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer 2010;127:2893-2917.
2. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. CA Cancer J Clin 2005;55:74-108.
3. Baris D, Zahm SH. Epidemiology of lymphomas. Curr Opin Oncol 2000;12:383-394.
4. Weisenburger DD. Epidemiology of non-Hodgkin's lymphoma: recent findings regarding an emerging epidemic. Ann Oncol 1994;5 Suppl 1:19-24.
5. Hoppe RT, Burke JS, Glatstein E, Kaplan HS. Non-Hodgkin's lymphoma: involvement of Waldeyer's ring. Can-

cer 1978;42:1096-1104.
6. Yuen A, Jacobs C. Lymphomas of the head and neck. Semin Oncol 1999;26:338-345.
7. Yong W, Zhang Y, Zheng W, Wei Y. Prognostic factors and therapeutic efficacy of combined radio-chemotherapy in Waldeyer's ring non-Hodgkin lymphoma. Chin Med J (Engl) 2000;113:148-150.
8. Jacobs C, Weiss L, Hoppe RT. The management of extranodal head and neck lymphomas. Arch Otolaryngol Head Neck Surg 1986;112:654-658.
9. Ko YH, Lee JD, Kim CM, Kim IS, Lee MJ. Malignant lymphomas of the nasal cavity and Waldeyer's ring: clinicopathologic and immunohistochemical study. J Korean Med Sci 1992;7:314-324.
10. Yamanaka N, Harabuchi Y, Sambe S, et al. Non-Hodgkin's lymphoma of Waldeyer's ring and nasal cavity: clinical and immunologic aspects. Cancer 1985;56:768-776.
11. Swerdlow SH, Campo E, Harris NL, et al., eds. WHO Classification: Pathology and Genetics of Tumors of Haematopoietic and Lymphoid Tissues. 4th ed. Lyon: International Agency for Research on Cancer, 2008.
12. Jaffe ES, Harris NL, Stein H, et al., eds. WHO Classification: Pathology and Genetics of Tumors of Haematopoietic and Lymphoid Tissues. 3rd ed. Lyon: International Agency for Research on Cancer, 2001.
13. Wang SS, Cozen W, Cerhan JR, et al. Immune mechanisms in non-Hodgkin lymphoma: joint effects of the TNF G308A and IL10 T3575A polymorphisms with non-Hodgkin lymphoma risk factors. Cancer Res 2007;67:5042-5054.
14. Ryu MH, Kim BS, Kim TW, et al. Subclassification of diffuse large B-cell lymphomas according to the real classification: distinction of immunoblastic and non-immunoblastic subtypes. Korean J Med 2003;65:71-80.
15. Krol AD, Le Cessie S, Snijder S, Kluin-Nelemans JC, Kluin PM, Noorduk EM. Waldeyer's ring lymphomas: a clinical study from the Comprehensive Cancer Center West population based NHL registry. Leuk Lymphoma 2001;42:1005-1013.
16. Kwong YL, Anderson BO, Advani R, et al. Management of T-cell and natural-killer-cell neoplasms in Asia: consensus statement from the Asian Oncology Summit 2009. Lancet Oncol 2009;10:1093-1101.
17. Harabuchi Y, Tsubota H, Ohguro S, et al. Prognostic factors and treatment outcome in non-Hodgkin's lymphoma of Waldeyer's ring. Acta Oncol 1997;36:413-420.
18. Chadburn A, Hyjek E, Mathew S, Cesarman E, Said J, Knowles DM. KSHV-positive solid lymphomas represent an extra-cavitary variant of primary effusion lymphoma. Am J Surg Pathol 2004;28:1401-1416.
19. Matsuoka M. Human T-cell leukemia virus type I and adult T-cell leukemia. Oncogene 2003;22:5131-5140.
20. Engels EA, Cerhan JR, Linet MS, et al. Immune-related conditions and immune-modulating medications as risk factors for non-Hodgkin's lymphoma: a case-control study. Am J Epidemiol 2005;162:1153-1161.
21. A predictive model for aggressive non-Hodgkin's lymphoma. The International Non-Hodgkin's Lymphoma Prognostic Factors Project. N Engl J Med 1993;329:987-994.
22. Lopez-Guillermo A, Colomo L, Jimenez M, et al. Diffuse large B-cell lymphoma: clinical and biological characterization and outcome according to the nodal or extranodal primary origin. J Clin Oncol 2005;23:2797-2804.
23. Ezzat AA, Ibrahim EM, El Weshi AN, et al. Localized non-Hodgkin's lymphoma of Waldeyer's ring: clinical features, management, and prognosis of 130 adult patients. Head Neck 2001;23:547-558.
24. Rosenwald A, Wright G, Chan WC, et al. The use of molecular profiling to predict survival after chemotherapy for diffuse large-B-cell lymphoma. N Engl J Med 2002;346:1937-1947.
25. Alizadeh AA, Eisen MB, Davis RE, et al. Distinct types of diffuse large B-cell lymphoma identified by gene expression profiling. Nature 2000;403:503-511.
26. de Leval L, Bonnet C, Copie-Bergman C, et al. Diffuse large B-cell lymphoma of Waldeyer's ring has distinct clinicopathologic features: a GELA study. Ann Oncol 2012;23:3143-3151.
27. Hans CP, Weisenburger DD, Greiner TC, et al. Confirmation of the molecular classification of diffuse large B-cell lymphoma by immunohistochemistry using a tissue microarray. Blood 2004;103:275-282.
28. Mohammadianpanah M, Omidvai S, Mosalei A, Ahmadloo N. Treatment results of tonsillar lymphoma: a 10-year experience. Ann Hematol 2005;84:223-226.

http://dx.doi.org/10.3904/kjim.2014.29.3.352