

TREATMENT OUTCOME IN EXTRANODAL NON-HODGKIN'S LYMPHOMA OF DIFFERENT SUBSITES IN HEAD AND NECK REGION

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ABSTRACT

BACKGROUND

HNENL (Head and Neck Extra nodal Non-Hodgkin's Lymphoma) contributes for <20% of all extra nodal NHL and <5% of all head and neck cancers. With limited literature, the outcomes of extra nodal lymphomas also vary depending on specific sites mostly because of different management strategies. Hence, the present study was undertaken to review the outcome of the primary extra nodal NHL of head and neck patients treated in our institute.

MATERIALS AND METHODS

A retrospective descriptive study was conducted among all the extranodal NHL cases of head and neck region treated in a regional cancer care centre during January 2010 to June 2013 except those who already had recurrences or distant metastasis. All the patients were followed up for a period of 6-36 months.

RESULTS

Among 29 patients, the mean age of the participants was 53.72 ± 11.37 years, males predominated (55.2%), the tonsillar group constituted the highest (48.3%) and 34.5% had lymph nodes. The over-all survival was 100.0% and the median disease-free survival was better in the tonsillar group (32.0 months) and among those with no lymph nodes (30.0 months). The disease-free survival rates were 28.6% in tonsillar group, 22.2% in nasopharyngeal group and 33.3% among others; it was 31.6% among those with no lymph nodes and 20.0% with lymph nodes.

CONCLUSION

Tonsillar group has relatively better prognosis compared to nasopharyngeal group of NHL patients and lymphadenopathy implicated a relatively bad prognosis.

KEYWORDS

Non-Hodgkin's Lymphoma, Head and Neck extra nodal NHL, Tonsillar Group, Nasopharyngeal Group, Lymphadenopathy.

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BACKGROUND

Non-Hodgkin Lymphoma (NHL), a group of malignant lympho-proliferative disorders arise from lymph nodes with varied manifestations.¹ Nevertheless 25% of NHL also arise from tissues other than lymph nodes and even from sites

that do not contain lymphoid tissue commonly. Such forms are referred to as primary extra nodal lymphomas (pENL).^{2,3} Various studies from the western countries have reported extra nodal NHL occurrence ranging between 24-48% of all NHL.²⁻⁵ In Asia, a range of 42-61% has been reported from Pakistan, Kuwait, Japan, Korea, Thailand and China.^{6,7} In India, the incidences reported varied from 22-36% in South India, 22% in Eastern India, 54% in Rajasthan.⁷⁻¹⁰ It has been stated that though several papers dealing with extra nodal NHL have been published, the literature on primary extra nodal lymphomas as a group is limited. 4-15% of NHL patients constitute head and neck extra nodal NHL (HNENL).¹¹ Although tonsil is the most common primary extra nodal site of head and neck NHL, it accounts for less than 1%.¹² The outcomes of extra nodal lymphomas vary depending on specific sites of primary extra nodal

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lymphomas. This can be explained partially due to differences in natural history and mostly to differences in management strategy related to organ-specific problems.¹³ Hence, the present study was undertaken.

Objective

To determine the outcomes of stage I and II primary extra nodal NHL of head and neck treated in our hospital, with chemotherapy and radiotherapy in terms of survival rate (over-all and disease free) and its duration.

MATERIALS AND METHODS

Study Setting

Our hospital is a tertiary care high volume centre where 20000 cases of cancers get registered over a year and among which only 29 cases of HNENL were detected, implicating a very less incidence of the disease.

Study Design

This is a retrospective descriptive study.

Study Duration

3 years.

Study Subjects

All the diagnosed 29 extranodal NHL cases of head and neck region treated at our tertiary care center during the study period between January 2010 to June 2013 were included as study subjects.

Inclusion Criteria

- Biopsy proven Non-Hodgkin's lymphoma, irrespective of histological subtype of the lymphoma
- Patients who have not received any chemotherapy previously for any other disease than present one.
- Patients who have not received any radiotherapy previously for any disease.
- Patient whose performance status was good.
- Patients with stage I and II limited to head and neck region.

Exclusion Criteria

- Patients who had developed recurrence or had distant metastasis.

Study Procedure

We retrieved the treatment charts of patients of extranodal NHL cases of head and neck region treated in our institute from January 2010 to June 2013 and the demographic, treatment details and outcome of HNENL cases using predesigned proforma.

Investigations

All the patients had undergone USG neck, axilla, abdomen, pelvis and inguinal regions, along with contrast enhanced CT scan of thorax or contrast enhanced CT scan of head & neck, thorax, abdomen and pelvis for the purpose of staging. All patients under went bone marrow biopsy to rule out any bone marrow involvement.

Treatment Details

Chemotherapy

All the patients were treated with 4 to 6 cycles of CHOP based regimen every three weekly once:

- Cyclophosphamide 750 mg/m²
- Vincristine 1.4 mg/m²
- Adriamycin 50 mg/m²
- Prednisolone 60 mg/m²

None of the patients received rituximab due to cost issue.

According to hospital protocol all patients were reviewed after 4 cycles of chemotherapy. The patients with good response then received consolidation radiotherapy whereas with partial response completed 6 cycles of chemotherapy followed by consolidated radiotherapy.

Radiotherapy

All patients received radiotherapy of 40 Gy in 20 fractions with 2Gy per fraction over 4 weeks, to the primary site and if any involved neck node with 3-Dimensional Conformal Radiotherapy (3DCRT) or Intensity Modulated Radiotherapy (IMRT) technique.

After analysing the charts, patients were initially divided into 3 groups-

- a. Disease arising from tonsil
- b. Disease arising from nasopharynx
- c. Disease arising from other site of head and neck region.

All the three groups were subdivided into 2 subgroups- with nodal or without nodal diseases along with primary sites, then were followed up for a minimum of 6 months and a maximum of 36 months.

Follow Up

During the follow up, complete haemogram, USG of the nodal regions or CT scan were done to rule out the disease status. If any new lesion that appeared in the follow up were biopsied to confirm the disease involvement. As per requirement even bone marrow biopsy was also done.

Statistical Analysis

The data was tabulated in Microsoft excel sheet. Patient and tumor characteristics were expressed in means and proportions. The median duration of survival, overall and disease-free survival probabilities were estimated using Kaplan-Meier method and were tested for significance with log rank tests. Data for patients who were alive and free of disease were censored at date of last follow-up. The analysis was done using a SPSS version-18.0. Statistical tests were considered significant at 5% significance level.

RESULTS

Among the 29 patients, the mean age was 53.72 ± 11.37 yrs. and the age ranged between 30-71 yrs. Males predominated (55.2%) and the tonsillar group constituted

the highest (48.3%). Only 34.5% of them presented with lymph nodes (Table-1).

With a followup of 36 months (range 6 to 36 months) over-all survival was 100.0% and over-all disease-free survival (DFS) was 30 months. Though, the median disease-free survival was not significantly different based on the sites affected, it was better in the tonsillar group 32.0 months (95% CI 29.7-34.3) compared to nasopharyngeal group 20.0 months (95% CI 17.2-22.7) and was worse in other sites group 12.0 months (95% CI 9.7-14.3). (Table-2)

Among the tonsillar group, 3 had residual disease and 7 had developed recurrence during 30th- 34th month of follow up. Among the nasopharyngeal group, 2 had residual disease and 4 developed recurrence during 12th-21st months.

Among the other group 4 developed recurrences during 6th-12th month of follow up (Figure-1)

The median disease-free survival was better among those with no lymph nodes [30.0 months (95% CI 23.8-36.1)] compared to those with lymph nodes [20.0 months (95% CI 9.1-30.8)], however the difference was not statistically significantly (P>0.05). (Table-3)

The probability of disease free survival at the end of 3 years was 28.6% (95% CI 9.6-57.9) in tonsillar group, 22.2% (95% CI 3.9-59.9) in nasopharyngeal group and 33.3% (95% CI 5.9-75.9) among others; on combining, tonsillar and nasopharyngeal group as a part of Waldeyer’s ring, it was 26.1% (95% CI 11.1-48.7). The DFS was 31.6% (95% CI 13.6-56.5) among those with no lymph nodes and 20.0% (95% CI 3.5-55.8) with lymph nodes.

Variables	No. of Patients (n)	Column Percentage (%)
1. Age Group		
< 60 years	18	62.1
> 60 years	11	37.9
2. Sex		
Males	16	55.2
Females	13	44.8
3. Sites of head and neck extranodal NHL		
Tonsillar	14	48.3
Nasopharynx	09	31.0
Others	06	20.7
4. Lymph Nodes		
Present	10	34.5
Absent	19	65.5

Table 1. Patient and Tumor Characteristics

Site	Median Disease-Free Survival (Months)	95% C.I.	Log-Rank (P-Value*)
Tonsil	32.0	29.7 – 34.3	0.19
Nasopharynx	20.0	17.2 – 22.7	
Others	12.0	9.7 – 14.3	

Table 2. Comparison of Disease-Free Survival among the Patients with Different Sites of Extra-Nodal NHL

Lymph Nodes	Median Disease-Free Survival (Months)	95% C.I.	Log-Rank (P-Value*)
Present	20.0	9.1 – 30.8	0.53
Absent	30.0	23.8 – 36.1	

Table 3. Comparison of Disease-Free Survival among Patients With and Without the Presence of Lymph Nodes in Extra-Nodal NHL

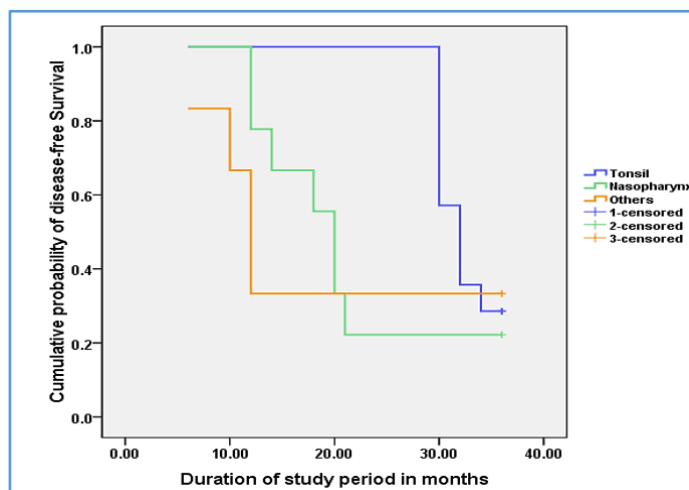


Figure 1. Kaplan-Meier Survival Curve Indicating the Disease-Free Survival Among the Three Sites

DISCUSSION

There are very limited literatures available with respect to prospective studies comparing the prognosis of HNENL affecting different sub-sites in head and neck region because of the very less incidence of the disease. Similarly, due to lack of number of patients based on previous year's data on incident cases in our hospital, the decision of conducting a retrospective study was made. Similarly, it is also noted that, HNENL shares <20% of all extra nodal NHL and <5% of all head and neck cancers as it often remains localized to the primary site.¹⁴

Al Diab AR et al., reported in their study that the mean age of patients with extranodal NHL was 55±18 years and most patients presented in the age range of 41-60 years which is similar to the findings in the current study. However older population (age >60 years) predominated in the NHL of head and neck (particularly nasopharyngeal NHL) which is not in line with the current study wherein younger age group predominated which may be due to different study settings.¹⁵ In the same study by Al Diab AR et al., among the patients with tonsillar, nasopharyngeal and other sites involvement, tonsillar group constituted more and males predominated the study in tonsillar and other sites similar to the current study.¹⁵ For Waldeyer's ring involvement as reported by Horiuchi et al., the 5 year survival was 62.7% per cent however in the current study the 3 year survival was assessed wherein 100.0% over-all survival was noted.¹⁶ The difference noted may be due to the different stage of presentation or the difference in the years of follow up; however it was noted in the same study that Waldeyer's ring lymphomas had the highest survival rate. In the same study the disease-free survival was noted to be 53.1% for Waldeyer's ring wherein, tonsils and nasopharynx also form a part and majority of the relapses occurred within 2 years which is similar to the current study, however the disease-free survival was noted still lesser in our study.¹⁶ The difference may be due to the change in the techniques used. The median event-free survival was 82.3 months, with the primary tonsillar site according to Ezzat AA et al., however in the present study median disease free survival was 32 months as the follow up period was limited to 3 years and in the compared study it was more.¹⁷ Abnormal neck lymph nodes were shown to have poor influence on prognosis as noted by Chi HS et al., and similarly in our study the proportion of those who survived with lymph nodes was 20.0%.¹¹

Limitations

While conducting the study, we did not consider the grade and subtype of lymphomas. Other parameters used in international prognostic indices for lymphoma were not taken into consideration for calculating the prognosis. Waldeyer's ring includes tonsil, nasopharynx and base of tongue, but in our study, there were no patients with lymphoma of base of tongue site. In the current study, even the follow up was limited to 3 years however it has been mostly compared to the literature which followed patients up to 5 years and also for those with whole Waldeyer's ring

involvement as literature comparing the subsites as such only tonsils and nasopharynx are very scarce. As the number of treated cases is limited, the results cannot be generalized.

CONCLUSION

From the above study, we conclude that tonsillar group of extra nodal NHL has better prognosis compared to nasopharyngeal group of NHL patients. Although patients of other sites had better outcome in terms of survival at 3 years, the disease-free interval was lesser compared to tonsillar and nasopharyngeal group, thus implicating poor response to treatment. Though the lymph node status did not make a significant difference, it relatively indicated a bad prognosis.

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