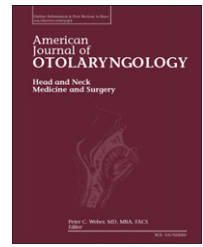


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Extra-nodal B-cell non-Hodgkin's lymphomas of the head and neck: A study of 68 cases

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ABSTRACT

Objectives: The objectives of this study are to describe the distinctive characteristics of extra-nodal B-cell non-Hodgkin's lymphomas (BNHLs) located in the head and neck in a series of patients, to discuss patient survival, and to compare the oral versus the non-oral locations of the extra-nodal BNHLs of the head and neck.

Material and methods: We studied 68 patients with BNHL of the head and neck. We analyzed the clinical and survival characteristics. Additionally, we performed Kaplan–Meier and Cox regression analyses to determine the influence of the different factors on survival.

Results: This study included 68 non-nodal lymphomas; 30 lymphomas (31.9%) were located intraorally, with the gingiva as the most frequent location. The oral lymphomas in stages 1 and 2 showed a prevalence of 60% (18/30). The Kaplan–Meier analysis showed that the stage of disease and the oral versus non-oral extranodal lymphomas were significant prognostic factors ($p < 0.05$). However, the multivariate Cox analysis indicated that only complete remission and oral versus non-oral location were significant prognostic factors ($p < 0.01$).

Conclusions: The gingiva was the most common location of the intraoral lymphomas. Complete remission and non-oral location were the only significant survival factors in the multivariate Cox regression analysis.

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1. Introduction

Oral squamous cell carcinoma is the most common oral malignant lesion [1]. Nonepithelial oral malignancies comprising sarcomas, lymphomas, metastasis and other rare tumors have an incidence of lower than 5% [2,3]. Malignant lymphomas (MLs) are a group of processes with widely varying clinical

features, histological characteristics, immunophenotypes and genetic abnormalities [4,5].

MLs can be found in the form of Hodgkin's lymphoma (HL) and non-Hodgkin's lymphoma (NHL). The latter group comprises B-cell, T-cell and NK cell lymphomas [6]. NHLs are the most prevalent of all head and neck lymphomas, representing nearly 75% of cases [7]. Of the NHLs, the B-cell lymphomas are

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the most common in the head and neck, with the diffuse large B-cell lymphoma (DLBCL) being the most frequent [8-10].

NHL can present as nodal or extranodal forms. Nodal NHLs are characterized by multiple and painless nodes in different locations, such as the neck, and in others areas, such as the axilla, mediastinum and abdomen. Extranodal lymphomas represent 55.5% of all NHLs in the head and neck, whereas the remaining 44.5% are nodal forms [8]. The extranodal lesions are the dominant types in the head and neck [11].

The head and neck is the second most common site of extranodal lymphomas after the gastrointestinal tract. They are located submucosally and are sometimes present as ulceration with bone destruction [12]. Little information is available regarding the characteristics of extra-nodal NHLs located in the oral cavity. We investigated this particular aspect in our series of cases collected over 15 years.

There are no publications that compare the survival rate between the oral and non-oral extra-nodal BNHLs of the head and neck. The objective of this clinical study is to present a series of extra-nodal BNHLs in which their primary presentation was in the head and neck region. In addition, we focused special attention on the intraoral manifestations. We analyzed their clinical characteristics, as well as the five-year survival rate and prognostic factors in patients comparing the oral and the non-oral locations.

2. Materials and methods

We collected 68 patients with a histological diagnosis of extranodal BNHL of the head and neck, who were seen at the University General Hospital of Valencia, Spain in the last 15 years. All patients presented with their first signs of symptoms to the Department of Ear, Nose and Throat (ENT) and to the Department of Stomatology, Oral and Maxillofacial Surgery.

This study was approved by the Ethics Committee of Valencia University (Spain) (Reference: H1382188167460), and we followed ethical principles, including the World Medical Association Declaration of Helsinki.

Each case was registered with the location in the head and neck. We distinguished the intraoral versus the non-intraoral locations of the extra-nodal BNHLs of the head and neck. We also analyzed the histological type of BNHL, the presence of B-symptoms, the affectionation of the bone marrow, and the stage of the lymphoma. We grouped stages 1 and 2 as initial stages, and stages 3 and 4 as late stages [5,6].

The treatment was established in the service of hematology following the standard recommendations as described previously [13]. The most common treatment combination was rituximab and cyclophosphamide, hydroxydaunorubicin, vincristine, and prednisolone (R-CHOP) in 25.5% of our patients, followed by CHOP and radiotherapy (CHOP + RT) in 16% of the cases. The remaining patients were treated with other combinations. The patients were regularly followed and we performed survival analysis in 55 cases. For non-survivors, the survival time was recorded from the time of diagnosis to the time of death.

To determine the significance in the survival study, we performed a Kaplan-Meier analysis with the log rank test (Mantel-Cox); for the prognostic analysis, we performed the

Cox regression with the B regression coefficient to determine the significance, the $\text{Exp}(B)$ -hazard ratio and the 95% confidence interval for $\text{Exp}(B)$.

We also used the χ^2 test and Student's t-test. Statistical significance was set at $p < 0.05$.

3. Results

This study included 68 patients (mean age, 59.7 ± 17 years), of which 38 (55.9%) were male and 30 (44.1%) were female. Most of the BNHLs were DLBCLs (46 cases, 67.6%). Thirty (44.1%) of the patients with extranodal NHLs had an intraoral location, and the remaining 38 cases (55.9%) were located in the ENT area. We found 49 cases (72.1%) in states 1 and 2 while in stages 3 and 4 there were 19 (27.9%). Other data such as immunodeficiency (HIV), B symptoms and bone marrow affectionation are described in Table 1.

The clinical characteristics of the 30 intraoral lymphomas are described in Table 2. The average age of patients with oral BNHLs was 57.03 ± 16.8 years; of the 30 patients, 18 were male (60%) and 12 (40%) were female. We detected 54.5% of the cases in stages 1 and 2, and the remaining 45.5% in stages 3 and 4. The most common location was the gingiva (16 cases, 53.3%), followed by the palate (6 cases, 20%). Most of the cases (93.3%) were located in the soft tissues, with only two cases found in the jawbones—one in the mandible and another one

Table 1 – Characteristics of the 68 extranodal non-Hodgkin's lymphomas of the head and neck.

	Extranodal (68 cases)
Mean age (\pm SD)	59.7 \pm 17
Gender	
Male	38 (55.9%)
Female	30 (44.1%)
Type of lymphoma	
DLBCL	46 (67.6%)
Follicular lymphoma	9 (13.2%)
Marginal lymphoma	5 (7.4%)
Mantle lymphoma	1 (1.5%)
Plasmablastic lymphoma	3 (4.4%)
Lymphocytic lymphoma	2 (2.9%)
Not classified	2 (2.9%)
Primary extranodal sites	
Tonsils	9 (9.3%)
Cavum	8 (8.2%)
Base of tongue	2 (2.1%)
Larynx and epiglottis	2 (2.1%)
Nose	1 (1%)
Maxillary sinus	2 (2.1%)
Pharynx	1 (1%)
Parotid	12 (12.4%)
Submandibular gland	1 (1%)
Thyroid	1 (1%)
Eyebrow	1 (1%)
Intraoral	30 (44.1%)
Immunodeficiency (HIV)	10 (14.7%)
B symptoms	12 (17.6%)
Bone marrow affectionation	11 (16.1%)

DLBCL: diffuse large B-cell lymphoma.

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