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HEAD AND NECK

Oral lesion as the primary diagnosis of non-Hodgkin's lymphoma: a 20-year experience from an oral pathology service and review of the literature

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Abstract

Purpose We aimed to investigate the frequency and clinicopathological features of oral NHL in our institution as well as to compare the data gathered from other oral pathology and general pathology services published in the literature.

Methods Clinical records of patients diagnosed with NHL exclusively affecting the oral cavity were reviewed from 1997 to 2017. Additionally, a review of the literature over a 20-year period was conducted aiming to examine articles on oral NHLs.

Results Oral NHLs represented 0.1% ($n=98$) of the total number of biopsies (68,229) received during the period evaluated (1997–2017). The mean age at the diagnosis was 47 years. Most patients were white (67.3%). A nodular lesion was the most frequent presentation (54.9%) and pain was described in 47.1% of the cases. The most common diagnosis was diffuse large B cell lymphoma (42%) followed by plasmablastic lymphoma (24%). Only 19 articles were included in the review of the literature.

Conclusions Although NHLs are rare in the oral cavity, clinicians and surgeons have an important role in promptly diagnosing lymphomatous lesions to refer the patient to a proper treatment.

Keywords Hematolymphoid neoplasms · Non-Hodgkin lymphoma · Head and neck · Oral cancer

Introduction

Non-Hodgkin's lymphoma (NHL) is a group of lymphocytic neoplasms derived from the uncontrolled proliferation of B, T or NK cells. NHL represents almost 90% of all lymphomas and shows a variety of histological subtypes [1]. The development of genetic testing and laboratory techniques has improved the diagnosis as well as the knowledge of the clinical management of patients [2], even though the diversity of cell types and histological overlapping may hamper the diagnosis [3].

NHL is either a nodal and/or extranodal disease that may occur at different anatomic sites, including the head and neck region [4–6]. In that region, an increase in the frequency of NHLs may be associated to the HIV infection [7]. The involvement of oral cavity seems to be rare, accounting for approximately 2–10% of the neoplasms affecting the mouth [1]. The Waldeyer's ring is usually pointed out as the main site of NHL occurrence, but many other sites within the oral cavity may be affected [7, 8].

Therefore, in the present study, we aimed to investigate all cases diagnosed as lymphomas originated from the oral cavity in the oral pathology service of the University of São Paulo. This oral pathology service is one of the largest of this type in Latin America, where only oral biopsies are received for diagnosis. We also aimed to compare the data gathered from other oral pathology and general pathology services published in the literature.

Materials and methods

The study was approved by the Ethics Committee of the University of São Paulo, SP, Brazil (1.824.822). This was a retrospective descriptive study conducted in the oral pathology service of the University of São Paulo. The records of the patients diagnosed with lymphoma from a period of time

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comprising 1997 to 2017 were reviewed and the data regarding histological type, lesion site, age at diagnosis, gender and clinical features were collected. Only cases located exclusively in the oral cavity and without other lesion reported by the clinician were included in the analysis, meaning that the oral lesion was the first signal of lymphoma presented. Cases from oropharynx were excluded. Data were obtained from the software "Laudo&Imagem" (São Paulo, Brazil) where the files are stored. Diagnosis was based in tumour morphology and immunohistochemical reactions. Diagnosis was reviewed by the pathologists to uniformize them according to the latest WHO classification of hematologic diseases [9].

For the review of the literature, all retrospective studies on oral NHLs, published in PUBMED database between 1997 and 2017, were reviewed. The research was performed combining the descriptors "non-Hodgkin lymphoma" AND "oral", "oral cavity" or "head and neck" AND "retrospective". Only articles in the English language were included.

Results

From 1997 to 2017, 98 cases were diagnosed as primary NHLs affecting oral tissues. This represented 0.1% of all the biopsies diagnosed in the period (68,229 cases). Men and women were almost equally affected (men = 50; women = 48). The mean age at the diagnosis was 47 years (women = 49; men = 45). Most patients were white ($n = 69$; 67.3%) and black ($n = 15$; 15.3%). The clinical appearance of a nodule was the most frequent sign reported by clinicians (54.9%) and pain was described in 47.1% of the cases. History of HIV and EBV infection was known for only 12 and 1 patients, respectively at the moment of the biopsy. The most common diagnosis was diffuse large B cell lymphoma followed by plasmablastic lymphoma (Fig. 1). Figure 2 shows the distribution of the age according to the histological subtype of NHL. The main site affected was the mucosa comprising alveolar ridge and gingiva (37.7%) followed by the palate (25.5%). Figure 3 shows the distribution of NHLs according to the site of occurrence.

Table 1 displays all the published retrospective studies on oral NHL between 1997 and 2017. First, 31 articles were found based on the title and abstract. Then, after reading the full article, 11 studies were excluded, mostly because they lacked cases affecting the oral cavity or because they were poorly designed. One additional study was excluded because the authors duplicated the same cases in two different studies.

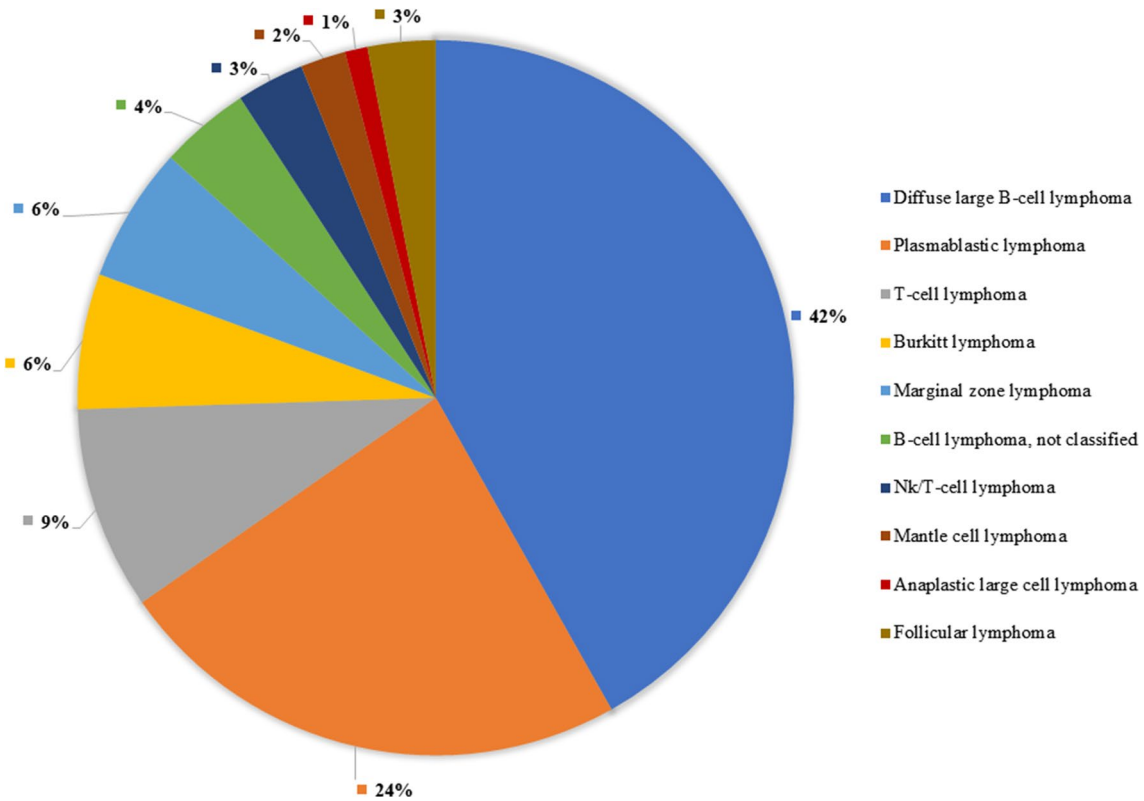

Fig. 1 Frequency of each subtype of NHL diagnosed in the pathology service

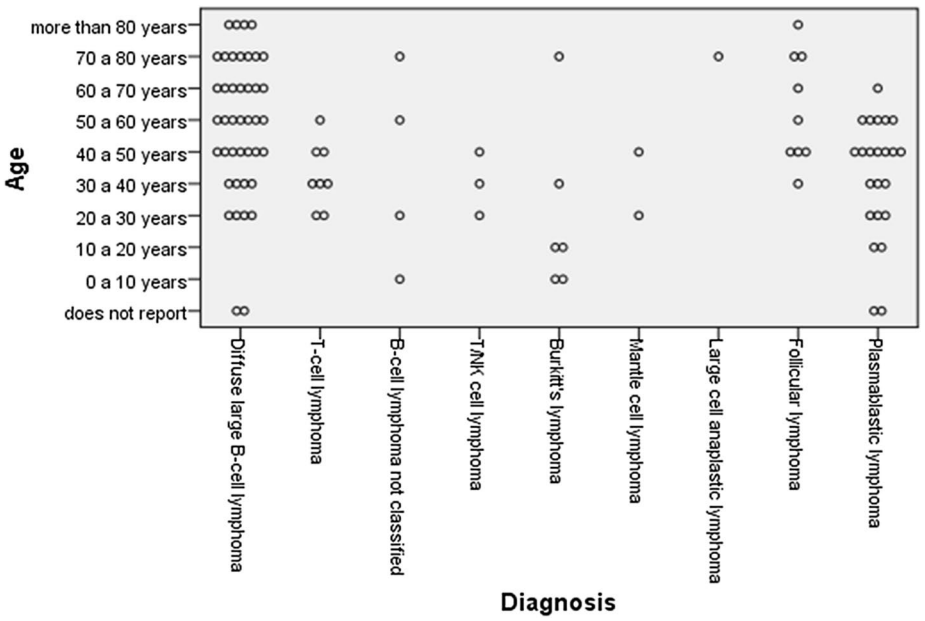

Fig. 2 Distribution of the patient's age according to the histological subtype of NHL

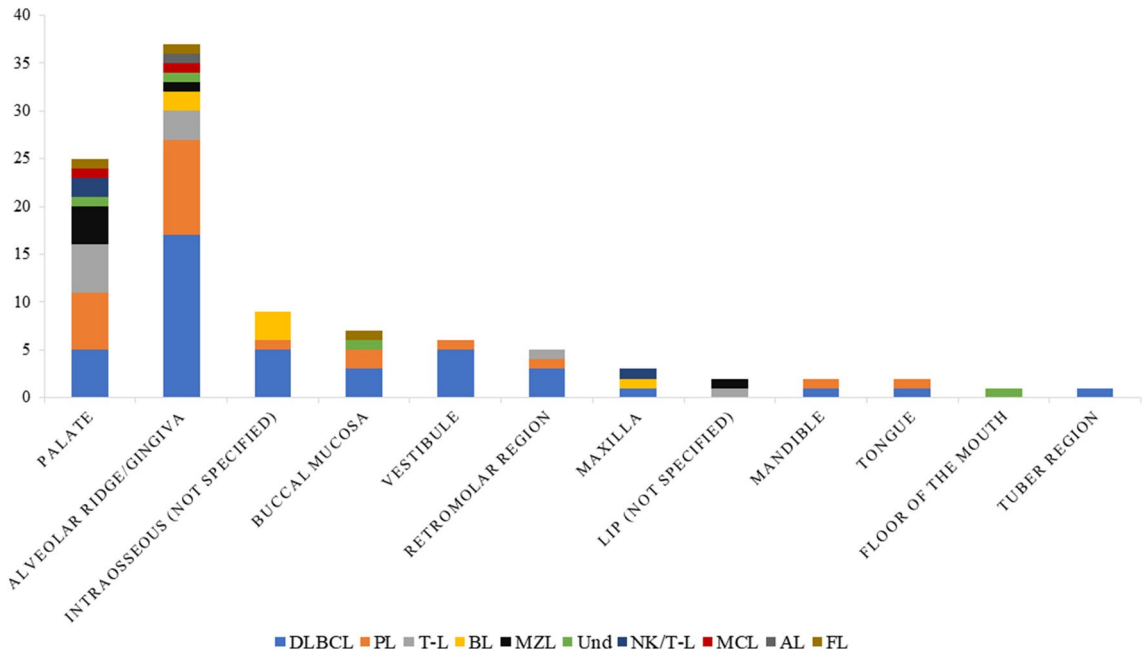

Fig. 3 Distribution of NHLs according to the site of occurrence in the oral cavity (*DLBCL* diffuse large b cell lymphoma, *PL* plasmablastic lymphoma, *BL* Burkitt lymphoma, *MZL* marginal zone lymphoma, *Und* B cell lymphoma, not classified, *NK/T-L* NK/T cell lymphoma, *MCL* mantle cell lymphoma, *AL* anaplastic large-cell lymphoma, *FL* follicular lymphoma)

Discussion

Most retrospective studies of the last 20 years have a limited number of NHLs affecting the oral cavity [4, 10–13]. That is in part because most reviews focus on head and neck lymphomas or because they are from medical pathology services [4–6]. In our oral pathology service, we found 98 NHLs exclusively affecting the oral cavity, comprising diverse subtypes of lymphomas. We found only one study with a larger sample compared to the one presented in this paper, i.e. 287 cases [7]. Another study showed 151 cases, but it lacked clear information about which neoplasms occurred within the oral cavity and which ones occurred in the maxillofacial region [1].

Table 1 Review of the studies involving oral NHLs in the last 20 years

Author/year	Time period of the study	Number of extranodal NHLs in the study	Number of cases affecting the oral cavity	Histological subtype of oral cases	Location within the oral cavity
Ajayi et al. [21]	1992–2003	28	26	Burkitt lymphoma = 18 Other types not informed = 8	Maxilla = 14 Mandible-maxilla = 8 Mandible = 3 Palate = 1
Kemp et al. [14]	1999–2006	40	40	Diffuse large b cell lymphoma = 23 Follicular lymphoma = 6 Extranodal marginal zone lymphoma = 5 Plasma cell tumours = 3 Small lymphocytic lymphoma = 2 T cell lymphoma = 1	Maxilla or palate = 11 Mandible = 8 Palatal soft tissue = 8 Vestibule and gingiva = 7 Buccal mucosa = 4 Floor of mouth = 1 Lower lip = 1
Elarbi et al. [11]	1991–2007	4	4	Burkitt lymphoma = 4	Maxilla = 3 Mandible = 1
Hansra et al. [20]	2000–2009	12	6	Plasmablastic lymphoma = 6	Alveolar mucosa = 2 Mandible = 2 Gingiva = 1 Hard palate = 1
Etemad-Moghadam et al. [5]	1981–2001	100	18	Not informed	Jaw bone = 16 Gingiva = 2
Shah et al. [8]	1990–2008	15	15	Not informed	Gingivobuccal complex = 12 Buccal mucosa = 1 Tongue = 1 Labial mucosa = 1
Iguchi et al. [12]	2004–2010	79	1	Peripheral T cell lymphoma, not specified = 1	Not informed
Scherfler et al. [6]	1993–2010	42	16	Not informed	Mandible = 5 Mandibular soft tissue = 4 Maxilla and hard palate = 4 Soft palate = 2 Floor of the mouth = 1
Chi et al. [4]	1990–2007	86	2	Not informed	Hard palate = 2
Matsuzaki et al. [15]	1993–2009	13	12	Diffuse large b cell lymphoma = 7 MALT lymphoma = 2 Follicular lymphoma = 2 Adult t cell leukemia/lymphoma = 1	Palate = 4 Buccal mucosa = 3 Gingiva = 3 Tongue = 1 Maxilla = 1
Anacak et al. [13]	1986–2006	63	2	MALT lymphoma = 2	Minor salivary gland = 2
Guevara-Canales et al. [1]	1980–2005	151	Not informed	Not informed	Not informed
Abadi et al. [18]	1979–2011	34	12	Low-grade b cell lymphoma = 9 Peripheral t cell lymphoma = 2 Diffuse large b cell lymphoma = 1	Maxilla = 5 Mandibular soft tissue = 5 Tongue = 2
Ramanathan et al. [16]	1980–2012	42	38	B cell lymphoma, not otherwise specified = 14 T cell lymphoma, not otherwise specified = 7 Burkitt lymphoma = 5 Diffuse large b cell lymphoma = 3 NK/T cell lymphoma = 3 Lymphoma, not otherwise specified = 6	Mandible = 9 Cheek = 8 Palate = 7 Maxilla = 7 Soft palate = 2 Gingiva = 2 Lip = 1 Tongue = 1 Floor of the mouth = 1

Table 1 (continued)

Author/year	Time period of the study	Number of extranodal NHLs in the study	Number of cases affecting the oral cavity	Histological subtype of oral cases	Location within the oral cavity
Sirsath et al. [23]	2001–2011	7	7	Plasmablastic lymphoma = 4 Diffuse large b cell lymphoma = 2 Peripheral t cell lymphoma, not otherwise specified = 1	Tongue = 3 Alveolus = 2 Hard palate = 1 Gingivobuccal sulcus = 1
Picard et al. [22]	2001–2013	67	8	Not informed	Tongue = 6 Soft palate = 2
Philipone et al. [19]	1997–2012	47	47	Diffuse large b cell lymphoma = 13 Small lymphocytic lymphoma = 8 Follicular lymphoma = 6 Extranodal marginal zone lymphoma = 5 Plasma cell neoplasms = 5 Plasmablastic lymphoma = 3 Mantle cell lymphoma = 2 Other types = 5	Buccal mucosa = 8 Maxilla = 7 Palate = 7 Tongue = 6 Gingiva = 6 Mandible = 5 Vestibule = 5 Lip = 2 Floor of the mouth = 1
Akbari et al. [17]	2003–2008	426	23	Diffuse large b cell lymphoma = 7 Non-hodgkin lymphoma, not otherwise specified = 8 Marginal zone b cell lymphoma = 1 Plasmacytoma = 1 Small lymphocytic lymphoma = 5 Burkitt lymphoma = 1	Palate = 18 Gingiva = 5
Alli et al. [7]	1993–2012	363	287	Not informed	Maxilla = 34 Palate = 28 Mandible = 24 Gingiva = 23 Buccal mucosa = 19 Other locations = 159
Kusuke et al. (present study)	1997–2017	98	98	Diffuse large b cell lymphoma = 41 Plasmablastic lymphoma = 23 T cell lymphoma, not otherwise specified = 9 Burkitt lymphoma = 6 Other types = 19	Alveolar ridge/Gingiva = 37 Palate = 25 Intraosseous, not specified = 9 Buccal mucosa = 6 Other locations = 21

NHLs may affect basically any location within the oral cavity [14] and this information should be considered by the clinician when performing a biopsy. In our study, the region comprising the alveolar ridge/gingiva was the most affected followed by the palate. In other investigations, the palate seems to be more affected than gingiva and that may be due to the proximity to the Waldeyer's ring [14–17]. The soft tissues are usually more involved than jaws. However, over half of the studies in our review showed intraosseous lesions, whether affecting one or both jaws [7, 14, 18, 19].

Diffuse large B cell lymphoma was the main diagnosis in our study, accounting for 42% of the cases. Interestingly, despite most papers claim that this is the leading diagnosis among oral NHLs, only three articles in our review showed this trend [14, 15, 19]. That may be attributed to the fact that some recent papers are now focusing on more specific subjects or specific histological subtypes in their reviews [20, 21]. In

some cases, the pathology service named the neoplasm with a broader histological subtype, i.e. b cell lymphoma or t cell lymphoma without further subtyping [16, 18]. In other cases, the information regarding the subtype was lacking [7, 8, 22]. Taken together, this may hamper any kind of conclusions about the most prevalent histological types of oral NHLs.

The second most common diagnosis was plasmablastic lymphoma ($n=23$; 24%). Only in ten cases, the information on the patient's clinical record showed a history of HIV infection. Indeed, there are rare cases of plasmablastic lymphoma without relation to HIV and even some cases where lymphoma is the first sign of an underlying infection, unknown by the patient [7, 20, 23]. However, the lack of more detailed information was a problem we faced when conducting this retrospective study. Sometimes, basic information such as age, gender and location of the lesion were missing.

Certainly, another difficulty we found in performing this study was the lack of clinical follow-up. Our pathology service receives biopsy from many regions of our country but the patients diagnosed with oral NHL will be promptly referred to an oncology centre. Therefore, we usually lose their clinical outcome.

In summary, we presented a study with a high number of NHLs restricted to the oral cavity. Since most studies combine oral and extraoral NHLs of the head and neck, we considered the strict criteria for selecting our cases as a differential aspect of our study. Oral NHLs are rare neoplasms, even in specialised pathology services like ours, but clinicians and surgeons should be aware of their occurrence and their most prevalent subtypes. Early recognition of a lymphomatous process would allow a fastest referral to a specialised centre for both a definitive diagnosis and institution of treatment.

Compliance with ethical standards

Conflict of interest The authors state that they have no conflicts of interest.

Ethical approval All the procedures performed in this study involving the patient were in accordance with the ethical standards of the Institutional and/or National Research Committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The approval of the local ethics committee is present in the methods section in this article.

Informed consent For this type of study, formal consent is not required.

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