

# Non-Hodgkin lymphoma of a palate: A case report of a highly destructive lesion

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## Abstract

Non-Hodgkin lymphoma (NHL) is a haematolymphoid neoplasm that can affect nodal and extra-nodal sites. It is a rare disease in the oral cavity, accounting for only 2% of all extra-nodal lymphomas. Its aetiology is multi-factorial, being strongly associated with viral infections. The average age group most affected is 66 years old, with a slight predilection for males. The most common histological sub-type in the oral cavity is diffuse large B-cell lymphoma, with Waldeyer's ring being the most affected site in the nodal form, and extranodally, it may involve the tongue, hard/soft palate, maxilla, and mandible. It presents as a nodular lesion with a smooth or ulcerated surface. The initial treatment approach is chemotherapy, but this may vary according to the stage of lymphoma. The aim of this study was to report a case of NHL in the palate of a 54-year-old female patient, with extensive tissue destruction.

**Keywords:** Diffuse, large B-cell, lymphoma, mouth neoplasms, non-Hodgkin

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## INTRODUCTION

Lymphomas are malignant neoplasms of the lymphocyte cell lines, which account for about 14% of all head and neck malignancies.<sup>[1,2]</sup> Traditionally, lymphomas are divided into two sub-types, Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL), with differences in histology, clinical features, and prognosis.<sup>[1,3]</sup> HL often appears as a nodal disease, and NHL appears as a nodal and extra-nodal disease.<sup>[1,3-5]</sup> Involvement of the oral cavity by NHL is rare; however, despite being rare, lymphoma is the third most common malignancy in this region, followed by squamous cell carcinoma and salivary gland neoplasms.<sup>[1,3,4]</sup>

The aetiology of NHL is multi-factorial, being strongly associated with viral infections.<sup>[4]</sup> The mean age of the affected individuals is 66 years,<sup>[2-4,6]</sup> and there is a slight predilection for the male gender.<sup>[4,7,8]</sup>

NHL consists of more than 40 major sub-types with distinct genetic, morphologic, and clinical features.<sup>[9]</sup> Diffuse large B-cell lymphoma (DLBCL) is the most common in the oral cavity, and Waldeyer's ring is usually pointed out as the main site of NHL occurrence.<sup>[1,2,4,6,8,10]</sup> Oral NHL usually manifests as an enlarging swelling with an intact or ulcerated covering mucosa.<sup>[4]</sup> Radiographically, although this tumour might initially mimic the shape and form of the bone and

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be mis-diagnosed as a peri-apical lesion, the periphery is characteristically ill-defined because of its invasive nature.<sup>[7]</sup> The differential diagnosis may be challenging because of its low incidence and non-specific symptoms, which can mimic inflammatory odontogenic or peri-odontal diseases, leading to mis-diagnosis and/or delayed treatment.<sup>[11]</sup>

The stage of the disease is informative in the choice of NHL therapy, which can be chemotherapy, radiotherapy, stem cell transplantation, or surgical resection.<sup>[4,8,12]</sup>

This study aimed to report a case of NHL in the palate of a 54-year-old female patient, with extensive tissue destruction, leading to bucosinusal communication in a short period of time.

### CASE REPORT

A 54-year-old female came to our clinic with a chief complaint of discomfort in her palate for the past 2 months. Her medical history was remarkable for arthritis with no other systemic disease. The social history was negative for smoking, tobacco, and alcohol use.

Extra-oral examination did not reveal any abnormality. Intra-oral examination showed an enlarging mass in the posterior region of the left palate, with the covering mucosa presenting a central ulcer and dilatation of the superficial capillaries [Figure 1]. The lesion size was approximately 20 mm in diameter, and there was pain on palpation. A cone-beam tomography was requested, and it revealed no bone involvement.

The initial diagnostic hypothesis was mucoepidermoid carcinoma, and an incisional biopsy was indicated. Twelve days later, the patient returned for the biopsy, and a considerable growth of the central ulceration was

observed [Figure 2]. Aiming to relieve her pain, which was stronger at the time, paracetamol with codeine 30 mg was prescribed to be used every 8 hours in the case of pain.

The histopathological examination was inconclusive, suggesting infiltrative atypical cellular proliferation in the connective tissue [Figure 3]. The main diagnostic hypothesis included mucoepidermoid carcinoma, poorly differentiated squamous cell carcinoma, and NHL. Furthermore, immunohistochemical analysis was positive for KI-67; the co-expression of CD45, CD20, BCL-2, and BCL-6, associated to a high proliferative index to KI-67, established the diagnosis of DLBCL [Figure 4].

The patient was referred to the oncology service and subjected to positron emission tomography/computed tomography (PET/CT) for the disease staging. The examination showed a hyper-metabolic lesion in the left soft palate with extension to the hard palate and palatine tonsil. There was also the involvement of the cervical and right axillary lymph nodes and the left sacral bone.

The patient was subjected to six chemoimmunotherapy sessions and returned to our clinic every 15 days for the oral lesion follow-up. She was advised about the importance of maintaining good oral hygiene and received a prescription of chlorhexidine 0, 12% for daily mouthwash. The lesion growth was very fast, causing extensive bone destruction and bucosinusal communication in less than 90 days after the initial examination [Figure 5].

After the chemoimmunotherapy sessions, a new PET/CT was performed, and it showed a reduction in the

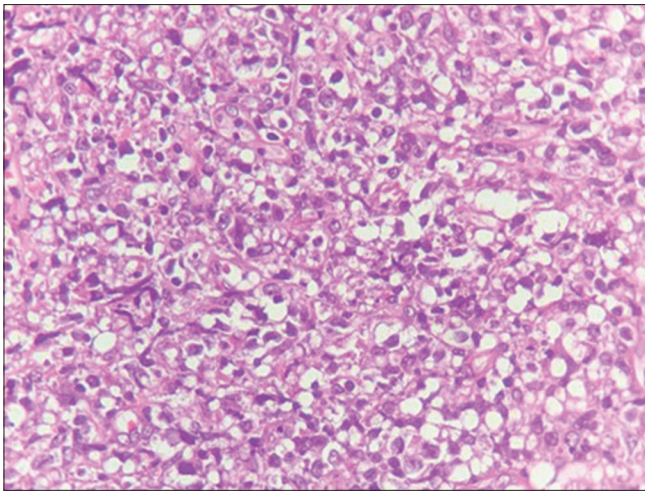


**Figure 1:** Initial intra-oral view, showing an enlarging mass with ulceration on the left posterior palate

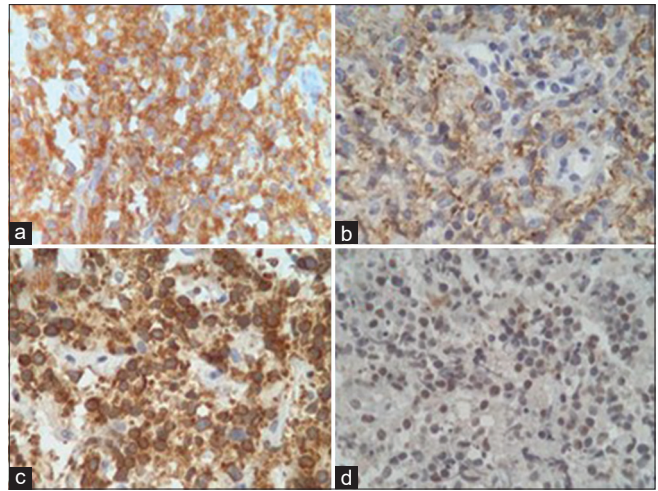


**Figure 2:** Intra-oral view 12 days after the initial examination, showing the growth of the central ulceration





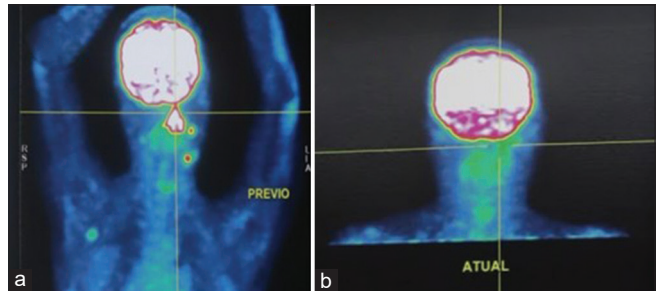
**Figure 3:** Histopathological examination showing infiltrative atypical cellular proliferation in the connective tissue with hematoxylin-eosin (HE) 400x



**Figure 4:** Immunohistochemical analysis showing the co-expression of CD45 (a), CD20 (b), BCL-2 (c), and BCL-6 (d) associated to a high proliferative index to Ki-67 and the negativity for the other markers



**Figure 5:** Intra-oral view 95 days after the initial examination showing extensive bone destruction



**Figure 6:** PET/CT: (a) Initial – expansive lesion in the left soft palate and involvement of cervical lymphnodes and (b) Final – reduction in the dimensions and the metabolism of the soft palate lesion and the cervical lymph nodes

dimensions and the metabolism of the soft palate lesion [Figure 6]. The sacral lesion also presented lower metabolism. The hyper-metabolic cervical, axillary, and inguinal lymph nodes previously described could not be seen anymore.

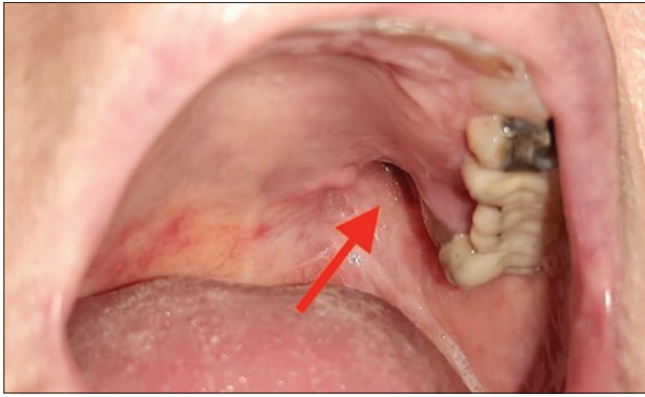
The patient continues to visit the clinic every month. The intra-oral lesion healed; however, the bucosinusal communication causes her a great discomfort [Figure 7]. She still has three chemoimmunotherapy sessions left, but she had not received medical authorization yet for the surgical closure of the bucosinusal communication. A temporary acrylic palatal obturator was inserted to improve the patient's quality of life [Figure 8].

The patient remains in oncological follow-up with no date for its completion.

## DISCUSSION

NHLs encompass a heterogeneous group of cancers, 85–90% of which arise from B lymphocytes; the remainder derive from T lymphocytes or NK lymphocytes.<sup>[12]</sup> Up to 40% of NHLs present at an extra-nodal site, most frequently occurring in the gastrointestinal tract, followed by the head and neck.<sup>[6]</sup> The involvement of the oral cavity seems to be rare, accounting for less than 5% of the extra-nodal lymphomas.<sup>[2,3,10]</sup>

Different aetiologies have been postulated for this tumour, but with no consensus.<sup>[5]</sup> The most well-established risk factor for the development of NHL is immunosuppression, and this is a common lesion in patients with the human immunodeficiency virus (HIV).<sup>[4,12]</sup> Epstein-Barr virus (EBV) infection has been identified in a varying number of cases, being strongly associated with B-cell lymphomas.<sup>[2,4,5,8,9,12]</sup> EBV-positive large B-cell lymphomas in young patients are more often nodal, whereas the preponderance of cases in the elderly has an extra-nodal component.<sup>[1]</sup> Other factors



**Figure 7:** Intra-oral view after the chemoimmunotherapy sessions showing the soft tissue recovering and a bucosinus communication (arrow)

such as host genetics (e.g., family history of haematologic malignancy), immune conditions (e.g., auto-immune and atopic disorders), infection (e.g., Hepatitis C. virus and *Helicobacter pylori*), modifiable risk factors (e.g., body mass index, alcohol consumption, and cigarette smoking), and occupation (e.g., farm or medical workers) play a role in non-Hodgkin lymphomagenesis.<sup>[9]</sup> The patient of the present study, however, was free of the aforementioned diseases.

Extra-nodal NHLs of the oral cavity have been recorded in all age groups; in one study with 58 cases, the patients' ages ranged from 7 to 81 years.<sup>[3]</sup> Ages between the fifth and seventh decades seem to be the most affected.<sup>[2,4,6,10,11]</sup> One study with 98 cases of NHL of the oral cavity found a mean age of 47 years;<sup>[10]</sup> in another series, with 42 and 40 cases, the mean age was higher, 64 and 71 years, respectively.<sup>[6,13]</sup> However, in a study of 45 reported cases of peri-apical lymphoma, the mean age was lower, 41.22 years; most patients (41%) were aged between 40 and 60 years, followed by 36.5% aging 20–40 years.<sup>[7]</sup>

The lymphomas of the oral and maxillofacial regions are more common in males than in females.<sup>[3,4,7]</sup> However, in some studies, no significant sex predilection was observed.<sup>[5,10-13]</sup>

Extra-nodal NHL in the head and neck is most commonly seen in Waldeyer's ring.<sup>[1,3,4,6,10]</sup> When the disease arises in the oral cavity, the maxilla, mandible, soft and hard palate, gingiva, and tongue can be involved.<sup>[11,13]</sup> In a study with 98 oral NHLs, the region comprising the alveolar ridge/gingiva was the most affected, followed by the palate.<sup>[10]</sup> In other investigations, the palate was more affected than the gingiva, and this may be because of the proximity to Waldeyer's ring.<sup>[5,6,13]</sup> The soft tissues are usually more involved than jaws.<sup>[10]</sup> When the jaws are affected, radiographs and/or CT images demonstrate ill-defined radiolucent/hypo-dense images, causing cortical bone expansion and destruction.<sup>[3,5]</sup>



**Figure 8:** Intra-oral view of the temporary acrylic palatal obturator covering the bucosinus communication

This lesion should be ranked in the differential diagnosis of a peri-apical lesion, especially in the case of unexplained numbness or pain without dental cause or unexplained tooth mobility with an irregular-shaped radiolucency, and if the patient has a known malignant disease.<sup>[7]</sup> Oral lymphoma often is a component of a disseminated disease process that may involve regional nodes as well.<sup>[13]</sup>

Most patients with NHL present with persistent painless lymphadenopathy, but some patients also present with constitutional symptoms, specifically drenching night sweats, persistent fevers, and unexplained weight loss;<sup>[8]</sup> in our patient, however, none of these were observed. Clinically, NHL in the oral cavity usually manifests as a symptomatic or asymptomatic enlarging swelling, with an intact or ulcerated covering mucosa.<sup>[4,6]</sup> The intra-oral lesions usually show rapid growth and can affect the underlying bone of the jaws.<sup>[3]</sup> These characteristics were all observed in our patient, especially the extensive and rapid bone destruction. 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 in a study with 98 oral NHLs.<sup>[10]</sup> In other series with 58 and 69 cases of oral NHL, the typical clinical picture of the lesions was an asymptomatic sub-mucosal swelling that gradually increased in size.<sup>[3,5]</sup>

The diagnosis of oral NHL is established by tissue biopsy, and an adequate specimen should be obtained to ensure an accurate diagnosis.<sup>[8]</sup> Histologically, the differential diagnosis of DLBCL includes the undifferentiated carcinomas, sarcomas, plasmacytomas, and malignant melanomas. Therefore, immunohistochemistry is pivotal for a definitive diagnosis.<sup>[4]</sup> DLBCL is negative for epithelial markers, CD3, CD138, myeloperoxidase, desmin, and S100, ruling out the aforementioned lesions included in the histological differential diagnosis.<sup>[4]</sup>



DLBCL constitutes approximately one-third of all NHLs, and it is the most common sub-type in the oral cavity.<sup>[2,8,10]</sup> However, other sub-types of NHL can occur in this region; a study with 58 patients with extra-nodal NHLs of the oral cavity and maxillofacial region found the mucosa-associated lymphoid tissue lymphoma as the most common sub-type, followed by DLBCL.<sup>[3]</sup> In another study, that plasmablastic lymphoma was more common than DLBCL.<sup>[11]</sup>

An accurate diagnosis, careful staging of the disease, and identification of adverse prognostic factors form the basis of treatment selection.<sup>[8]</sup> Pre-treatment PET scans can result in upstaging; however, PET scans are most widely used to assess response to therapy.<sup>[12]</sup> The therapeutic options in lymphomas of the oral and maxillofacial regions include chemotherapy, radiotherapy, and immunotherapy.<sup>[4,5,8]</sup> In the pre-rituximab era, more than a third of patients with this disseminated DLBCL were cured with chemotherapy alone, with most by the CHOP regimen (a combination of cyclophosphamide, doxorubicin, vincristine, and prednisone). The addition of the monoclonal CD 20 antibody rituximab to chemotherapy (R-CHOP) was the most important progress in treatment.<sup>[12]</sup> Actually, R-CHOP is the most used treatment.<sup>[6,8,12]</sup> Other sorts of treatments including the combined use of surgery, radiotherapy, and other chemotherapy approaches are reported.<sup>[5]</sup>

Diffuse large B-cell lymphoma is considered an aggressive yet treatable neoplasm with a variable clinical course.<sup>[13]</sup> The survival of extra-nodal NHL of the head and neck depends on the extent of the disease, the presence or absence of the HIV serology status, histopathology, and Ann Arbor staging.<sup>[11]</sup> In a study with 16 cases of DLBCL, the initial remission rate was 62.5%; however, the mean survival after the first diagnosis was only 17.5 months. The authors pointed that this median survival rate is an unexpectedly bad outcome for a disease with 70% curative potential and may be because of the low number of patients included in the study.<sup>[6]</sup> In another series of 69 cases of oral and oropharyngeal DLBCL, the overall survival rate was 48.9% and 44.4% after 2 and 5 years of follow-up, respectively; the authors stated that these results may be related to the presence of patients in their sample who were not subjected to any treatment because of health care assistance constraints, which may have negatively impacted the survival rates of their sample.<sup>[5]</sup>

## CONCLUSION

Although NHL is rare in the oral cavity, it should always be considered as a possible diagnosis by dentists who see patients with unspecific head and neck swelling. Timely

diagnosis is important for a good prognosis, with effective therapies available for the management of the disease, typically relying on chemoimmunotherapy. Despite the treatment being performed by oncologists, careful evaluations by the dentist at regular intervals are essential to recognize any recurrence or other local developments. Besides this, small interventions can be performed by the dentist to improve the patient's quality of life; in the present case, the manufacture of a palatal obturator significantly contributed to eliminating the discomfort caused by the bucosinusal communication.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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## Conflicts of interest

There are no conflicts of interest.

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