

## Oral manifestations of extranodal lymphomas – a review of the literature with emphasis on clinical implications for the practicing dentist

Malin Höglund Wetter<sup>a</sup> and Ulf Mattsson<sup>a,b</sup>

<sup>a</sup>Clinic of Medical Dentistry, Central Hospital, Karlstad, Sweden; <sup>b</sup>Department of Oral pathology, Faculty of Odontology, Malmö University, Sweden

### ABSTRACT

**Objective:** Lymphoma is a heterogenous group of malignant tumours with proliferation of lymphoid cells or their precursors. Lymphomas in the head and neck region are usually found in Waldeyer's ring. Intraoral lymphomas are rare and the clinical presentation and roentgenological appearance may resemble other and benign conditions, entailing a risk for diagnostic delay. The objective of the present literature review was to identify subjective symptoms, clinical presentations and roentgenological appearances which should raise suspicion of lymphoma.

**Materials and methods:** The literature review identified 41 case series with head and neck lymphomas ( $n=3880$ ) and 384 case reports ( $n=567$  cases) of intraoral lymphomas. Information of demographics, clinical presentation, subjective symptoms and roentgenological appearance was registered.

**Results:** The most common clinical presentation was a broad-based swelling or bulging mass with or without simultaneous ulceration, frequently with a relatively rapid growth pattern. Subjective symptoms varied considerably. Intraosseous lymphomas were frequently associated with paresthesia or numbness. The most common roentgenological finding was a radiolucency with diffuse demarcation.

**Conclusions:** The clinical presentation, symptomatology and roentgenological appearance of intraoral lymphomas varied. Diagnostic delay was usually associated with a lymphoma initially misdiagnosed as a lesion of dental aetiology or a reactive lesion. Inadequate healing after tooth extraction or symptoms of numbness or pain without obvious dental origin should merit further clinical and roentgenological examination. Biopsy is indicated when there is the slightest doubt of the true nature of mucosal lesion.

### ARTICLE HISTORY

Received 2 October 2021  
Revised 1 December 2021  
Accepted 11 December 2021

### KEYWORDS

Biopsy; lymphoma; mouth mucosa; oral manifestation; radiology

### Introduction

Lymphoma represents a heterogenous group of clonal malignant tumours with proliferation of lymphoid cells or their precursors with very varying clinical features, histological characteristics, immunophenotypes and genetic abnormalities [1,2]. Lymphomas are classically divided into Hodgkin's lymphoma (HL) and non-Hodgkin's lymphoma (NHL), where the latter group comprises B-cell, T-cell and NK-cell lymphomas. There are currently some 60 diagnostic forms of lymphomas [3].

Oral manifestations of HL are rare. NHL can present as nodal or extranodal forms. Nodal NHLs presents as multiple and painless lymph nodes in different locations including the head and neck area and many can be encountered as an incidental finding [4]. Despite the fact that oral involvement is rare, NHL is estimated to be the second most common oropharyngeal malignancy after squamous cell carcinoma [5] and may also appear in the oral cavity and encountered by a dentist in clinical practice.

Earlier studies have stated that the knowledge regarding characteristics of non-Hodgkin lymphoma is limited [6] and that symptoms may vary [7–9]. Also, to the best of our knowledge, there are very few studies on the roentgenological appearance of oral lymphoma. A study by Mulligan et al. [10] described primary lymphoma in bone in all parts of the

body. A few studies describe roentgenological appearance in a limited number of cases [2,11,12] but not in sufficient numbers to provide statistics to identify findings pathognomonic of or strongly related to lymphoma.

The literature on extranodal lymphomas in the head and neck is extensive and can broadly be divided into two groups. The first group is case series focussed on anatomical distribution, histopathological classification, treatment and prognosis. The second group is case reports which generally offer more extensive information on the clinical symptoms and/or roentgenological presentation of the lymphoma.

The aims of our literature review were twofold. The first aim was to estimate the frequency and localization of extranodal lymphomas in the head and neck area and how often they affect oral mucosa and maxillary and/or mandibular bone. The second aim was to analyse information from available case series and case reports to obtain information on subjective symptoms, clinical and roentgenological signs which should generate a clinical suspicion of lymphoma.

### Materials and methods

A literature search on PUBMED was performed in December 2020. The search was made with the following profiles:

- 'Lymphoma' AND 'oral' AND 'extranodal' AND 'case report'
- 'Lymphoma' AND 'oral' AND 'case report'
- 'Lymphoma' AND 'oral' AND 'case series'.

The search was limited to articles written in English and published later than 1982.

The definition of a case series was a manuscript including six or more lymphoma cases where the localization of the individual lymphoma and histopathological diagnosis could be registered. A few additional case series were identified through the reference lists of obtained articles.

Inclusion of case reports was limited to articles available online. To be included, the case report should include detailed information of clinical and subjective symptoms, histopathological diagnosis and preferably radiological appearance when the lymphoma affected the maxilla or mandible.

All studies were examined by both authors. Registration of data was done individually but subsequently checked by the other author. When there was discrepancy in registrations, the final registration of data was performed after discussion between the authors.

#### Data extraction from the case series

The search related to the first aim identified 41 case series describing localization and histopathological diagnosis of lymphomas in the head and neck area [2,6–9,11–46]. The following parameters were registered for analysis: Number of lymphoma cases, age, sex, localization of diagnosed lymphoma and histopathological diagnoses.

#### Data extraction from the case reports

A total of 384 case reports ( $n = 472$  cases) which fulfilled the inclusion criteria were identified. A few additional cases were found in reference lists from case reports identified in the PUBMED search. Five of the studies in the case series search [7,8,30,42,43] and 30 of the cases by Bagan et al. [6] included information of localization, size and presence of bone involvement and were also included.

The following parameters were registered for analysis: age, sex, localization of lymphoma, size of lymphoma, singular/multifocal lesion, type and duration of subjective symptoms, factors associated with debut of symptoms/lesion, clinical presentation of lymphoma, bone involvement, tentative diagnosis in referral or during examination process and histopathological diagnosis of confirmed lymphoma. The size of lymphoma, when not given in the text, was estimated from clinical images and registered as the largest visible diameter. If the patient had observed or felt a swelling, nodule or ulceration it was registered both as subjective symptom and as clinical appearance. Information regarding roentgenological appearance was copied verbatim from the case reports. A number of key words for these findings were identified and used for subsequent analyses.

*Statistics:* Mean values and SD for the various parameters were calculated.

## Results

### Results from case series

A total of 3880 cases were described with a slight predominance for men (56.4%). The mean/median age registered was 57.4 years (SD 13.6). A few cases had multiple lesions and a total of 3952 localizations were recorded. The most frequent localization for lymphomas was Waldeyer's tonsillar ring (Table 1). A total of 1124 (28.4%) registered lymphomas were located in the oral cavity (maxilla, mandible, palate, gingiva, tongue/base of tongue, buccal mucosa, vestibulum, floor of the mouth, oral cavity-unspecified, lip, minor salivary glands and alveoli). The most common histopathological diagnosis was diffuse large B-cell lymphoma (DLBCL) representing 1485 (38.3%) of all cases.

### Results from case reports

Three hundred and eighty-four case reports ( $n = 472$  cases) were identified. Together with 95 cases from the case series, a total of 567 cases were analysed. Three hundred and thirty-three were men (mean age 46.2 years, SD 20.7) and 234 women (mean age 54.7 years, SD 20.5).

#### Lymphoma located on gingiva and/or alveolar crest

Three-hundred and twenty-one cases (217 men and 104 women; mean age 45.6 years, SD 20.5) were found. The average time from debut of symptoms to clinical examination was 3.1 months (SD 5.3). The most common subjective symptom was that the patient had noted a swelling/tumour mass or ulceration, but the lesion itself was not necessarily accompanied by pain or major discomfort (Tables 2a and 2b). The

**Table 1.** Localization of lymphomas in the ear nose and throat region as registered in 41 case series with a total of 3880 patients.

Waldeyer's tonsillar ring	1173
Lymph nodes (unspecified)	362
Major salivary glands	343
Palate	294
Maxillary sinus or nasal cavity	282
Maxilla/mandible	271
Gingiva	226
Nasopharynx	163
Tongue/base of tongue	150
Oropharynx	135
Others, unspecified	112
Thyroid gland	110
Buccal mucosa	68
Orbital/conjunctival/lacrimal gland	53
Floor of the mouth	31
Vestibular mucosa	30
Lip	29
Skin/scalp	28
Multiple sites	25
Larynx	24
Minor salivary glands	17
Cavum	10
Hypopharynx	7
Skull	3
Periorbital bone	3
Alveol	2
Muscle	1
Total	3952

Some cases had multiple localizations.

clinical size varied, but the fact that 157 cases (63%) had a largest diameter exceeding 3 cm indicated that the growth rate could be relatively fast. A tentative diagnosis had been given in 167 cases and included a wide variety of both malignant and non-malignant alternatives. Malignancy of any sort was considered as a diagnostic alternative in 66 cases, but lymphoma or lymphoproliferative disease was only specified in 11 cases. Also, as shown in Table 3, a large number of patients were initially treated under a tentative diagnosis of dental origin.

Roentgenological information was described in 224 of the 321 cases. The most common finding in panoramic or intraoral radiographs was a radiolucency with diffuse demarcation, but individual cases were also described as well demarcated. Horizontal bone loss and/or bone loss consistent with or suggestive of marginal periodontitis was described in 22% of

the cases. Displacement or affected dental follicles or teeth were mainly found in patients with advanced lymphomas or Burkitt's lymphoma (BL). Individual cases could also display signs of bone resorption or destruction of bone walls (Table 2b). Computer tomography could in general provide more information regarding possible presence of resorption or destruction of cortical bone suggestive of a malignant lesion (Table 2b).

A total of 42 different lymphoma diagnoses were registered. The five most common were DLBCL ( $n=81$ ), BL ( $n=50$ ), NHL – unspecified ( $n=39$ ), plasmablastic lymphoma (PL) ( $n=32$ ) and extranodal T-cell lymphoma ( $n=16$ ).

### Lymphoma in palatal mucosa

Eighty-seven cases (49 men and 39 women) with a mean age of 56.7 years (SD 20.0) described isolated involvement of the palatal mucosa. The time from debut of symptoms to clinical examination/diagnosis was given in 39 cases with a mean value of 3.2 months (SD 2.9). Subjective symptoms mainly consisted of an awareness of a swelling or ulceration, but the lesions were not necessarily associated with pain, which was only described in 16% of the cases (Table 4a). Several of the symptoms described in Table 4a could likely be attributed to involvement of the nasal cavity or extension into the soft palate. Eight patients had no subjective symptoms at all. The clinical size was given or could be estimated in 62 cases. Twenty-five cases (40%) had a largest diameter exceeding 3 cm, suggesting that lymphoma in the palate can also grow rapidly. A tentative diagnosis was given in 29 cases and the most common were infection/stomatitis or necrotizing sialometaplasia ( $n=13$ ). Squamous cell carcinoma was suspected in three and salivary gland tumour in four cases. A tentative diagnosis of lymphoma was only given in two cases.

Roentgenological and magnetic resonance (MR) examinations were performed in 46 cases. MR was the only examination in four cases. The main findings for the remaining 42 cases are shown in Table 4b. Panoramic X-ray or intraoral radiographs could only in individual cases provide information suggestive of lymphoma or other malignant disease.

**Table 2a.** Frequency and percentage of clinical and subjective symptoms registered in 321 cases diagnosed with lymphoma on gingiva and/or alveolar crest.

Clinical presentation	$n=321$	%
Swelling/bulging mass	212	66.0
Ulcerated bulging mass	88	27.4
Ulceration	20	6.2
Erythema	1	0.3
Subjective symptoms	$n=308$	%
Swelling/tumour mass	273	88.6
Pain	98	31.8
Increased tooth mobility	83	26.9
Sensory disturbance	56	18.2
Tenderness	46	14.9
Ulceration	36	11.7
No symptoms	21	6.8
Fever, night sweats	19	6.2
Difficulties to eat	17	5.5
Bleeding	14	4.5
Fever	8	2.6
Dysphagia	7	2.3
Ill-fitting denture	4	1.3
Nasal congestion	4	1.3
Headache	2	0.6
Difficult to open mouth	2	0.6
Pericoronitis	2	0.6
Halitosis	2	0.6
Running nose	2	0.6
Difficulties to speak	1	0.3

**Table 2b.** Most prevalent roentgenological findings described in 224 case reports of lymphoma in gingiva or on alveolar crest.

#### Panoramic and intraoral x-ray ( $n=185$ )

	Radiolucency-diffuse demarcation	Radiolucency-well demarcated	Horizontal bone loss and/or bone loss consistent with periodontitis	Opacification in sinus	Destruction of bone walls
$N$	89	10	41	10	24
%	48.1	5.4	22.2	5.4	13.0
	Bone resorption of compact bone	Displacement or affected dental follicles or teeth	Abnormal trabecular pattern	Loss of lamina dura	Widening of the periodontal ligament space
$N$	17	24	11	14	16
%	9.2	13.0	5.9	7.6	8.6

#### Computer tomography ( $n=94$ )

	Bone resorption or bony defects	Osteolytic destruction of bone	Soft tissue density lesion with destruction of bone/sinus walls	Soft tissue mass without destruction of bone	Floating teeth
$N$	17	26	44	13	4
%	18.1	27.7	46.8	13.8	4.3

**Table 3.** Tentative diagnoses and treatment given prior to referral in 140 cases subsequently diagnosed with lymphoma.

	Marginal periodontitis	Apical periodontitis	Odontogenic infection-unspecified	Other specified diagnoses <sup>a</sup>
<i>Tentative diagnosis</i>				
Number	31	38	56	15
Men	24	25	37	13
Women	7	13	19	2
Mean age (SD)	43.3 (18.9)	44.3 (18.2)	41.2 (22.8)	36.7 (17.5)
Months from symptom to clinical examination (mean; SD)	3.3 (3.3)	4.7 (5.6)	3.4 (5.8)	2.3 (1.6)
<i>Treatments given before diagnosis of lymphoma</i>				
Extraction of teeth	15	19	41	8
Periodontal treatment	14	0	1	2
Apicectomy	0	5	0	0
Endodontic treatment	0	24	0	0
Antibiotics	10	17	27	9
Other antibacterial treatment	5	2	0	0

<sup>a</sup>The diagnoses included osteomyelitis, pericoronitis, traumatic lesion to the gingiva and influence from fixed prosthetics on mucosal tissue.

**Table 4a.** Clinical and subjective symptoms registered in 87 cases with lymphoma in palatal mucosa.

	<i>n</i>	%
<i>Clinical presentation</i>		
Swelling/tumour mass	37	42.5
Ulcerated tumour mass	49	56.3
Erythema	1	1.2
<i>Subjective symptoms</i>		
No symptoms	8	9.2
Swelling/tumour mass	50	57.5
Ulceration	36	41.4
Pain	14	16.1
Fever, night sweats	16	18.4
Nasal congestion	10	11.5
Dysphagia	8	9.2
Tenderness	7	8.0
Ill-fitting denture	5	5.7
Difficulties to speak	4	4.6
Increased tooth mobility	3	3.4
Difficulties to eat	3	3.4
Running nose	3	3.4
Headache	2	2.3
Difficult to open mouth	2	2.3
Sensory disturbance	1	1.1
Pharyngitis	1	1.1
Nasal speech	1	1.1

The most relevant findings were found with CT, CBCT or MR which could identify osteolytic lesions, bone resorption or destruction of bone/sinus walls.

Twenty-eight different diagnoses were registered. The most frequent were T-cell lymphoma, extranodal NK/T-cell lymphoma, nasal type and T-cell lymphoblastic lymphoma ( $n = 18$ ), DLBCL ( $n = 12$ ), MALT lymphoma ( $n = 8$ ), mycosis fungoides ( $n = 7$ ) and mantle cell lymphoma ( $n = 4$ ).

#### **Lymphoma in maxilla or mandible without visible mucosal lesions**

Twenty cases were found (11 men and nine women; mean age 50.3 years, SD 19.7). Seventeen were located in the mandible. One patient had involvement of both jaws. Information on subjective symptoms was given in 16 cases. The time from debut of symptoms to diagnosis was short (mean 1.0 month, SD 0.7) but was only described for four patients. The most common symptom was paresthesia, which was described in nine out of 16 cases, all of them with lymphoma in the mandible. Other subjective symptoms

included tenderness ( $n = 1$ ), pain ( $n = 2$ ) and increased tooth mobility ( $n = 2$ ). Two patients had no subjective symptoms at time of referral. A tentative diagnosis was given in five cases. Three of them included a malignant condition.

Nine of the 20 cases belonged to the case series and did not include any information on radiology. Roentgenological findings were described in 11 case reports. The clinical size varied considerably. Panoramic and/or intraoral X-ray was performed in six cases and the most common findings were destruction of bone walls ( $n = 4$ ), abnormal trabecular pattern ( $n = 3$ ), well demarked radiolucency ( $n = 2$ ), widening of mandibular canal ( $n = 4$ ) and narrowing of mandibular canal ( $n = 1$ ). Computer tomography was performed in seven cases, showing bone resorption or bone destruction in five cases.

*Histopathological diagnosis:* Eleven different lymphoma diagnoses were registered. The most common was DLBCL ( $n = 6$ ).

#### **Lymphoma on tongue and tongue base**

Thirty-eight cases (21 men and 17 women; mean age 57.0, SD 19.6) described lymphoma on the tongue ( $n = 29$ ) or tongue base ( $n = 9$ ). The mean time from debut of symptoms to clinical examination was given in 22 cases with a mean value of 6.6 months (SD 10.5). The clinical size varied between 1 and 6 cm in diameter.

The clinical presentations on the lateral border of the tongue varied. Thirteen lymphomas presented with ulceration and 15 with an expansive growth. One lesion was located on the dorsum of the tongue. Five cases reported pain and dysphagia. Tentative diagnoses were offered in nine cases and four were suggestive of malignancy or paraneoplastic lesion. None of them specified lymphoma. The two most common lymphoma diagnoses were mycosis fungoides ( $n = 9$ ) and extranodal T cell lymphoma ( $n = 5$ ).

Information of symptoms associated with lymphomas located on the tongue base ( $n = 9$ ) were only given in five cases. Three patients reported pain and one patient dysphagia. One patient had no subjective symptoms. Tentative diagnoses were only given for three patients and two suggested lymphoma.

Four cases were diagnosed as DLBCL, two as MALT lymphoma, and one case as non-Hodgkin-unspecified, PL and T-cell non-Hodgkin, respectively.

**Table 4b.** Roentgenological findings in 42 patients with lymphoma in palatal mucosa.

<i>Ortopanorhograms and intraoral x-ray (n = 12)</i>				
	No radiological findings	Radiolucency-diffuse demarcation	Radiolucency-well demarcated	Mixed radioopaque and radiolucent lesion
N	8	3	1	1
%	66.7	25.0	8.3	8.3
	Bone resorption of compact bone	Horizontal bone loss and/or bone loss consistent with periodontitis	Opacification in sinus	Destruction of bone walls
N	1	3	4	2
%	8.3	25.0	33.3	16.7
<i>Computer tomography (n = 30)</i>				
	Bone resorption or bony defects	Osteolytic destruction of bone	Soft tissue density lesion with destruction of bone/sinus walls	Soft tissue mass without destruction of bone
N	3	3	11	6
%	10.0	10.0	36.7	20.0

Four patients were evaluated with panoramic, intraoral radiographs and computer tomography.

**Table 5.** Data on lymphoma in buccal mucosa, floor of the mouth, lip and major salivary glands.

	Bucca	Floor of mouth	Lip	Major salivary glands <sup>a</sup>
Number	22	15	29	23
Men	8	5	10	8
Women	14	10	19	15
Mean age (SD)	59.6 (18.8)	68.1 (9.7)	47.2 (25.9)	51.6 (23.8)
Size registered/estimated (n)	17	11	27	15
<3 cm in diameter	10	4	20	8
>3 cm in diameter	7	7	7	7
Cases with registered clinical symptoms	22	12	28	23
Months from debut of symptoms to clinical examination	7.2 (8.5)	4.5 (7.6)	3.4 (2.4)	3.9 (5.0)
<i>Most common symptoms</i>				
Swelling/nodule	22	12	25	23
Ulceration			4	
Tenderness			1	4
Paresthaesia	2		2	
Pain	1	1	3	3
<i>Most frequent histopathological diagnosis</i>				
MALT lymphoma	7	6	14	5
Non-Hodgkin – unspecified	5	1	0	0
Diffuse large B-cell lymphoma	2	0	3	3
Mantle cell lymphoma	0	2	0	3
Extranodal T-cell lymphoma	0	0	2	1
Burkitt's lymphoma	1	0	0	3

<sup>a</sup>Nineteen out of 23 were localized in the submandibular gland.

### **Lymphoma in the buccal mucosa, lip, floor of the mouth and major salivary glands**

Data regarding lymphoma in these locations are summarized in Table 5. They were seldom associated with any pronounced subjective symptoms apart from the swelling or nodule itself. Differential diagnoses apart from suspicion of another tumour than lymphoma, were rare. Three cases of lymphoma in the lower lip and one case in the upper lip were tentatively diagnosed as mucocele.

### **Histopathological diagnoses**

A total of 44 different histopathological diagnoses of lymphoma were registered for the entire material. The most frequent were DLBCL ( $n = 119$ ), BL ( $n = 57$ ), MALT lymphoma ( $n = 46$ ), extranodal T cell or NK/T-cell lymphoma ( $n = 43$ )

and PL ( $n = 42$ ). Fifty-six cases were diagnosed as non-Hodgkin lymphoma – unspecified.

### **Diffuse large B-cell lymphoma**

DLBCL was diagnosed in 119 cases (68 men and 51 women; mean age 51.9 years, SD 19.1). The most common location was gingiva/alveolar crest ( $n = 85$ ) but DLBCL was found in all regions of the oral cavity.

### **Burkitt's lymphoma**

A separate analysis was made for the 57 cases (41 men and 16 women) of BL since the clinical course was frequently different from other lymphoma diagnoses. The mean age for BL was considerably lower (24.3 years, SD 17.8) and 28 of the cases were under 18 years. Also, the time from debut of symptoms to clinical examination was relatively short

**Table 6.** Roentgenological findings registered in 46 patients with Burkitt's lymphoma.*Panoramic and intraoral X-ray (n = 46)*

	Radiolucency–diffuse demarcation	Horizontal bone loss and/or bone loss consistent with periodontitis	Opacification in sinus	Destruction of bone walls	Bone resorption of compact bone	Floating teeth
N	22	11	3	9	5	2
%	47.8	23.9	6.5	19.6	10.9	4.3
	Displacement or affected dental follicles or teeth	Abnormal trabecular pattern	Loss of lamina dura	Widening of the periodontal ligament space	Displacement of teeth	Root resorption
N	6	5	11	6	11	5
%	13.0	10.9	23.9	13.0	23.9	10.9
<i>Computer tomography (n = 19)</i>						
	Bone resorption or bony defects	Osteolytic destruction of bone	Soft tissue density lesion with destruction of bone/sinus walls	Soft tissue mass without destruction of bone		
N	2	6	7	5		
%	10.5	31.6	36.8	26.3		

(2.2 months, SD 2.4) and with a more rapid growth pattern since 64% had a diameter over 3 cm. This pattern was even more pronounced in patients under 18 years where the corresponding time was 1.0 month (SD 0.7) and 70% were larger than 3 cm.

Localizations varied, but 50 out of 57 cases affected gingiva/alveolar crest, either as a swelling/bulging mass ( $n = 35$ ) or as an ulcerated bulging lesion ( $n = 15$ ). Other localizations were palate ( $n = 3$ ), bucca ( $n = 6$ ) and floor of the mouth ( $n = 4$ ). Thus, a few cases had multiple localizations. Roentgenological examinations with panoramic/intraoral X-ray and CT were performed in 46 cases. Pathological findings were frequent and are summarized in Table 6.

### Plasmablastic lymphoma

Plasmablastic lymphoma is a subgroup of DLBCL and was diagnosed in 42 of the case reports (34 men and eight women) with a mean age of 41.7 years (SD 13.8). The time from debut of symptoms to examination or diagnosis was relatively short (2.7 months, SD 2.6) and the tumour size was frequently large, with 69% of the cases larger than 3 cm in diameter. Plasmablastic lymphoma is frequently associated with HIV infection and 33 patients (26 men) were HIV-positive, but PL was also diagnosed in patients without a disease associated with immune deficiency. Thirty-one of the cases affected gingiva/alveolar crest and the clinical appearances varied. The most frequent clinical presentation was a convex swelling/bulging mass ( $n = 20$ ) or an ulcerated bulging mass ( $n = 11$ ). PL was also found in the palate ( $n = 6$ ), bucca ( $n = 3$ ) and floor of the mouth ( $n = 2$ ).

### Differential diagnosis and diagnostic delay

A frequent finding was lack of adequate response to given treatment, necessitating further examination which subsequently gave the correct diagnosis, but also with a certain delay. The results showed that 140 cases had prior to referral been treated under a tentative diagnosis of marginal or apical periodontitis, unspecified odontogenic infection or for

specified diagnoses such as pericoronitis, osteomyelitis, fracture or a traumatic lesion to gingiva. The results are summarized in Table 3.

### Discussion

Lymphoma is a relatively common malignancy accounting for 3.37% of all cancer cases worldwide, but with a substantial geographic variation. North America has an age-standardized incidence rate for all lymphomas of 16.1/100,000, where the corresponding figures for Europe, Japan and China are 11.1, 5.5 and 2.5, respectively. Non-Hodgkins lymphoma is mainly diagnosed in the sixth to seventh decade with a slight male predominance. The epidemiology of lymphoma is complex due to the great number of subtypes with unique biology, and their complex relationship with infection, immunological abnormality and genetic predisposition [47].

The first aim of our study was to estimate how frequent lymphoma are in the oral cavity and to put it into the clinical situation of the practicing dentist. A recent multicentre study by Dhanuthai et al. [48] showed that lymphoma represented 3.89% of all oral cancers. The following picture emerges if available data are put into a national perspective. Sweden has a population of approximately 10.3 million. According to the report from the Swedish National Quality Register for Lymphoma, 2212 patients were in 2016 diagnosed with this disease. Only 0.9% of extranodal lymphomas were located in the oral cavity and 0.8% in salivary glands, suggesting that intraoral manifestations of lymphoma amount to only 35–50 cases annually. The case series (Table 1) have focussed on lymphoma in the head and neck area and therefore only evaluate a portion of all diagnosed lymphomas in the population. Only 28.3% of 3880 registered lymphomas were located in the oral cavity and minor salivary glands, adding information that intraoral involvement is rare. Sweden has some 8000 practicing dentists. There is no available information of how many of annually diagnosed intraoral lymphomas which were initially seen by a dentist. Our interpretation

of existing information is that a general practitioner will most likely encounter, if any, no more than a single case during a professional career, a fact possibly entailing a risk for delayed diagnosis if the observed lesion is tentatively diagnosed as another and benign condition.

The second aim is a consequence of the first aim, to identify subjective, clinical and roentgenological findings which should raise suspicion of lymphoma, since several of the case reports noted a risk of diagnostic delay. It must be emphasized that the quality and amount of information given in the individual case reports varied between studies. Based on our inclusion criteria, a few identified case reports with very limited clinical information were therefore excluded. As can be seen in Tables 2a and 4a, clinical and subjective symptoms from intraoral lymphoma were varied. The most common symptom noted by the patient was a swelling or an ulceration, but the lesions were seldom accompanied by pain or discomfort, indicating that intraoral lymphoma do not necessarily cause any major symptoms. However, the fact that subjective symptoms may not have been presented in a case report does not mean that they did not exist, with the consequence that the prevalence of various subjective symptoms may be higher. But, it is our opinion that the large number of cases included in this report allows us to make some general conclusions regarding the symptomatology of intraoral lymphomas, but also that obtained percentages must be taken with caution.

From an overall perspective, there are medical conditions associated with increased risk of lymphoma. Fifty-seven cases described BL, which is a rare diagnosis in the population compared to DLBCL. BL is associated with endemic malaria, but also to Epstein Barr virus (EBV) and immunosuppression in AIDS. BL is a highly aggressive form of NHL which frequently affects the oral cavity with pronounced clinical findings such as an intraosseous mass, mobile or displaced teeth, intraoral swellings, trismus, jaw deviation, gingival swellings and ulcerations [49–51]. The majority of the cases with PL were associated with HIV, but PL can also be found in HIV-negative patients [52] with the oral cavity being the most common primary involved site [53]. Another risk factor for development of lymphoma is autoimmune disease or immunosuppression following solid organ transplantation [54,55]. Patients with Sjögren's syndrome have a 7.5% risk of developing lymphoma (mainly MALT type lymphoma) during the course of disease [56], and there are several other autoimmune diseases related to B or T cell responses which have an increased risk for development of lymphoma [57,58]. Consequently, presence of immunosuppression or autoimmune disease is an anamnestic finding which should be a cautionary factor when observing mucosal lesions of unclear origin with clinical features compatible with or suggestive of lymphoma.

The clinical presentation is important but varied considerably depending on location. Bulging lesions in the palate with or without ulceration (Table 4a) should clinically be regarded with caution and may also represent salivary gland tumours or squamous cell carcinoma. We advocate computer

tomography since it frequently showed pathology when panoramic and intraoral X-ray did not (Table 4b).

The perhaps most important aim of this study was to identify the risk for diagnostic delay. Diagnostic delay was described in many case reports and the results from our literature review correspond with the results described by Soderholm et al. [8] where the mean time from observation to referral was 2.8 months (range 0–8). Lymphomas in minor salivary glands, buccal mucosa, floor of the mouth and lip were obviously not interpreted as a lesion with possible odontogenic origin, but the time from observation to diagnosis of lymphoma was still several months (Table 5).

The diagnostic challenge for the dentist was, based on information in the case reports, mostly related to lymphomas in gingiva/alveolar crest or maxilla/mandible. The clinical presentations were frequently described as a broad-based swelling or bulging mass/ulcerated bulging mass, often with a rather rapid growth and considerable size at time of diagnosis. A common tentative diagnosis in the case reports was a reactive lesion, which is tumour-like hyperplasia associated with chronic local irritation or trauma. The gingiva is the most common location for reactive lesions (irritation hyperplasia, peripheral giant cell granuloma, pyogenic granuloma and cemento-ossifying fibroma), but they can also be found in other parts of the oral cavity [59,60]. The clinical appearance of reactive lesions is usually different from the descriptions given for intraoral lymphoma and present as clinically elevated, well circumscribed, often pedunculated lesions with a smooth or sometimes ulcerated appearance depending on the kind of reactive lesion [61]. They may vary in size but are usually only slightly larger than 1 cm [60] and therefore seldom reach the size of lymphomas described in the case reports. Clinical description of a lymphoma with a pedunculated lesion was extremely rare and only described in a single case [62]. Also, lymphomas located on gingiva frequently affected the underlying bone (Table 2b), which is in accordance with results by Bagan et al. [6]. Although there were individual cases where the initial biopsy only revealed a reactive lesion [63,64], a biopsy can most likely enable a correct diagnosis [60] and should be performed when there is any doubt on the nature of the lesion, not only to differentiate from lymphoma but also from other malignant diagnoses.

One common factor for misinterpretation and diagnostic delay was absence of effect from performed therapy, where the observed lesion was initially regarded as an infection (Table 3). Given the fact that oral manifestations of lymphoma are rare, it is not surprising that a lesion may be misinterpreted as a far more common diagnosis. The question is therefore if there are specific symptoms or clinical findings which should raise caution. One such finding from our review is lack of healing after tooth extraction which was described in 76 cases. Our conclusion corresponds with a systematic review by MacDonald and Lim [65] which described lymphoma arising in extraction alveolus. The authors concluded that the majority of case reports included a tentative diagnosis, where the most frequent was a dental infection followed by squamous cell carcinoma.

A number of cases showed clinical and roentgenological signs initially compatible with marginal periodontitis (Table 3) but later developed bulging [66,67] or ulcerated lesions [68,69] which promoted referral, or had roentgenological findings [70–73] suggesting another diagnosis.

Thirty-nine cases had a tentative diagnosis of apical periodontitis. However, several of the case reports described clinical and/or roentgenological symptoms which may raise suspicion of a non-endodontic aetiology. Six cases described paresthesia [74–79] which is a relatively uncommon finding in lesions of endodontic aetiology. Other authors emphasized that a positive sensitivity test, in combination with ill-defined radiolucencies should raise suspicion of lymphoma [80–82]. Also, a clinical presentation with non-tender painless swellings with roentgenological findings not immediately consistent with endodontic aetiology should be a warning signal [77,78,82–84]. A recent review by Mortazavi et al. [4] focussed on periapical lymphoma and concluded that 49% of the cases had been misdiagnosed as pulpal pathology and the average time lapse to correct diagnosis was 4.3 months. They emphasized that a positive pulp test should suggest a tentative diagnosis of lymphoma. They also stated that unexplained numbness or pain without obvious dental cause, unexplained tooth mobility and radiolucency with irregular borders should raise suspicion of lymphoma. We agree with this, but also suggest that CBCT is a valuable roentgenological examination in cases with numbness and pain since panoramic X-ray does not always reveal any obvious pathology.

The examination of the patients frequently included a roentgenological examination. The roentgenological findings were copied verbatim from the case reports and then analysed according to a set of keywords/criteria created by the authors. This procedure entails a possible bias or confounding factor in the analyses. With this in mind, we still think it is justified to conclude that the roentgenological appearance in lymphomas affecting maxilla and mandible is varied, with several different findings not necessarily pathognomonic for lymphoma. The most prevalent observation in panoramic or intraoral X-ray was a radiolucency with diffuse demarcation, but 10 lesions were described as well demarcated by the authors (Table 2b). There were also cases where the roentgenological appearance resembled horizontal bone loss consistent or comparable with marginal periodontitis. Computer tomography or cone beam computed tomography (CBCT) was frequently found to give valuable additional information, especially to identify resorption or destruction of cortical bone or bone walls, suggesting a malignant diagnosis. Consequently, roentgenological examination is of great value in the examination, and findings may raise suspicion of a non-odontogenic condition including lymphoma. But, there are in our opinion no roentgenological findings found exclusively in oral lymphoma and other diagnoses must be also considered.

## Conclusions

Intraoral manifestations of extranodal lymphoma are rare, which entails a possible risk for delayed diagnosis, especially

in lymphomas located in gingiva or alveolar crest. The clinical appearance may vary depending on location, but usually presents as a swelling or bulging mass with or without ulceration and with no apparent abscess. The growth is usually rather rapid. Subjective symptoms like pain or discomfort are most common in lesions located on gingiva/alveolar crest or palate, but many lymphomas do not generate major symptoms.

Clinical findings such as inadequate healing after tooth extraction or lack of effect from antibiotic treatment should raise concern of a non-odontogenic lesion. Symptoms of paresthesia, numbness or pain without obvious odontogenic origin should also merit further clinical and roentgenological examination, especially in cases where the roentgenological appearance is not consistent with an apical or marginal periodontitis. Computer tomography may provide more valuable information than panoramic or intraoral X-ray. We strongly advocate biopsy when there is the slightest doubt of the true nature of mucosal lesion.

## Disclosure statement

No potential conflict of interest was reported by the author(s).

## References

- [1] Mawardi H, Cutler C, Treister N. Medical management update: non-Hodgkin lymphoma. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2009;107(1):e19–e33.
- [2] van der Waal RI, Huijgens PC, van der Valk P, et al. Characteristics of 40 primary extranodal non-Hodgkin lymphomas of the oral cavity in perspective of the new WHO Classification and the International Prognostic Index. *Int J Oral Maxillofac Surg.* 2005; 34(4):391–395.
- [3] Swerdlow SH, Campo E, Pileri SA, et al. The 2016 revision of the world Health Organization Classification of Lymphoid Neoplasms. *Blood.* 2016;127(20):2375–2390.
- [4] Mortazavi H, Baharvan M, Rezaeifar K. Periapical lymphoma: review of reported cases in the literature. *J Stomatol Oral Maxillofac Surg.* 2020;121(4):404–407.
- [5] DePena CA, Van Tassel P, Lee YY. Lymphoma of the head and neck. *Radiol Clin North Am.* 1990;28(4):723–743.
- [6] Bagan JV, Carbonell F, Gomez MJ, et al. Extra-nodal B-cell non-Hodgkin's lymphomas of the head and neck: a study of 68 cases. *Am J Otolaryngol.* 2015;36(1):57–62.
- [7] Howell RE, Handlers JP, Abrams AM, et al. Extranodal oral lymphoma. Part II. Relationships between clinical features and the Lukes-Collins classification of 34 cases. *Oral Surg Oral Med Oral Pathol.* 1987;64(5):597–602.
- [8] Soderholm AL, Lindqvist C, Heikinheimo K, et al. Non-Hodgkin's lymphomas presenting through oral symptoms. *Int J Oral Maxillofac Surg.* 1990;19(3):131–134.
- [9] Shima N, Kobashi Y, Tsutsui K, et al. Extranodal non-Hodgkin's lymphoma of the head and neck. A clinicopathologic study in the Kyoto-Nara area of Japan. *Cancer.* 1990;66(6):1190–1197.
- [10] Mulligan ME, McRae GA, Murphey MD. Imaging features of primary lymphoma of bone. *AJR Am J Roentgenol.* 1999;173(6): 1691–1697.
- [11] Kemp S, Gallagher G, Kabani S, et al. Oral non-Hodgkin's lymphoma: review of the literature and World Health Organization Classification with reference to 40 cases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2008;105(2):194–201.
- [12] Kolokotronis A, Konstantinou N, Christakis I, et al. Localized B-cell non-Hodgkin's lymphoma of oral cavity and maxillofacial region:

- a clinical study. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2005;99(3):303–310.
- [13] Horiuchi J, Okuyama T, Matsubara S, et al. Extranodal non-Hodgkin's lymphoma in the head and neck. Irradiation and clinical course. *Acta Radiol Oncol.* 1982;21(6):393–399.
- [14] Eisenbud L, Sciubba J, Mir R, et al. Oral presentations in non-Hodgkin's lymphoma: a review of thirty-one cases. Part I. Data analysis. *Oral Surg Oral Med Oral Pathol.* 1983;56(2):151–156.
- [15] Takahashi H, Tsuda N, Tezuka F, et al. Primary extranodal non-Hodgkin's lymphoma of the oral region. *J Oral Pathol Med.* 1989; 18(2):84–91.
- [16] Wolvius EB, van der Valk P, van der Wal JE, et al. Primary extranodal non-Hodgkin lymphoma of the oral cavity. An analysis of 34 cases. *Eur J Cancer B Oral Oncol.* 1994;30B(2):121–125.
- [17] Shindoh M, Takami T, Arisue M, et al. Comparison between submucosal (extra-nodal) and nodal non-Hodgkin's lymphoma (NHL) in the oral and maxillofacial region. *J Oral Pathol Med.* 1997; 26(6):283–289.
- [18] Epstein JB, Epstein JD, Le ND, et al. Characteristics of oral and paraoral malignant lymphoma: a population-based review of 361 cases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2001; 92(5):519–525.
- [19] Jaehne M, Ussmuller J, Jakel KT, et al. The clinical presentation of non-Hodgkin lymphomas of the major salivary glands. *Acta Otolaryngol.* 2001;121(5):647–651.
- [20] Hart S, Horsman JM, Radstone CR, et al. Localised extranodal lymphoma of the head and neck: the Sheffield Lymphoma Group Experience (1971–2000). *Clin Oncol (R Coll Radiol).* 2004;16(3): 186–192.
- [21] Frata P, Buglione M, Grisanti S, et al. Localized extranodal lymphoma of the head and neck: retrospective analysis of a series of 107 patients from a single institution. *Tumori.* 2005;91(6): 456–462.
- [22] Otmami N, Khattab M. Oral Burkitt's lymphoma in children: the Moroccan experience. *Int J Oral Maxillofac Surg.* 2008;37(1):36–40.
- [23] Etemad-Moghadam S, Tirgary F, Keshavarz S, et al. Head and neck non-Hodgkin's lymphoma: a 20-year demographic study of 381 cases. *Int J Oral Maxillofac Surg.* 2010;39(9):869–872.
- [24] Corti M, Villafane MF, Solari R, et al. Non-Hodgkin lymphomas of the oral cavity in AIDS patients in a reference hospital of infectious diseases in Argentina: report of eleven cases and review of the literature. *J Gastrointest Cancer.* 2011;42(3):143–148.
- [25] Chi HS, Lee KW, Chiang FY, et al. Head and neck extranodal lymphoma in a single institute: a 17-year retrospective analysis. *Kaohsiung J Med Sci.* 2012;28(8):435–441.
- [26] Iguchi H, Wada T, Matsushita N, et al. Anatomic distribution of hematolymphoid malignancies in the head and neck: 7 years of experience with 122 patients in a single institution. *Acta Otolaryngol.* 2012;132(11):1224–1231.
- [27] Scherfler S, Freier K, Seeberger R, et al. Cranio-maxillofacial non-Hodgkin's lymphoma: clinical and histological presentation. *J Craniomaxillofac Surg.* 2012;40(7):e211–e213.
- [28] Triantafyllidou K, Dimitrakopoulos J, Iordanidis F, et al. Extranodal non-Hodgkin lymphomas of the oral cavity and maxillofacial region: a clinical study of 58 cases and review of the literature. *J Oral Maxillofac Surg.* 2012;70(12):2776–2785.
- [29] Mian M, Capello D, Ventre MB, et al. Early-stage diffuse large B cell lymphoma of the head and neck: clinico-biological characterization and 18 year follow-up of 488 patients (IELSG 23 study). *Ann Hematol.* 2014;93(2):221–231.
- [30] Cozzolino I, Vigliar E, Todaro P, et al. Fine needle aspiration cytology of lymphoproliferative lesions of the oral cavity. *Cytopathology.* 2014;25(4):241–249.
- [31] Owosho AA, Bilodeau EA, Surti U, et al. Large B-cell lymphoma of the base of the tongue and oral cavity: a practical approach to identifying prognostically important subtypes. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2014;118(3):338–347.
- [32] Ramanathan A, Mahmoud HA, Hui LP, et al. Oral extranodal non-Hodgkin's lymphoma: series of forty two cases in Malaysia. *Asian Pac J Cancer Prev.* 2014;15(4):1633–1637.
- [33] Sirsath NT, Lakshmaiah KC, Das U, et al. Primary extranodal non-Hodgkin's lymphoma of oral cavity—a single centre retrospective study. *J Cancer Res Ther.* 2014;10(4):945–950.
- [34] Akbari ME, Bastani Z, Mokhtari S, et al. Oral lymphoma prevalence in Iranian population: a multicenter retrospective study. *Iran J Cancer Prev.* 2015;8(6):e4124.
- [35] Picard A, Cardinne C, Denoux Y, et al. Extranodal lymphoma of the head and neck: a 67-case series. *Eur Ann Otorhinolaryngol Head Neck Dis.* 2015;132(2):71–75.
- [36] Takano S, Matsushita N, Oishi M, et al. Site-specific analysis of B-cell non-Hodgkin's lymphomas of the head and neck: a retrospective 10-year observation. *Acta Otolaryngol.* 2015;135(11): 1168–1171.
- [37] Walter C, Ziebart T, Sagheb K, et al. Malignant lymphomas in the head and neck region—a retrospective, single-center study over 41 years. *Int J Med Sci.* 2015;12(2):141–145.
- [38] Anacak Y, Miller RC, Constantinou N, et al. Primary mucosa-associated lymphoid tissue lymphoma of the salivary glands: a multicenter rare cancer network study. *Int J Radiat Oncol Biol Phys.* 2012;82(1):315–320.
- [39] Guggisberg K, Jordan RC. Mantle cell lymphoma of the oral cavity: case series and comprehensive review of the literature. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2010;109(1): 98–104.
- [40] Nathu RM, Mendenhall NP, Almasri NM, et al. Non-Hodgkin's lymphoma of the head and neck: a 30-year experience at the University of Florida. *Head Neck.* 1999;21(3):247–254.
- [41] Ratech H, Burke JS, Blayney DW, et al. A clinicopathologic study of malignant lymphomas of the nose, paranasal sinuses, and hard palate, including cases of lethal midline granuloma. *Cancer.* 1989;64(12):2525–2531.
- [42] Kaplan I, Shuster A, Frenkel G, et al. Non-Hodgkin lymphoma of the lips: a rare entity. *Acta Histochem.* 2019;121(8):151449.
- [43] Sirosis DA, Miller AS, Harwick RD, et al. Oral manifestations of cutaneous T-cell lymphoma. A report of eight cases. *Oral Surg Oral Med Oral Pathol.* 1993;75(6):700–705.
- [44] Hanna E, Wanamaker J, Adelstein D, et al. Extranodal lymphomas of the head and neck. A 20-year experience. *Arch Otolaryngol Head Neck Surg.* 1997;123(12):1318–1323.
- [45] de Arruda JAA, Schuch LF, Conte Neto N, et al. Oral and oropharyngeal lymphomas: a multi-institutional collaborative study. *J Oral Pathol Med.* 2021;50(6):603–612.
- [46] Tseng CH, Wang WC, Chen CY, et al. Clinical manifestations of oral lymphomas – retrospective study of 15 cases in a Taiwanese population and a review of 592 cases from the literature. *J Formos Med Assoc.* 2021;120(1 Pt 2):361–370.
- [47] Huh J. Epidemiologic overview of malignant lymphoma. *Korean J Hematol.* 2012;47(2):92–104.
- [48] Dhanuthai K, Rojanawatsirivej S, Thosaporn W, et al. Oral cancer: a multicenter study. *Med Oral Patol Oral Cir Bucal.* 2018;23(1): e23–e29.
- [49] Mlotha J, Naidoo S. Oro-facial manifestations of Burkitt's lymphoma: an analysis of 680 cases from Malawi. *SADJ.* 2011;66(2): 77–79.
- [50] Rodrigues-Fernandes CI, de Souza LL, Santos-Costa SFD, et al. Clinicopathological analysis of oral plasmablastic lymphoma: a systematic review. *J Oral Pathol Med.* 2018;47(10):915–922.
- [51] Fonseca FP, Robinson L, van Heerden MB, et al. Oral plasmablastic lymphoma: a clinicopathological study of 113 cases. *J Oral Pathol Med.* 2021;50(6):594–602.
- [52] Castillo JJ, Reagan JL. Plasmablastic lymphoma: a systematic review. *ScientificWorldJournal.* 2011;11:687–696.
- [53] Tchernonog E, Faurie P, Coppo P, et al. Clinical characteristics and prognostic factors of plasmablastic lymphoma patients: analysis of 135 patients from the LYSA group. *Ann Oncol.* 2017;28(4): 843–848.
- [54] Ojha J, Islam N, Cohen DM, et al. Post-transplant lymphoproliferative disorders of oral cavity. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2008;105(5):589–596.

- [55] Taylor AL, Marcus R, Bradley JA. Post-transplant lymphoproliferative disorders (PTLD) after solid organ transplantation. *Crit Rev Oncol Hematol*. 2005;56(1):155–167.
- [56] Delli K, Villa A, Farah CS, et al. World Workshop on Oral Medicine VII: biomarkers predicting lymphoma in the salivary glands of patients with Sjögren's syndrome—a systematic review. *Oral Dis*. 2019;25 Suppl.1:49–63.
- [57] Khanmohammadi S, Shabani M, Tabary M, et al. Lymphoma in the setting of autoimmune diseases: a review of association and mechanisms. *Crit Rev Oncol Hematol*. 2020;150:102945.
- [58] Herber M, Mertz P, Dieudonne Y, et al. Primary immunodeficiencies and lymphoma: a systematic review of literature. *Leuk Lymphoma*. 2020;61(2):274–284.
- [59] Naderi NJ, Eshghyar N, Esfehanian H. Reactive lesions of the oral cavity: a retrospective study on 2068 cases. *Dent Res J*. 2012;9: 251–255.
- [60] Zhang W, Chen Y, An Z, et al. Reactive gingival lesions: a retrospective study of 2,439 cases. *Quintessence Int*. 2007;38:103–110.
- [61] Kfir Y, Buchner A, Hansen LS. Reactive lesions of the gingiva. A clinicopathological study of 741 cases. *J Periodontol*. 1980;51(11): 655–661.
- [62] Ajila V, Gopakumar R, Hegde S, et al. Intraoral Burkitt's lymphoma in an HIV positive patient. *Indian J Sex Transm Dis Aids*. 2012; 33(2):118–120.
- [63] Eisenbud L, Sciubba J, Mir R, et al. Oral presentations in non-Hodgkin's lymphoma: a review of thirty-one cases. Part II. Fourteen cases arising in bone. *Oral Surg Oral Med Oral Pathol*. 1984;57(3):272–280.
- [64] Keyes GG, Balaban FS, Lattanzi DA. Periradicular lymphoma: differentiation from inflammation. *Oral Surg Oral Med Oral Pathol*. 1988;66(2):230–235.
- [65] MacDonald D, Lim S. Extranodal lymphoma arising within the maxillary alveolus: a systematic review. *Oral Radiol*. 2018;34(2): 113–126.
- [66] Matsumoto N, Ohki H, Mukae S, et al. Anaplastic large cell lymphoma in gingiva: case report and literature review. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2008;106(4):e29–e34.
- [67] Theofilou VI, Katsoulas N, Tosios KI, et al. Richter transformation in the oral and maxillofacial area: report of 2 cases and literature review. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2021;131(1): e14–e20.
- [68] Groot RH, van Merkesteyn JP, Bras J. Oral manifestations of non-Hodgkin's lymphoma in HIV-infected patients. *Int J Oral Maxillofac Surg*. 1990;19(4):194–196.
- [69] Donkor P, Punnia-Moorthy A, Painter DM. A case of AIDS presenting as intra-oral malignant lymphoma. *Aust Dent J*. 1991;36(1): 22–28.
- [70] Nittayananta W, Apinawatavorngul S, Chungpanich S, et al. Burkitt-like lymphoma presenting as a periodontal disease in AIDS patients: a report of two cases. *Oral Dis*. 1998;4(4):281–284.
- [71] Buric N, Jovanovic G, Radovanovic Z, et al. Radiographic enlargement of mandibular canal as first feature of non-Hodgkin's lymphoma. *Dentomaxillofac Radiol*. 2010;39:383–388.
- [72] Maxymiw WG, Wood RE, Lee L. Primary, multi-focal, non-Hodgkin's lymphoma of the jaws presenting as periodontal disease in a renal transplant patient. *Int J Oral Maxillofac Surg*. 1991;20(2):69–70.
- [73] Manganaro AM, Phillips KM. Rapidly growing periodontal enlargement. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2000; 89(5):535–538.
- [74] Alderson GL, Jones AC, McGuff HS, et al. Oral and maxillofacial pathology case of the month. Malignant lymphoma, diffuse large B cell type. *Tex Dent J*. 2006;123:300–304.
- [75] Cabras M, Arduino PG, Chiusa L, et al. Case report: sporadic Burkitt lymphoma misdiagnosed as dental abscess in a 15-year-old girl. *F1000Res*. 2018;7:1567.
- [76] Cox DP, Treseler P, Dong R, et al. Rare oral cavity presentation of a B-cell lymphoblastic lymphoma. A case report and review of the literature. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2007;103(6):814–819.
- [77] Pereira DL, Fernandes DT, Santos-Silva AR, et al. Intraosseous non-Hodgkin lymphoma mimicking a periapical lesion. *J Endod*. 2015;41(10):1738–1742.
- [78] Saund D, Kotecha S, Rout J, et al. Non-resolving periapical inflammation: a malignant deception. *Int Endod J*. 2010;43(1):84–90.
- [79] Spatafore CM, Keyes G, Skidmore AE. Lymphoma: an unusual oral presentation. *J Endod*. 1989;15(9):438–441.
- [80] Fischer DJ, Klasser GD, Kaufmann R. Intraoral swelling and periapical radiolucency. *J Am Dent Assoc*. 2012;143(9):985–988.
- [81] Dolan JM, DeGraft-Johnson A, McDonald N, et al. Maxillary and mandibular non-Hodgkin lymphoma with concurrent periapical endodontic disease: diagnosis and management. *J Endod*. 2017; 43(10):1744–1749.
- [82] Hopp RN, Marchi MT, Kellermann MG, et al. Lymphoma mimicking a dental periapical lesion. *Leuk Lymphoma*. 2012;53(5): 1008–1010.
- [83] Jessri M, AbdulMajeed AA, Matias MA, et al. A case of primary diffuse large B-cell non-Hodgkin's lymphoma misdiagnosed as chronic periapical periodontitis. *Aust Dent J*. 2013;58(2):250–255.
- [84] Mendonca EF, Sousa TO, Estrela C. Non-Hodgkin lymphoma in the periapical region of a mandibular canine. *J Endod*. 2013;39(6): 839–842.