CASE REPORT

Primary non-Hodgkin's lymphoma of the tongue: a diagnostic dilemma of unusual case presentation

Natheer Hashim Al-Rawi

Department of Oral & Craniofacial Health Sciences, University of Sharjah, Sharjah, UAE

Correspondence to
Professor Natheer Hashim Al-Rawi, nhabdulla@sharjah.ac.ae

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SUMMARY

Primary non-Hodgkin's lymphoma of the tongue is extremely uncommon, which makes its diagnosis quite challenging. A panel of 11 markers is used based on morphological differential diagnosis to elucidate the lymphoma subtype. A case of 43-year-old Egyptian man suffering from nodular mass on the right side of the tongue of 4 months duration is presented. No cervical lymphadenopathy was detected. No abdominal organomegaly was noted. The histological evaluation of incisional biopsy revealed a sheet of pleomorphic lymphoid cells with abnormal mitotic figures. A large number of histiocytes were infiltrating the lymphoid cellular sheet. The results of immunophenotyping were extranodal T-cell lymphoma. A proper immunohistochemical workup is crucial for the correct diagnosis and proper management.

BACKGROUND

Extranodal non-Hodgkin's lymphomas (NHLs) include a diverse and complex group of solid malignant tumours with variable clinical and histopathological features. In total, 8–13% of lymphomas involve the head and neck region.^{1–2} Pazoki *et al*³ reported four cases of primary extranodal NHL of jaw bones and reviewed the literature about extranodal NHL affecting the hard tissue. Primary NHL of the tongue is extremely rare, and this makes its diagnosis quite challenging. Van der Waal *et al*⁴ in their case series analysis of 40 primary extranodal NHL of oral cavity found the most common sites involved were the palate and gingiva. Meheshwari *et al*⁵ reviewed 12 cases of tongue lymphoma. Shah *et al*⁶ in their case series analysis found alveolar bones and hard palate were the most common sites. The primary NHL of the oral cavity appear as non-tender soft or firm nodules of the area often with surface ulcerations⁷ which may be misdiagnosed with other oral lesions. Primary lymphoma of the tongue usually present as soft, bulky nodular mass covered by normal or ulcerated mucosa.⁸ We encountered a rare case of primary T-cell lymphoma of the tongue as a nodular swelling on the right side of the tongue.

CASE PRESENTATION

A 43-year-old Egyptian man attended oral medicine clinic at College of Dental Medicine, University of Sharjah, UAE, with a 4 months history of slow growth of nodular mass on the right side of the tongue. The patient was heavy smoker and regular alcohol drinker. He had negative history of neck mass, febrile illnesses, weight loss and night sweats.

The oral lesion presented as a 3×3 cm nodular mass involving the middle portion of the right side of the tongue. The deep central groove of the tongue separates the mass from the rest of the tongue ([figure 1](#)). The movement of the tongue was normal. The right pharyngeal wall and the tonsils were normal. No cervical lymphadenopathy was detected. No abdominal organomegaly was noted on CT scan. The patient underwent surgery for an incisional biopsy. The histological evaluation revealed a sheet of pleomorphic lymphoid cells and abnormal mitotic figures. A large number of histiocytes were infiltrating the lymphoid cellular sheet ([figure 2](#)).

INVESTIGATIONS

To differentiate between lymphoma subtypes, immunohistochemistry was performed for proliferation (Ki67), PAN-T (CD3), B-cell antigen (CD20), leucosialin (CD43), granzyme B, CD68, CD4, CD8, CD30, CD56 and ALK to confirm the diagnosis which was extranodal T-cell lymphoma. [Figure 3A–F](#) revealed strong to mild expression against Ki67, CD3, CD20, CD43, granzyme B and CD68. However, [figure 4A–E](#) demonstrates weak to negative expression against CD4, CD8, CD30, CD56 and Alk1 (CD246).

Figure 1 The 3×3 cm nodular mass is seen at presentation.

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Figure 2 Histological sections show the atypical lymphocytes with abnormal mitotic figures (arrows) with macrophages infiltrates (H&E, original magnification $\times 400$).

DIFFERENTIAL DIAGNOSIS

- ▶ B-cell lymphoma
- ▶ T-cell lymphoma
- ▶ Natural killer (NK)-cell lymphoma
- ▶ Histiocytic lymphoma

OUTCOME AND FOLLOW-UP

The patient was staged as Ann Arbour stage IE and referred to oncology clinic to start CHOP chemotherapy (cyclophosphamide, hydroxydaunomycin, oncovin, prednisolone) followed by radiotherapy. The results of immunophenotyping are depicted in [table 1](#).

DISCUSSION

NHLs are a group of highly diverse malignant cells that tend to affect organs and tissues that are not ordinarily composed of lymphoid cells. WHO classifies peripheral tumours of lymphoid tissues as B-cell lymphoma, T-cell lymphoma, peripheral T-cell/NK-cell lymphoma and peripheral T-cell lymphoma, and NOS (not otherwise specified). Extranodal NHLs constitute about 20–30% of NHLs.⁸ The head and neck is the second most common site for extranodal lymphomas after the gastrointestinal tract.⁹ Waldyer's ring lymphomas are the most common area of malignant lymphoma.¹ The intraoral location is not

Figure 3 Immunophenotyping demonstrates strong reaction against Ki67 (A), CD3 (B) and CD43 (C); moderate reaction with granzyme B (D) and CD68 (E); and mild reaction with CD20 (F).

Figure 4 Immunophenotyping demonstrate weak or negative reaction against CD4 (A), CD8 (B), CD30 (C), CD56 (D) and Alk1 (E).

Table 1 Immunohistochemical markers used for the case

Marker	Ki67	CD3	CD20	CD43	Gran B	CD68	CD4	CD8	CD30	CD56	CD246
Present case	+	+	– (+)	+	+	– (+)	–	–	– (+)	–	–
T-cell lymphoma	+	+	–	+	– (+)	– (+)	– (+)	– (+)	–	–	–
B-cell lymphoma	+	–	+	–	– (+)	– (+)	–	–	–	–	Variable
NK-cell/T-cell lymphoma	+	(cytoplasm –; membrane +)	–	+	+	– (+)	–	–	+	+	–

NK, natural killer.

common; it comprises only 2% of all extranodal lymphomas.^{10–11} Tonsils and palate are the most frequent sites.⁸ Epstein *et al*¹² in 2001 reported 361 cases in the oral and perioral region; they found that the most common sites were tonsils (118 cases; 32.6%), parotid gland (58 cases; 16%) and then nasopharynx (40 cases; 11%). Most intraoral lymphomas were of large cell types (137 cases; 38%), followed by small cell type (99 cases; 27.4%) and then lymphoma NOS (82 cases; 22.7%). Kemp *et al*¹³ in 2008 reported 40 cases of NHL; maxilla was the most common site (27.5%) and the most common clinical presentation was swelling and ulceration. Guevara-Canales *et al*¹⁴ in their systematic review of 714 patients from 1990 to 2010 found that Waldeyer's ring was the most frequent extraoral site, whereas gingiva was the most frequent intraoral site.

The predisposing factors of oral NHLs have not been identified yet, although few cases have reported an association with HIV infection.^{1–2} Oral NHLs have similar clinical appearance of a more commonly benign oral lesions.¹⁵ Thus, these lesions may be easily misdiagnosed. Lymphomas and more commonly carcinomas could not be differentiated clinically; therefore, awareness of this clinical entity inside the mouth is very important. The tongue itself is an extremely unusual site for isolated primary NHL.^{16–17} Few cases reported primary extranodal NHL of the tongue though most of them presented as submucosal mass with no ulceration.^{18–20} Of these, only two cases presented without cervical lymph nodes involvement.^{19–20} The case presented in this paper involved one side of the tongue with deep central fissure separating the mass from normal tissue with

no cervical lymph nodes involvement. Inchingolo *et al*²¹ reported an unusual case of NHL of tongue in a 73-year-old man involving the whole tongue with enlarged subcranial and right pulmonary hilar lymph nodes. Tongue lymphoma could be easily mistaken for hypertrophic lingual tonsil, benign neoplasms like peripheral nerve sheath tumours, benign salivary gland tumours, leiomyoma and rhabdomyosarcoma, beside infective processes such as tongue abscess, fungal infection and bite-related trauma could have been possible differentials. According to Colmenero *et al*,²² intraoral lymphomas first signs may appear as infection in 50% of cases. Asymptomatic soft swelling with or without ulceration might be seen when tonsils, palate, buccal mucosa, gum, tongue and floor of mouth were involved.²³ Alveolar bone loss with oedema and pain has been reported which often mimics periodontal disease.²⁴ Lip paraesthesia and pathological fracture may be reported as a common sign of jaw involvement.²⁵ On histology, these tumours typically demonstrated a mixture of pleomorphic malignant T cells with few reactive cells infiltrate, such as eosinophil and histiocytes. Tongue lymphomas are usually made of B-cell origin.^{1–8} The patient's tumour of the presented case was of the T-cell type as confirmed by immunohistochemical phenotyping. Immunohistochemistry is almost compulsory for the correct diagnosis and characterisation of immunophenotype in most of the lymphomas. A panel of 11 markers is decided based on morphological differential diagnosis. The cells expressed high Ki67 labelling index, more than 90% of atypical cells were positive against this antigen. This indicates a bad clinical course of the disease.²⁶ PAN-T marker (CD3) and B-lymphocyte antigen (CD20) were used²⁷ to distinguish between B-cell and T-cell variants. More than 90% of malignant cells examined in this case were positive for CD3 marker and <25% of cells were positive for CD-20. Leucosialin (sialophorin) immunohistochemical marker which is a major sialoglycoprotein on the surface of human T lymphocytes was positive over 90% of T-cell lymphoma.²⁸ Isacson *et al*²⁹ used CD20+ (a PAN-B-cell marker) and CD3– (a PAN-T-cell marker) to profile extranodal follicular lymphomas of the head and neck region. Granzyme B was used to discriminate between T and NK cells.³⁰ Nearly 50% of malignant cells of the present case were granzyme B positive. In the present case, histiocytes were infiltrating the lymphoid cellular sheet; therefore, CD68 was used to distinguish between malignant histiocytosis and histiocytic lymphoma.¹⁰ The atypical cells of the present case were positive in <50% of cells. The increase in tumour-associated macrophages is usually related to the high proliferative index of the tumour.³¹ CD4 and CD8 were always negative in cases of extranodal NK-cell/T-cell lymphoma especially in nasal type. Both markers were also negative in the studied case. NK cells and activated T cells were always positive for CD56. However, this marker was negative in the present case. This eliminates the presence of NK cells in the case studies. The present case was also negative for CD30 and CD246, which eliminates the probable diagnosis of anaplastic large cell lymphoma.^{32–34} NHLs are very responsive to radiation and chemotherapy therefore, differentiating this lesion from carcinoma is very crucial for proper management.^{2–8}

CONCLUSION

Primary NHL of the tongue is a rare disease entity particularly of T-cell type. It usually misdiagnosed as squamous cell carcinoma clinically. Therefore, this possibility should be kept in mind when diagnosing benign and malignant lesions of this area. A proper diagnostic assessment with adequate immunohistochemical phenotyping like (PAN-T, PAN-B, CD3, CD20, etc) are essential to

confirm diagnosis and improve management and long-term survival. Differentiating NHL from carcinoma is critical for treatment of these lesions, since NHLs are highly sensitive to radiotherapy and chemotherapy.⁵ The prognosis of patients with extranodal NHLs mainly depends on the tumour stage, tumour grade and aggressiveness beside patient's response to treatment.

Learning points

- Primary non-Hodgkin's lymphoma (NHL) of the tongue is extremely uncommon, which makes its diagnosis quite challenging.
- Differentiating a NHL from other reactive or malignant oral lesions is critical for the management of these lesions.
- A proper immunohistochemical workup is necessary for the correct diagnosis and proper management.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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