

Lymphoma in an extraction socket

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Abstract

Non-Hodgkin's lymphoma (NHL) is a lymphoproliferative malignancy that can involve both lymph node and lymphoid organs as well as extranodal organs and tissues. The aim of presenting this case of NHL is to highlight the suspicion of its occurrence in the region of unhealed extraction sockets and the significance of its awareness. NHL can be presented in various forms; therefore, a thorough knowledge regarding this malignancy is essential for arriving at the earliest possible diagnosis and therapy for the patient.

Keywords: B-cell, cyclophosphamide, extranodal, hydroxydoxorubicin, lymphoma oncovin and prednisone

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INTRODUCTION

Lymphomas account for 2%–5% of all oral malignancies. From the past decade, after oral squamous cell carcinoma, salivary gland tumors and odontogenic tumors, lymphomas, although less frequently, have been reported in the oral cavity. The most common site affected is tonsil (34%) followed by salivary glands (16%).^[1,2] The majority of head-and-neck lymphomas arise in lymphoid tissue, especially in the cervical group of nodes (nodal lymphomas) and Waldeyer's ring. Primary extranodal lymphomas account for 25%–40% of non-Hodgkin's lymphomas (NHLs).^[2-4] After Kaposi's sarcoma, NHL is the second most common malignancy associated with acquired immunodeficiency syndrome, and almost 75% of lymphomas in HIV-positive patients are extranodal in presentation.^[3,4,5] Oral extranodal lymphomas account for 1.4% of all lymphomas, affecting the vestibule, gingiva and mandible commonly. Furthermore, the palatal soft tissue, maxilla and tongue are affected.^[5,6,7] The present report is about a case of NHL occurring in the region of an unhealed extraction socket.

CASE REPORT

An 85-year-old elderly female patient reported to our outpatient department with a chief complaint of swelling in her right lower back tooth region, accompanied with mild pain for 3 months. Her previous dental history revealed a tooth extraction in the same region 3 months earlier, following which she noticed a growth from the unhealed extraction socket. There was no relief of symptoms on medication. Medical history revealed that she was hypertensive and suffered from hyperlipidemia and cardiac problems for 6 years for which she was under medication. Upon extraoral examination, a diffuse swelling on the right side of the mandible was observed that extended anteroposteriorly from the symphysis to the posterior lower border of the mandible and superoinferiorly 1 cm below the tragus line to 1 cm beyond the lower border of the mandible. On palpation, the swelling was firm, nontender and noncompressible, with the overlying skin being normal. The right and left submandibular lymph nodes

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were palpable, firm in consistency, tender and fixed. The left middle cervical lymph node was palpable, round, soft in consistency, tender and freely movable [Figure 1a and b].

Intraoral examination revealed a localized, well-defined swelling of size 4 cm × 5 cm in its greatest dimension obliterating the buccal, labial and lingual vestibules in the region of the nonhealed extraction sockets of 43, 44 and 45. The lesional mass was extending anteroposteriorly from the distal aspect of 42 to the distal aspect of 46, obliterating the buccal vestibule. Lingually, the swelling extended from the mesial aspect of 41 to the mesial aspect of 46 [Figure 2a and b]. On palpation, the swelling was firm in consistency, tender and with smooth and shiny surface with cortical expansion on the lingual aspect. The superficial surface of the swelling exhibited ulceration covered by pseudomembranous slough. Based on the clinical findings, carcinoma of alveolus was considered as a provisional diagnosis. Radiographic examination revealed an ill-defined radiolucency of 2 cm × 1 cm dimension on an orthopantomogram, extending anteroposteriorly from 42 to 46. Based on the radiographic findings, a radiological diagnosis of alveolar carcinoma in relation to 44 and 45 regions was made [Figure 3]. An occlusal radiograph also revealed the presence of cortical defect in the area extending between

42 and 46 [Figure 4], following which an incisional biopsy from 44 and 45 regions was advised.

Upon histopathological examination, hematoxylin and eosin-stained section revealed the proliferation of small, uniform, round, hyperchromatic, neoplastic lymphocytes with prominent nuclei and scanty cytoplasm, arranged diffusely. Some areas exhibited multilobulated cells, resembling Reed–Sternberg cells [Figures 5a, b and 6a, b]. The histopathological features were suggestive of malignant lymphoproliferative lesion, following which an immunohistochemical (IHC) analysis was done using antibodies against CD20 and BCL-2, which showed a positive expression [Figure 7a and b]. The IHC profile confirmed the clinical and histopathological diagnoses of NHL (B-cell lymphoma), following which the patient was referred to a regional cancer institute for further management. Whole-body contrast-enhanced computed tomography and positron-emission tomography were performed which revealed intensely hypermetabolic

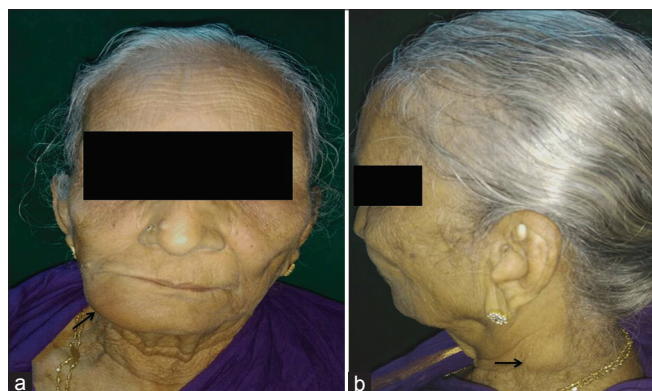


Figure 1: (a) Extraoral image presenting right facial asymmetry. (b) Left profile view exhibiting detectable cervical lymph node enlargement



Figure 3: Orthopantomogram revealing approximately 2 cm × 1 cm, ill-defined radiolucency in the 44 and 45 regions



Figure 2: (a) Intraoral examination of the lesion; (b) well-defined intraoral swelling obliterating the buccal, labial and lingual vestibules in the region of nonhealed extraction sockets of 43–45

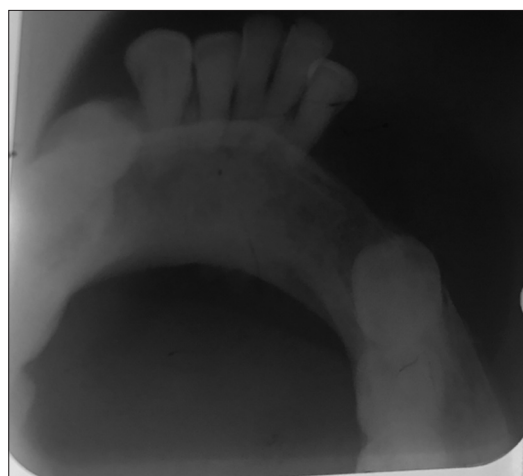


Figure 4: Occlusal radiograph revealing the presence of cortical defect in the region extending between 42 and 46

lesions involving the suboccipital region with intracranial extension, the mandible, bilateral cervical lymph nodes, left axillary nodes and pelvis, which were likely sites of disease involvement in the current clinical context [Figures 8a-c and 9].

DISCUSSION

NHL is a lymphoproliferative malignancy of the immune system with an unique capacity to arise almost anywhere in the body, but most frequently (80%) developing in the lymph nodes.^[2,6,8] Oral cavity is an uncommon site for NHL with an incidence rate of 0.1%–5%.^[3,7] Extranodal NHL was first described as a distinct entity by Isaacson and Wright in 1983. NHL is subclassified according to the precursor cell, cytological features and histological pattern; thus, they may be of T-cell or B-cell lineage, poorly or well-differentiated and diffuse or follicular. Up to 97% of these oral extranodal lymphomas may be of B-cell lineage.^[7,8] Thus, classification (by histology and phenotype) of NHL is important for determining proper treatment and predicting prognosis.

The first classification that was used before the immunologic study of lymphoma was the “Rappaport Classification,” in 1956. Then, in 1975, “Lukes–Collins Classification” was based on the origin of a tumor from either T-lymphocytes or B-lymphocytes. In Europe, in 1975, the “Kiel’s” classification has been widely used. Based on cell composition and pattern, a “New Working

Formulation for Clinical Use” was introduced in 1982, a clinically relevant morphologic classification, that presented three groups, namely low, intermediate, and high grade.^[9-11,12] Later, in 1994, the Revised European American Lymphoma Classification was in widespread use, but yet it requires immunologic or phenotypic information. The modifications of old classifications and to the invention of new schemes by the application of modern immunologic concepts led to the classification of malignant lymphoma. Based on this, the WHO Classification of Lymphomas is as follows: precursor B-cell neoplasms, peripheral B-cell neoplasms, precursor T-cell neoplasms, peripheral T-cell and NK cell neoplasms and Hodgkin’s lymphoma (HL).

In the head-and-neck region, extranodal NHL manifests frequently as a submucosal mass accompanied by polypoidal, bulky masses with a smooth mucosal surface. Burkitt’s lymphoma, diffuse large B-cell lymphoma (DLBCL) and NK-/T-cell lymphomas are clinically aggressive lymphomas that are characterized by the destruction of the mandible, maxilla and bones around the paranasal sinuses, which are

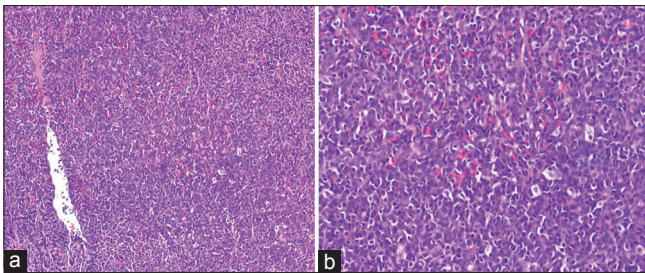


Figure 5: (a) Section presenting diffusely arranged small, round, uniform lymphocytes (H and E, ×4). (b) Section presenting proliferating lymphocytes (H and E, ×10)

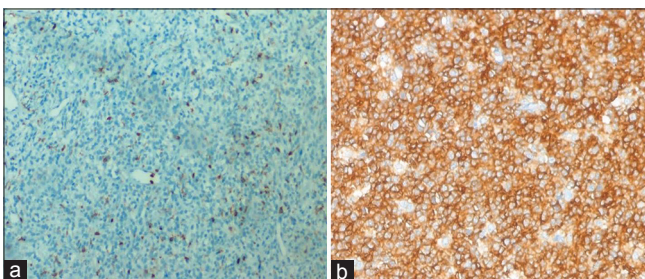


Figure 7: (a) Bcl2 positivity (×4), (b) CD20 positivity (×10)

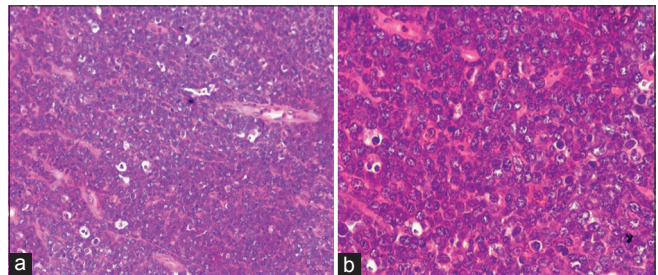


Figure 6: (a) Section presenting proliferating lymphocytes along with some Reed–Sternberg-like cells (H and E, ×10). (b) Section presenting diffusely proliferating large lymphocytes (H and E, ×40)

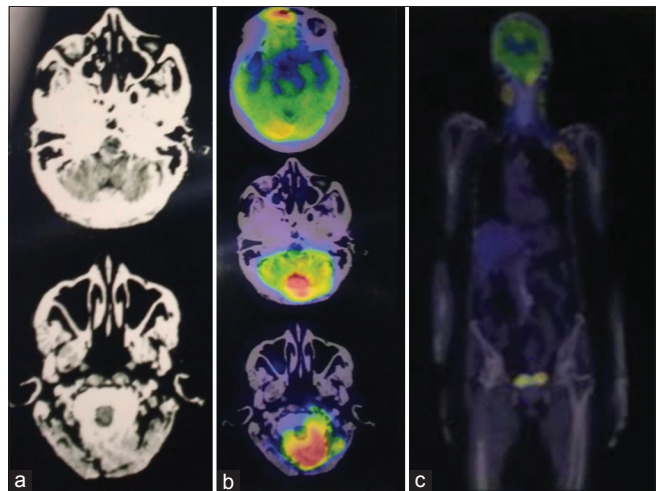


Figure 8: Contrast-enhanced computed tomography (a) and positron-emission tomography (b and c) images revealing intensely hypermetabolic lesions in the suboccipital region, mandible, bilateral cervical lymph nodes, left axillary nodes and pelvis

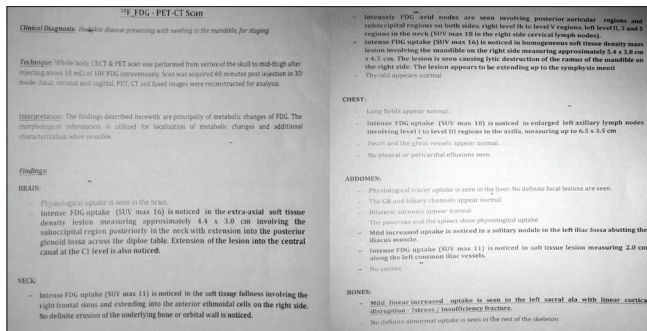


Figure 9: Positron-emission tomography-computed tomography scan report

often indistinguishable from bony destruction in other malignant tumors, such as squamous cell carcinoma.^[11,13] HLs involve the lymph nodes predominantly and only approximately 5% arise in extranodal sites, whereas 30% of NHLs present in extranodal sites.^[11,13,14] Marginal-zone lymphoma has an affinity for ocular adnexa, salivary glands, larynx and thyroid gland. DLBCL in the oral cavity is considered to be a high-grade lymphoma. It is the most common diagnosis, comprising approximately 60% of the cases.^[15,16] DLBCL is commonly encountered in the paranasal sinuses, mandible, maxilla and Waldeyer's ring. Among children and young adults, Burkitt's lymphoma occurs most frequently in the maxilla and mandible, with a greater distribution of involvement at a lower frequency.^[17,18] Oral NHLs are shown to be predominantly of B-cell lineage and are of DLBCL subtype. The greater predominance of DLBCL in the oral cavity is unknown, but has been explained as a natural inclination for this site. It may occur at all ages, but generally in patients more than 40 years of age and females account for 64% of the total population.^[19,20] Parihar *et al.*^[21] have reported NHL of gingiva in a 50-year-old Indian female in the anterior mandible that was positive with CD20 marker. Furthermore, Basavaraj *et al.*^[22] and Patil *et al.*^[23] in their case reports presented NHL of gingiva in HIV-positive patients.

To understand the pathology of lymphomas, it is necessary to know the cell lineage, the degree of cell differentiation and the location of the cell of origin (humoral factors, i.e., growth factors). For the diagnosis of NHL, the important criteria are as follows: (1) partial or complete obliteration of the lymph node by a usually monomorphous lymphoid cell type and (2) the pattern of growth. Follicular and diffuse growth patterns are most often encountered. Follicular or nodular pattern presents follicular center structures, whereas in diffuse pattern, the lymphoid cells proliferate in an apparently unorganized fashion. Occasionally, lymphoma will be distributed within lymph nodal sinuses.^[24,25]

The important IHC markers for B-cell-associated lymphomas are CD10, 19, 20, 21 and 23; that of T-cell-associated lymphomas are CD1, 3, 4, 5 and 8; that of macrophage-associated are CD11c, 13, 14, 15, 33 and 64 and that of NK-cell-associated are CD16 and 56. It is suggested that MUM1 positivity represents the activated state of the B/T cells as MUM1 expression in peripheral blood B/T-lymphocytes was upregulated by mitogenic stimuli. Chromosomal translocations and molecular rearrangements are commonly used to confirm the diagnosis. The most common chromosomal abnormality in NHL is the translocation of t(14;18)(q32;q21) that is found in 85% of follicular lymphomas and 28% of DLBCLs. The translocation of the bcl-2 gene from 18q21-14 at a site adjacent to the J-region of the Ig-heavy chain results in unregulated expression of the bcl-2 protein. t(8;14) or MYC in Burkitt's lymphoma, t(2;5) or anaplastic lymphoma kinase in anaplastic large-cell lymphoma, t(11;14) or bcl-1 in mantle cell lymphoma and trisomy 3 or trisomy 18 in marginal zone lymphomas are noticed.^[25,26]

Treatment of head-and-neck NHL involves chemotherapy, radiotherapy or a combination of both. The standard chemotherapeutic regimen is a combination of cyclophosphamide, hydroxydoxorubicin, oncovin and prednisone therapy. The presence of bcl-2 and MUM-1 proteins has been associated with a less favorable prognosis and the possibility of a nongerminal center DLBCL subtype, requiring more aggressive treatment.

CONCLUSION

Oral lymphomas can resemble dental abscesses, tumors or other diseases such as osteonecrosis. Malignant lymphomas from nonhealing extraction socket or in the form of any suspicious alteration of the mucosal membrane of the oral cavity should be considered as a differential diagnosis to other primary lesions encountered often. Due to the unspecific symptoms, a histopathological verification of the diagnosis is crucial.

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.

REFERENCES

- Savarrio L, Gibson J, Dunlop DJ, O'Rourke N, Fitzsimons EJ. Spontaneous regression of an anaplastic large cell lymphoma in the oral cavity: First reported case and review of the literature. *Oral Oncol* 1999;35:609-13.
- Freeman C, Berg JW, Cutler SJ. Occurrence and prognosis of extranodal lymphomas. *Cancer* 1972;29:252-60.
- Aozasa K, Tsujimoto M, Sakurai M, Honda M, Yamashita K, Hanada M, *et al.* Non-Hodgkin's lymphomas in Osaka, Japan. *Eur J Cancer Clin Oncol* 1985;21:487-92.
- Hicks MJ, Flaitz CM, Nichols CM, Luna MA, Gresik MV. Intraoral presentation of anaplastic large-cell Ki-1 lymphoma in association with HIV infection. *Oral Surg Oral Med Oral Pathol* 1993;76:73-81.
- Howell RE, Handlers JP, Abrams AM, Melrose RJ. Extranodal oral lymphoma. Part II. Relationships between clinical features and the Lukes-Collins classification of 34 cases. *Oral Surg Oral Med Oral Pathol* 1987;64:597-602.
- Fukuda Y, Ishida T, Fujimoto M, Ueda T, Aozasa K. Malignant lymphoma of the oral cavity: Clinicopathologic analysis of 20 cases. *J Oral Pathol* 1987;16:8-12.
- Takahashi H, Fujita S, Okabe H, Tsuda N, Tezuka F. Immunophenotypic analysis of extranodal non-Hodgkin's lymphomas in the oral cavity. *Pathol Res Pract* 1993;189:300-11.
- Handlers JP, Howell RE, Abrams AM, Melrose RJ. Extranodal oral lymphoma. Part I. A morphologic and immunoperoxidase study of 34 cases. *Oral Surg Oral Med Oral Pathol* 1986;61:362-7.
- Isaacson P. Gastric Lymphoma and *Helicobacter pylori*. *New England Journal of Medicine* 1994;330:1310-11.
- Alkan S, Karcher DS, Newman MA, Cohen P. Regression of salivary gland MALT lymphoma after treatment for *Helicobacter pylori*. *Lancet* 1996;348:268-9.
- Kolokotronis A, Konstantinou N, Christakis I, Papadimitriou P, Matiakis A, Zaraboukas T, *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;99:303-10.
- Epstein JB, Epstein JD, Le ND, Gorsky M. Characteristics of oral and paraoral malignant lymphoma: A population-based review of 361 cases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2001;92:519-25.
- van der Waal RI, Huijgens PC, van der Valk P, van der Waal I. 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;34:391-5.
- Gawęda A, Jach E, Wojciechowicz J, Sokolowska B, Tomaszewski T. Diffuse large B cell lymphoma of the oral cavity – Case report. *J Pre Clin Clin Res* 2014;8:27-9.
- Hart S, Horsman JM, Radstone CR, Hancock H, Goepel JR, Hancock BW, *et al.* Localised extranodal lymphoma of the head and neck: The Sheffield lymphoma group experience (1971-2000). *Clin Oncol (R Coll Radiol)* 2004;16:186-92.
- Mawardi H, Cutler C, Treister N. Medical management update: Non-Hodgkin lymphoma. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2009;107:e19-33.
- Reddy I, Sreenath G, Reddy YR, Prakash AR, Swathi TR. Non-Hodgkin's lymphoma in buccal vestibule – Case report. *J Clin Diagn Res* 2014;8:QD01-2.
- Sahoo SR, Misra SR, Mishra L, Mishra S. Primary diffuse large B-cell lymphoma in the anterior hard palate: A rare case report with review of literature. *J Oral Maxillofac Pathol* 2014;18:102-6.
- Colovic N, Jurisic V, Terzic T, Atkinson HD, Colovic M. Immunochemotherapy for Bcl-2 and MUM-negative aggressive primary cutaneous B-cell non-Hodgkin's lymphoma. *Arch Dermatol Res* 2009;301:689-92.
- Zhang HW, Cheng NL, Chen ZW, Wang JF, Li SH, Bai W, *et al.* Clinical impact of t(14;18) in diffuse large B-cell lymphoma. *Chin J Cancer Res* 2011;23:160-4.
- Parihar S, Garg RK, Narain P. Primary extra-nodal non-Hodgkin's lymphoma of gingiva: A diagnostic dilemma. *J Oral Maxillofac Pathol* 2013;17:320.
- Basavaraj KF, Ramalingam K, Sarkar A, Muddaiah S. Primary non-Hodgkin's lymphoma of gingiva in a 28-year-old HIV-positive patient. *J Nat Sci Biol Med* 2012;3:189-91.
- Patil K, Mahima VG, Srikanth HS. Extranodal non-Hodgkin's lymphoma of the gingiva in an HIV seropositive patient. *Indian J Sex Transm Dis AIDS* 2010;31:112-5.
- Manjunatha BS, Gowramma R, Nagarajappa D, Tanveer A. Extranodal non-Hodgkin's lymphoma presenting as gingival mass. *J Indian Soc Periodontol* 2011;15:418-20.
- Wolvius EB, van der Valk P, van der Wal JE, van Diest PJ, Huijgens PC, van der Waal I, *et al.* Primary extranodal non-Hodgkin lymphoma of the oral cavity. An analysis of 34 cases. *Eur J Cancer B Oral Oncol* 1994;30B: 121-5.
- Shankland KR, Armitage JO, Hancock BW. Non-Hodgkin lymphoma. *Lancet* 2012;380:848-57.