

Primary oral non-Hodgkin's lymphoma – A clinicopathologic study with immunohistochemical analysis

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Abstract

Context: Non-Hodgkin's lymphoma (NHL) is a group of highly diverse malignancies whose prognosis depends on the histologic type and associated factors like HIV positivity. **Aims:** The aim of this study was to evaluate eight cases of NHL for their histologic type and HIV positivity, since both are major prognostic factors for NHL. **Settings and Design:** Eight cases of primary NHL of the oral cavity were evaluated for age, sex, clinical presentation, and the histologic type, along with immunohistochemistry. These cases were also evaluated for HIV positivity. **Materials and Methods:** NHL cases which were diagnosed through the dental OPD and subsequent biopsy procedure were chosen. The patient data, including age, sex, location, clinical presentation, radiographic presentation, metastasis, and histologic subtype, according to the World Health Organization (WHO) classification were tabulated. Immunohistochemical markers were used to confirm the cell type. CD20 and CD3 were used for B cell and T cell, respectively. Subsequent western blot analysis was carried out for HIV detection. **Results:** 75% of the NHL was of B-cell type; of this, 83% was found to be diffuse large B-cell lymphoma, which is an aggressive variant. 62.5% of cases were found to be HIV positive. **Conclusions:** This study emphasizes the need for HIV investigation in NHL cases and the need to determine the histologic type, both of which significantly affect the treatment outcome and prognosis.

Key words: HIV, non-Hodgkin's lymphoma, oral cavity

INTRODUCTION

Non-Hodgkin's lymphoma (NHL) is a group of diverse malignancies and has a tendency to also affect the tissues that usually do not contain lymphoid cells. From 20 to 30% of NHL arises from extranodal sites.^[1] The hard palate and gingiva are commonly involved. Other sites

such as tongue, buccal mucosa, lips, and floor of the mouth have been reported quite infrequently.^[2]

T-cell NHL is aggressive and patients have poorer prognosis compared to the B-cell type. Hence, this differentiation is needed.^[3]

The aim of this study is to emphasize the need for HIV investigation in NHL cases and the need to determine the histologic type, both of which significantly affect the treatment outcome and prognosis.

MATERIALS AND METHODS

NHL cases which were diagnosed through the dental OPD and subsequent biopsy procedure were chosen.

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The patients complained of a swelling or ulcerated growth. The patient data, including age, sex, location, clinical presentation, radiographic presentation, metastasis, and histologic subtype, according to the World Health Organization (WHO) classification were tabulated. CD20 and CD3 were used to differentiate B-cell lymphomas and T-cell lymphomas.

Paraffin-embedded tissue blocks were cut to produce 4 µm thick sections and stained by the Novolink™ Max Polymer detection system (Novocastra TM, London, UK). After the sections were re-hydrated through a graded series of alcohol, epitope retrieval was performed. Endogenous peroxidase was blocked by using a peroxidase block of the kit. Protein block was used to prevent non-specific binding. The sections were subsequently incubated with optimally diluted primary antibodies. The primary antibodies used were: Mouse antihuman CD3 and mouse antihuman CD20. The polymer recognizes the primary antibody.

The sections were then incubated with the substrate/ chromogen 3',3'-diaminobenzidine (DAB). Sections were then counterstained with hematoxylin and coverslipped.

The slides were observed under a microscope and the results interpreted. The cases were also tested for HIV positivity by enzyme-linked immunosorbent assay (ELISA) and western blot analysis.

RESULTS

The following results were obtained. Patients were in the 3rd to 6th decade of life, with one case being of age 15 years. Majority were of B-cell type [75% (6 cases)]; among these, 83% (5 cases) were found to be diffuse large B-cell lymphoma (DLBCL), which is an aggressive variant. 62.5% (5 cases) were males and the mean age was 42 years.

Maxilla was involved in six cases and mandible in two cases which were also intraosseous, and the greatest size reported was 8 × 4 cm [Figure 1a–1c].

The lesions appeared as swellings and were ulcerated in a few cases; their color varied from pinkish to erythematous [Figure 2a and 2b].

Metastasis to regional nodes was present in one case which involved the posterior palate. 62.5% (5 cases) of the cases were found to be seropositive for HIV on performing ELISA and subsequent western blot [Table 1]. Among the five HIV-positive patients,

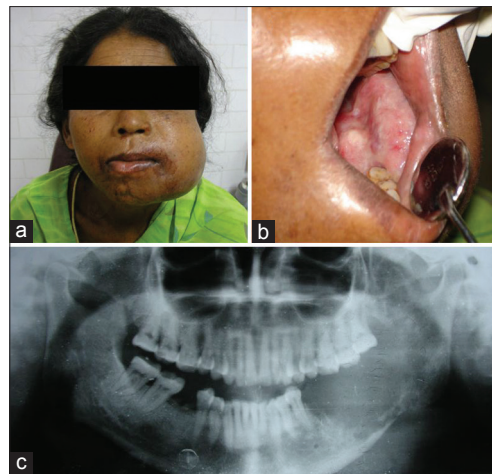


Figure 1: (a) Extraoral view of the mandibular swelling. (b) Large destructive lesion involving the both cortical plates. (c) orthopantomogram (OPG) showing pathologic fracture

one had developed a recurrence of NHL and another had died during the course of treatment.

The microscopic pattern was predominantly that of round malignant cells fitting into the diagnosis of NHL. Nuclear pleomorphism, hyperchromatism, altered nuclear–cytoplasmic ratio, mitosis, and vascular invasion were present in most of the cases [Table 2].

Immunohistochemistry was done using anti-CD3 for T-cell lineage and anti-CD20 for B-cell lineage; six cases were positive for CD20 and two cases for CD3. Among the six B-cell lymphomas, five were diffuse large cell and one was follicular B-cell lymphoma [Figure 3a and 3b]. Both the T-cell lymphomas were anaplastic large T-cell lymphomas [Figure 4a and 4b].

DISCUSSION

Twenty-five to forty percent of HIV-positive patients would develop a malignancy, with approximately 10% developing NHL. NHL is a heterogeneous malignancy characterized by abnormal proliferation of lymphoid cells and/or their precursors.^[4]

The risk factors include exposure to pesticides and radiation, long-term immunosuppression, and autoimmune diseases including rheumatoid arthritis, systemic lupus erythematosus, and Sjögren syndrome. Certain infections, including Epstein–Barr virus (EBV), human T-cell lymphotropic virus 1 (HTLV-1), HIV, *Helicobacter pylori*, *Chlamydia*, and human herpesvirus-8 (HHV-8, KSHV), are known to be associated with a risk for development of NHL and, in particular, mucosa-associated lymphoid tissue (MALT) lymphomas.^[5]

Oral lesions may appear as an erythematous, painless enlargement, often with surface ulceration secondary to trauma. In patients with removable oral prosthetics, the tissue enlargement may interfere with proper seating and function. NHL rarely presents with deep oral ulceration.^[6]

Patients with HIV infection are at higher risk of developing NHL and the aggressive B-cell lymphoma is one of the most commonly seen variants in these individuals.^[7]

The age of AIDS-related lymphoma patients seems to vary. Five of our eight cases turned out to be HIV

positive. The age group affected by NHL related to AIDS is considerably younger than that of unrelated NHL.^[7]

DLBCL is considered an aggressive, yet treatable neoplasm with a variable clinical course. An initial remission of 60–80% has been reported with chemotherapy.^[8]

The cells of DLBCL are roughly 3 times the diameter of small lymphocytes and have a vesicular appearing nucleus, usually with prominent membrane-bound



Figure 2: (a) Ulcerative growth involving the right retromolar region. (b) Erythematous lesion of the maxillary gingiva

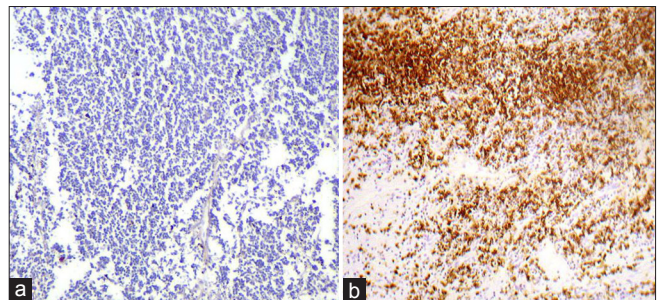


Figure 3: (a) Histologic section showing the malignant lymphocytes in a B-cell lymphoma (H and E stain at 10 × magnification). (b) Immunohistochemistry showing positivity for CD20 marker (IHC stain at 10 × magnification)

Table 1: The clinical features of the cases of NHL

Case no	1	2	3	4	5	6	7	8
Age/gender (years, male/female)	45/female	38/female	42/female	63/male	65/male	38/male	15/male	37/male
Radiographic features	Bony erosion of maxillary alveolar ridge	Erosion of cortices of mandible	No involvement	No involvement	No involvement	Destruction of lingual cortex of mandible	Bony erosion of maxillary alveolar ridge	Bony erosion of maxillary alveolar ridge
Appearance	Diffuse swelling	Diffuse swelling	Ulcerated lesion	Lobulated mass	Ulcerated lesion	Diffuse swelling	Lobulated mass	Diffuse swelling
Location	Maxillary alveolar ridge	Posterior mandible	Posterior palate	Maxillary gingiva	Posterior palate	Posterior mandible	Maxillary alveolar ridge	Maxillary alveolar ridge
Tumor size (cms)	4×1.5	8×4	3×3	2×1	2×2	3×1.5	2.5×2.5	3×2
HIV positivity	+ve	-ve	-ve	+ve	+ve	+ve	-ve	+ve

NHL=Non-Hodgkin's lymphoma

Table 2: The microscopic analysis of the cases of NHL

Case no	Nuclear pleomorphism	Altered N: C ratio	Mitosis	Perivascular invasion	Histopathology	Immuno-histochemistry CD3/CD20
1	Present	Present	Absent	Absent	Diffuse large cell	Bcell type CD20+
2	Present	Present	Present	Present	Angioimmunoblastic	Tcell type CD3+
3	Present	Present	Absent	Absent	Follicular	Bcell type CD20+
4	Present	Present	Present	Present	Angioimmunoblastic	Tcell type CD3+
5	Present	Present	Present	Present	Diffuse large cell	Bcell type CD20+
6	Present	Present	Present	Absent	Diffuse large cell	Bcell type CD20+
7	Present	Present	Absent	Absent	Diffuse large cell	Bcell type CD20+
8	Present	Present	Absent	Present	Diffuse large cell	Bcell type CD20+

NHL=Non-Hodgkin's lymphoma

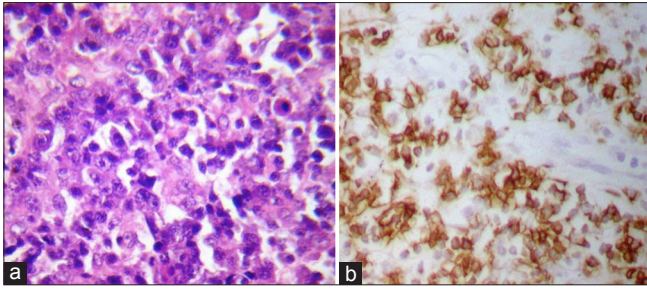


Figure 4: (a) Histologic section showing large malignant lymphocytes in a T-cell lymphoma (H and E stain at 40 × magnification). (b) Immunohistochemistry showing positivity for CD3 marker (IHC stain at 40 × magnification)

chromatin. Nucleoli are usually prominent.^[9] These findings were similar to cases. In the present study, out of the six B-cell lymphomas, five were DLBCL and one was a follicular lymphoma.

Angioimmunoblastic T-cell lymphoma is a common T-cell lymphoma which accounts for 15–20% of the reported cases and 4–6% of the lymphomas. It is an aggressive lesion showing rapid growth, destruction of the adjacent tissue, and is associated with poor prognosis. Average age at presentation is about 64 years, with a slight male predilection.^[10] These findings are similar to those observed in the present study. Among the eight NHL cases, two were T-cell lymphomas.

High-dose chemotherapy followed by stem cell transplantation has only been evaluated in a few patients. Treatment with anthracycline-based combination results in satisfactory remission rates of 50–70%. Only 10–30% of subjects have shown good survival rates.^[11] This emphasizes the need to differentiate B-cell lymphomas from T-cell lymphomas which have a different regimen.

In our cases, the B-cell lymphomas were given four cycles of CHOP (Cyclophosphamide, Hydroxydaunorubicin, Oncovin, and Prednisone) chemotherapy. The T-cell lymphomas which require aggressive therapy were treated by additional anthracycline. Our patients have remained disease-free for 5 years now. Among the HIV-positive cases, one died due to the disease and another patient has had a relapse after four cycles of chemotherapy.

CONCLUSION

This study clearly shows the poorer prognosis of NHL associated with HIV. A proper histopathologic analysis along with immunohistochemical evaluation aids in

the accurate diagnosis that helps in ideal management. This article emphasizes the need for HIV investigation in NHL cases and the need to determine the histologic type, both of which significantly affect the treatment outcome and prognosis.

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