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Dentistry

UNVEILING THE UNUSUAL: ORAL CAVITY B-CELL NON-HODGKIN'S LYMPHOMA

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ABSTRACT Lymphomas are malignant neoplasms of lymphoid tissue that account for a significant proportion of head and neck cancers, with Non-Hodgkin's lymphoma (NHL) comprising a smaller but clinically important subset. NHLs are heterogeneous lymphoproliferative disorders of B, T or natural killer cells, often arising in extranodal sites such as Waldeyer's ring, paranasal sinuses, orbit, salivary glands and thyroid gland. Oral NHL is rare, most commonly involving the palate and gingiva and typically presents as a painful swelling with ulceration. The majority of oropharyngeal lymphomas are of B-cell origin. We report a 55-year-old male with pain in the maxillary left posterior tooth region and a history of smoking. Histopathology revealed highly cellular stroma with sheets of monotonous round cells and immunohistochemistry confirmed B-cell NHL. This case highlights the importance of considering oral NHL in the differential diagnosis of intraoral malignancies, with histopathology and IHC essential for accurate classification. Early recognition and multidisciplinary management are critical for improving patient outcomes.

KEYWORDS : Oral Cavity, B-cell, Non-Hodgkin's Lymphoma, Palate, CD20.

INTRODUCTION

Lymphomas are malignant neoplasms arising from lymphocyte cell lines and account for approximately 14% of all head and neck malignancies. They are divided into Hodgkin's lymphoma (HL) and Non-Hodgkin's lymphoma (NHL), which differ in histopathology, clinical presentation and prognosis. HL usually appears as nodal disease, while NHL can involve nodes and extranodal sites.[1] NHL arises from B or T lymphocytes, with B-cell types being most common, around 20 cases per 100,000 annually in high-income countries.[2,3] Extranodal NHL often affects the gastrointestinal tract, Waldeyer's ring, bone and skin. Oral cavity involvement is rare, with an incidence reported between 0.1–5% of cases of extranodal lymphomas.[4,5]

Case History

A 55-year-old Indian male presented to the Department of Oral Medicine and Radiology, Government Dental College and Hospital, Hyderabad with pain in the upper left posterior tooth region since three months, accompanied by swelling in the left middle third of the face for the past two months. He reported a history of trauma following a fall from a tree four months earlier, after which he experienced loosening of teeth in the left maxillary and mandibular regions. There was no associated history of dysphagia, dyspnea, paraesthesia or difficulty in mouth opening. The patient's personal history revealed cigarette smoking for 20 years with frequency of 2 packet per day and alcohol consumption with frequency of 250 ml per day for 30 years.

Extraorally, diffuse swelling was observed over the left middle and lower third of the face, extending superoinferiorly from 1.0 cm below the infraorbital region to the inferior border of the mandible and anteroposteriorly from the ala of the nose to approximately 3.0 cm anterior to the tragus on the left side. The swelling was soft to firm in consistency and tender on palpation. On examination, the left submandibular lymph nodes were palpated and found to be enlarged, mobile and firm in consistency. (Figure-1A)

On intraoral examination, a swelling was noted in the muco-buccal vestibule and palatal alveolar mucosa, extending from tooth 24 to the 28 tooth region and reaching the maxillary tuberosity. Obliteration of bucco-gingival sulcus was seen. The lesion was sessile and firm to hard on palpation and measuring approximately 3.5 × 2.0 × 1.0 cm^2, with an erythematous overlying mucosa (Figure-1B). On palpation, the swelling was tender and exhibited induration. Based on the clinical features, a provisional diagnosis of carcinoma of the left maxillary alveolus was considered.

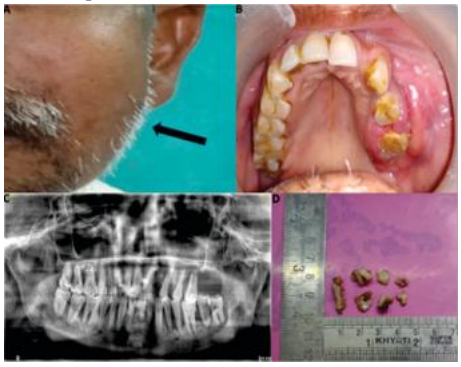


Figure-1 A Mild Diffuse Swelling Noticed on Left Middle and Lower 1/3rd of Face. B Swelling Seen in the Buccal Vestibule Extending from Distal Side of 24 to Tuberosity Anterio-posteriorly. C OPG Revealed ill-defined Radirolucency

Extending Antero-posteriorly from Distal Side of 24 to Maxillary Tuberosity. D Received Multiple (7) Creamish-brown Soft Tissue Bits Measuring About 2.6 × 2.1 cm², Which Were Firm in Consistency.

On radiographic examination, orthopantomography (OPG) revealed an ill-defined radiolucency extending antero posteriorly from the distal aspect of tooth 24 to the maxillary tuberosity. A floating-tooth appearance and haziness in the maxillary sinus were also noted (Figure-1C).

A positron emission tomography/computed tomography (PET-CT) scan performed using FDG revealed a metabolically active, single extranodal (extra-lymphatic) lesion located above the diaphragm in the left maxilla, measuring approximately 3.5 cm (AP) × 2.0 cm (ML) × 1.0 cm (CC).

Differential diagnosis of carcinoma of left maxillary sinus, minor salivary gland malignancy and benign tumours were considered clinically.

Under local anesthesia, the lesion was incised and sent for histopathological analysis. Grossly, the specimen comprised multiple creamish-brown soft tissue bits (2.6 × 2.1 cm²) (Figure-1D).

Microscopically, the lesion revealed an infiltrative, highly cellular stroma composed of sheets of uniform, monotonous round cells measuring approximately 10–15 μm in diameter, separated by delicate connective tissue septa. These lesional cells were diffusely arranged and exhibited pleomorphic, hyperchromatic nuclei, with mitotic figures 2-3 per HPF. The cells possessed only a thin rim of cytoplasm, imparting a crowded and atypical appearance. (Figure-2A and B).

The intervening stroma showed moderate vascularity, with conspicuous areas of extravasated red blood cells, reflecting vascular fragility. In addition, scattered chronic inflammatory cells had been present within the stroma, further contributing to the reactive background.

Collectively, microscopic analysis demonstrated a densely cellular neoplastic proliferation of round cells exhibiting nuclear atypia, mitotic figures and scant cytoplasm. The stroma showed prominent vascularity, with haemorrhagic foci and chronic inflammatory infiltrates. These features collectively suggested an aggressive round-cell lesion with stromal involvement.

For definitive diagnosis, immunohistochemical analysis revealed strong positivity for CD45 and CD20 (Figure-2C and D). CD45, a pan-leukocyte marker expressed on nearly all hematopoietic cells, is crucial for distinguishing lymphoid neoplasms from epithelial or mesenchymal tumors. CD20, a transmembrane protein on B lymphocytes, has both diagnostic and therapeutic importance in Non-Hodgkin's lymphoma (NHL). As a lineage-specific marker, CD20 confirms the B-cell origin of the neoplasm.

In this case, combined CD45 and CD20 expression excluded epithelial origin, established hematopoietic nature and confirmed B-cell lineage. Correlated with histopathology showing monotonous round cells in sheets, these findings strongly supported the diagnosis of B-cell NHL.

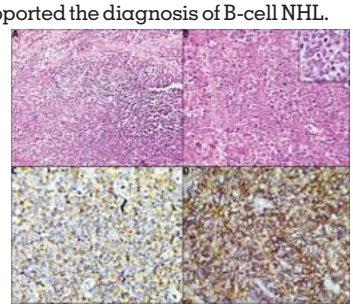


Figure-2, A Sheets of Uniform, Monotonous Round Cells (H&E 10x). B Round Cells Show Pleomorphic and Hyperchromatic Nuclei with Inset Showing Mitotic Figures (H&E 20x & 40x). C&D IHC Shows Membrane Positivity for CD45 and CD20 (40x).

According to the Ann Arbor staging system, the disease was classified as Stage IE, reflecting isolated extranodal involvement. The patient received four cycles of R-CHOP chemotherapy at three-week intervals, followed by involved site radiotherapy totaling 36 Gy in 2 Gy fractions. At 24 months of follow-up, the patient remained disease-free, with no recurrence or treatment-related adverse effects, underscoring the effectiveness of combined modality therapy in localized oral B-cell Non-Hodgkin's lymphoma.

DISCUSSION

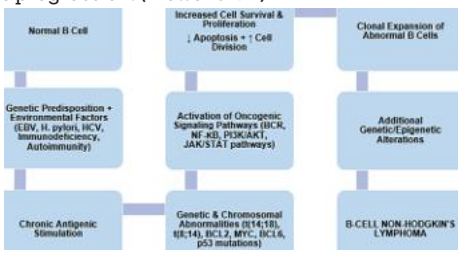
Malignant lymphomas are heterogeneous neoplasms of lymphoid tissue, classified into Hodgkin's disease and Non-Hodgkin's lymphoma (NHL). NHLs arise from B, T or NK cells, with 85–90% from B-cell lineage. Extranodal NHL accounts for 20–30% of cases, commonly in the gastrointestinal tract and head and neck (14%). Oral cavity involvement is rare, reported in 0.1–5% of extranodal lymphomas, but should be considered in differential diagnosis due to varied clinical features and risk of misdiagnosis.[4,5,6]

Diffuse large B-cell lymphoma (DLBCL) is the most common B-cell NHL subtype in the head and neck. B-cell NHLs predominate overall, while T-cell and NK/T-cell lymphomas are rarer, aggressive and linked to poor prognosis.[7,8,9]

Major risk factors for Non-Hodgkin's lymphoma (NHL) include immunosuppression and HIV infection, while Epstein–Barr virus, genetic predisposition and immune-related conditions also contribute. Lifestyle factors such as smoking and alcohol further increase risk. In this case, the patient was HIV negative but reported long-term tobacco and alcohol use.

The pathogenesis of Non-Hodgkin's lymphoma involves malignant transformation of lymphocytes arrested at specific stages of differentiation. Chromosomal translocations, often balanced reciprocal recombinations, are a hallmark of lymphoid malignancies and contribute to oncogene activation or tumor suppressor inactivation. Additional genetic alterations, including deletions and point mutations, further drive uncontrolled proliferation.

In B-cell Non-Hodgkin's lymphoma, pathogenesis is a multistep process shaped by genetic abnormalities, environmental influences and dysregulated signaling pathways. Chronic antigenic stimulation, infectious agents and inherited or acquired mutations promote the transformation of normal B lymphocytes into malignant cells, ultimately leading to diverse clinical presentations and disease progression. (Flowchart-1) [6,10]



Flow Chart-1 Pathogenesis of B-cell Non-Hodgkin's Lymphoma.

Cervical lymphadenopathy is the most common presentation of head and neck Non-Hodgkin's lymphoma, typically appearing as multiple, painless, mobile nodes. About half of extranodal cases arise in Waldeyer's ring, most often the palatine tonsils. Symptoms include dysphagia, sore throat or

tonsillar enlargement, while tongue base involvement remains exceedingly rare.[6]

Oral NHL generally affects individuals in the fifth to seventh decades, with a slight male predominance and is more common in HIV-positive patients. Clinical features include swelling, pain and ulceration, most frequently involving the gingiva, palate and tongue. Rapid growth may extend into jaw bones, producing lytic destruction. In our patient, maxillary swelling and tooth mobility reflected this aggressive pattern of oral NHL.

Jaw involvement in Non-Hodgkin's lymphoma is relatively uncommon compared to soft tissue disease. When present, radiographic findings typically reveal ill-defined radiolucent areas with cortical bone destruction, consistent with aggressive infiltration, as observed in our patient's orthopantomogram.

FDG-PET imaging complements radiography by detecting metabolically active disease, with aggressive B-cell lymphomas demonstrating intense uptake. PET remains essential for staging, monitoring treatment response, and prognostication.[2,3]

Non-Hodgkin's lymphoma (NHL) demonstrates two principal growth patterns: nodular and diffuse. The nodular variant is characterized by clusters of neoplastic lymphoid cells, whereas the diffuse pattern shows a monotonous distribution with complete effacement of lymph node architecture and absence of germinal centers.[6]

Microscopically, NHL typically reveals sheets of poorly differentiated lymphoid cells with vesicular nuclei, scant cytoplasm, and numerous mitotic figures, reflecting high proliferative activity and aggressive biological behavior. In our patient, biopsy findings demonstrated similar morphology, confirming the presence of a malignant lymphoid neoplasm.

A definitive diagnosis of Non-Hodgkin's lymphoma requires tissue biopsy, with histopathological and immunohistochemical evaluation essential to distinguish it from other lesions with overlapping features. Several conditions may mimic NHL microscopically: (Table 1)[2,4]

Table 1: Histopathological Differential Diagnosis.

Reactive hyperplasia	Characterized by hyperplastic stratified squamous epithelium, elongated rete ridges, fibroblastic proliferation, chronic inflammatory infiltrates and increased vascularity.
Follicular lymphoma	Exhibits follicular architecture, composed of neoplastic lymphocytes including centrocyte-like small cells and centroblast-like large cells, often showing mitotic activity.
Plasmablastic lymphoma	Presents as large solitary cells with eccentric nuclei, prominent nucleoli and vesicular chromatin.
Undifferentiated carcinoma	Shows sheets of malignant round or oval cells with marked pleomorphism.
Ewing's sarcoma	Defined by monotonous round blue cells with scant cytoplasm, prominent nuclei and occasional pseudo-rosette formation.
Plasmacytoma	Characterized by monoclonal plasma cells displaying the classic cartwheel nuclear appearance.

These overlapping morphologic features highlight the importance of correlating histopathology with immunohistochemistry to achieve diagnostic accuracy and avoid misclassification.[2,4]

Immunohistochemistry is crucial for diagnosing Non-Hodgkin's lymphoma. In this case, CD45 and CD20 positivity confirmed both hematopoietic origin and B-cell lineage. CD45 or leukocyte common antigen, is expressed on most nucleated hematopoietic cells and distinguishes lymphomas from non-hematopoietic tumors. CD20, present on mature B lymphocytes, provides specificity by confirming B-cell derivation and excluding T-cell types. The combined expression of CD45 and CD20 established the lesion's hematopoietic nature and classified it as B-cell Non-Hodgkin's lymphoma.

Accurate diagnosis, staging, and recognition of prognostic factors are vital in managing Non-Hodgkin's lymphoma (NHL). PET imaging may occasionally alter staging but is primarily used to monitor treatment response. Standard therapy includes chemotherapy, radiotherapy or both, with CHOP as the conventional regimen. Rituximab combined with CHOP is widely adopted, especially in younger, low-risk patients, and CD20-directed antibody therapy is standard for most B-cell subtypes. Prognosis depends on stage, histology and patient factors, with HIV-associated cases showing poorer survival.[11,12,13,14]

In the present case, the patient demonstrated a favorable response to R-CHOP combined with radiotherapy, achieving disease-free survival. As the patient was classified as Stage IE, prognosis was favorable, since early-stage disease typically responds well to standard therapy.

CONCLUSION

Non-Hodgkin's lymphoma of the oral cavity, though rare, should be considered in the differential diagnosis of intraoral malignancies due to its diverse presentation and potential for misinterpretation. Oral involvement presents unique diagnostic and therapeutic challenges, making histopathology and immunohistochemistry essential for accurate classification and distinction from other lesions. A thorough evaluation incorporating medical history, clinical examination, imaging and biopsy is critical. Early recognition and timely multidisciplinary management significantly improve outcomes. This case emphasizes the need for vigilance in atypical oral presentations and highlights the pivotal role of histopathology in guiding effective treatment strategies.

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