INTRODUCTION

The diverse group of neoplasms affecting lymphoreticular system is known as lymphomas. These are the malignant neoplasms mainly affecting lymph nodes, spleen and other nonhematopoietic tissues. They are divided into Hodgkin’s and non-Hodgkin’s subtypes and are of B-cell or T-cell origin. The majority of Hodgkin’s lymphomas presents as a nodal disease involving mainly cervical and axillary nodes.\(^\text{[1,2]}\)

Among the 40% non-Hodgkin’s lymphomas presenting extranodally, gastrointestinal tract, Waldeyer’s ring, spleen, salivary gland are the most common sites of occurrence and are rarely seen in the oral cavity. It may arise from preexisting low-grade lymphomas or as a de novo neoplasms.\(^\text{[3,4]}\) In the paraoral and primarily oral lymphomas, diffuse large B-cell lymphomas (DLBCL) are most common and is show a male predominance. The most common sites of involvement intraorally are palate, buccal mucosa and tongue with the prevalence of only 3–5%.\(^\text{[4,5]}\)

CASE REPORT

A 79-year-old male patient reported to the Department of Oral Pathology and Microbiology with a chief complaint of pain and swelling on the upper left buccal mucosa since 1-month. The swelling was insidious and gradually increased in size. The patient also reported reduced sensation on cheek mucosa of the left side.

Extraorally, facial asymmetry was noticed with diffuse swelling on the left sided cheek region, approximately 3 cm × 2 cm in size, irregular in shape, vertically extending from inferior border of zygomatic arch up to 1–2 cm above corner of mouth and was extending from ala of nose up to tragus of the ear mediolaterally. The swelling was firm and nontender on palpation with normal appearing overlying skin. The swelling was not fixed to the underlying structures. On intraoral examination, the swelling was diffuse, soft and roughly oval in shape [Figure 1]. The color of the overlying

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mucosa was normal as that of the surrounding mucosa. The swelling was situated in maxillary buccal vestibule extending anteroposteriorly from 26 to 28 region and mediolaterally from buccal mucosa of left side obliterating the vestibule, crossing the alveolar ridge and extending onto palatal mucosa. The swelling was approximately 4 cm × 2 cm in size and was of smooth surface texture. On palpation, the swelling was tender and not fixed to underlying structures.

Radiologically, on Waters view haziness was noticed in the left maxillary sinus region as compared to the right side, extending from superior border up to inferior border of sinus vertically and extending from medial to the lateral border of sinus mediolaterally [Figure 2].

An incisional biopsy was advised from buccal mucosa of left side under local anesthesia after routine blood investigations, which were within the normal limits. Human immunodeficiency virus (HIV) Tridot screening test was also negative.

On histopathological examination, the hematoxylin and eosin stained tissue section showed diffuse, monotonous proliferation of round cells, in the form of sheets within the loose fibrillar connective tissue stroma [Figure 3]. These cells were having large nuclei with a small amount of cytoplasm resembling lymphoid cells. It also revealed the presence of cells with large nuclei showing prominent nucleoli arranged at the periphery, exhibiting condensation and vesiculation of chromatin with cellular and nuclear pleomorphism. These cells resembled centroblasts [Figure 4] and immunoblastic cells [Figure 5]. The adjacent minor salivary gland tissue with mucous acini showed infiltration of these cells, disturbing the normal architecture.

Overall histopathological features suggest the diagnosis of atypical lymphoproliferative lesion. For confirmation, further immunohistochemical evaluation was done.

On immunohistochemical analysis, CD45 (leukocyte common antigen) [Figure 6] positivity distinguished malignant lymphomas from other non-lymphoid neoplasms, strong positivity for CD20 (B-cell marker) [Figure 7] and weak expression of CD3 (T-cell) marker suggests the B-cell origin of the lesion and Ki-67 (proliferation marker) positivity indicates the proliferative potential of the lesion. Thus, the overall histopathological and immunohistochemical findings were suggestive of DLBCL.

**DISCUSSION**

In head and neck region, lymphomas are the second most common neoplasms. Among 40% extranodal non-Hodgkin’s lymphomas majority of cases are of B-cell origin. B-cell lymphomas are classified as precursor B-cell neoplasm and peripheral B-cell neoplasm. According to Revised European-American Lymphoma classification of non-Hodgkin’s lymphomas, DLBCL is a peripheral B-cell
neoplasm.\textsuperscript{[6,7]} World Health Organization in 2008 further categorized aggressive B-cell lymphomas as:

- DLBCL not otherwise specified
- DLBCL associated with chronic inflammation
- Large B-cell lymphoma arising in human herpes virus (HHV)-8 associated Castelman’s disease
- B-cell lymphoma unclassifiable and
- Burkitt’s lymphoma.\textsuperscript{[8]}

The Kiel classification subdivided large B-cell lymphomas by pure morphology into centroblastic and immunoblastic lymphomas. The working formulation, on the other hand, subdivided large B-cell lymphomas according to their biological behavior into an intermediate-grade (large cleaved and large noncleaved) and a high-grade (immunoblastic) category.\textsuperscript{[9,10,11]}

Among DLBCLs, DLBCL not otherwise specified is the most common subtype and it accounts for up to 20–30% cases seen in elderly, above 70 years of age.\textsuperscript{[10]} It is characterized by large neoplastic B lymphocytes diffusely proliferating, with nuclei larger than or equal to normal macrophage nuclei in size, or more than twice the size of normal lymphocyte and are seen arising \textit{de novo}.\textsuperscript{[9,10]} Various studies have shown that DLBCLs shows an average age of presentation that is above 50–55 years with a male predominance.\textsuperscript{[12]} The present case was also reported in elderly (79-year-old) male patient.

Gastrointestinal tract, thyroid, bone, skin and lungs are the most frequent extranodal sites\textsuperscript{[8]} and in orofacial region Waldeyer’s ring, salivary gland, tonsils, nasopharynx, base of the tongue are frequently involved.\textsuperscript{[6]} Intraorally it shows maxillary predominance (77%) and the majority of cases are reported on the palate.\textsuperscript{[13]} This is in accordance with the present case which was also reported in maxillary vestibular region and extended towards the palate.

Histopathologically, the pattern of invasion in lymph nodes or extranodal sites is diffuse, with frequent peripheral tissue involvement. Malignant cells show variants such as...
centroblastic, immunoblastic or anaplastic cell types. The plasmablastic form is another morphologic variant but is more commonly associated with Epstein-Barr virus or anaplastic lymphoma kinase positive B-cell lymphomas. In the present case, there was a presence of diffuse involvement of mucosa and infiltration of adjacent minor salivary glands, main cell types seen in this case were centroblastic and immunoblastic variants showing cells with larger nuclei and prominent nucleoli, chromat in condensation and pleomorphism.

Differential diagnosis includes – reactive non-neoplastic processes in which aggregates of lymphocytes are evident but they did not show atypical features. In case of Burkitt's lymphoma the cells are of homogeneous size and shape giving starry sky appearance due to presence of macrophages which were absent in this case. In plasmablastic lymphomas predominantly plasma cells were evident showing cartwheel-shaped nuclei. Classic Hodgkin's lymphoma is predominantly the disease of lymph nodes and rarely affects oral cavity showing Reed–Sternberg cells as a classic feature which were not evident in this case. Other malignancies such as liposarcoma, round cell type show sheets of poorly differentiated round cells with finely vacuolated or granular cytoplasm and cells may appear epitheloid or pericytoid type. Carcinomas of poorly differentiated type show atypical round cells with eosinophilic cytoplasm, but centroblastic and immunoblastic cells are not seen. Thus, after excluding all these possibilities and the presence of centroblastic and immunoblastic cells a diagnosis of DLBCL was suggested.

The beginning IHC panel includes CD20, CD3, CD45 and if alteration of B-cell areas are seen then antibodies against CD5, CD10, CD23, CD43, BCL2, BCL6 protein, etc., would be useful. Previous studies have done an immunohistochemical analysis of leukocyte common antigen (LCA), CD20, CD5 to confirm the diagnosis. Here, in the present case Ki-67 (proliferative marker), CD45 (common leukocyte antigen), CD20 (B-cell marker) analysis were done, which showed strong positivity. CD3 (T-cell marker) was weakly positive in this case. Thus, these findings confirm the diagnosis of extranodal large B-cell lymphoma.

DLBCL represents intermediate and high-grade lymphomas. It can be best treated by surgical excision with adjuvant radiotherapy if the lesion is localized; chemotherapy is the treatment of choice in case of diffuse and aggressive lesions. No significant difference in prognosis has been found between the three major groups: Centroblastic, immunoblastic and anaplastic. In diffuse cases and HIV patients, the prognosis is worse than that in follicular, nodal and HIV-negative cases.

**CONCLUSION**

The diagnosis of these lesions is challenging due to their resemblance to inflammatory and benign lesions, chances of misdiagnosis are more and the treatment is prolonged. Hence, the clinicians must consider it as a possible differential diagnosis since the lesions are aggressive and efforts should be taken to diagnose these lesions as early as possible as they demonstrate fatal outcomes.

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**Conflicts of interest**

There are no conflicts of interest.

**REFERENCES**

1. 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.
2. Higgins RA, Blankenship JE, Kinney MC. Application of immunohistochemistry in the diagnosis of non-Hodgkin and Hodgkin lymphoma. Arch Pathol Lab Med 2008;132:441-61.
3. Stein H, Warnke RA, Chan WC. Diffuse Large B-Cell Lymphoma, Not Otherwise Specified. Lyon, France: IARC Press; 2008.
4. Sankaranarayanan S, Chandrasekhar T, Rao S, Rooban T, Ranganathan K. Maxillary non hodgkins lymphoma. J Oral Maxillofac Pathol 2005;9:34-6.
5. 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.
6. Zucca E, Roggero E, Bertoni F, Conconi A, Cavalli F. Primary extranodal non-Hodgkin’s lymphomas. Part 2: Head and neck, central nervous system and other less common sites. Ann Oncol 1999;10:1023-33.
7. Rajendran R editor. Shafer’s Textbook of Oral Pathology. 7th ed. New Delhi: (Reed) Elsevier publications; 2012. p. 81-222.
8. Jaffe ES, Pittaluga S. Aggressive B-cell lymphomas: A review of new and old entities in WHO classification. Hematology Am Soc Hematol Educ Program 2011;2011:506-14. doi: 10.1182/ashedducation-2011.1.506.
9. De Paep P, De Wolf-Peeters C. Diffuse large B-cell lymphoma: A heterogeneous group of non-Hodgkin lymphomas comprising several distinct clinicopathological entities. Leukemia 2007;21:37-43.
10. Gurbuxani S, Anastasi J, Hyjek E. Diffuse large B-cell lymphoma – More than a diffuse collection of large B cells: An entity in search of a meaningful classification. Arch Pathol Lab Med 2009;133:1121-34.
11. Jaffe ES, Harris NL, Stein H, Vardiman J. World Health Organization Classification of Tumors. Pathology and Genetics of Tumors of Haematopoietic and Lymphoid Tissues. Lyon, France: IARC Press; 2001.
12. Kini R, Saha A, Naik V. Diffuse large B-cell lymphoma of mandible: A case report. Med Oral Patol Oral Cir Bucal 2009;14:e421-4.
13. Jham BC, Duarte EC, Fernandes AM, Johann AC, Aguiar MC, Gomez RS, et al. Primary diffuse large B-cell lymphoma of the oral cavity. J Bras Patol Med Lab 2007;43:369-72.
14. Higgins RA, Blankenship JE, Kinney MC. Application of immunohistochemistry in the diagnosis of non-Hodgkin and Hodgkin lymphoma. Arch Pathol Lab Med 2008;132:441-61.

15. Cohen SM, Petryk M, Varma M, Kozuch PS, Ames ED, Grossbard ML. Non-Hodgkin’s lymphoma of mucosa-associated lymphoid tissue. Oncologist 2006;11:1100-17.