Case Report

# Monocytoid B cell lymphoma: A case report and evaluation

Adesh Singh Manchanda, Ramandeep Singh Narang, Harshveer Kaur

Department of Oral and Maxillofacial Pathology and Microbiology, Sri Guru Ram Das Institute of Dental Sciences and Research, Amritsar, Punjab, India

**Abstract**

Lymphomas are a group of malignant blood cell tumors that develop from lymphocytes. Two main categories of lymphomas are Hodgkin and non-Hodgkin lymphomas (NHL), of which 90% are of the NHL type. The objectives of classifying is to help in the identification of homogenous group of well-defined entities and facilitating the recognition of uncommon diseases that further require classification as it affects prognosis and therapeutic implications. Nodal marginal zone lymphoma, also known as monocytoid B–cell lymphoma (MBCL), is an uncommon form of lymphoma representing 1.5%–1.8% of lymphoid neoplasms, with only rare reports in the literature that have attempted morphologic or immunophenotypic characterization. Specific markers for MBCLs are still lacking, so its diagnosis is based on exclusion of other small B-cell lymphomas. This article illustrates a case report of MBCL highlighting the intricacies and difficulties involved in establishing a diagnosis.

**Keywords:** Immunohistochemistry, lymphoma, monocytoid B-cell lymphoma

**Address for correspondence:** Dr. Adesh Singh Manchanda, Department of Oral and Maxillofacial Pathology and Microbiology, Sri Guru Ram Das Institute of Dental Sciences and Research, Amritsar, Punjab, India.
E-mail: adesh_manchanda@yahoo.com

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## INTRODUCTION

Malignant tumors of oral cavity are infrequent, representing only 5% of all those occurring in the human body. Among malignant tumors of oral cavity, squamous cell carcinomas are the most frequent type (90%–98%), and malignant lymphomas are the most outstanding among the remaining 2%–10%.[1]

Previous classification used for classifying lymphoma were Rappaport, Lennert/Kiel, Working formulation and Revised European American Classification (REAL).[2] In 1995, the WHO started the project of classifying hematopoietic and lymphoid tissue tumors which was first published in 2001 and updated in 2008 and is based on foundations laid within REAL. The 2001 classification is the first world system of consensus classification and is based on a combination of morphological and immunophenotypical data, molecular genetics and clinical aspects. It also predicts the clinical aggressiveness of the subtype. It was re-edited in 2008 with the participation from the Hematolopathology Society and the European Association of Hematopathologists. Apart from the 2001 classification, it defined new entities and gave solutions to diagnose accuracy problems; this included the recognition of small clonal lymphoid populations and identification of diseases characterized by the participation of certain anatomical sites or the clinical characteristics such as age.[3]

Recently, the classification was reassessed and modified in 2016 with limited alterations. This present classification

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incorporated a large body of information published over the last 8 years relating to the existing entities with some important diagnostic, prognostic and therapeutic implications. It clarifies the diagnosis and management of lesions at very early stages of lymphomagenesis, refines the diagnostic criteria for some entities, details the expanding genetic/molecular landscape of numerous lymphoid neoplasm and their clinical correlates and refers to investigations leading to more targeted therapeutic strategies. The classification maintains the goal of helping to identify homogeneous group of well-defined entities and facilitating the recognition of uncommon diseases that require further classification.[4]

Lymphomas are malignant neoplasms of the lymphocytic cell lines. They mainly involve lymph nodes, spleen and other nonhematopoietic tissues. They are generally classified as either Hodgkin's lymphoma (HL) or non-HL (NHL) and may be either B-lymphocyte or T-lymphocyte origin. Nearly 24%–48% of NHL can arise in extranodal locations, and 3%–5% are primarily located in the oral cavity.[5]

HL corresponds to approximately 14% of all lymphomas and NHL approximately 86% of lymphomas.[3] In head-and-neck regions, common sites are Waldeyer ring (63%), oral cavity (12%), thyroid gland (9%), paranasal sinus, palate, gingiva and buccal mucosa.[6] Patients have signs of localized or diffuse swelling, ulceration of mucosa, paresthesia, anesthesia and tooth loss.

Although lymphomas of the oral cavity and maxillofacial region are rare pathological entities, and are often difficult to diagnose as they mimic other pathologies, it is important to describe the complete manifestation of their natural history in order to provide knowledge of their development.

B-cell lymphomas arise as a result of deregulation and clonal expression of B-cells at distinct developmental stages.[7] In B-lymphocyte group, two major categories are recognized: precursor and mature B-lymphocytes. Mature B-cell lymphomas comprise more than 30% of NHLs and, based on their clinical course, lymphomas can be classified as indolent and aggressive type. Low-grade follicular lymphoma (FL), marginal zone lymphoma (MZL) and chronic lymphocytic leukemia (CLL) show indolent behavior, in contrast high-grade FLs have aggressive behavior.[8] Nodal MZL (NMZL) is a rare form of indolent small B-cell lymphoma constituting <2%. NMZL are thought to arise from marginal zone B-cells of the lymphoid follicle.[9] Most of the B-cell lymphomas have overlapping features, so definitive diagnosis is challenging. Treatment and prognosis may vary from one subtype to the next, thus it is important to make the most definitive diagnosis as possible.[8]

In this article, a case of monocytoid B-cell lymphoma (MBCL) is illustrated, highlighting the intricacies and difficulties involved in establishing a diagnosis.

## CASE REPORT

A 45-year-old male reported with a complaint of swelling in the lower right posterior region of jaw for 5 months. Intraoral examination revealed ovoid, nontender, firm swelling extending from #43 to #45 region measuring approximately 3.5 cm × 2 cm with normal overlying mucosa. Lymph nodes were not palpable. Peripheral blood examination was within normal limits. Radiographic examination revealed multilocular radiolucency in interdental area in relation to #43 and #44, with well-defined unilocular radiolucency at apical third in relation to #44 and #45 [Figure 1]. Based on these findings, a provisional diagnosis of odontogenic cyst/tumor was given. Microscopic examination revealed small, round lymphoid cells among minor salivary gland tissue. The ducts and acini of salivary gland tissue were lined by multilayered epithelial cells [Figure 2]. Numerous small nest and well-defined islands of epithelial cells were also seen. The overlying epithelium was stratified squamous in nature. It was diagnosed as lymphoepithelial lesion on microscopic examination. Immunohistochemistry showed these lymphoepithelial lesions to be comprising of MBCs with abundant eosinophilic cytoplasm and clefted nuclei. The tumor cells were immunopositive for CD20/BCL2 and focally immunoreactive for CD43 [Figure 3]. The lymphoid tumor cells were immunonegative for pancytokeratin/CD3/CD5/CD10/CD11c. The diagnosis of MBCL, low grade,

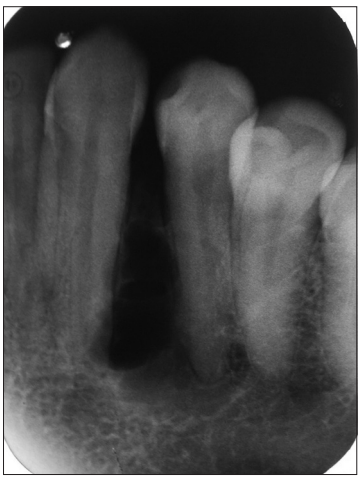

**Figure 1:** Radiographic examination reveals multilocular radiolucency in interdental area in relation to #43 and #44, with well-defined unilocular radiolucency at apical third in relation to #44 and #45

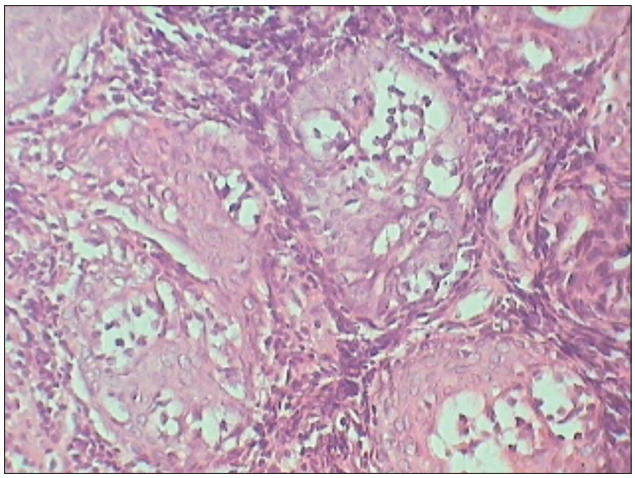

**Figure 2:** Microscopic examination reveals small round lymphoid cells among minor salivary gland tissue. The ducts and acini of salivary gland tissue were lined by multilayered epithelial cells. Numerous small nest and well-defined islands of epithelial cells were also seen (H and E, ×40)

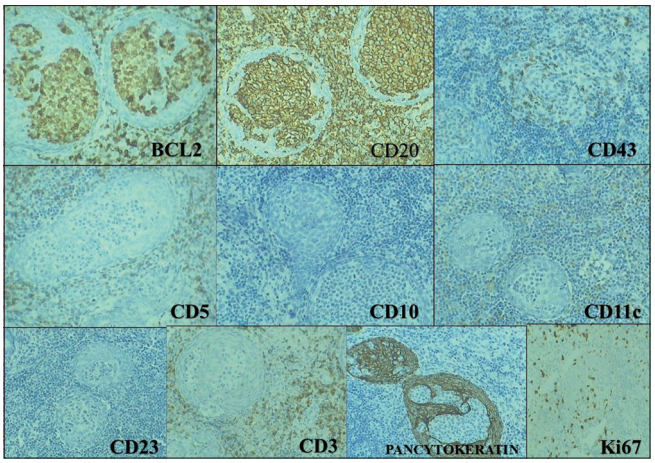


**Figure 3:** Immunohistochemistry shows the tumor cells were immunopositive for CD20/BCL2 and focally immunoreactive for CD43 and immunonegative for pancytokeratin/CD3/CD5/CD10/CD11c. Ki67 index is 8%

was made based on clinical, radiographic, histopathologic and immunohistochemical investigations. The Ki67 proliferative index was 8% approximately. The patient was given localized radiation therapy and follow-up was done for 1 year, in which the patient had an uneventful postoperative course.

## DISCUSSION

The WHO classification of marginal zone neoplasms comprises three entities: extranodal mucosa-associated lymphoid tissue (MALT) lymphoma, splenic MZL (SMZL) with and without villous lymphocytes and NMZL with and without MBCs.[10] NMZL is a distinct primary nodal B-cell lymphoma recognized as having morphologic and immunophenotypic similarities with SMZL and MALT lymphomas, but displays differences in terms of clinical presentation, molecular findings, treatment and prognosis.[9] Historically, different terminologies have been used to describe NMZL. It was first described by Sheibani *et al*. in 1986 and termed "monocytoid B-cell lymphoma," taking its name from the predominant morphology of neoplastic cells resembling monocytes. Cousar *et al*. described it as a "parafollicular B-cell lymphoma, while Piris *et al*. reported a relationship to marginal zone cells. In 1990, the revised Kiel classification included the provisional entity "nodal monocytoid B-cell lymphoma," which was renamed in 1994 in the RREAL as "nodal marginal zone lymphoma with or without monocytoid B-cells."[9] NMZL was ultimately included as one of three MZL types in the 2001 and 2008 WHO classifications.[2] NMZL is an uncommon form of lymphoma representing 1.5%–1.8% of lymphoid neoplasms, with only rare reports in the literature that have attempted morphologic or immunophenotypic characterization.[8] Campo *et al*. classified growth patterns in NMZL into splenic type and MALT type which subsequently become subject of debate.[11]

On high power, NMZL cells show heterogeneous morphology, varying from centrocyte-like cells to monocytoid cells to plasmacytoid cells and plasma cells with varying numbers of interspersed centroblasts and immunoblasts. Monocytoid cells have a central nucleus with condensed chromatin and indistinct nucleoli, surrounded by ample pale cytoplasm. Centrocyte-like cells, resembling the centrocytes of the germinal center, have nuclei with slightly irregular nuclear membranes and a coarser chromatin structure. Lymphoplasmacytoid cells have some, but not all features of plasma cells; in comparison to plasma cells, they have less cytoplasm that is basophilic. Predominance of monocytoid cells is rare and should prompt the consideration of secondary lymph node involvement by MALT lymphoma.[12]

Specific markers for MBC are still lacking, and this makes it difficult to analyze their relationship with other B-cell populations and to confirm the existence of tumors derived from this cell population. This difficulty is reflected in the denomination of the tumors that are thought to derive from MBCs, which have been recently termed as nodal MZB-cell lymphoma/MBCL.[13]

Diagnosis of MBCL requires exclusion of other small B-cell lymphomas. The present case showed immunopositivity for CD20 which is a pan B-cell marker and BCL2 gene. BCL2 is located at chromosome 18q21, encodes inner mitochondrial membrane protein that prevents apoptosis. CD43, known as sialophorin, is a product of SPN gene and encodes a sialoglycoprotein found on the surface of

thymocytes, T-lymphocytes, monocytes, granulocytes and some B-lymphocytes. It is useful in the evaluation of MZL as it may be expressed on the neoplastic lymphoid cells.[8] CD43 expression has also been detected in benign lymphoepithelial lesions or expansion of MBC halos in the salivary gland.[14]

Immunohistologic staining for CD43 and BCL2 can be helpful in the diagnosis of NMZL, but shows significant variation among cases and in rates of positivity reported in previously published studies. Staining for CD43 is reported to range from 20% to 75%, whereas the staining for BCL2 has been reported to range from 62% to 100%.[7] Immunohistologic stains for CD43 and BCL2 are helpful when present and aid in identifying the neoplastic B-cell infiltrates on which they are co-expressed; however, their expression is not essential for the diagnosis of NMZL. In addition, other B-cell NHL such as mantle cell lymphoma (MCL) (frequently positive for both CD43 and BCL2) and FL (particularly, diffuse follicle center lymphoma) should also be carefully eliminated from the differential diagnosis.[8] FL showed higher expression of germinal center markers, i.e., CD10, LMO2 in comparison to NMZL.[12] CD10 is negative in this case, thus excluding FL. MCL can be distinguished from NMZL by its positivity for CD5 which is involved in T- and B-cell receptor signaling pathways. It is a useful T-cell marker and is present on postthymic T-cells as well as thymocytes and on small subset of normal B-cells.[8] CLL can be differentiated from NMZL by its expression of CD5 and CD23. CD 23 is a low affinity receptor for IgE and has role in cell–cell interactions and is expressed on a variety of cell types including activated B-cells and subset of follicular dendritic cells.[8] Thus, immunonegativity for CD10, CD5 and CD23 differentiates it from FL, MCL and CLL. Immunonegativity for CD3 excludes T-cell lymphomas. Expression of CD11c is highly associated with SMZL which rarely presents with lymphadenopathy. It virtually always infiltrates the bone marrow with a characteristic intertrabecular and intrasinusoidal pattern, which is not typical of NMZL.[13] Cells show immunoreactivity for epithelial cells and immunonegativity for monocytoid cells which excludes the diagnosis of epithelial tumors. Ki67 expression of 8% in this case suggests a low-grade tumor with good prognosis.

Accurate diagnosis of most mature small B-cell lymphomas can be achieved with a meticulous morphologic evaluation and a concise immunohistochemical panel.

## CONCLUSION

NMZL is a distinct entity among NHLs, and particularly among the indolent small B-cell lymphomas, representing unique clinical and morphological characteristics. Diagnosis of lymphomas requires the integration of clinical, morphologic, immunophenotypic and genetic information to reach a definitive diagnosis. Immunophenotyping although indispensable in the diagnosis and classification of lymphoid neoplasms has to be used cautiously with knowledge of the antibodies used.

### 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.

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