

CASE REPORT

Primary B-cell MALT lymphoma of the palate: A case report and distinction from benign lymphoid hyperplasia (pseudolymphoma)

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ABSTRACT

Diagnosis of palatal swellings is a challenge. Benign and malignant tumors may be misinterpreted as lesions of inflammatory origin. We present a case of B-cell non-Hodgkin lymphoma on the palate of a 40-year-old male. A number of factors can make the diagnosis of oral lymphoma difficult. Many lymphomas are extranodal, there is usually a prominent superimposed nonspecific inflammatory response and thus they mimic benign lymphoid hyperplasia. It is important for the pathologist to be familiar with features that distinguish benign from malignant lymphoid proliferations.

Key words: B-cell lymphoma, benign lymphoid hyperplasia, extranodal non-Hodgkin lymphoma, MALT, monocytoid B-cell lymphoma, pseudolymphoma

INTRODUCTION

The diagnosis of palatal lesions is a challenge for any clinician. The palate is a complex area of the mouth, with a variety of native tissue types that give rise to a plethora of pathological conditions, both benign and malignant [Table 1].^[1,2] 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 lymphoma or non-Hodgkin lymphoma (NHL) and may be of either B-lymphocyte or T-lymphocyte origin.^[3] Lymphoma is the second most common neoplasm of the head and neck region after squamous cell carcinoma. Nearly 24%–48% of NHL can arise in extranodal locations, and 3%–5% are primarily located in the oral cavity.^[4,5]

Oral lymphomas are relatively rare and are often difficult to diagnose as they may mimic other pathologies such as periodontal diseases, osteomyelitis, or some other malignancy.^[6] Lymphoid lesions of the palate can be divided

into three categories, the management and prognosis of each category being different:^[7]

1. Primary lymphoma of the palate, with no other lymphomatous lesion detected elsewhere in the body
2. Lymphoma of the palate occurring as one of the lesions in a case of disseminated lymphoma
3. Benign lymphoid hyperplasia (BLH) of the palate

In addition, histologically, lymphoid lesions of the palate may be misinterpreted as inflammatory in nature. The purpose of our report is to present a case of B-cell lymphoma on the palate and distinguish it from benign lymphoid hyperplasia (BLH).

CASE REPORT

A 40-year-old man with a swelling in the right palatal region was referred to the department of oral pathology for evaluation and diagnosis. The painless mass was noticed 4 months ago by the patient.

Intraoral examination exhibited a firm, exophytic, oval mass with an intact overlying mucosa in the region of the right hard palate measuring 3 × 4.5 cm in size [Figure 1]. There were no signs of ulceration, bleeding, discharge, or numbness in the area. The patient did not have the habit of chewing tobacco or betel nut. On general examination, he was found to be afebrile, with no palpable lymph nodes in the head and neck region.

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Table 1: Differential diagnosis of palatal swellings

Developmental
Palatal torus
Inflammatory/reactionary
Periapical abscess
Periodontal abscess
Fibroepithelial polyp
Pyogenic granuloma
Adenomatous hyperplasia
Atypical lymphoproliferative disorder/follicular lymphoid hyperplasia
Cysts
Radicular (periapical) cyst
Dentigerous cyst
Nasopalatine cyst
Incisive canal cyst
Odontogenic keratocyst
Neoplasms
Salivary gland
Pleomorphic adenoma
Adenoid cystic carcinoma
Mucoepidermoid carcinoma
Polymorphous low-grade adenocarcinoma
Adenocarcinoma NOS
Carcinoma ex-pleomorphic adenoma
Necrotizing sialometaplasia
Odontogenic
Ameloblastoma
Adenomatoid odontogenic tumor
Odontogenic myxoma
Others
Fibrous histiocytoma
Schwannoma
Neurofibroma
Lymphomas
Osteosarcoma
Chondrosarcoma
Fibrosarcoma

He did not mention any sudden weight loss in the recent past and the medical history was noncontributory.

CT scan revealed a mass on the right side of the hard palate, with no involvement of the maxillary sinus [Figure 2]. A provisional diagnosis of benign tumor of salivary glands was given.

An excisional biopsy [Figure 3] was performed under local anesthesia. and a bony crater-like defect was seen on the palatal bone after soft tissue removal. Histopathological examination of sections of the resected specimen revealed an intact stratified squamous epithelium with underlying vaguely follicular and diffuse proliferation of lymphoid cells [Figure 4a and b]. The follicle-like structures were composed of central large cells (giving a ‘washed-out’ appearance) surrounded by a thin rim of small, round lymphocytes. The central large cells had abundant pinkish cytoplasm and convoluted nuclei with inconspicuous



Figure 1: Clinical photograph showing swelling on the palate

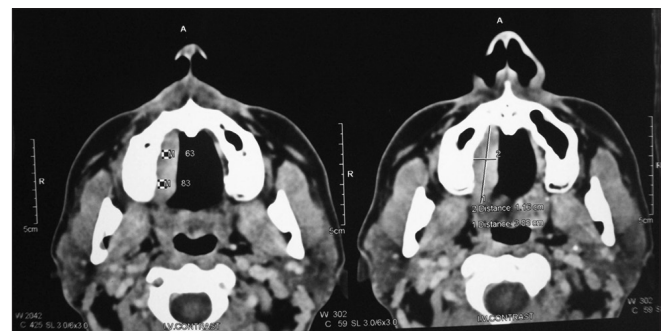


Figure 2: Computed tomography scan of patient

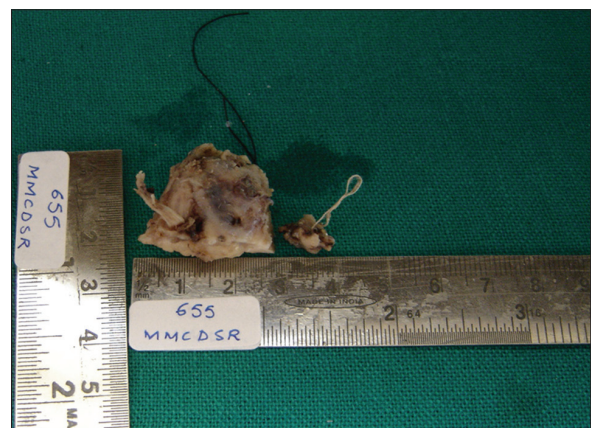


Figure 3: Photograph of gross excisional tissue

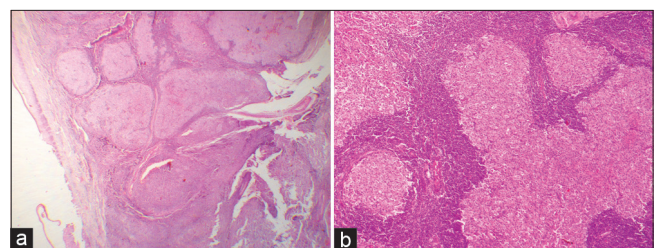


Figure 4: (a) The overlying epithelium is seen separated from follicles. The histological picture in this view gives the impression of reactive follicular hyperplasia of the lymphoid tissue (H and E, stain; original magnification, ×2.5). (b) High-power view of the follicular pattern gives the impression of a reactive lesion (H and E, stain; original magnification, ×10)

nucleoli [Figure 5]. Epimyoeptithelial islands were also observed. On microscopic examination of hematoxylin and eosin (H and E)–stained sections, there was a conflict of opinion over the distinction between benign (reactive) lymphoid hyperplasia (pseudolymphoma) and non-Hodgkin lymphoma. Immunohistochemical investigations were performed to resolve the issue. The large lymphoid cells showed immunoreactivity for CD20 and the rim of small lymphocytes were positive for CD5 [Figure 6]. The large lymphoid cells were negative for CD5, Bcl-2, and CD10 [Figures 7–9]. The Ki67 proliferative index was 1% [Figure 10].

The patient was referred to a general physician for systemic evaluation and was found to be free of other systemic manifestations. There were no palpable lymph nodes found anywhere in the body. A final diagnosis of low-grade B-cell lymphoma of mucosa-associated lymphoid tissue (MALT) was accorded based on the clinical, radiographic, histopathologic, and immunohistochemical investigations.

DISCUSSION

Lymphoma constitutes a diverse and complex group of malignancies of lymphoid histogenesis. According to the revised European–American Classification of Lymphoid Neoplasms (REAL), classification the category of marginal zone B-cell lymphoma includes lymphomas that were originally designated as monocytoid B-cell lymphoma and low-grade B-cell lymphoma of MALT. Both these neoplasms were thought to represent different clinical presentations of a B-cell lymphoma believed to arise from normal marginal zone B-cells in the lymph node or their extranodal counterparts, respectively.^[8]

The most frequent location of extranodal lymphoma in the head and neck is the palate. Lymphoma usually appear as a nontender diffuse mass and are rarely ulcerated. Many salivary gland lymphocytic infiltrates of the palate are usually non-Hodgkin B-cell lymphomas of MALT.^[9]

Extranodal marginal B-cell lymphomas of MALT (B-MALT) are known to show histologic features similar to benign lymphoid hyperplasias (BLH). In the past, many low-grade lymphomas were probably misdiagnosed and inappropriately categorized as BLH. Extranodal infiltration composed of small round or slightly irregular lymphoid cells—often admixed with plasma cells, histiocytes and lymphoid follicle—were classified as ‘pseudolymphomas’ since clinical studies showed that in patients with these lesions, the disease pursued an indolent clinical course.^[10]

The term pseudolymphoma/benign lymphoid hyperplasia should be restricted to tumefactive lesions with prominent lymphoid infiltrate that by routine morphology appears to be reactive and that on ancillary immunophenotypic and

molecular genetic analysis lacks evidence of clonality.^[11] There appears to be no appreciable clinical difference between BLH and the palatal lymphomas. Both can present as unilateral or bilateral swellings that may be soft or firm. Both lesions usually have intact surface mucosa. Our case also had no mucosal ulceration. Even histopathologically, palatal lymphoma is very similar to BLH. The subtle distinctions in interpretation of the histological characteristics between benign and malignant lymphoid proliferations makes the diagnosis of these lesions difficult. Several papers have dealt with the histologic features of BLH and nodular lymphoma.^[12–14] Fortunately, with the advent of advanced immunophenotyping and molecular genetic techniques, it is now possible to differentiate the two lesions. Table 2 lists out the essential features that help us distinguish BLH from B-cell MALT lymphomas.^[11,15]

BLH is characterized by numerous well-demarcated germinal centers of varying size and shape often rimmed by a mantle of small lymphocytes. While many B-cell lymphomas have a nodular growth pattern, these nodules are neoplastic and should not be considered germinal centers.^[16,17] In addition, in lymphomas, these neoplastic nodules tend to be ovoid to round and show little variation in size. In BLH, the cells demonstrate all stages of follicular center cell transformation, including plasma cells. Mitosis may be abundant, although never atypical and never seen outside the germinal centers. Nuclear debris and evidence of phagocytosis are often prominent. The cells comprising malignant lymphomas, on the other hand, are neoplastic and do not show the wide range of cell types seen in reactive lesions. Nuclear atypia as well as mitosis (occasionally atypical) may be seen, but the mitotic rate rarely approaches that seen in benign lesions.

In our case, the follicle-like structures showed variation in size and were composed of central large cells surrounded by a thin rim of small, round lymphocytes. Mitotic activity was found to be quite low. Hence, it was quite difficult to give a confirmative diagnosis solely on the basis of routine histopathologic examination. Therefore we performed immunohistochemical analysis on the lesional tissue for the following markers: CD20, CD5, CD10, Bcl2, and Ki-67. The result was positive for CD20 and negative for CD5, CD10, and bcl2, while Ki-67 showed positivity of 1%. Immunophenotypic studies have shown that low-grade B-cell lymphomas of MALT typically do not express the B cell-associated antigens CD10, CD21, or Cd23, or the T-cell antigens (including CD5).^[8,18] These findings were consistent with the immunohistochemistry profile of our case and thus confirmed our diagnosis of low-grade B-cell lymphoma of MALT.

MANAGEMENT

Patients with localized low-grade B-cell lymphomas follow a very indolent clinical course. Therapeutic strategies for this kind of disease are not standardized yet due to the small number of MALT lymphomas described in the head and neck region.

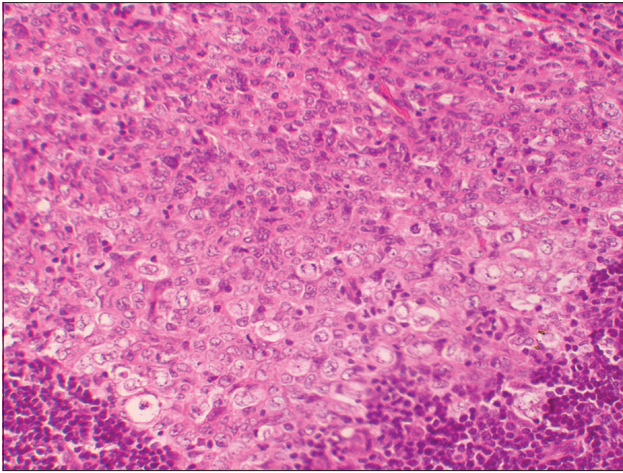


Figure 5: Magnified view showing central larger cells with mitotic figures, convoluted nuclei, and inconspicuous nucleoli. Peripherally, small round lymphocytes are seen (H and E, stain; original magnification, ×20)

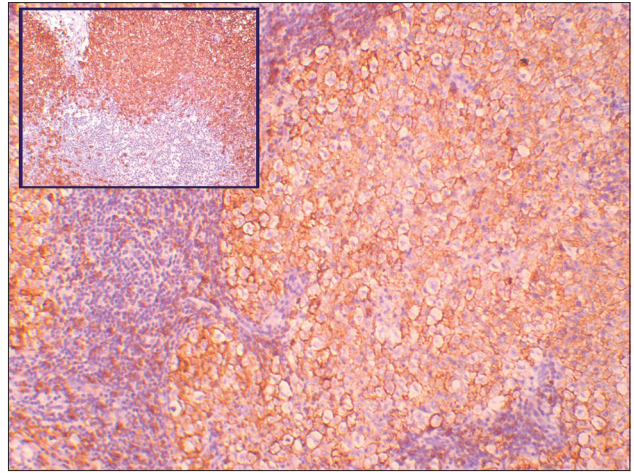


Figure 6: The large lymphoid cells show positive immunoreactivity for CD20, whereas the peripheral small lymphocytes are negative. Inset shows control stain (original magnification, ×10)

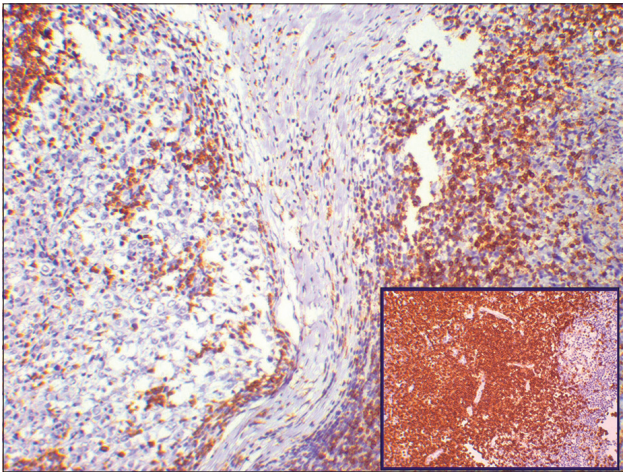


Figure 7: The peripheral small lymphocytes show positive immunoreactivity for CD5, whereas the central large cells are negative. Inset shows control stain (original magnification, ×10)

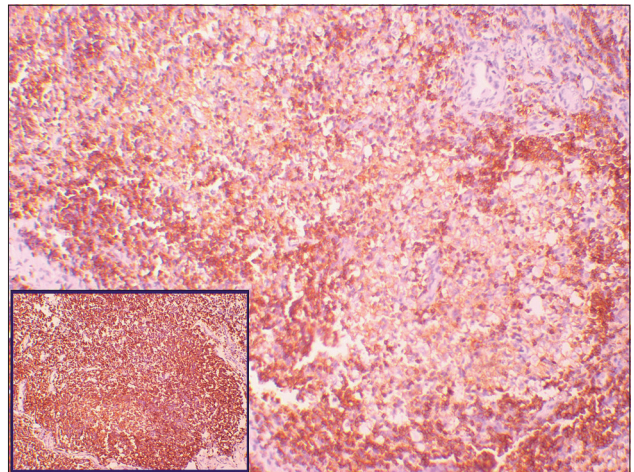


Figure 8: The peripheral small lymphocytes show positive immunoreactivity for Bcl2, whereas the central large cells are negative. Inset shows control stain (original magnification, ×10)

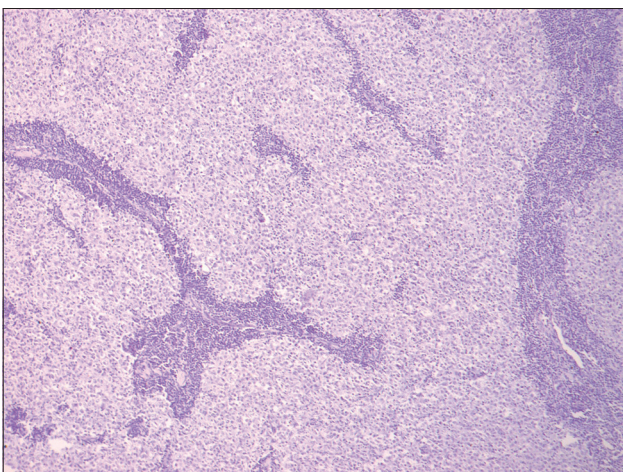


Figure 9: Negative immunoreactivity for CD10 (original magnification, ×10)

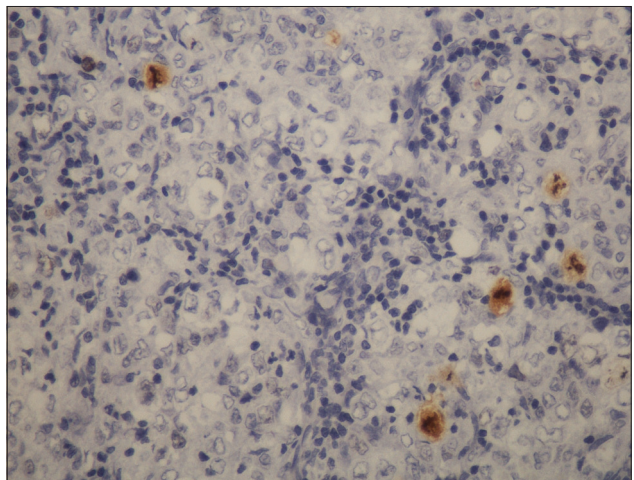


Figure 10: Immunohistochemistry profile showing very low Ki67 proliferative index (original magnification, ×20)

Table 2: Lymphoid hyperplasia vs B-cell MALT lymphoma

	Lymphoid hyperplasia	B-cell MALT lymphoma
Clinical		
Size	Small	Large
Presentation	Localized mass/consolidation	Single or multiple nodules/consolidation
Behavior	Self-limited	Persistent
Number	Single or multiple	Single or multiple
Histology		
Architecture	Top-heavy	Bottom-heavy
Density	Moderate, sometimes dense	Dense
Germinal centers	Present, normal appearing	Usually present with thick cuff of lymphoid tissue; colonization of germinal centers by monocytoid or centrocytic cells
Cellular composition around germinal centers	Polymorphous cellular composition, usually lymphocytes and plasma cells, with occasional histiocytes and giant cells	Mixed, including variable numbers of lymphocytes, monocytoid/centrocytic cells, transformed lymphocytes, and plasma cells
Epithelial infiltration by lymphoid cells	Lymphoepithelial lesions inconspicuous	Lymphoepithelial lesions often prominent
Cytologic atypia	Minimal	Present
Immunophenotyping	CD20+ B-cells usually confined to follicular and immediate perifollicular regions, with the remainder of the cells being predominantly T-cells; polytypic plasma cells	Predominant population of CD20+ B-cells (CD5-, CD10-, CD23-negative) with appreciable background population of T-cells positive for CD3+; plasma cells may be monotypic or polyclonal
Aberrant antigen expression	Absent	Present, e.g., bcl-2
Molecular studies	No clonal population identified; polyclonal	Clonal population identified in most cases

Remedial measures include combined radiochemotherapy for advanced cases and either radiation therapy or surgery for small lesions. Our patient underwent surgical excision of the lesion and continues to be well after 6 months of follow-up.^[19]

CONCLUSION

A number of factors can make the diagnosis of oral lymphoma difficult, despite the fact that the histological features are the same as at other sites. Many lymphomas are extranodal and there is almost always a prominent superimposed, nonspecific, inflammatory response. Clinically obvious lymphomas present primarily to the medical rather than the dental practitioner or oral surgeons. Hence to see a spectrum of lymphomas in oral pathology practice is unusual. Early recognition and biopsy are extremely important because the lymphoma may be confined entirely to the palate in the early stages and such localized palatal lymphomas respond well to irradiation, whereas disseminated disease necessitates chemotherapy.

Malignant B-cell lymphoma mimics BLH, both clinically and histologically. The pathologist must be familiar with the features that distinguish between these two diseases. Light microscopy supported by immunohistochemistry is essential for providing the final diagnosis.

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