CASE REPORT

Case Report: Activated B-cell-diffuse large B-cell lymphoma

[version 1; peer review: 1 approved with reservations]

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Abstract

Lymphomas of the oral and oropharyngeal regions are rather uncommon, and diagnosis can be challenging and confusing due to the multiple histological subgroups. Lymphomas are the third most common type of tumor in the head and neck region and are brought on by the lymphoreticular system. The two forms of lymphoma are Hodgkin's lymphoma and non-Hodgkin's lymphoma (NHL). Herein, we present a case report of oropharyngeal lymphoma. The female patient reported with a complaint of swelling over the palatal region for two to three months. An ulceroproliferative lesion was evident over the posterior palatal region. We diagnosed reactive lymphadenitis based on an incisional biopsy. To confirm the diagnosis and rule out other conditions, a punch biopsy followed by immunohistochemical studies were done. Features suggestive of activated B-cell-diffuse large B-cell lymphoma were confirmed. Among malignant lymphomas, diffuse large B-cell lymphoma is the most prevalent variety. Much progress has been made in recent years in understanding the molecular pathophysiology of this disease. In this case report, we aim to correlate the clinical presentation, histology features and immunohistochemical significance in order to promote early discovery, diagnosis, and treatment for a better prognosis of the patient.

Keywords

diffuse large B cell lymphoma, immunohistochemistry, lymphocytes, non-Hodgkin's lymphoma, oral cavity

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Introduction
Samuel Wilks coined the term “Hodgkin’s disease,” which is now known as “Hodgkin lymphoma,” in recognition of the earlier report by Thomas Hodgkin from Guy’s hospital in London.1 Lymphomas are a diverse group of lymphoid malignancies with a range of clinical behaviour patterns and therapeutic responses. The histologic type, clinical variables, and more recently, molecular traits all affect the prognosis.2 In terms of prevalence, lymphomas rank ninth among males and tenth among women worldwide. Lymphomas are the second most prevalent type of cancer in the head and neck region, and they rank third after squamous cell carcinoma and salivary gland cancers in the oral cavity. Even though lymphomas account for 3% to 5% of all reported cases in the head and neck region, they are the most prevalent non-epithelial malignant tumors in the same region.1 Typically, no underlying cause of lymphoma is found in any specific occurrence. Nonetheless, other environmental, viral, and genetic risk factors for lymphoma have been discovered. Certain lymphomas have been linked to a number of infectious agents, including Helicobacter pylori, Borrelia burgdorferi, Chlamydia psittaci, and Campylobacter jejuni.4 We adhere to the CARE reporting guidelines to report this Case report.5

Case report
A 63-year-old female, presented to the outdoor patient department of our institution in January 2023, with a complaint of a non-healing ulcer over the posterior palatal region for two to three months. She described no symptoms before two to three months but later observed swelling over the posterolateral region of the soft palate. Initially, it was 2 × 1 cm in size and increased to the current size of 4 × 3 cm approximately. She described difficulty in mastication and swallowing. A change in consistency and quantity of saliva was reported by the patient. No history of trauma was present. Intraorally, a single ulceroproliferative lesion present over the anterior faucial pillar was observed (Figure 1, marked with a red circle). The lesion was oval, reddish pink in color, with ill-defined borders, soft to hard in consistency, nonmobile, and had an irregular surface. Uvula deviated to the left side. Lymph nodes in the left submandibular region were palpable, of size 1 × 2 cm, non-tender, and firm in texture. In December 2022, an incisional biopsy was taken with a histopathological diagnosis of reactive lymphadenitis. This was followed by a punch biopsy (Figure 2) in January 2023, with histopathological features suggestive of a lymphoproliferative lesion. No extraoral extension of the growth was evident.

Figure 1. Clinical photo of the patient showing swelling on the posterolateral portion of the soft palate.

Figure 2. Punch biopsy specimen (2 × 1.7 cm).
Histological features
Haematoxylin and Eosin-stained sections showed predominantly a diffuse infiltrate of large-sized atypical B cell population comprising of scant cytoplasm. The nucleus was double the size of the nucleus of a normal lymphocyte, vesicular chromatin, and prominent nucleoli (Figure 3A, marked with red arrows). Complete effacement of normal lymphoid tissue architecture was present.

Immunohistochemical findings
Immunohistochemical features with cytokeratin staining were negative, CD45 was strongly positive with an intensity score of 3, proportionate scores of 4 (Figure 3B), and CD20 positive. On the basis of histopathological and immunohistochemical features, the lesion was suggestive of an activated B-cell (ABC) subset of diffuse large B-cell lymphoma (DLBCL).

Radiographic features
A contrast-enhanced computerized tomography (CECT) presented evidence of a soft tissue density lesion with few non-enhancing necrotic areas noted in the left tonsillar fossa measuring 2.2 × 2 × 2.7 cm (Figure 4A, marked with a red circle) with the following extensions: a. Anteromedially extending into the oropharynx causing partial obstruction with non-visualization of uvula suggestive of involvement abutting the base of the tongue and vallecula (Figure 4B, marked with a}

Figure 3. A: Diffuse infiltration of large lymphocytes (marked by red arrow); B: CD45 positive.

Figure 4. A: Non-enhancing necrotic areas noted in the left tonsillar fossa; B: Anteromedial extension abutting to the base of the tongue.
red circle). b. Posteroinferiorly involves the posterior pharyngeal wall. c. Laterally involving the peritonsillar space including the pharygobasilar fascia, styloglossus and stylopharyngeus, and the posterior belly of the digastric.

**Treatment**
DLBCL becomes less fatal and may even be cured with combination chemotherapy, which only successfully treats less than 50% of patients. The type of therapy will either be curative, where survival is the goal, or palliative, where the goal is to improve the patient’s quality of life, depending on the patient’s status. Rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) is the standard treatment for DLBCL patients. Approximately 60–70% of DLBCL patients who continue this regimen are free of illness.

In the present case, chemotherapy (cyclophosphamide, hydroxy doxorubicin, oncovin, and prednisone) was used to treat the patient. The patient continued receiving CHOP chemotherapy, and her overall health is improving. A four-month follow-up showed regression of the swelling. The patient is still on treatment.

**Discussion**
Malignant lymphomas are a category of neoplasms with variable degrees of malignancy that are derived from the lymphoid tissue’s fundamental cells, the lymphocyte, and histiocytes at any stage of development. The classification of lymphomas originating from these normal lymphoid populations is challenging since the physiologic immunological roles of lymphocytes vary depending on lineage and degree of development. NHL and Hodgkin lymphoma (HL) are the two main categories into which lymphomas are frequently categorized. NHLs are a variety of lymphoproliferative malignancies that have a far higher propensity to disseminate to extranodal locations than Hodgkin’s lymphoma. A class of neoplasms, occurs due to the uncontrolled proliferation of B-, T-, or Natural Killer (NK) cells. T-cell or NK cell-derived illnesses account for 10 to 15 percent of all NHL cases. DLBCL, which accounts for 30–40% of cases in various parts of the world, is the most common NHL. It is most commonly seen in the sixth to seventh decade of life. DLBCL is a diverse entity in terms of clinical presentation, genetic advances, therapeutic options, and prognosis. There was a significant advancement when gene expression profiling (GEP) was applied to further detect this variety and provide a rationale for categorizing patients in the study of DLBCL. DLBCL patients are divided into subtypes named germinal center B-cell-like (GCB), ABC, and 10–15% remain unclassified. The ABC subtype is derived from B cells that are undergoing plasma cell development. Patients with the ABC subtype often have the worst prognosis than those with the GCB subtype. However, there is morphological and clinical heterogeneity in DLBCL. However, patients with GCB DLBCL still do considerably better than those with ABC DLBCL. Expression of CD20 (cluster of differentiation antigens) in lymphoma cells is essential for both making an accurate diagnosis and creating a strategy for biological therapeutic therapy. CD20 antigen is expressed on the surface of neoplastic cells in the majority of B-cell lymphomas, albeit the degree of CD20 expression varies depending on the type of lymphoma and the degree of lymphoma B-cell differentiation. Hence, it is assumed that CD20 expression is high in DLBCL and hairy cell leukemia cells, and low in B-cell chronic lymphocytic leukemia (CLL). Particularly, ABC DLBCLs express X-box binding protein-1 (XBP-1), a significant modulator of the secretory phenotype of plasma cells. About 25% of ABC DLBCL samples taken from patients have BLIMP1-inactivating mutations in the PRDM1 gene. By inhibiting the expression of the majority of mature B-cell differentiation genes, BLIMP1 promotes plasmacytic differentiation. Consistent activation of the nuclear factor-kappa B (NF-kB) signaling pathway, which stimulates cell survival and proliferation while inhibiting apoptosis, is another pathogenic characteristic of ABC DLBCLs. In order to ensure the most effective use of investigational treatments or currently accessible, frequently expensive therapeutic agents, pathologists must also evaluate the markers required to support their usage. Additionally, pathologists must prioritize sufficient and viable tumor tissue for high-throughput molecular analysis.

According to the location and histologic type, clinical presentation differs substantially. Biopsy in conjunction with immunohistochemical investigations of biopsy tissue is the only accurate way to identify and classify these lesions. No single antibody has been useful for subdividing DLBCL or determining prognosis, according to research by Meyer et al. Because of this, many antibody combinations or methods have been created. For the differential diagnosis of 40 cases of oral NHL, Van der Waal et al. used the following antibodies: L26 (CD20, a pan B-cell marker), CD 79a (the immunglobulin anchoring molecule, so a B-cell marker), CD3, and UCHL 1 (CD45RO), both pan T-cell markers, BerH2 (CD30), and Mib1 (staining primarily B cells). Forty cases of oral cavity NHL were studied by Kemp et al. for sex, age, location, clinical presentation, and WHO histological subtype. They found that 98% of the lymphomas in their investigation had a B cell lineage, and the majority of these were histologically subtype as diffuse large B cell lymphomas (58%). Our study is in accordance with Kemp et al., who used an immunohistochemical panel that included CD3, CD5, CD20, CD45RO, CD79a, leukocyte common antigen, Bcl-2, CD10 and CD23 to validate the lineage and help characterize the subtype. According to them, molecular testing is typically useful in determining genetic infiltration and seems to be a useful supplement to diagnosis. In nonimmunocompromised patients, diffuse large B-cell lymphoma in
the head and neck region was the most prevalent form observed, according to Hicks and Flaitz, 2001. Hashimoto and Kurihara (1982), reviewed pathological characteristics of oral NHL and according to his nine cases and review of the literature, he concluded that B-cell lymphoma is the most common histotype in oral NHL. Therefore, in order to diagnose a rare condition, this case report emphasizes the value of early biopsies of oral lesions and the use of a definitive marker among other available immunohistochemical markers.

**Limitations**
The study has limitations due to the patient’s ongoing treatment and the relatively short follow-up time.

**Conclusions**
Oral NHL is a very uncommon disorder that may cause localized swelling, inflammation, or discomfort in the vestibule, gingiva, or posterior hard palate. DLBCL is a genetically heterogeneous disease with equally different clinical manifestations. Hence, one can determine the malignant nature and prognosis of various kinds of lymphomas by correlating the histological characteristics of these entities. Pathologists should evaluate immunophenotypic and genetic markers that are useful for determining prognosis. In order for the patient to receive therapy at an early stage and have a favorable prognosis, a thorough evaluation of the patient and appropriate investigations are needed for a precise diagnosis.

**Consent**
Written informed consent for publication of their clinical details and clinical images was obtained from the patient.

**Data availability**

**Underlying data**
All data underlying the results are available as part of the article and no additional source data are required.

**Reporting guidelines**

Data are available under the terms of the Creative Commons Attribution 4.0 International license (CC-BY 4.0)

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**References**


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Reviewer's comments to Author:
1. Is there any laboratory test data that can be presented in this case report? Such as EBV or Serology detection?

2. Does the patient have enlarged lymph nodes on other imaging?

3. Physical examination for lymph node lesions in other parts?

4. What should be included in the imaging differential diagnosis and clinical differential diagnosis? Can it be determined that he has primary lymphoma?

5. Is there detection of EBV-related staining or molecular detection in pathological diagnosis?

6. What are the learning objectives of this case report?

Is the background of the case's history and progression described in sufficient detail?
Partly

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?
No

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?
Yes

Is the case presented with sufficient detail to be useful for other practitioners?
Yes

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Cancer, Pathology, Immunology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

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