

Unusual Presentation of Oropharyngeal B-Cell Lymphoma

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ABSTRACT

We present the intriguing case of a 64-year-old woman in good health complaining of dysphonia and odynophagia for about 2 months. Flexible fiberoptic laryngoscopy revealed an excavated lesion on the right side of the base of the tongue, which was in communication with the laryngeal vestibule through the epiglottis. The patient underwent biopsy of the lesion by microlaryngoscopy under general anesthesia. Histological evaluation of the surgical specimen revealed a high-grade diffuse large B-cell lymphoma of non-germinal center type. Excavated lesion at the base of the tongue may be of various types, and it is important to consider rarer differential diagnoses, especially in patients with clinical histories not suggestive of squamous cell carcinomas or lesions of infectious origin. Non-Hodgkin's lymphomas arising from the base of the tongue are very rare. Moreover, this lesion is usually described in the literature as a swelling with an intact and smooth surface, totally different from that of our patient. The aim of this report is to examine clinically, endoscopically, and radiologically the main differential diagnoses of an excavated lesion of the base of the tongue, focusing on one of the rarest ones, large B-cell lymphoma of the oropharynx.

Keywords: Cancer, dysphonia, dysphagia, head and neck cancer, chemotherapy, swallowing

Introduction

All of the procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Before the procedure, a thorough counseling was performed with the patient and a written informed consent was obtained.

Case Presentation

A 64-year-old woman in good health presented to our center complaining of dysphonia and odynophagia for about 2 months. Six months before, she had complained of painless cervical lymphadenopathy that resolved with cortisone and antibiotic therapy and tested negative for malignancy on ultrasound-guided needle aspiration. She denied any associated symptoms such as fever, unwanted weight loss, fatigue, or altered appetite. She also had no history of voice changes or laryngeal trauma in the past. The patient was not a smoker or alcohol user. Her laboratory values were normal.

Radiologic and Clinical Findings

Flexible fiberoptic laryngoscopy revealed an excavated lesion on the right side of the base of the tongue (BOT), which was in communication with the laryngeal vestibule through the epiglottis (Figure 1A and 1B). Cervical lymphadenopathies could not be appreciated on palpation of the neck. Findings of other systemic examinations were within normal limits. A computed tomography (CT) scan of the neck revealed a tissue thickening at the right BOT that involved the epiglottis caudally with extension through it into the laryngeal vestibule. The lesion had a transverse diameter of approximately 3.5 × 3 cm and extended 3 cm craniocaudally (Figure 2A). Some lymphadenomegaly was evident in the cervical region, particularly on the left side. Computed tomography scan of the chest was negative for lesions. The patient then underwent biopsy of the lesion by microlaryngoscopy under general anesthesia.

Histologic Findings and Diagnosis

Histological evaluation of the surgical specimen revealed a deep diffuse infiltration of monomorphic large cells with normal surface epithelium (Figure 3A and 3B). Immunohistochemistry shows positivity for CD20, BCL2, BCL6, and MUM1 in large

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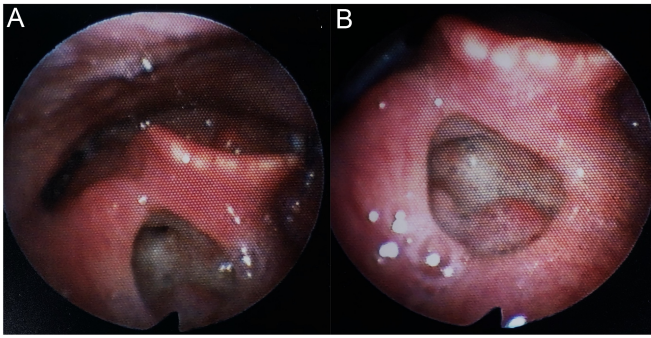


Figure 1. (A-B) Fiberoptic laryngoscopy shows an excavated lesion on the right side of the base of the tongue, which is connected to in communication with the laryngeal vestibule through the epiglottis.

lymphoid cells, while CD10, CD5, and EBER were negative (Figure 4). The proliferation index was high (ki67: 70%). Fluorescence in situ analysis shows no cMyc, BCL2, or BCL6 rearrangements.

The final diagnosis was of a diffuse large B-cell lymphoma of non-germinal center type.

Complete staging with positron emission tomography computed tomography (FDG/PET-CT) (Figure 2B–2D) showed increased metabolic activity on the right side of the BOT (SUV 29) which extended to the epiglottis and right pyriform sinus, confirming the absence of secondary foci. The patient received 6 cycles of cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) chemotherapy.

The patient has responded well to the therapy, no longer complains of dysphagia, and is currently 6 months post-treatment free of disease.

Discussion

The majority of malignancies of the BOT are SCC, but other malignant processes may occur, including lymphoepithelial carcinomas, hematolymphoid tumors, salivary gland tumors, and mucosal melanomas. Lymphomas are the second most

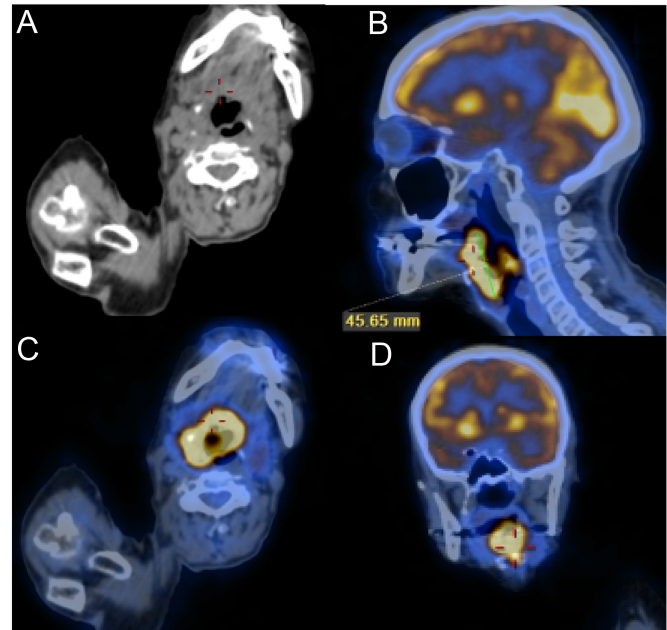


Figure 2. (A) Computed tomography scan of the neck reveals a tissue thickening at the right base of the tongue that involves the epiglottis caudally. (B-D) Positron emission tomography computed tomography shows increased metabolic activity on the right side of the base of the tongue (SUV 29) which extends to the epiglottis and right pyriform sinus, without secondary foci.

common primary malignancies in the head and neck region after SCC, with non-Hodgkin lymphoma (NHL) accounting for 65%-90% of all lymphomas in this region. The head and neck region is, after the gastrointestinal tract, the second most frequent site for extranodal lymphomas. However, lymphomas occurring primarily in the oral cavity are rare and even rarer are those at the BOT.^{1,2} Because of the small number of cases, it is difficult to determine the biological behavior and treatment options of lymphomas occurring in this district.

The etiologic factors associated with lymphomas of this region, apart from EBV and HIV, are poorly understood.³ There is a logarithmic increase in incidence with age and there are no sex differences in NHL of the head and neck.^{4,5}

The clinical features of involvement of the BOT by NHL are not specific, therefore, such tumors are misdiagnosed as proliferative or infectious lesions in the early stages.² The most common symptoms are more or less severe discomfort in the pharynx, such as the sensation of a pharyngeal foreign body or choking when drinking. Involvement of the extrinsic tongue musculature can lead to restricted movement, dysarthria, and dysphagia.⁶ Late stages can cause dyspnea.⁷

Imaging examination can help identify lesions. The best way to diagnose NHL of the BOT is a biopsy. In special cases, multiple biopsies are required. Differential diagnoses include carcinoma, benign lymphoid hyperplasia, and abscess. Current standard therapy consists of cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) alone or in combination with rituximab (R-CHOP). Therapeutic response depends on the pathological subtype and several factors, such as advanced age, high-grade histology, and advanced stage.^{5,8} Pathologically, diffuse large B-cell lymphoma (DLBCL) is the most common

Main Points

- The head and neck region is, after the gastrointestinal tract, the second most frequent site for extranodal lymphomas. However, lymphomas occurring primarily in the oral cavity are rare and even rarer are those at the base of the tongue.
- The patient came to our attention with aggravating dysphagia and dysphonia.
- Flexible fiberoptic laryngoscopy revealed an excavated lesion on the right side of the base of the tongue, which was in communication with the laryngeal vestibule through the epiglottis.
- Lymphomas in this region are usually described in the literature as a swelling of the base of the tongue with an intact and smooth surface, totally different from that of our patient.
- Excavated lesion at the base of the tongue may be of various types and it is important to consider rarer differential diagnoses, especially in patients with clinical histories not suggestive of squamous cell carcinomas or lesions of infectious origin.

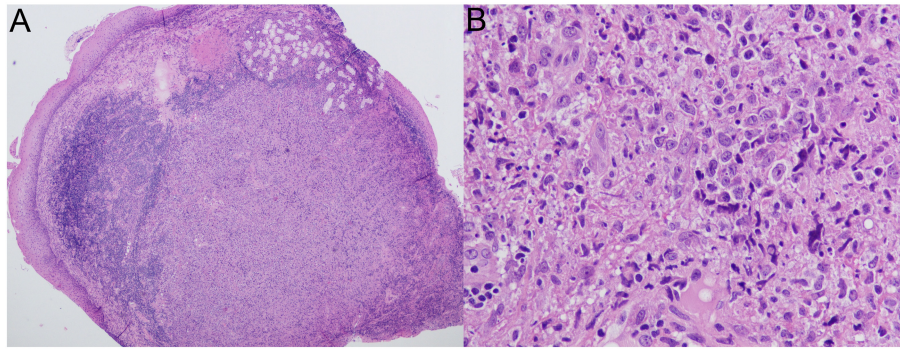


Figure 3. (A-B) Low-power (4x) hematoxylin and eosin-stained microscopic image shows the tongue biopsy with normal epithelium on the surface and underlying diffuse infiltration by neoplasia. At high power, the image demonstrates big atypical cells and necrosis.

diagnosis among all NHL cases and accounts for about 70% of patients.⁹ Studies on survival of patients with DLBCL in the head and neck region are controversial.^{8,10} Many authors state that lymphomas originating from the BOT have a good prognosis.⁶ Moreover, patients with DLBCL at the Waldeyer's ring (BOT) often have a better prognosis than patients with nodal DLBCL.¹⁰

Non-Hodgkin lymphoma primarily derived from the BOT is rare. This lesion is usually described in the literature as a swelling with an intact and smooth surface,⁶ totally different from that of our patient.

The differential diagnosis for excavated lesion at the BOT is broad but is managed with the assistance of clinical correlation. As reported, the majority of malignancies of the BOT are SCC. The risk factors for oropharyngeal SCC such as smoking, alcohol use, and poor oral hygiene do not correspond with the patient's medical history. Clinically, however, HPV-related oropharyngeal SCC could not be ruled out, the incidence of which has increased markedly in the past decade.¹¹⁻¹²

Among the primary clinical differential diagnoses is also laryngocele, which may also resemble the described lesion in clinical and endoscopic presentation. Clinical presentation depends on the extension of the lesion into the endolarynx including

foreign body sensation in the throat, hoarseness, dysphagia, and stridor.¹³⁻¹⁴ Currently, CT imaging is the most accurate imaging modality for the diagnosis of laryngocele. The CT image of the laryngocele appears as an air-filled structure in the space near the laryngeal sacculus,¹⁵ which is very different from that of the lesion under examination.

Another lesion that falls under the differential diagnosis is an infectious lesion of the base of the tongue. Abscesses arising in the posterior portion of the tongue are rarely seen and usually occur as a result of periodontal infections (e.g., extension of an apical infection from a first or second molar), infected thyroglossal duct remnants and lingual tonsillitis. Lingual trauma, poor oral hygiene, immunodeficiency, diabetes, and drug use are the leading predisposing factors. However, our patient does not have any of these risk factors and, moreover, she presented to our attention afebrile and with normal inflammatory indices.

Last but not least, epidermolysis bullosa (EB) belongs to a group of rare¹⁶ inherited diseases characterized by marked mechanical fragility of the epithelial tissue with blistering and erosion after mild trauma. Epidermolysis bullosa is caused by mutations in several genes encoding structural proteins that form the intraepidermal adhesion and dermo-epidermal anchoring complexes within the basement membrane zone of the skin and mucosae.^{17,18}

Depending on the severity of the disease, the lesions usually appear at birth or in infancy, but may occur later, even in the third decade of life.¹⁹ An acquired form has also been described that can occur at any age and appears to be associated with other forms of disease such as multiple myeloma, amyloidosis, lymphoma, inflammatory bowel disease, and lupus erythematosus.

Typically, the skin is affected, but manifestations in the oral cavity are not uncommon.²⁰ These include soft tissue and dental abnormalities such as intraoral blisters and superficial erosions, ulceration that can lead to ankyloglossia, obliteration of the vestibula, and loss of the lingual papillae. In particular, scarring and loss of normal intraoral soft tissue architecture can mimic oral malignancies.

Diagnosis is based on a careful history of recurrent mucocutaneous lesions and objective evaluation of the entire skin and appendages. Biopsy of suspicious lesions with

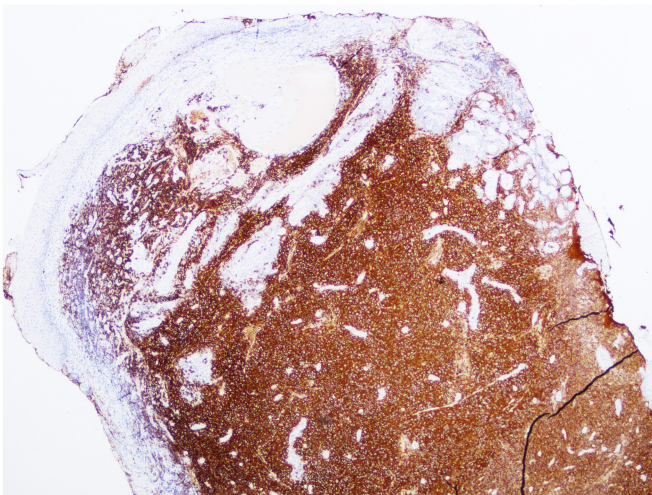


Figure 4. Immunohistochemical staining with CD20 (low-power view) illustrates diffuse and strong positivity according with the diagnosis of B-cell lymphoma.

immunofluorescence testing and genetic analysis usually provides the definitive diagnosis.

In conclusion, a careful history, combined with endoscopic and radiological evaluation, is essential for the classification of suspected malignant lesions of the head and neck region.

To date, NHL primarily derived from the BOT, is rare, and, to our knowledge, this is the first described case of tongue-based lymphoma presenting as an excavated lesion.

Excavated lesion at the BOT may be of various types and it is important to consider rarer differential diagnoses, especially in patients with clinical histories not suggestive of SCC or lesions of infectious origin.

Informed Consent: Written informed consent was obtained from the patient who agreed to take part in the study.

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