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Case Report

Diffuse Large B-Cell Lymphoma of the Midface: A Diagnostic Challenge

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Abstract

Background: Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of non-Hodgkin lymphoma, characterized by aggressive behavior and extranodal involvement in 40% of cases. Midface presentation is rare, often leading to diagnostic challenges due to nonspecific symptoms and the need for histopathological confirmation.

Case Report: We present the case of a 56-year-old male with a gradually enlarging, painless malar swelling, initially managed as a possible infection following recent dental extractions. Despite antibiotic therapy, there was no clinical improvement. Imaging revealed a subcutaneous mass without bone erosion, and histopathological evaluation through core biopsy suggested a lymphoproliferative disorder. A definitive diagnosis was delayed by six months, requiring specialized review. During this period, the mass demonstrated local progression. Final histopathological analysis confirmed DLBCL, stage I-E. The patient was managed with combined chemotherapy and radiotherapy.

Conclusions: This case underscores the diagnostic challenges associated with DLBCL in the midface region. Persistent facial swellings with atypical progression should prompt comprehensive evaluation for potential neoplastic etiologies. Early multidisciplinary intervention is essential to optimize patient outcomes.

Keywords: Diffuse Large B-Cell Lymphoma; Midface; Extranodal Lymphoma; Diagnostic Challenge; Otorhinolaryngology; Histopathology; Multidisciplinary Approach

Introduction

Diffuse large B-cell lymphoma (DLBCL) is the most common subtype of non-Hodgkin lymphoma, accounting for approximately 30-40% of all cases worldwide. It is characterized by a heterogeneous clinical presentation and aggressive behavior, with a rapid proliferation rate and a tendency for early dissemination. Most DLBCL cases involve lymph nodes, but approximately 40% exhibit extranodal involvement. These cases may affect any organ system, such as the gastrointestinal tract, central nervous system, skin, and bones. Extranodal presentations of DLBCL pose significant diagnostic challenges due to their diverse clinical manifestations, which often mimic more common, benign conditions [1,2].

DLBCL involving the midface is exceptionally rare and can be difficult to distinguish from other facial tumors or inflammatory conditions. The midface region, including the maxillary sinuses, nasal cavity, and orbit, is an uncommon site for primary lymphoma, with DLBCL representing only a small fraction of cases. Patients with midface DLBCL may present with nonspecific symptoms such as swelling, pain, facial asymmetry, or nasal obstruction, which can

lead to misdiagnosis or delays in diagnosis. Initial presentations may be mistaken for dental infections, sinusitis, or other benign conditions, as seen in other reported cases where initial management focused on infectious or inflammatory etiologies [3,4].

The diagnostic process is further complicated by the need for histopathological confirmation. Although imaging techniques, like computed tomography (CT) or magnetic resonance imaging (MRI), can reveal the presence and extent of a mass, findings are often nonspecific, frequently showing soft tissue masses without bone erosion.

Biopsy remains the gold standard for diagnosis, but even with tissue sampling, distinguishing DLBCL from other lymphoproliferative disorders or inflammatory conditions can be challenging. Immunohistochemistry and molecular studies, including testing for CD20, BCL2, BCL6, and MYC rearrangements, are crucial for confirming the diagnosis and subclassifying DLBCL, which has implications for prognosis and treatment [5].

The standard treatment for DLBCL involves combination chemotherapy, typically with the R-CHOP regimen (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone), often followed by involved-field radiotherapy in localized cases. Early-stage DLBCL in the head and neck region may benefit from combined modality therapy to achieve local control and reduce recurrence risk. However, DLBCL prognosis depends on various factors, such as the International Prognostic Index (IPI), tumor biology, and timeliness of diagnosis and treatment initiation [6].

This case report highlights the complexities involved in diagnosing midface DLBCL. Given the rarity and nonspecific symptoms of this presentation, DLBCL should be considered in the differential diagnosis of persistent or atypical facial swellings, particularly when initial treatments fail. A multidisciplinary approach—including otolaryngologists, radiologists, pathologists, and oncologists—is crucial for timely diagnosis, accurate staging, and appropriate management. Early recognition and intervention are vital to improving patient outcomes, as delays in diagnosis can lead to disease progression and impact overall survival [7].

Objective

This report aims to describe an atypical presentation of DLBCL in the midface region, emphasize the importance of clinical suspicion and prompt referral, discuss the diagnostic challenges in achieving a definitive histopathological diagnosis, and highlight the need underscore the necessity of timely, multidisciplinary treatment to improve patient outcomes.

Case Report

We present a 56-year-old male with no significant past medical history, who presented to the emergency department with a progressively enlarging left malar mass over one month. The patient reported a recent dental extraction (teeth 2.3 and 2.4), following which he completed two courses of antibiotics (amoxicillin-clavulanic acid and clarithromycin) with no clinical improvement. He was referred to the Otolaryngology department for further evaluation.

On examination, there was a firm, non-tender swelling in the left malar region, extending to the nasal dorsum with obliteration of the nasolabial fold. The overlying skin was intact, with no ulceration (Figure 1). The patient denied nasal or systemic symptoms, including B symptoms, and there were no signs of nasal or oral cavity infection.

A computed tomography (CT) scan was ordered, revealing a

Figure 1: Left malar swelling extending to the nasal dorsum with obliteration of the nasolabial fold.

"subcutaneous mass in the left malar region measuring 4.2 x 2.8 x 3 cm, without underlying bone erosion and of indeterminate nature" (Figure 2). A repeat CT one month later showed no significant changes. Magnetic resonance imaging (MRI) was then conducted, which confirmed a "well-defined subdermal mass (4.5 x 1.7 cm), adherent to the maxillary sinus wall without evidence of bone ero-

sion" (Figure 3). To determine the etiology, an ultrasound-guided core biopsy was performed, revealing an "exuberant reactive lymphoproliferative lesion".

Subsequently, the patient underwent surgical excision via a sublabial approach, with intraoperative findings confirming an intact anterior maxillary sinus wall. The frozen section analysis was inconclusive. Histopathological analysis of the excised specimen described a "lymphoproliferative lesion with morphological, histochemical, and immunohistochemical features favoring a reactive process, in correlation with clinical context." Given the diagnostic uncertainty, the specimen was sent to an external pathology center for further review. This resulted in a six-month delay for the final diagnosis.

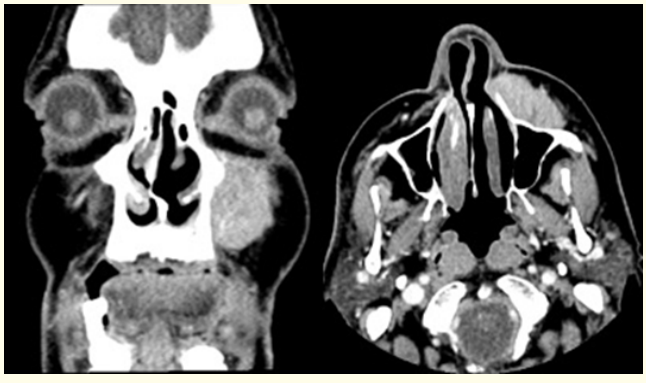

Figure 2: Coronal and axial maxillofacial CT scan showing a subcutaneous mass in the left malar region without underlying bone erosion.

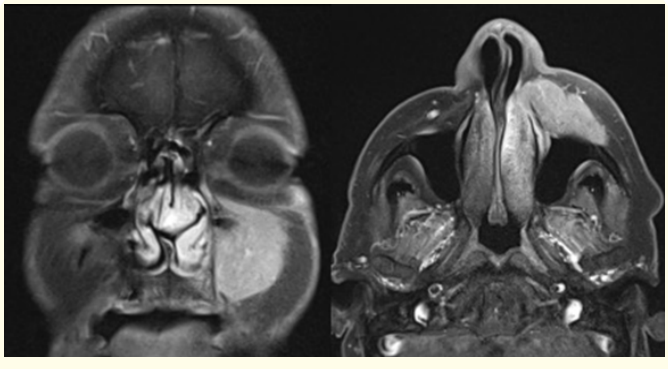

Figure 3: Coronal and axial MRI scan showing a well-defined subdermal mass (4.5 x 1.7 cm), adherent to the maxillary sinus wall without evidence of bone erosion.

During this period, the patient remained clinically stable. However, follow-up CT imaging indicated disease progression, with extension into the maxillary frontal process, anterior and medial maxillary sinus walls, nasal vestibule, and inferior meatus. The mass extended laterally into the soft tissues surrounding the anterior maxillary sinus wall and frontal process, superiorly to the infraorbital rim, and was now elevating the skin over the eyelid and nasal pyramid (Figure 4).

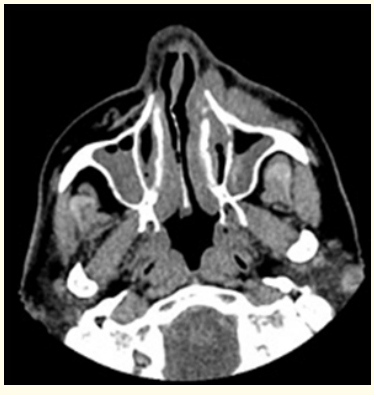

Figure 4: Follow-up axial CT scan indicated disease progression into the maxillary frontal process, anterior and medial maxillary sinus walls, nasal vestibule, and inferior meatus.

Final histological analysis showed large cells with regular nuclei and prominent nucleoli. Immunohistochemistry demonstrated CD20 and BCL-6 positivity, CD10 and MUM1 negativity, with a proliferative index (Mib1/Ki67) of 75%, consistent with diffuse large B-cell lymphoma (DLBCL).

The patient was evaluated by a multidisciplinary oncology team and referred to oncohematology service. Staging, including bone marrow biopsy and 18F-FDG PET-CT (Figure 5), confirmed the disease as stage I-E. He was started on combined chemoimmunotherapy with the R-HCVAD regimen (rituximab, cyclophosphamide, vincristine, dexamethasone, doxorubicin), alongside planned radiotherapy.

Discussion

DLBCL often presents heterogeneously and follows an aggressive course, particularly in rare extranodal sites like the midface region. This rarity complicates diagnosis, as midface DLBCL often presents with nonspecific symptoms that resemble common be-

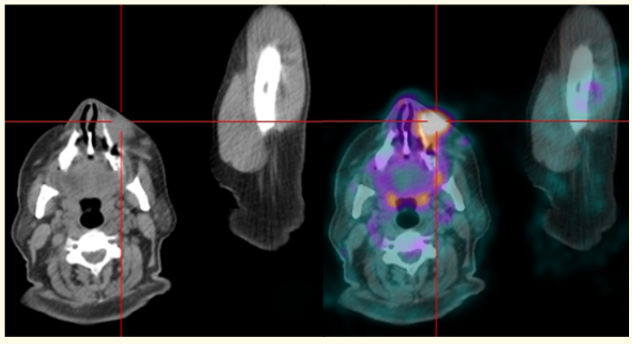

Figure 5: Staging 18F-FDG PET-CT showing malignant lymphomatous involvement in the left hemiface with increased 18F-FDG uptake (SUVmax: 7.4).

nign conditions such as sinusitis or dental infections, leading to initial misdiagnosis. In this case, the patient's initial presentation of malar swelling, coupled with a recent dental procedure, led to a presumptive diagnosis of an inflammatory or infectious process. Such scenarios are not uncommon, as midfacial DLBCL can mimic a range of pathologies, thereby causing diagnostic delays that can impact the prognosis [3].

Imaging, including CT and MRI, is essential in evaluating facial masses; however, findings in DLBCL are often nonspecific. In this case, the CT revealed a subcutaneous mass without bone erosion, contributing to diagnostic ambiguity. Soft tissue masses lacking bone erosion, for example, may not immediately suggest malignancy [4]. In this case, the initial imaging described a subcutaneous mass without bone involvement, which contributed to the diagnostic ambiguity. While imaging can aid in assessing the extent of the disease, histopathological analysis remains the gold standard for a definitive diagnosis. However, as seen here, even with biopsy, the diagnosis can be complicated, requiring immunohistochemical and molecular studies to distinguish DLBCL from other lymphoproliferative disorders. Immunohistochemical markers such as CD20, BCL2, BCL6, and MYC are invaluable for diagnosing and determining the prognosis of DLBCL [5].

The diagnostic delay, spanning several months, enabled local disease progression. This underscores the need for rapid referral and evaluation by a multidisciplinary team when faced with persistent or atypical facial swellings. The role of otorhinolaryngologists is particularly important in recognizing and pursuing further investigation for potential neoplastic processes. This aligns with current literature emphasizing the importance of early and accurate diagnosis in extranodal DLBCL to initiate timely treatment, thereby improving outcomes [7].

Standard DLBCL management includes systemic chemotherapy with the R-CHOP regimen, sometimes supplemented by radiotherapy for local control in localized cases. In this case, a combined modality approach was chosen, aligning with evidence that suggests better survival rates for early-stage patients receiving such therapy [6]. Early detection and therapy initiation are crucial to prevent disease progression and improve prognosis. Prognostic tools like the International Prognostic Index (IPI) are essential for guiding treatment strategies and predicting outcomes, as they consider factors such as age, tumor stage, and performance status [1].

Conclusion

This case highlights the challenges of diagnosing midface DLBCL, where nonspecific symptoms often resemble benign conditions, delaying definitive diagnosis. Persistent, atypical facial swellings unresponsive to standard treatment should prompt early consideration of neoplastic causes like DLBCL. The diagnostic delay in this case led to disease progression, highlighting the need for a multidisciplinary approach to facilitate rapid, specialized evaluation. Timely referral and comprehensive assessment are critical for improving prognosis through early intervention, potentially preventing local progression and reducing complication risks.

Acknowledgements

There are no acknowledgements.

Conflict of Interest

There are no financial interest or any conflict of interest.

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