2026, e-ISSN: 2674-7103

Jornal Memorial *da* Medicina

DOI: 10.37085/jmmv8.n1.2026.pp.1-5

Case Report

Diffuse large B-cell lymphoma in the maxillary sinus: case report

Linfoma difuso de grandes células B em seio maxilar: relato de caso

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Editado por:

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Abstract

Diffuse large B-cell lymphoma (DLBCL) is the most frequent subtype of non-Hodgkin lymphoma, accounting for 30-40% of cases. Symptoms are nonspecific and can range from nasal obstruction to visual disturbances, making diagnosis difficult and easily confused with benign inflammatory conditions and upper respiratory tract infections. In this article, we report the case of a 79-year-old female patient who sought care due to frontal headache and left hemifacial pain. After imaging studies, which revealed an infiltrative lesion in the maxillary sinus extending to the nasal cavity, orbit, and lateral wall, and biopsy, the patient was diagnosed with diffuse large B-cell lymphoma and referred for oncological treatment. The signs and clinical manifestations of diffuse large B-cell lymphoma (DLBCL) in the maxillary sinus are nonspecific. Diagnosis requires biopsy for evaluation, showing high proliferation of large B cells, with fibrosis and necrosis. Initial treatment for DLBCL involves chemotherapy using monoclonal antibodies.

Resumo

O linfoma difuso de grandes células B (LDGCB) é o subtipo mais frequente do Linfoma Não Hodgkin, constituindo de 30-40% dos casos. Os sintomas são inespecíficos e podem se apresentar desde obstrução nasal até alterações visuais, o que dificulta o diagnóstico e facilita com que seja confundido com condições inflamatórias benignas e infecções do trato respiratório superior. Neste artigo relatamos o caso de uma paciente do sexo feminino, de 79 anos que procurou atendimento devido à cefaleia frontal e dor hemifacial à esquerda. Após a realização de exames de imagem, que evidenciaram lesão infiltrativa no seio maxilar, com extensão para a cavidade nasal, órbita e parede lateral, e biópsia, a paciente recebeu o diagnóstico de linfoma difuso de grandes células B e foi encaminhada para tratamento oncológico. Os sinais e manifestações clínicas do linfoma difuso de grandes células B (LDGCB) no seio maxilar são pouco específicos. O diagnóstico requer biópsia para avaliação, apresentando alta proliferação de células B grandes, com fibrose e necrose. O tratamento inicial do LDGCB envolve quimioterapia com o uso de anticorpos monoclonais.

Keywords:
Lymphoma
Maxillary sinus
Diffuse Large B-cell Lymphoma

Keywords:
Linfoma, Seio Maxilar
Linfoma Difuso de Grandes Células B

Received: December 11, 2025
Revised: January 17, 2026
Accepted: January 29, 2026

Introduction

Lymphomas are malignant neoplasms of non-epithelial origin that develop from lymphocytes or their precursor cells and can arise at different stages of cell differentiation (1). They are broadly classified into Hodgkin lymphomas and non-Hodgkin lymphomas (NHL), with NHL accounting for approximately 90% of all cases (2). Based on cell lineage, NHLs are subdivided into B-cell, T-cell, and Natural Killer (NK) cell types, with B-cell lymphomas being the most prevalent (2). Approximately one-third of NHL cases involve extranodal sites, most commonly the gastrointestinal tract and the head and neck regions (3). Notably, NHL is also the second most frequent non-epithelial malignant neoplasm affecting the oral cavity and maxillofacial region (3).

Lymphomas affecting the nasal cavity and paranasal sinuses are unusual and generally present with nonspecific symptoms, such as nasal congestion, discharge, facial swelling, or visual impairment, these manifestations often lead to delays in diagnosis, which can compromise the patient's overall prognosis (4,5). Between of the NHL subtypes, diffuse large B-cell lymphoma (DLBCL) is the most common, representing 30–40% of cases. DLBCL is a biologically heterogeneous entity, characterized by the clonal proliferation of malignant B cells originating from germinal or post-germinal centers, resulting in diverse clinical behaviors, treatment responses, and prognoses (6).

Primary involvement of the maxillary sinus by diffuse large B-cell lymphoma (DLBCL) is rare. When present, it often mimics infectious or inflammatory processes, which can delay diagnosis and allow disease progression before identification and appropriate treatment. Late recognition can lead to local invasion of adjacent structures, with significant implications for morbidity and mortality (5,7).

Case Report

A 79-year-old female patient sought medical attention due to a frontal headache associated with left hemifacial pain. Magnetic resonance imaging (MRI) revealed an infiltrative lesion in the left maxillary sinus (Figure 1). The patient underwent endoscopic endonasal biopsy with intraoperative frozen section examination, which confirmed malignancy (Figure 2). Immunohistochemistry results showed diffuse large B-cell lymphoma, positive for CD20 (diffuse), Ki-67 (99%), BCL2 (diffuse), BCL6 (diffuse), C-MYC (60-70%), and CD79a. After hospital discharge, the patient was referred for oncological treatment.

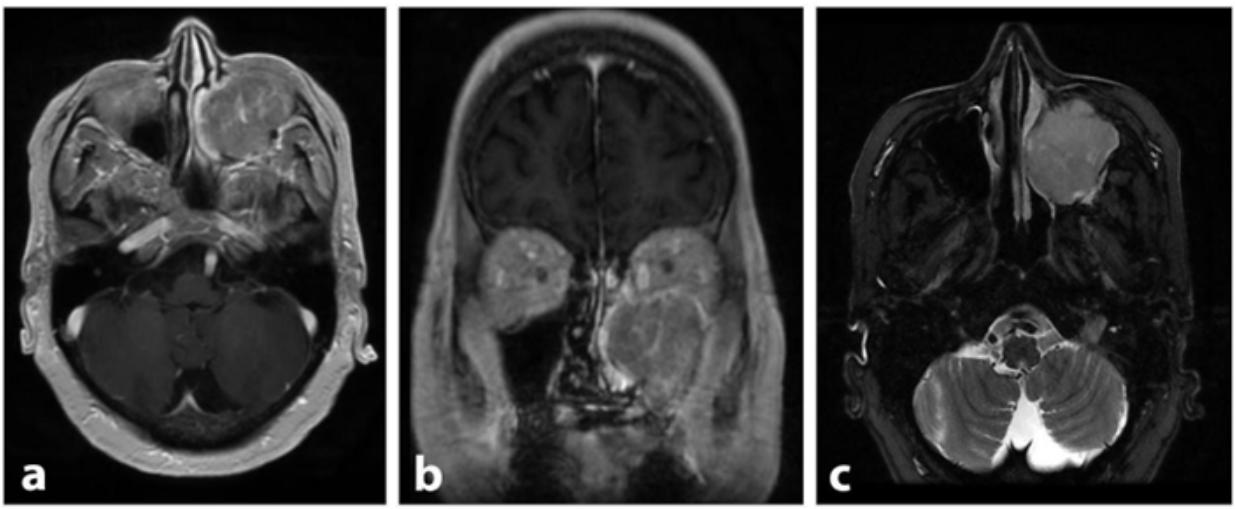

Figure 1. Preoperative magnetic resonance imaging. a) Axial T1-weighted magnetic resonance imaging with gadolinium, showing an infiltrative mass within the left maxillary sinus, protruding into the nasal cavity. b) Coronal T1-weighted magnetic resonance imaging with gadolinium, showing the infiltrative mass within the left maxillary sinus, protruding into the nasal cavity and left orbit. c) Axial T2-weighted magnetic resonance imaging, confirming the extra-axial aspect of the mass within the left maxillary sinus.

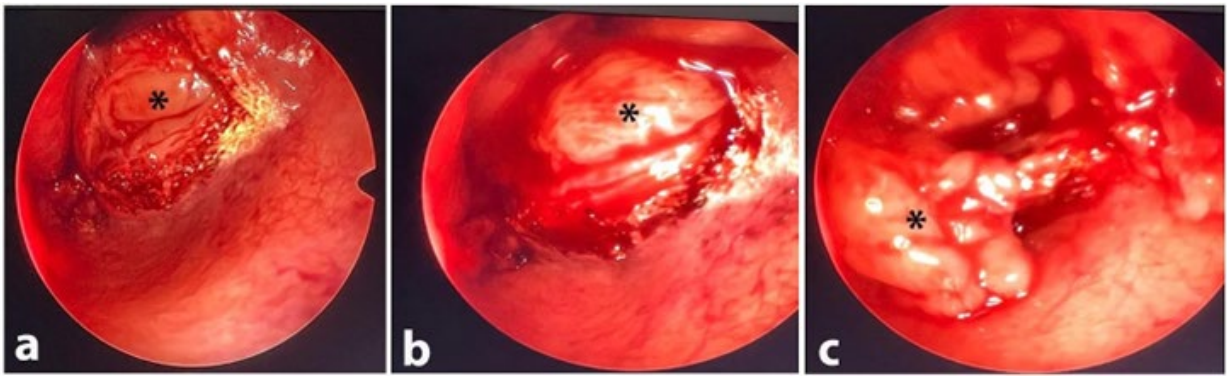

Figure 2. Intraoperative findings. a) Initial exposure, revealing a protruding mass (*) on the lateral wall of the nasal cavity, below the middle turbinate. b) After mucosal incision, the mass becomes apparent (*). c) Partial resection of the mass (*), for biopsy and improvement of nasal physiology.

Discussion

The clinical presentation of diffuse large B-cell lymphoma (DLBCL) in the maxillary sinus is remarkably heterogeneous. Reported symptoms include pain along the maxillary nerve distribution, diplopia, ptosis, and ipsilateral hyperexophoria (8). Some cases also describe palatal gingiva edema progressing to ulceration with surrounding erythema, as well as mildly painful edema on the affected side and nasal obstruction (9,10). In the present report, however, the patient presented only with frontal headache and hemifacial pain ipsilateral to the affected side. Malignant lesions of the paranasal sinuses can manifest with nonspecific or even absent symptoms, which can delay diagnosis and lead to misinterpretation as benign conditions, until extension to adjacent structures occurs, as observed in this case (11).

Lymphomas, such as diffuse large B-cell lymphoma (DLBCL), frequently demonstrate bone destruction affecting the maxilla, mandible, and adjacent paranasal structures. On computed tomography (CT), these lesions typically present with muscle-like density and well-defined contours. In cases of extranodal extension, the margins may appear less defined, and necrotic areas may be identified within the mass. Magnetic resonance imaging (MRI) is the method of choice for evaluating facial compartment involvement and possible intracranial spread. On T1-weighted sequences, DLBCL generally appears hypointense, while on T2-weighted images, the signal is more pronounced. intensity intervals of low to high. After gadolinium-DTPA administration, improvement varies, but tends to be low (12).

The diagnosis of diffuse large B-cell lymphoma (DLBCL) requires a comprehensive approach that includes morphological, immunophenotypic, cytogenetic, and molecular assessments (13,14). To ensure the accuracy of these assessments, it is essential to obtain a feasible evaluation and a representative tissue sample — preferably obtained through excisional lymph node biopsy, with fine-needle aspiration as an alternative when excision is not feasible. Proper sampling allows for a complete assessment of nodal architecture, which is fundamental for accurate interpretation (13,15). Morphologically, tumor cells exhibit a diffuse growth pattern, replacing part or all of the normal structure of nodal or extranodal fabrics. These cells are composed mainly of centroblasts and immunoblasts, with one cytotype predominating over the other in approximately 10–15% of cases (13). Fibrosis and necrosis may be observed, and in approximately 10% of cases, the pattern termed "starry sky" indicates a high rate of cell proliferation (13).

Gene expression profiling (GEP) analysis is considered the gold standard for identifying the main forms of DLBCL, as it allows classification based on the cell of origin (COO) into two molecular subtypes: germinal center B cell-like (GCB) and activated B cell-like (ABC). However, this method is not yet commercially available on a large scale (16). Approximately 10–15% of cases remain unclassified. Studies show that patients with the GCB subtype have superior overall survival compared to patients with the ABC subtype, even when treated with CHOP or R-CHOP (16). Furthermore, next generation sequencing (NGS) allows the detection of specific genetic alterations and reveals distinct mutational profiles among subtypes, supporting a more individualized approach to disease management (13).

Immunophenotypic analysis, being more widely available than molecular methods such as gene expression profiling, can be performed by immunohistochemistry (IHC) or flow cytometry, allowing the identification of neoplastic B cell markers such as CD19, CD20, CD22, and CD79a, as well as transcription factors including PAX5, BOB1, and OCT2 (13,17,18). This immunophenotypic profile is crucial not only for the diagnosis of confirmation, but also for the identification of therapeutic targets and to estimate treatment response and prognosis (19). Evaluation of MYC and BCL2 protein expression by IHC is essential for detecting double-expressing lymphomas, which represent 20–30% of cases and are associated with unfavorable clinical outcomes (20,21).

Conventional cytogenetic analysis offers a broad view of chromosomal abnormalities and contributes to prognostic stratification.

More aggressive and treatment-refractory tumors often exhibit complex karyotypes (19). For example, translocations involving the MYC gene (8q24) occur in about 10–15% of cases and are strongly associated with high-grade morphological features. and the greater genomic complexity (22). In the absence of fresh tissue, fluorescence in situ hybridization (FISH) can be performed on paraffin-embedded sections for the detection of genetic rearrangements. However, although highly specific, FISH does not replace comprehensive cytogenetic analysis (19).

Ultimately, the DLBCL diagnostic approach is expected to continue evolving in parallel with advances in precision medicine, fostering the development of increasingly effective and personalized therapeutic strategies (19).

Diffuse large B-cell lymphoma (DLBCL), the most prevalent subtype of non-Hodgkin lymphoma, is typically treated with the R-CHOP regimen as first-line therapy. This protocol includes four chemotherapeutic agents (cyclophosphamide, doxorubicin, vincristine, and prednisone) in combination with the monoclonal antibody rituximab, which specifically targets CD20-positive B cells. R-CHOP is generally administered in six to eight cycles, depending on the stage of the disease, the response to treatment, and the patient's overall condition. Its efficacy is well established and it remains the gold standard for initial treatment of DLBCL (6).

If an unsatisfactory response is observed after the fourth cycle, and if disease progression is identified, or if complete remission is not achieved by the end of the eighth cycle, the protocol should be interrupted and second-line chemotherapy regimens should be initiated (16).

Although it is the standard therapy, it is estimated that between 40% to 45% of patients experience relapse. Rituximab, which targets the CD20 antigen expressed on the surface of B lymphocytes, when combined with the CHOP regimen, promotes higher remission rates and improves overall survival. However, its use is not recommended in patients with reduced CD4 lymphocyte counts, such as those who are HIV-positive (16).

In cases of initial therapy failure, second-line chemotherapy regimens include DHAP, ESHAP, EPOCH, ICE, or MINE. These protocols aim to identify patients whose disease is responsive to chemotherapy and who may therefore benefit from autologous hematopoietic stem cell transplantation. As with first-line treatment, if remission is not achieved or if disease progression occurs after the fourth cycle of second-line therapy, treatment should be discontinued (16).

In the absence of response to previous treatments or in the presence of disease progression, third-line chemotherapy is indicated, generally with palliative intent. Patients who develop severe neutropenia may receive granulocyte colony-stimulating factor. Furthermore, hematopoietic stem cell transplantation remains a viable option for patients with relapse responsive to second-line chemotherapy who are clinically eligible for the procedure (16).

Conclusion

Diffuse large B-cell lymphoma (DLBCL) is the most common non-Hodgkin lymphoma (NHL), predominantly affecting individuals around the sixth decade of life. Involvement of the nasal cavity and paranasal sinuses is a rare and aggressive condition, requiring early diagnosis due to its high growth rate. In this context, the involvement of a multidisciplinary team is fundamental from diagnosis to the completion of treatment. Detailed medical history, imaging studies, laboratory tests, and biopsy are essential tools for the diagnostic workup of these cases.

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Authors contribution: PMMF: Writing - Analysis & Edited by FPS: Resources; ADP: Writing - Original DPAC: Writing - Analysis & Edited by AHK: Writing - Original Draft; AFO: Writing - Original Draft; MRQ: Writing - Original Sketch
Conflict of interest: None.
Funding: None.