Non-Hodgkin's Lymphoma Mimicking Orbital Cellulitis: A Diagnostic Dilemma

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Abstract: We reported a rare case of disseminated diffuse large B-cell lymphoma (DLBCL) initially presenting as refractory orbital cellulitis in a 53-year-old male. The patient presented with acute periorbital swelling, pain, and restricted ocular motility, unresponsive to broad-spectrum antibiotics. Magnetic resonance imaging (MRI) revealed extensive sinusitis with a peripherally enhancing medial extraconal orbital mass and adjacent bony erosions. A prompt functional endoscopic sinus surgery and histopathology revealed a poorly differentiated malignant neoplasm. Immunohistochemistry confirmed DLBCL, non-germinal center B-cell subtype. Systemic evaluation with whole-body MRI and fluorodeoxyglucose-positron emission tomography demonstrated widespread dissemination involving the lungs, gastrointestinal tract, adrenal glands, and skeleton. The patient was initiated on required chemoimmunotherapy with central nervous system prophylaxis and remains under oncology follow-up. This case highlights the diagnostic challenge posed by orbital lymphoma mimicking infectious orbital cellulitis and underscores the need for early imaging and tissue diagnosis in culture-negative, non-resolving cases. A high index of suspicion and multidisciplinary collaboration are essential for timely diagnosis and effective management.

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Introduction

Orbital cellulitis is a serious ophthalmic emergency with potential for both vision and life-threatening complications, characterized by infectious and inflammatory involvement of the orbital soft tissues (American Academy of Ophthalmology: Basic and Clinical Science Course 2019–2020). The condition most commonly arises from contiguous spread of infection from adjacent periorbital structures such as the paranasal sinuses, facial skin, eyelids, lacrimal sac, or odontogenic sources. Additional etiologies include exogenous insults – such as trauma, retained foreign bodies, or iatrogenic introduction during surgical interventions – and hematogenous dissemination via septicemia or bacteremia with embolic phenomena. Less commonly, primary orbital infections, including endophthalmitis and dacryoadenitis, may serve as the nidus (Singh et al., 2018).

Although bacterial sinusitis remains the predominant cause, atypical and non-infectious etiologies must be carefully considered in cases with poor therapeutic response. Notably, masquerading neoplastic processes – including choroidal melanoma (Singh et al., 2018) and metastatic lesions from primary bronchogenic (Kumar and Issing, 2011) or urothelial carcinomas (Bobadilla-Romero et al., 2022) – have been documented and warrant inclusion in the differential diagnosis of refractory orbital cellulitis.

Case report

A 53-year-old male presented to the ophthalmology outpatient department with a 15-day history of acute-onset right side periorbital swelling (Figure 1)

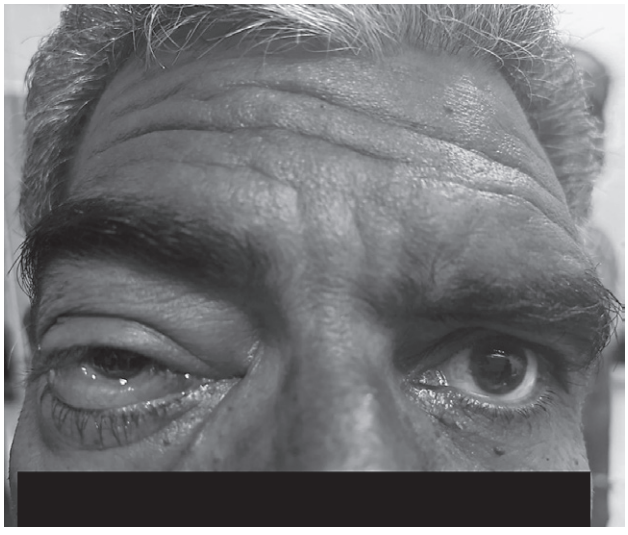

Figure 1: Presentation with right side periorbital swelling, lid swelling and conjunctival chemosis.

associated with pain, particularly aggravated by ocular movements. On clinical examination, best-corrected visual acuity (BCVA) in the right eye was 6/12 with an intraocular pressure of 14 mm Hg. Notable findings included mechanical ptosis, marked conjunctival congestion, severe chemosis, and gross restriction of extraocular movements in all directions (Figure 2). The pupillary reaction to light was preserved, and fundus evaluation was unremarkable. Ocular examination of left eye was normal. Based on the clinical features, a provisional diagnosis of right-sided orbital cellulitis was made. The patient was admitted and initiated on broad-spectrum intravenous antibiotics – ceftriaxone 1 g twice daily and metronidazole 400 mg thrice daily – after sending appropriate blood and urine samples for required investigations.

Despite appropriate medical therapy, the patient exhibited clinical deterioration, marked by worsening chemosis and pupillary involvement. Magnetic resonance imaging (MRI) of the brain, orbits, and paranasal sinuses demonstrated extensive mucosal thickening in the right maxillary, ethmoidal, and frontal sinuses with signal alterations along the maxillary floor, as well as a peripherally enhancing soft tissue lesion in the medial extraconal orbital space with suspected erosions of the lamina papyracea, orbital roof, and posterior maxillary wall. In light of these findings, the otorhinolaryngology team proceeded with functional endoscopic sinus surgery (FESS), during which representative tissue specimens were obtained for histopathological analysis. Given the radiological evidence of atypical enhancement and osseous destruction, a whole-body MRI was subsequently performed, revealing infiltrative lesions in the apical lung segments, humerus, radius, and multiple vertebral bodies – highly suggestive of systemic malignant dissemination.

Histopathological examination of tissue obtained via endoscopic debridement (including intra-orbital, paranasal, turbinate, and medial wall specimens) revealed a poorly differentiated malignant neoplasm composed of medium to large syncytial atypical cells arranged in diffuse sheets accompanied by dense lymphoplasmacytic infiltration. Special stains were negative for fungal or acid-fast organisms. The undifferentiated morphology gave the differentials suggestive of either nasopharyngeal carcinoma or non-Hodgkin lymphoma. Immunohistochemistry (IHC) demonstrated strong positivity for LCA, CD20, MUM1, BCL6, and BCL2, with negativity for CD3, CD30, CD10, and C-MYC, confirming a diagnosis of diffuse large B-cell lymphoma (DLBCL), non-germinal center B-cell (non-GCB) subtype.

A prompt referral to the oncology department with a whole-body fluorodeoxyglucose-positron

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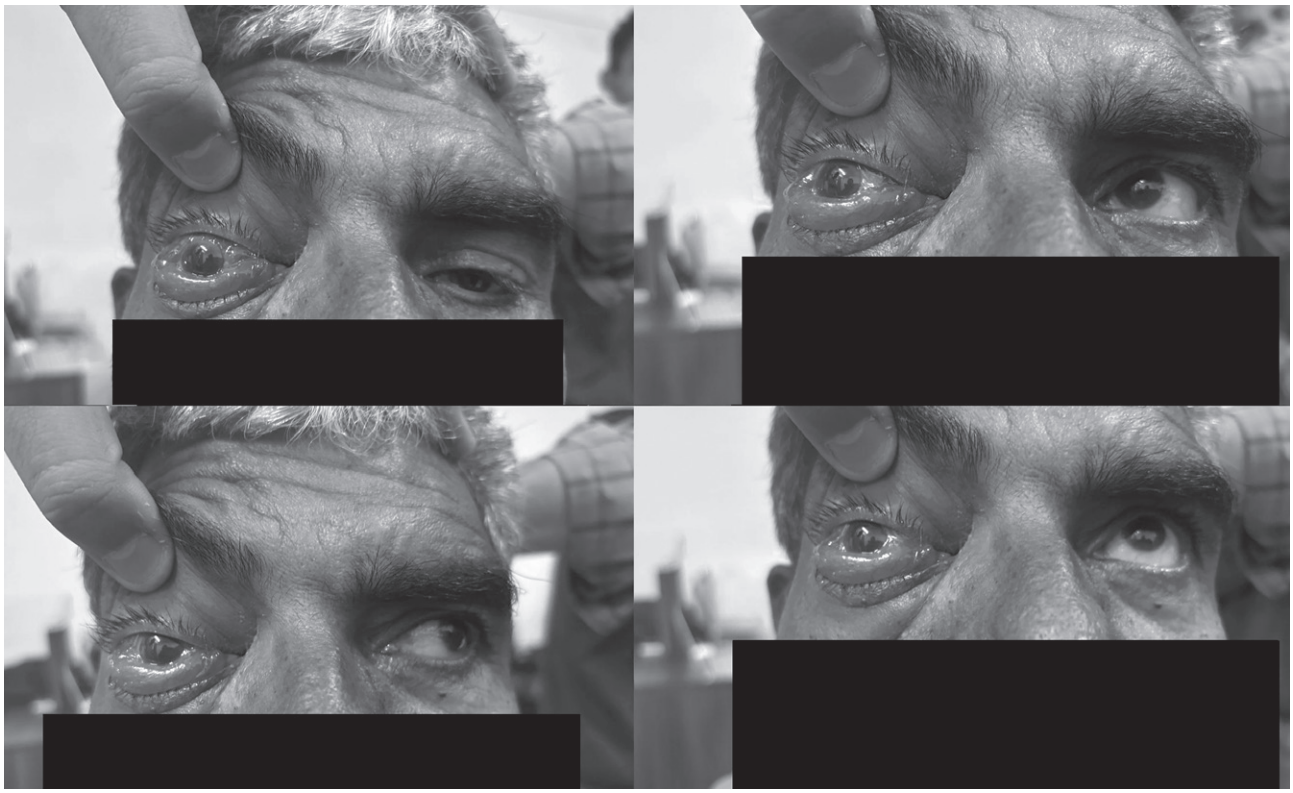

Figure 2: Restriction of extra-ocular movement in all gaze position.

emission tomography (FDG-PET) scan revealed a metabolically active mass involving the right orbit, paranasal sinuses, and adjacent naso-oropharyngeal structures, with intraconal extension and widespread lymphadenopathy. Systemic dissemination was evident, including pulmonary, gastrointestinal, peritoneal, adrenal, and osseous involvement – consistent with advanced hemato-lymphoid malignancy. A multidisciplinary tumour board recommended initiation of combination chemoimmunotherapy tailored to the diagnosis of high-grade B-cell lymphoma. The patient was started on the R-CHOP regimen, comprising Rituximab (600 mg), Cyclophosphamide (1,000 mg), Vincristine (2 mg), Doxorubicin (Adriamycin, 65 mg), and oral Prednisolone. Pegfilgrastim (6 mg subcutaneously) was administered for hematopoietic support, and intrathecal Methotrexate (1.5 mg) was included as prophylaxis against central nervous system involvement.

The patient successfully completed the prescribed chemotherapy cycles and is currently under maintenance surveillance, with ongoing follow-up at the oncology center.

Discussion

Non-Hodgkin lymphoma (NHL) represents a heterogeneous group of lymphoid malignancies derived from B, T, or NK cells, and is classified into indolent or aggressive subtypes. Risk factors include immunosuppression, chronic infections, and autoimmune conditions. Extranodal involvement – such as in the central nervous system, gastrointestinal tract, bone marrow, or orbit – is not uncommon. Diagnosis relies on histopathology, immunohistochemistry, and positron emission tomography-computed tomography (PET-CT) imaging, while treatment ranges from observation in indolent cases to systemic chemoimmunotherapy (e.g., R-CHOP) for aggressive forms. Prognosis is influenced by disease stage, age, lactate dehydrogenase levels, and extent of extranodal disease.

Although rare, orbital lymphoma can closely mimic the clinical features of orbital cellulitis, leading to diagnostic delays and suboptimal early management. Several case reports have illustrated this diagnostic pitfall. Ishak et al. (2024) described a 71-year-old woman with recurrent periorbital swelling, erythema, and progressive vision loss – initially misinterpreted as sphenoid meningioma or metastatic disease on imaging – who exhibited only transient improvement with intravenous antibiotics. Subsequent histopathological analysis confirmed high-grade B-cell lymphoma, underscoring the need for early consideration of neoplastic etiologies in atypical presentations (Ishak et al., 2024).

Other reports have documented cases of diffuse large B-cell lymphoma and small lymphocytic lymphoma presenting with classical features of orbital cellulitis but demonstrating poor or absent response to standard antimicrobial regimens, with final diagnosis established only after biopsy and immunohistochemical analysis (Mak et al., 2010; Chaurasiya et al., 2021). Extranodal NK/T-cell lymphomas have also been shown to present with clinical signs such as periorbital edema, erythema, and orbital soft tissue inflammation, closely resembling infectious etiologies and further compounding diagnostic challenges (Barkhuysen et al., 2008; Shah et al., 2017).

Scientific highlights

This case provides several important scientific insights into the management of orbital cellulitis. First, it demonstrates that refractory orbital cellulitis requires a high index of suspicion for underlying malignancy, especially in older patients. The role of MRI in identifying atypical patterns and guiding further diagnostic procedures is critical. Second, it emphasizes the importance of obtaining tissue for histopathological examination in cases with non-resolving clinical features. Finally, the addition of systemic steroids, while providing temporary relief, highlighted the aggressive nature of the underlying metastatic carcinoma, influencing our understanding of inflammatory responses in malignancy-related orbital cellulitis.

Conclusion

This case illustrates the importance of maintaining a broad differential diagnosis when managing cases of orbital cellulitis that do not respond to standard treatment. A multidisciplinary approach involving ophthalmology, radiology, otorhinolaryngology, and pathology was essential in reaching the correct diagnosis. Clinicians should be vigilant in recognizing atypical presentations and ensure timely investigation and referral in refractory cases of orbital cellulitis.

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