Othman et al
Brunei International Medical Journal
2025;21:144-148

Brunei International

Case Report

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Diffuse Large B-Cell Lymphoma Presenting with Rapid Painless Orbital Proptosis: A Case Report

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Abstract

Orbital lymphoma is a rare malignancy, with diffuse large B-cell lymphoma (DLBCL), a less common but more aggressive subtype. It commonly manifests with progressive proptosis and visual disturbances mimicking conditions such as thyroid eye disease, benign masses, or idiopathic orbital inflammation. A 69-year-old woman presented with right eye proptosis secondary to a progressively enlarging temporal orbital mass. Her condition rapidly deteriorated, with worsening visual acuity, increased proptosis, and elevated intraocular pressure. Imaging revealed an extraconal orbital lesion with widespread systemic involvement, including lytic lesions, hypermetabolic lymph nodes, splenomegaly and skeletal involvement. Fine needle aspiration confirmed DLBCL. She was treated with six cycles of CHOP chemotherapy (Cyclophosphamide, Hydroxydaunorubicin, Oncovin, and Prednisone) and intrathecal methotrexate. Her symptoms resolved, and vision was restored. This case highlights the importance of considering orbital lymphoma as a potential indicator of disseminated disease, and prompt diagnosis and interventions can restore visual functions.

Keywords: Diffuse Large B-Cell Lymphoma; Non-Hodgkin Lymphoma; Orbital Lymphoma; Proptosis

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INTRODUCTION

Orbital lymphoma represents a rare yet significant cause of orbital masses, commonly presenting with painless proptosis, that mimics more benign condition such as thyroid eye disease, benign orbital masses, or idiopathic orbital inflammation. Lymphoma is the most common primary malignant orbital tumour and accounts for 55% of all orbital malignancies.[1] These lymphomas may originate primarily within the orbital

cavity or may reflect secondary involvement from systemic disease, including non-Hodgkin lymphoma (NHL), leukaemia, or other hematologic malignancies. Common sites of origin include the conjunctiva, lacrimal gland, eyelids, and extraocular muscles, and they are typically extraconal in location. Orbital lymphomas comprise 1–10% of all NHL cases and occur more frequently in females within the age range of 15–70 years, with an increase incidence reported in Asia and Europe. [2,3]

Histologically, orbital lymphomas represents a wide range of subtypes, from less aggressive variants such as extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT, accounting for up to 70% of cases) to more aggressive forms, including diffuse large B-cell lymphoma (DLBCL) and mantle cell lymphoma.[4] DLBCL, despite its lower prevalence compared to MALT lymphoma within the orbital region, is significant because of its aggressive nature and potential for widespread systemic involvement.

This case is unique and clinically significant for numerous reasons. First, it showcases an unusual and rapidly advancing DLBCL in a patient devoid of prior systemic symptoms, initially resembling less severe orbital pathologies. Second, it illustrates the secondary orbital involvement resulting from systemic NHL, a relatively rare clinical manifestation. Finally, while orbital lymphoma is increasingly acknowledged in Southeast Asia, there remains limited published literature on secondary orbital DLBCL, particularly those exhibiting marked clinical progression over a short timeframe.

This case is presented to raise awareness regarding DLBCL as an aggressive cause of proptosis, to highlight the diagnostic complexities associated with orbital masses, and to emphasises the necessity of early multidisciplinary intervention. Furthermore, this case serves to reinforce the importance of integrating clinical, radiological, and histopathological findings to facilitate timely diagnosis and treatment.

CASE REPORT

A 69-year-old woman presented to the community eye clinic that accepts walk-in patients, with a one-week history of the following symptoms: right eye proptosis with a painless palpable mass on her right temporal region (**Figure 1**). There was no history of trauma, no vision loss, no diplopia or any other systemic symptoms. She has diabetes, hypertension and hyperlipidaemia, and is on regular medications of metformin, gliclazide, atorvastatin, gemfibrozil and perindopril. Systemic symptoms such as fever, night sweats, and weight loss were specifically inquired about and were not present at the time of initial evaluation. The patient is currently retired, a non-smoker, and is usually independent with basic activities of daily living (ADLs). Following the initial assessment, she was referred to the Eye Centre, RIPAS Hospital, for specialist evaluation. No formal diagnosis was made at the initial visit, but an orbital mass due to the proptosis was suspected. The patient reported no pain or discomfort associated with the proptosis. Although no formal pain scale was applied, she consistently denied pain during clinical evaluation.

Her visual acuity (VA) at presentation was 6/12 in both eyes and intraocular pressure (IOP) was mildly raised in the right eye – 21 mmHg and the left eye was 16 mmHg. The anterior segments were otherwise unremarkable apart from early lens changes. She had normal reactive pupils and fundi showed some retinal changes of mild non-proliferative diabetic retinopathy. There was no relative afferent pupillary defect, cranial nerve examination was grossly intact and both colour vision and visual field were also normal, indicating

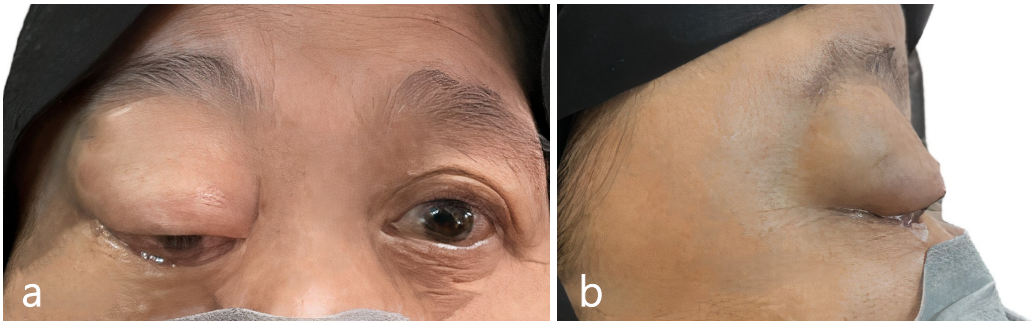

Figure 1: a) Frontal and b) lateral views of the patient showing marked right-sided proptosis with ptosis, obscuring the visual axis in primary position. The lateral view demonstrates anterior globe displacement consistent with orbital mass effect.

preserved optic nerve function and visual pathway despite the orbital mass. On further inspection, the right globe was protoptic by 3 mm and was displaced downwards with resistance to retropulsion. This was confirmed with an exophthalmometer. There was hypotropia (downward deviation of the affected eye) and full lid closure with no lid retraction. Noticeably, there was fullness over the superotemporal orbit with diffuse hard swelling occupying the temporal fossa. However, extraocular movements were full and there was no pain on eye movements.

An optical coherence topography (OCT) was performed, and it was unremarkable. In contrast, ultrasound B-scan revealed a well-defined, extraconal lesion superotemporal orbit with medium to high internal reflectivity, which was non-reducible in the right orbit, suggesting a solid mass.

Subsequent, computerised tomography (CT) scan of the orbit and brain (**Figure 2**) showed a well-defined homogenous, hyperintense lesion with distinct margin borders. The size measured 5 x 3 cm extraconal mass in the right orbit, involving the greater wing of the sphenoid with subcutaneous extension and small extra axial component in the middle cranial fossa. The mass appeared to be moulding around its surrounding structures, rather than infiltrating.

At third week of review, the right proptosis got dramatically worse. It was irreducible, intense and VA dropped to counting fingers at three meters. Her IOP was digitally high, and she had restricted eye movement in all gazes. She was then admitted and immediately treated for her raised IOP and urgent investigations. On initial assessment by the ophthalmology team, the differential diagnoses included idiopathic dacryoadenitis and thyroid eye disease, given the localised superotemporal orbital swelling and absence of systemic features. There were no clinical signs of inflammation such as tenderness or erythema, but dacryoadenitis remained a consideration due to the lesion's anatomical location. Thyroid eye disease was considered due to proptosis, though thyroid function tests were within normal limits and there were no other signs of systemic thyroid dysfunction. Lymphoma was not the leading diagnosis initially, as the patient lacked systemic "B symptoms," palpable lymphadenopathy, or prior hematologic history. Given the atypical presentation and the lesion's rapid progression, further imaging and tissue sampling were pursued to establish a definitive diagnosis.

Magnetic resonance imaging (MRI) of the head showed lytic lesion with large soft tissue involving

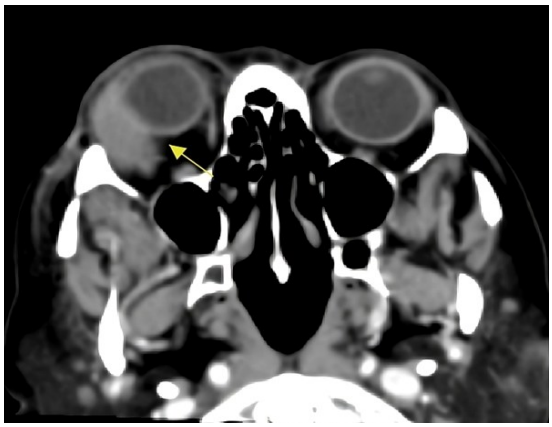

Figure 2: Axial CT scan of the orbits showing a well-defined, extraconal soft tissue mass in the right superotemporal orbit (yellow arrow). The lesion is slightly hyperdense compared to orbital fat and is causing inferomedial displacement of the right globe, suggestive of an orbital mass.

greater wing of sphenoid, consistent with the CT findings. There was also a heterogenic mass in the left orbit extraconal too. Positron emission tomography (PET) scan showed a hypermetabolic extraconal mass in the right orbit, thickening of the right temporalis muscle, and hypermetabolic lymph nodes above and below the diaphragm. Diffuse splenic hypermetabolism with splenomegaly and widespread hypermetabolic lesion including few adjacent muscle involvements, were also observed – findings consistent with disseminated systemic disease.

Fine needle aspiration cytology (FNAC) was performed on the temporal mass and histopathology investigation confirmed diffuse large B cell Lymphoma (DLBCL). The histopathology slide (**Figure 3 A & B**) stained with haematoxylin and eosin, showed a diffuse infiltrate of round cells containing thin rim of cytoplasm hyperchromatic nuclei with nucleoli. There was a uniform arrangement of the lymphoma cells with irregular nuclei and prominent nucleoli, suggestive of a malignant lymphoma. **Figure 3 (C—E)** showed almost all the cells show positive staining with cluster of differentiation 20 (CD20), which predominantly shows B cells. Overall, it was confirmed diagnosis of (DLBCL), - non germinal centre (activated cell) type (of right orbital/ temporal region) – NHL type. From the radiology findings and histopathology findings, it was staged as Stage IV Non-Hodgkin Lymphoma.

The patient was then referred to oncology and treatment was started with intrathecal methotrexate and chemotherapy – rituximab and prednisolone 100 mg once daily, along with cyclophosphamide, doxorubicin,

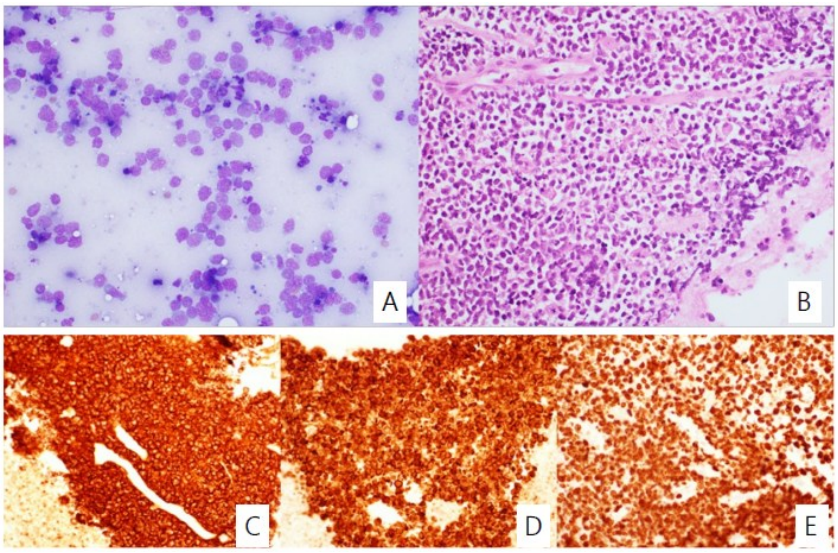

Figure 3: Slides showing discohesive intermediate to large sized round cells containing irregular hyperchromatic nuclei, small nucleoli and minimal cytoplasm. (A - Leishman 400x, B - H&E 400x).
Lymphoma cells are positive for B-lymphocytic markers, CD20 (C) and CD79a (image not shown). Positive staining for Bcl-2 (D) and high Ki67 (E) proliferation are seen. CD3, CD5, Bcl-6, CD10, cyclin D1, CD30 and CD15 are negative (image not shown). (A-C IHC 400x).

vincristine, and prednisone (CHOP).

After completion of six cycles of chemotherapy, patient's symptoms had resolved. There was no more evidence of proptosis. The temporal mass was completely gone. Patient's vision and IOP returned to normal. She had full range of eye movement and was on her way of recovery. At the time of reporting, she was stable and awaiting her next PET scan to monitor for any recurrence.

DISCUSSION

Orbital lymphoma is a rare yet important condition to consider in the differential diagnosis of proptosis, particularly in elderly patients. Over the past decade, there has been an observable increase in orbital lymphoma cases presenting in our clinic. It has now become a common diagnosis with varying types of lymphoma. Lymphoma is the most common malignant tumour of the orbit, accounting for approximately 11% of all orbital tumors, and 55% of malignant orbital lesions. While orbital lymphoma includes several subtypes, primary orbital lymphoma remains relatively uncommon. In contrast, secondary orbital involvement is seen in about 5% of patients with disseminated non-Hodgkin lymphoma (NHL),[6] as in our patient. However, patient may present initially with eye symptoms rather than any systemic symptoms. Therefore, it is important for general ophthalmologist to identify and quickly act upon investigations so that patients can be treated earlier for better prognosis. Patients may present with a rapidly growing mass which is painless, unilateral or proptosis. If patients present with these symptoms, but does not have thyroid disease, one should think immediately of neoplastic causes. Radiotherapy has been widely used to treat ocular adnexal lymphoma. However, orbital and periorbital lymphoma are preferred to have systemic chemotherapy.[7] Diffuse large B-cell lymphoma (DLBCL) typically presents with systemic "B symptoms" such as fever, weight loss, and night sweats. However, our patient did not report any of these symptoms, making the presentation atypical. The absence of systemic features initially made a lymphoma diagnosis less likely. In case of this patient, the rapid and aggressive progression over three weeks raised clinical suspicion for an underlying malignant process, prompting further imaging and histopathological evaluation. Based on these findings, the team had decided to hit the disease full on with systemic chemotherapy and it worked well for the patient. Her symptoms were resolved. Careful clinical judgment and diagnosis play an important role in managing these conditions.

Early detection and diagnosis are important in orbital lymphoma as early treatment can potentially cure the disease. These diseases cannot be taken lightly as we all know eye diseases and symptoms can be the first clue to other plethora of systemic issues. Ophthalmologists must be aware of these conditions and work closely with other specialties to ensure prompt diagnosis with correct treatment, to have a better outcome for the patients.

CONCLUSION

Orbital lymphoma, particularly diffuse large B-cell lymphoma, is a rare but significant cause of proptosis and should be considered in differential diagnosis for patients experiencing progressive orbital symptoms. The combination of timely diagnosis, achieved by imaging and biopsy, followed by appropriate treatment, is essential for achieving optimal patient outcome. The prognosis of orbital lymphoma is generally favourable with chemotherapy and radiation, especially when detected early and confined to the orbit.

Take Home Message

- Clinicians should consider a broad differential diagnosis when evaluating patients with isolated proptosis, beyond common causes like thyroid eye disease.
- Orbital lymphoma can present solely with proptosis and minimal or no systemic symptoms.
- Early imaging and tissue diagnosis are essential to distinguish malignant from benign orbital conditions.
- Prompt systemic evaluation and treatment can significantly improve outcomes and prevent further disease progression.

Abbreviations

DLBCL	Diffuse large B-cell lymphoma
CHOP	Cyclophosphamide, Hydroxydaunorubicin, Oncovin, and Prednisone
MALT	Mucosal associated lymphoid tissue
NHL	Non-Hodgkin lymphoma
ADL	Activity of daily living
VA	Visual acuity
IOP	Intraocular pressure
OCT	Optical Coherence tomography
CT	Computerised tomography
MRI	Magnetic resonance imaging
PET	Positron emission tomography
FNAC	Fine needle aspiration cytology

Declarations

Conflict of interests

The authors declare no conflict of interests.

Patient Consent

Patient consent has been obtained.

Acknowledgement

The authors wish to acknowledge the Department of Radiology and the Laboratory Services and Pathology Department at the Raja Isteri Pengiran Anak Saleha Hospital for their support in the diagnostic workup and for providing the clinical images included in this report.

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