

# Marginal Zone Mucosa Associated Lymphoid Tissue Diffuse Large B Cell Lymphoma

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## Abstract

**Context:** Non-Hodgkin's lymphomas (NHL) primarily involving the orbit, is relatively uncommon. Rarely two pathologically different NHL cell types have been found to be coexistent. **Case Report:** We report a case of orbital lymphoma in a 62-year-old male with rare histopathological findings secondary to transformation of once cell type into another. Tissue diagnosis and molecular studies led to revelation of diffuse large B cell lymphoma evolving from MALT lymphoma. **Conclusion:** Proliferation of two morphologically and phenotypically different B cells resulting in malignancy has not been found in the orbit so far. They are usually aggressive tumors and require chemo-immunotherapy.

**Keywords:** Diffuse large B cell lymphoma, Marginal zone mucosa-associated lymphoid tissue lymphoma, Orbital lymphoma, Rituximab

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## Introduction

The orbit is a rare primary site for non-Hodgkin's lymphoma (NHL), accounting for 1% of primary presentations and an estimated 5-14% of all extra nodal presentations. However, lymphomas are the most common primary orbital tumor in adults 60 years of age and older.<sup>[1]</sup>

Transformation from marginal zone mucosa-associated lymphoid tissue (MALT) lymphoma to a different form of lymphoma is a very rare occurrence<sup>[2]</sup>, and has not been previously described in orbital lymphomas. We present a case of bilateral orbital MALT lymphoma that transformed into a diffuse large B-cell lymphoma (DLBL), both of which were incidentally found to be coexistent at the time of diagnosis.

## Case Presentation

A 62-year-old Caucasian male with a past medical history of hypertension and diabetes, presented with bilateral eye protrusion since 1 week. He had been experiencing double vision and throbbing frontal headaches for the past 2 weeks. Physical examination was remarkable only for bilateral exophthalmos [Figure 1a], without any palpable lymphadenopathy. Magnetic resonance imaging (MRI) of the orbit revealed  $3.8 \times 3.0 \times 1.5$  cm enhancing orbital mass involving the lateral and superolateral aspect of the peripheral right orbit as well as an irregular  $1.1 \times 1.1 \times 2.4$  cm mass along the inferior aspect of left orbit [Figure 1c]. Also noted were abnormal signal enhancements within the lesser sphenoid wing and the anterior body of the mandible on the right. Given this constellation of findings, there was suspicion for lymphoma or other metastatic disease.

Biopsy of right eye mass was done that revealed extensive soft tissue involvement by two separate lymphomatous populations [Figure 2a and b], comprising small and large neoplastic lymphocytes. The large cells were positive for CD20 B cells with co-expression of CD10 BCL6 and MUM-1. By corresponding flow cytometry, they were found to be kappa chain restricted. These features were consistent with high grade large B

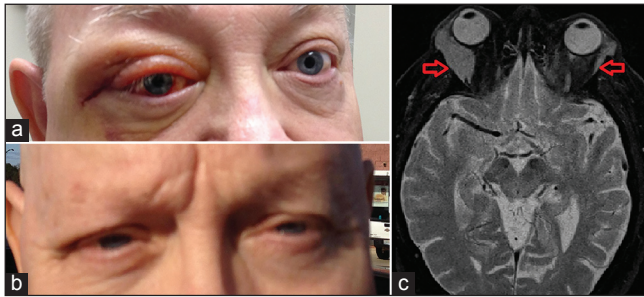
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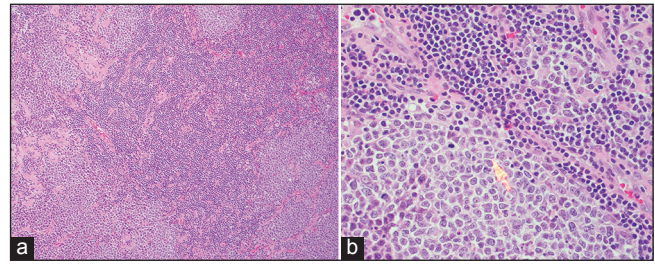
**Figure 1:** (a) Photograph of the patient showing bilateral swelling and proptosis of the eyes, more prominent on the right side. (b) Photograph of the patient after 1 month of chemotherapy, showing significant improvement on both sides. (c) MRI of the orbits, T2 cross section view. Red arrows showing lateral hyperintense infiltration in both orbits

cell lymphoma. The small lymphoma cells were CD20+ B cells with co-expression of BCL2 and aberrant CD43 and partial CD5. Flow cytometry revealed lambda restriction. These morphological and phenotypic features were consistent with MALT lymphoma. B cell immunoglobulin gene rearrangement by polymerase chain reaction (PCR) was done to detect clonality. Peaks migrating at 318, 255, and 274 bases were present on B-cell immunoglobulin heavy chain (IgH). In addition, there were peaks present migrating at 195 and 273 bases on B-cell immunoglobulin kappa light chain (IgK). The intensities of these peaks were consistent with clonal neoplasm. Gene rearrangement studies were also done on the different aberrant lymphocyte population with diagnosis of MALT lymphoma. Those areas also shared common peaks at 318 and 255 bases in IgH as well as 273 bases in IgK light chain.

Metastatic work-up with computed tomography (CT) scans and positron emission tomography (PET) scan was negative. He was started on Rituximab and cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP). By the time of his 1-month follow-up, the orbital swelling had disappeared [Figure 1b]. His lymphoma is currently under remission. Repeat PET is negative for any metastatic disease, and only residual disease is present in the orbit.

## Discussion

Orbital lymphomas (OL) usually present with eyelid swelling, palpable eyelid mass, diplopia, proptosis, and lid erythema. The most commonly infiltrated structures are found within the superior-lateral quadrant, such as the superior rectus muscle, lateral rectus muscle, lacrimal gland, and eyelid. Systemic lymphoma has been diagnosed in 67% of patients with bilateral orbital tumor and in 34% with unilateral orbital tumor. About 84% of OL have shown regression with treatment.<sup>[3]</sup>



**Figure 2:** (a) Low magnification view of lacrimal gland histopathology, showing two morphologically different lymphocytes. (b) High power magnification shows malignant large lymphocytes in the lower half with abundant cytoplasm, round nuclei with prominent nucleoli and occasional mitoses. This is consistent with diffuse large B cell lymphoma. Seen in the upper half of the figure are small lymphoid cell with a narrow rim of clear cytoplasm and condense chromatin. This is consistent with MALT lymphoma

Majority of the OL are MALT type lymphomas, accounting for 40% to 70% of the cases.<sup>[4]</sup>

Although initially described in gastric mucosa and in association with *Helicobacter pylori* infection, MALT lymphomas have subsequently been observed to arise in other epithelial structures, including the thyroid, parotid gland, lung, uterus, and breast, as well as in the orbit.<sup>[5,6]</sup>

Age greater than 60 years, elevated lactate dehydrogenase (LDH), and coexistent other malignancies, have been identified as independent risk factors for transformation into aggressive lymphomas.<sup>[4,7]</sup>

Management of orbital lymphoid tumors includes surgical excision, chemotherapy, immunotherapy, or radiotherapy, depending on the size, shape, location, and grade of the lesion and on the systemic status of the patient.<sup>[8,9]</sup> Some aggressive tumors may require chemo-immunotherapy as in this case.

What is unusual about our case is that it combines two morphologically and phenotypically different mature B-cell lymphomas arising in the same tissue. In the pathological sample, there is a defined demarcation between the two lymphoma cells without any intermixing. It may represent either two different co-existent lymphomas or a transformation from one to the other.

In this case, immunoglobulin gene rearrangement studies revealed common peaks at 318 bases and 254 bases in the IgH, and 273 bases peak in the IgK light chain, in both MALT lymphoma as well as DLBL. These findings suggest a common initial clonal process evolving from MALT lymphoma to a diffuse large B cell lymphoma with light chain switch (from lambda to kappa).

Transformation of MALT lymphoma is a rare event, and there are only a few cases of this occurrence

that have been reported<sup>[6,10]</sup>, but to our knowledge, no such pathological transformation has been identified in the orbit.

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