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# Extranodal Marginal Zone B Cell Lymphoma of the Orbit In a Patient with Sarcoidosis: A Case Report

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**Abstract.** *Objective:* To describe a case of extranodal marginal zone B-cell lymphoma (EMZL) "mucosa associated lymphoid tissue (MALT)" of the orbit that presented with stage IV disease in a patient with sarcoidosis. *Design:* Clinicopathologic case report. *Methods:* Biopsies of the lesion were performed in the operating room and the samples were submitted for pathology processing. Pathology analysis identified the lesion as an extranodal marginal zone B-cell lymphoma "mucosa associated lymphoid tissue (MALT)" via flow cytometry, histopathology, cytogenetics, and immunohistochemical staining and fluorescent in situ hybridization (FISH). The institutional review board of Howard University Hospital waived the need for IRB approval for this intraoperative finding. *Results:* A 70-year-old Black woman with biopsy-proven sarcoidosis presented complaining of foreign body sensation, redness, swelling of her left upper eyelid and tearing. The patient was found to have an orbital lymphoproliferative malignancy. *Conclusions:* It is still unclear if the presence of immunosuppression or an autoimmune disease increases the risk of lymphoproliferative malignancies {6}. Malignancy should always be suspected and investigated. *(Sarcoidosis Vasc Diffuse Lung Dis 2014; 31: 252-255)*

**Key words:** immunohistologic staining, flow cytometry, lymphoproliferation

This is a report of an unusual case of a metastatic marginal zone B cell lymphoma of the orbit in a patient with sarcoidosis. A 70-year-old black woman presented complaining of foreign body sensation, redness, swelling of her left upper eyelid and tearing of four months duration. Her past medical history was significant for hypertension, heart block with pacemaker, and sarcoidosis. Her sarcoidosis was managed chronically with prednisone 5 mg daily along with alendronate to reduce osteoporosis. On examination, her uncorrected visual acuity was 20/25 in the right eye and 20/30 in the left eye. She had a superotemporally located subconjunctival area of redness extending from the limbus to the left upper eyelid fornix. There was significant swelling of the left upper eyelid which was thought to be secondary to a lacrimal gland process. There was also noticeable left orbital fullness. Exophthalmometry measurements were 18 mm/104mm/23 mm.

There was radiologic evidence, via orbital computed tomography (CT) of an intraconal and extraconal mass of the left orbit measuring 31.19 mm x 32.62 mm involving the lacrimal gland and molding to all surrounding structures without bony erosion

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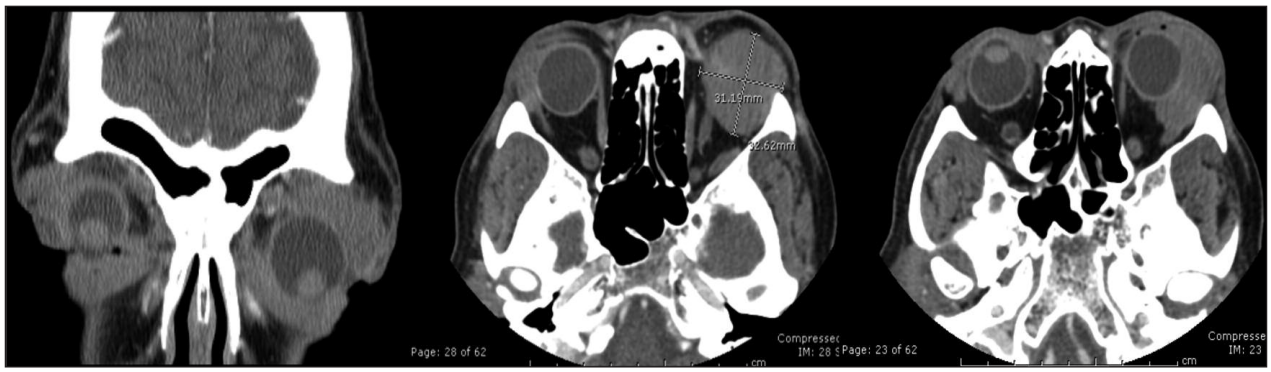


**Fig. 1.** Coronal and axial CT images of intraconal and extraconal orbital mass.
Postcontrast CT orbital images. Postcontrast CT of the orbit demonstrates intraconal and extraconal mass of the left orbit measuring 31.19 mm x 32.62 mm involving the lacrimal gland and molding to all surrounding structures without bony erosion.

(figure 1). The right lacrimal gland was also enlarged. Precontrast and postcontrast findings were the same. The patient's pacemaker prohibited the use of magnetic resonance imaging (MRI).

The patient therefore underwent a lateral orbitotomy with bone flap to allow for complete removal of the lacrimal gland and excisional biopsies of the surrounding areas. Initial intraoperative frozen section analysis suggested a lymphoproliferative process. Specimens included the lacrimal gland in its entirety, orbital bone flap and subconjunctival mass. The specimens were fixed for histologic examination and immunohistologic staining. The remaining tissue was processed for flow cyotmetry and submitted for FISH analysis.

The pathology report noted diffuse infiltration of orbital tissue and lacrimal gland by small lymphocytes with "centrocyte-like" contours along with atypical lymphoid proliferation of the marrow of the bone flap (figure 3a, 3b). Flow cytometry revealed small and

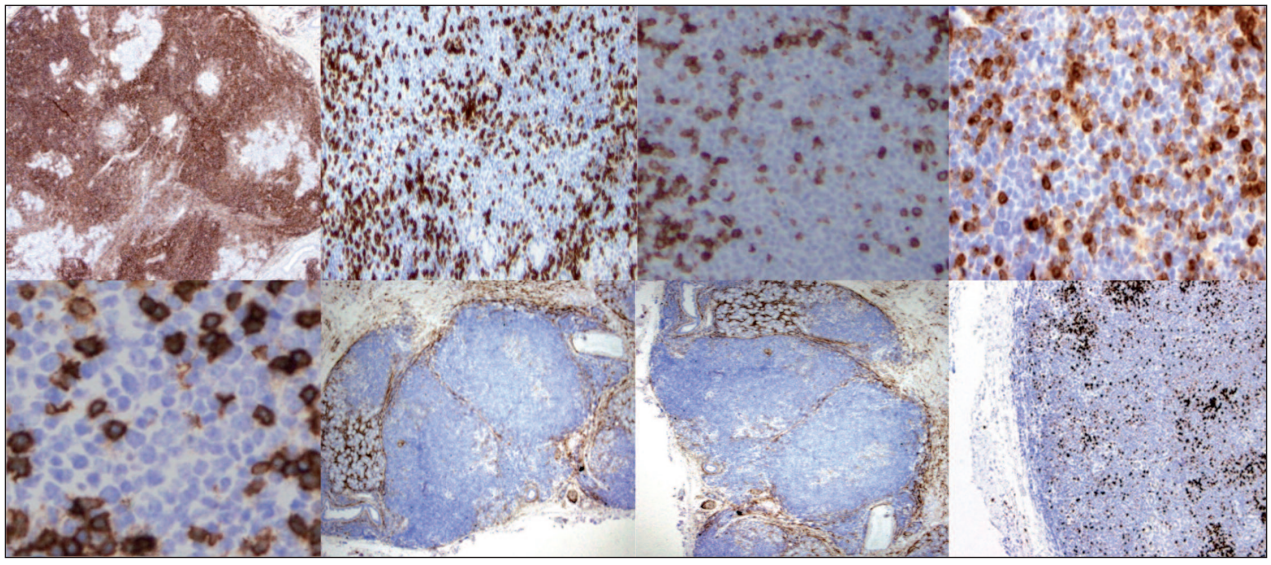

**Fig. 2.** Immunohistochemical staining of ocular adnexal tissue.
Immunohistochemical staining slides of lacrimal gland and orbital fibrous septal connective tissue. Lacrimal gland and orbital fibrous septal connective tissue from left orbit after a myriad of immunohistochemical stains as listed (top left = CD-20, top middle = bcl-2, top right = CD-5, middle left = CD-43, middle center = CD-10, middle right = bcl-6, botton left = CD-3, botton middle = Ki-67). Immunohistochemical staining results were as follows: negative for CD-3, CD 5, CD 10, CD 23, CD 43, bcl-2 and bcl-6 positive for CD-20 with some positivity of Ki-67. Magnification was as follows: 4x, 10x, 40x, 60x, 20x, 20x, 40x, 10x
Figure 3a. Histopathology slides of lacrimal gland.

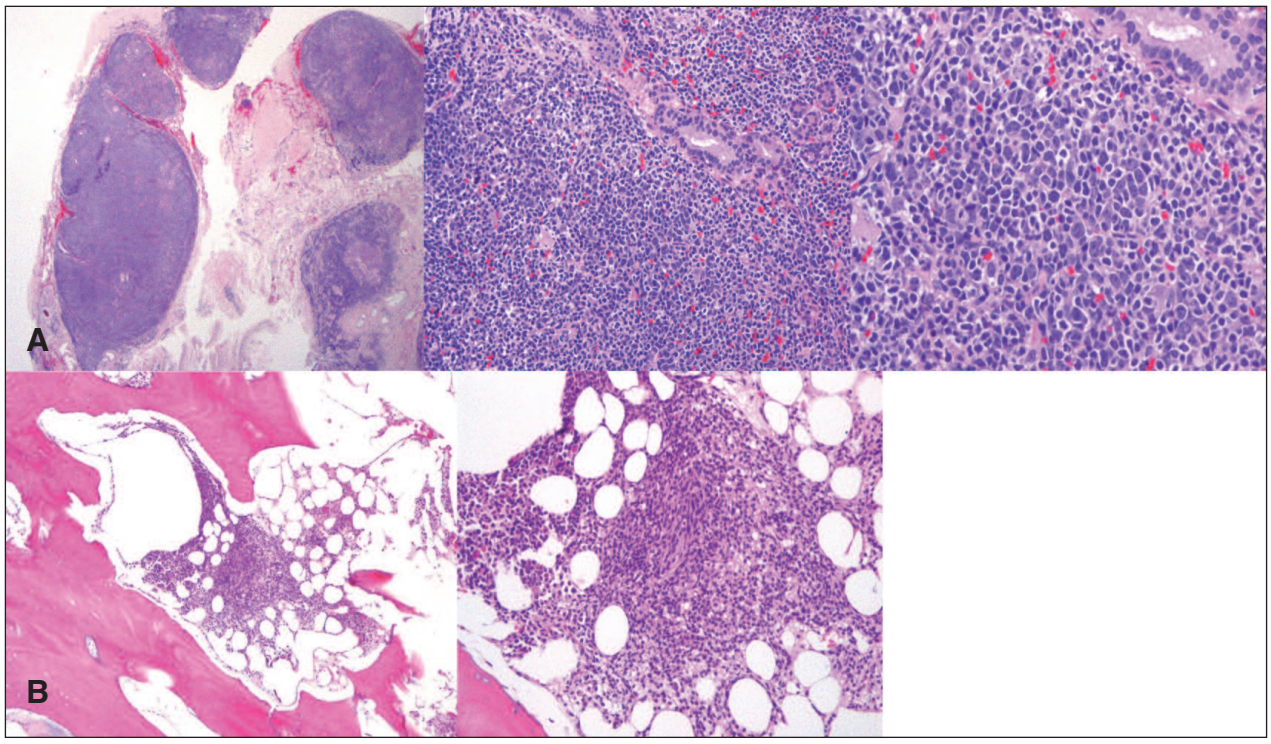


**Fig. 3.** A) Histopathology slides of lacrimal gland.
Histopathology slides of lacrimal gland infiltrated with lymphomatous cells. Mucosa-associated lymphoid tissue-type (MALT) lymphoma of the left lacrimal gland (low power, medium power, high power).
B). Histopathology slides of lateral orbital wall bone flap.
Histopathology slides of bone flap. Left lateral orbital wall section bone flap demonstrating marrow infiltration with lymphomatous cells (low and high power).

medium-sized lymphocytes, 21% of which were CD 20-positive B cells expressing monotypic surface kappa light chain. Immunohistochemical staining results were as follows: negative for CD 5, CD 10, CD 23, CD 43, bcl-2 and bcl-6 (figure 2). The result of the FISH analysis was negative for any kind of rearrangement which is consistent with the literature findings. Immunohistochemical staining profiles for ocular adnexal lymphoproliferative lesions demonstrated the most likely diagnosis of our patient's mass was extranodal marginal zone B-cell lymphoma (EMZL), the most common of the orbital lymphomas (1, 3, 4, 7, 8).

Our patient subsequently underwent staging via a CT angiogram of the chest, abdomen, and pelvis along with bone marrow biopsy and PET scan. The chest CT showed multiple small left upper lobe lung nodules, left supraclavicular large lymph nodes, and multiple bilateral subclavicular lymph nodes. There were also bilateral large axillary lymph nodes and large mediastinal and hilar lymph nodes, and splenomegaly. The bone marrow aspirate smear showed low grade B-cell lymphoma which was previously noted from the pathology report of the orbitotomy bone flap. Our patient was therefore started on pentamustine and rituximab to treat stage 4 EMZL.

## Discussion

It is widely accepted that the extent of disease at the time of diagnosis is the most important clinical prognostic factor (2, 6). In 2000, Jenkins et al investigated the applicability of the Revised European-American Lymphoma (REAL) classification which was originally developed for the properties of all lymphomas. They concluded that there exists an association between histological grade, as defined by the REAL classification system, and survival of patients with ocular adnexal lymphoma (2, 3). According to Kao et al, patients with lacrimal gland MALT

lymphoma are at a relatively high rate of synchronous bilateral involvement and extraorbital involvement at diagnosis (6).

There is a wide spectrum of diseases encompassing bilateral orbital lymphoid lesions. These lesions typically have no overt inflammatory signs (7). Even though fluorescent in situ hybridization (FISH) and real-time polymerase chain reaction (RT-PCR) have emerged as useful diagnostic modalities of lymphoproliferative lesions, biopsy provided specimens for immunohistochemical staining remains as the standard method for differentiating these disorders involving the orbit (1).

The three chromosomal translocations t(11;18) (q21;q21), t(14;18) (q32;q21), and t(1:14) (p22;q32) are associated with MALT lymphoma (10). Although t(11:18) (q21:q21) is the most common structural abnormality in EMZL, t(14;18) (q32;q21) has been observed in cytogenetic analysis of MALT lymphoma outside of the gastrointestinal tract (GI) and lung (9). Furthermore, those with t(14;18) (q32;q21), may harbor additional genetic abnormalities such as trisomy 3 and/or 18 (9). T(3;14) (p14.1;q32) may also harbor additional genetic abnormalities such as trisomy 3 (9). Our patient's negative result of the FISH analysis for any kind of rearrangement is consistent with the literature findings further supports the diagnosis of EMZL.

The etiology of primary orbital lymphoma is presently unknown. Ferreri et al provided evidence for an association between Chlamydia psittaci and ocular adnexal lymphomas but no evidence to elucidate the origin of primary orbital lymphomas (7). It has been postulated there may be an association of autoimmune disorders with an increased risk of lymphoproliferative malignancies (6). In the study of Kao et al reviewing 13 patients with MALT lymphoma in the lacrimal gland, two of them had prior autoimmune disease and both were stage IV disease at presentation just like our patient. It is not known, however, if patients with autoimmune disease or immunosuppression are prone to advanced disease (6).

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