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CE Credit - Topic Review

Ocular Findings in a Case of Systemic Lymphoma

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ABSTRACT

Purpose: To report a case of systemic lymphoma with ocular manifestations.
Methods: Case presentation.
Results: A 75-year-old male with a history of B-cell chronic lymphocytic leukemia and peripheral T-cell lymphoma presented to the eye clinic with painless swelling along his right upper eyebrow and binocular double vision. The patient was diagnosed with diplopia and dacryoadenitis, both presumably due to progression of his pre-existing lymphoma diagnosis. Neuroimaging results also suggested progressive lymphoma with central nervous system (CNS) and orbit involvement. The patient was hospitalized and ultimately passed away from advancement of his condition.
Conclusion: While this patient had an unfavorable outcome, his case demonstrates how lymphoma can manifest in the eye. Eye care providers can play a role in identifying the condition, alleviating ocular symptomatology, and coordinating care with other specialists to ensure patients' well-being.

INTRODUCTION

Lymphoma is a hematological malignancy with a variety of systemic and localized signs and symptoms. Ophthalmic involvement can be localized or part of a more disseminated disease; it can impact the globe or ocular adnexa, prompting a variety of symptoms or findings during an ophthalmic exam. Eye care providers can help identify ocular lymphoma and mitigate visual symptoms associated with the disease. This case report demonstrates one such ocular presentation in a patient with B-cell chronic lymphocytic leukemia and peripheral T-cell lymphoma.

CASE REPORT

A 75-year-old male presented to the optometry clinic to address a one-week history of binocular diplopia in all non-primary gaze positions, other than left gaze. He also reported epiphora, swelling, soreness, and redness around his right eyebrow. The patient's ocular history included ocular hypertension and mild cataracts in both eyes. His medical history was significant for hyperlipidemia, anemia, bacteremia, and Lyme disease. Of note, he was undergoing treatment for peripheral t-cell lymphoma and B-cell chronic lymphocytic leukemia with chemo-immunotherapy.

Upon examination, the patient's best-corrected visual acuity was 20/25 and 20/20 in his right and left eye, respectively. Prism cover test demonstrated a 2-prism diopter exophoria in primary position of gaze, an 8 prism diopter right hypotropia in left and right gaze, and no misalignment on left and right head tilt. Externally, a painless, flesh-colored, elevated, dome-shaped mass was evident along the superior temporal quadrant of his right orbit. The patient was diagnosed with diplopia and presumed right dacryoadenitis with a concern that these findings were related to his lymphoma. He was referred to the clinic's ophthalmology service for further evaluation.

At his ophthalmology visit two days later, the patient's diplopia had worsened to include primary position of gaze. He also exhibited extraocular motility restriction on up-gaze

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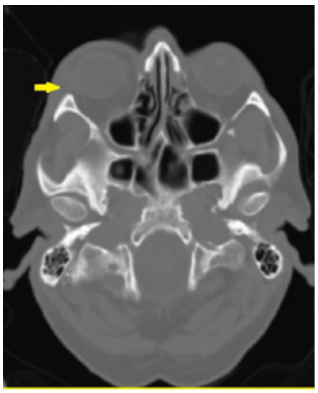
in the right eye and his right superior conjunctiva showed 2+ injection. Due to the advancement of his symptoms, the patient was sent to the emergency room the same day for a computed tomography (CT) scan of his head and maxillofacial region with contrast. The objective was to visualize the location and extent of his abnormalities to guide the diagnostic process and to encourage a targeted treatment plan. The patient was also referred to an oculoplastic ophthalmologist for a biopsy of the orbital mass; unfortunately, this was never completed.



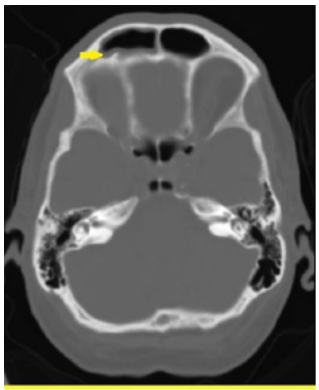


Image 1: Right orbital and adnexal soft tissue infiltration.

Image 2: Mucosal thickening of the right frontal sinus.

The CT scan demonstrated pansinusitis disease without significant orbital abnormality (Images 1 and 2 above). At the emergency room, the patient was empirically prescribed amoxicillin/clavulanic acid and probiotics for sinusitis. Infiltration from his systemic lymphomatous condition was of greatest concern. The patient opted to be discharged from the emergency room and he was strongly advised to follow up with ophthalmology, hematology, oncology, and his primary care physician.

6 days later, the patient was hospitalized at another facility for neurologic deficits including dysphonia, vertical diplopia, progressive weakness, and hemibody sensory loss. Magnetic resonance imaging (MRI) of the brain and spine demonstrated abnormal leptomeningeal enhancement involving the right trigeminal nerve, cranial nerve III, bilateral internal auditory canal fundus, orbital apex, cavernous sinus, foramen ovale, superior rectus muscle, and lacrimal gland. A repeat CT scan of the head exhibited mucosal thickening of the right frontal sinus and sphenoid sinus as well as bilateral thickening within the ethmoid air cells and maxillary sinuses. The CT scan also revealed an asymmetrically enlarged right superior rectus and mild infiltration of right orbital fat. A biopsy from the left middle turbinate exposed squamous metaplasia and abnormal lymphoid tissue, which may have represented T-cell lymphoma or mucosal inflammation. His primary team deemed his case findings highly suggestive of progressive lymphoma with CNS and orbit involvement. 17 days after being seen in our clinic, the patient unfortunately passed away from this escalation of his condition.

DISCUSSION:

Lymphoma is a hematological malignancy which arises from clonal proliferation of lymphocytes, including B-cells, T-cells, and natural killer (NK) cells.[1] Given this abnormal immune activity, it is not surprising that non-Hodgkin lymphomas are more common in individuals with autoimmune disease.[2] There are two main lymphoma subtypes, Hodgkin and non-Hodgkin, which comprise approximately 10% and 90% of all cases, respectively. B-cell lymphomas account for 85% of all non-Hodgkin lymphomas, while T-cell and NK/T-cell lymphomas account for the remaining 15%. One to 2% of all non-Hodgkin lymphomas and 5 to 15% of all extranodal non-Hodgkin lymphomas are primary ophthalmic lymphoma, meaning they arise in the eyes. Ocular adnexal involvement has been identified in in 5.3% of generalized systemic lymphoma cases.[3] The patient in this case report had non-Hodgkin lymphoma with ocular adnexal involvement.

While it is rare for eye care providers to make the initial diagnosis of lymphoma, it is important for them to be well-versed in the myriads of ways in which this cancer can present in the eye. A thorough history of the case and targeted questioning can help a practitioner make an initial diagnosis of lymphoma or identify an instance of recurrence or progression. Given that the lymphatic system is found throughout the body, lymphoma can develop in various places. Ocular lymphomas can be either primary or secondary;[2] they can be limited to the eye or present in the eye in addition to other places in the body. For example, lymphoma may spread to the eye from the sinuses, given their proximity. There are three subtypes of ocular lymphoma, which are ocular adnexal, uveal, and vitreoretinal (Table 1).

Table 1: Three subtypes of ocular lymphoma.[14,15,4]

	Affected Structures	Signs
Ocular Adnexa	Conjunctiva Lacrimal gland	Pink conjunctival lesion Dacryoadenitis
Uveal	Iris Ciliary body Choroid	White mass in the iris Ciliary body mass Multifocal yellow-white choroidal infiltrates
Vitreoretinal	Vitreous humor Retina	Anterior chamber cells Yellow subretinal lesions

This paper is focused on ocular adnexal lymphoma, given that our patient had this form of the disease. Ocular adnexal lymphoma can affect the eyelid, conjunctiva, lacrimal gland, or other orbital structures.[4] Of all ocular adnexal lymphomas, 46 to 74% affect the orbital cavity, 20 to 33% the conjunctiva, 25% the lacrimal gland, and 5 to 20% the eyelid.[2] Symptoms of ocular adnexal lymphoma include: conjunctival hyperemia (32% of patients), exophthalmia (27% of patients), orbital or palpebral mass (19% of patients), reduced visual acuity and ptosis (6% of patients), and diplopia (2% of patients).[5] Most cases of orbital and sinonasal lymphomas are diagnosed in the 7th decade of life.[6,7] There is an equal gender distribution with a slight male preponderance.[2]

Due to the widespread nature of lymphomas, it can be difficult to parse out when closer scrutiny of a diagnosis and etiology of symptoms is warranted and, therefore, the differential diagnosis is endless. In the case of this patient, dacryoadenitis was highest on our differential diagnosis given the presentation of a flesh-colored, elevated, dome-shaped mass along the superior temporal quadrant of his right orbit. Dacryoadenitis, which can be a sign of ocular adnexal lymphoma, is a general term for inflammation of the lacrimal gland. The elevation is evident superotemporally relative to the globe and tends to be unilateral. Acute dacryoadenitis, most frequently presenting in children and young adults, usually resolves within 4 to 6 weeks. Bacterial etiologies necessitate antibiotic administration, whereas viral etiologies do not. Dacryoadenitis can also be inflammatory and associated with conditions such as Sjogren syndrome, sarcoidosis, Crohn disease, and granulomatosis with polyangiitis. While the condition generally does not require a biopsy or comprehensive laboratory evaluation, there are circumstances in which these actions are indicated. An additional workup is warranted in cases where dacryoadenitis is not resolving or worsening with treatment after 3 months. Further investigation is also necessary when it occurs in older adults, especially if they have systemic symptoms, as this may raise suspicion for a malignant or systemic autoimmune process. Dacryoadenitis can mimic adenoid cystic carcinoma, mixed malignant carcinoma, mucoepidermoid carcinoma, thyroid eye disease, or lymphomatous infiltration of the lacrimal gland.[8] Given our patient's age and medical history of lymphoma, further investigation was necessary.

In addition to viral or bacterial dacryoadenitis, lymphoma with ocular involvement can be misdiagnosed as a common cold or a sinus infection. Symptoms of sinonasal lymphoma, such as nasal blockage, rhinorrhea, epistaxis, and sinusitis, can mimic a common cold or sinus infection. Both of these conditions may be affiliated with intermittent ocular pain, bulging around the affected sinuses, and proptosis.[5] While both lymphoma and sinus infections can cause night sweats and swelling of the lymph nodes, unexpected weight loss or treatment of sinusitis without resolution may signal the need for a more detailed examination.[5] The lymphoma disease process is also slowly progressive; therefore, severe, or rapid onset of symptoms would warrant further investigation.[6] Furthermore, ophthalmic signs of lymphoma tend to be unilateral, although bilateral manifestations are possible. Of note, vision is characteristically preserved in cases of lymphoma, as the optic nerve and globe are rarely infiltrated.[6,10]

If a patient's case history and physical examination are suspicious for the disease, communication with a medical internist is warranted and, from there, radiology and oncology specialists will become involved. Laboratory studies, neuroimaging, and a biopsy are necessary for diagnosis.[11] Once ocular lymphoma has been diagnosed through the analysis of a biopsy, an oncologist will be consulted to determine if it is elsewhere in the body and stage the lymphoma (See Table 2).

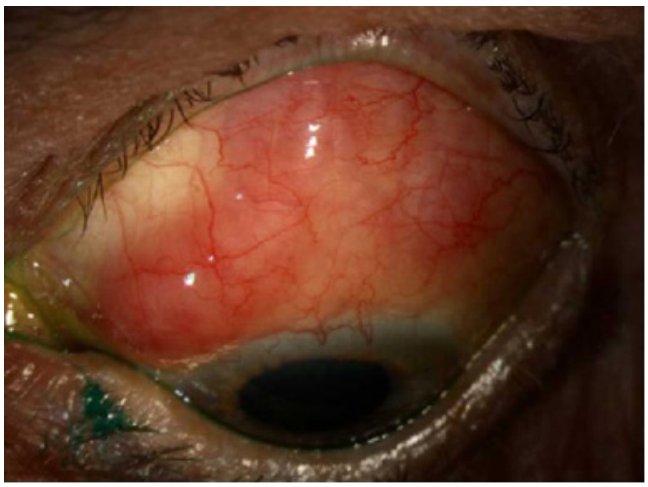


Image 3: Pink "salmon patch" clinical presentation of conjunctival lymphoma.[17]

Table 2: Lugano classification for staging of lymphomas[4,16]

Stage	Involvement
Stage 1	One node or group of adjacent nodes.
	Stage IE: a single site outside of the lymph nodes.
Stage 2	Two or more nodal groups on the same side of the diaphragm.
Stage 3	Nodes on both sides of the diaphragm or nodes above the diaphragm in addition to the spleen.
Stage 4	One or more extranodal organs.

This will steer a provider's treatment plan and provide a clearer prognosis. Adnexal and uveal lymphomas tend to occur at visceral sites, such as the chest, abdomen, or bone marrow, in addition to manifesting in the eye. Contrastingly, vitreoretinal lymphoma tends to involve the brain, spine, or cerebrospinal fluid.[4]

An initial laboratory investigation may include a complete blood count (CBC) with differential, coagulation studies, and serum chemistries, including electrolytes, renal function tests, liver function tests, lactate dehydrogenase (LDH), and uric acid. Hypercalcemia, anemia, thrombocytopenia, leukopenia, lymphocytosis, hyperuricemia, and elevated serum LDH may suggest NHL.[12] The extent of involvement and bone destruction can be evaluated and early detection can be achieved with MRI, CT, and positron emission tomography (PET)/CT.[11] Image studies may also encompass a chest x-ray in addition to CT and MRI of the orbit, abdomen, thorax, and pelvis.[6] While neuroimaging is necessary to evaluate nasal tumors and can add to the story by illustrating structural abnormalities and explaining subsequent functional defects, a biopsy is essential for diagnosis. A biopsy will help rule out other sinonasal malignancies, narrow down the diagnosis, and lead to targeted care.7

TREATMENT

Treatment options for lymphoma include surgery, radiotherapy, chemotherapy, and immunotherapy.[11,2] While surgery can be diagnostic and therapeutic, incomplete excision usually leads to relapse. Radiotherapy is the most common and preferred treatment modality. Chemotherapy is usually employed for lymphoma at stage 2 or higher and may be used after surgery or in combination with radiation.[2] Disease-free survival at 5 years could exceed 90% after systemic treatment for lymphoma.[10] However, current treatments are unable to prevent disease recurrence in patients with intraocular and CNS lymphoma.[4]

Preservation of vision is important, especially given that patients with ocular and CNS lymphomas tend to live long after their diagnosis.4 The survival rate for non-Hodgkin lymphoma is 72% at five years.[1] Treated patients can be followed by optometrists or ophthalmologists every three months for two years then every six months for the subsequent three years and then annually. In addition to identifying signs of lymphoma and monitoring for recurrence, eye care providers manage ocular side effects, such as keratitis, corneal ulceration, cataract, or radiation retinopathy, from treatment. Eye care providers may help alleviate symptoms associated with the condition, such as diplopia.[6] Diplopia can be mitigated with prismatic correction in spectacles for deviation magnitudes of up to 12 diopters. Larger misalignments necessitate occlusion of either eye with a patch or the application of tape to one lens in the eyeglasses.[13] If abnormal exam findings are suggestive of recurrence and secondary tumor formation, communication with an internist, oncologist, or radiologist is necessary.[6]

CONCLUSION:

Lymphoma, whether spread throughout the body or limited to one node area or organ, can manifest in the eye. Eye care providers can help make an initial diagnosis of lymphoma or, as exemplified in this case report, identify recurrence or progression. In addition to coordinating targeted care, practitioners may also play a role in alleviating ocular discomfort from treatment sequelae or from the disease itself.

REFERENCES

1. Baker-Schena L. Demystifying ocular lymphoma. *American Academy of Ophthalmology*. April 28, 2016. https://www.aao.org/eyenet/article/demystifying-ocular-lymphoma.
2. Bitner B, Htun N, Wang B et al. Sinonasal lymphoma: A primer for otolaryngologists. *Investigative Otolaryngology*. October 2022.
3. Moslehi R, Schymura MJ, Nayak S, Coles FB. Ocular adnexal non-Hodgkin's lymphoma: a review of epidemiology and risk factors. *Expert Rev Ophthalmol*. 2011;6(2):181-193. doi:10.1586/eop.11.15
4. Freedman AS, Friedberg JW, Aster JC. Clinical presentation and initial evaluation of non-Hodkin lymphoma. UptoDate. August 22, 2024.
5. Decaudin D, de Cremoux P, Vincent-Salomon A, Dendale R, Rouic LL. Ocular adnexal lymphoma: a review of clinicopathologic features and treatment options. *Blood*. 2006;108(5):1451-1460. doi:10.1182/blood-2006-02-005017
6. Greenwald M et al. Conjunctival Lymphoma. *EyeRounds.org*. September 26, 2016. http://eyerounds.org/cases/243-conjunctival-lymphoma.htm#gsc.tab=0
7. Jamil A, Mukkamalla SKR. Lymphoma. *StatPearls*. July 17, 2023. https://www.ncbi.nlm.nih.gov/books/NBK560826/
8. Patel R, Patel BC. Dacryoadenitis. [Updated 2023 Apr 3]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/sites/books/NBK535384/
9. Zhu BJ, Li B, Zhang MH, Wang NL. Predicting the prognosis of primary orbital lymphoma by clinical characteristics and imaging features. *International Journal of Ophthalmology*. May 18, 2023. 16(5):705-711. doi:10.18240/ijo.2023.05.06
10. Kakkassery V, Coupland SE, Heindl LM. Iris lymphoma—a systematic guide for diagnosis and treatment. *Survey of Ophthalmology*. 2021. 66(1):41-53. doi:https://doi.org/10.1016/j.survophthal.2020.06.003
11. Kiratli H, Ağın A, Büyükeren B, Söylemezoğlu F. Primary Diffuse Large B-Cell Lymphoma of the Ciliary Body. *Ocul Immunol Inflamm*. 2019. 27(3):407-409. doi:10.1080/09273948.2017.1415362
12. Knipe H. Lugano staging classification. Radiopaedia. August 26, 2024. doi:https://doi.org/10.53347/rid-63811
13. Meer EA, Gonzalez-Candial M, Scawn R et al. Orbital Lymphoma. *EyeWiki*. May 9, 2024. https://eyewiki.org/Orbital_Lymphoma
14. Najem K, Asuncion RMD, Margolin E. Diplopia. *StatPearls*. February 29, 2024. https://www.ncbi.nlm.nih.gov/books/NBK441905/
15. Sharma T and Kamath M. Diagnosis and Management of Orbital Lymphoma. *American Academy of Ophthalmology*. October 12, 2016.
16. Urbanelli A, Testi F, Riva G, Pecorari G. Diffuse Large B-Cell Lymphoma of the Frontal Sinus: A Case Report. *Hematol Rep*. September 12, 2023. 15(3):524-531. doi:10.3390/hematolrep15030055
17. Vishal RR, Mruthyunjaya P, Singh AD. Ocular and Adnexal Lymphoma. *Essentials in Ophthalmology*. 2023.