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Title: Stepping Back to Take a Bird's Eye View

Abstract

Purpose: To present a case of conjunctival and uveal mucosa-associated lymphoid tissue (MALT) lymphoma masquerading as an anterior sclerouveitis in a patient with ulcerative colitis.

Case presentation: A 42-year-old male with a past medical history of ulcerative colitis was referred to the anterior segment service for redness of one eye. Examination was consistent with unilateral nodular anterior sclerouveitis secondary to a pre-existing autoimmune inflammatory disorder. There were atypical features including elevated intraocular pressure, anterior chamber inflammation, and optic neuropathy. After failure of response with adequate treatment, re-examination showed posterior segment changes including a birdshot-like retinopathy. Biopsy of the subconjunctival nodule confirmed the diagnosis of MALT lymphoma. The patient was referred to oncology for further management which included immunotherapy and subsequent improvement of his ocular symptoms.

Conclusion: Masquerade syndromes such as adnexal MALT lymphoma present a diagnostic dilemma, as the presentation can easily be confused with other or concurrent ophthalmic disease. Clinicians must remain vigilant to consider masquerade conditions in the differential diagnosis with any condition that shows atypical features or inadequate response to treatment. If there is concern for adnexal lymphoma, obtaining ocular tissue for pathologic evaluation is important to establish a diagnosis.

History

A 42-year-old male was referred to the Geisinger Eye Institute by an outside optometrist for redness of the right eye for four months. The redness had not improved over this time with topical lubrication. His ophthalmic history included myopia and there was no history of previous ophthalmic surgery. The patient had a past medical history of ulcerative colitis which at the time of presentation was controlled on oral mesalamine. There was no history of trauma, review of systems was negative, there was no introduction of new ocular or systemic medication, and he had no known drug allergies.

Examination

At presentation, the patient had a best corrected visual acuity of 20/20 with an intraocular pressure of 34mm Hg by applanation in the right eye. His pupillary exam was normal and negative for a relative afferent pupillary defect.

External lid examination was normal, while the anterior segment was notable for an elevated subconjunctival nodule with 3+ temporal injection and chemosis (**Figure 1**), keratic precipitates on the inferior endothelium, and 2+ cell and flare in the anterior chamber. Gonioscopy

revealed a Spaeth angle classification of D45f 1+PTM. Anterior segment of the left eye was normal.

The posterior segment revealed a cup to disc ratio of 0.9, the vitreous was negative for inflammatory cells, the media was clear, and the posterior segment was otherwise normal. Of note, cup to disc ratio in the left eye was 0.3. Optical coherence testing (OCT) confirmed an optic neuropathy of the right eye (**Figure 2**).

Discussion and Diagnosis

Our patient presented with evidence of a subconjunctival injected nodule with an anterior chamber inflammatory response and secondary optic neuropathy. Given his history of ulcerative colitis, treatment with oral non-steroidal anti-inflammatory drugs (NSAIDs) was initiated. There was no change in clinical findings with NSAIDs, therefore topical and oral corticosteroids were instituted. Gastroenterology was consulted given suspicion for uncontrolled ulcerative colitis and colonoscopy was performed; biopsy and pathology results yielded no active colitis.

After three months of treatment with minimal improvement, repeat comprehensive evaluation showed evidence of multifocal yellow deposits in the post-equatorial region in a birdshot-like pattern (**Figure 3**). Fluorescein angiography was performed which showed patchy choroidal filling with hypofluorescent choroidal lesions in the mid periphery without optic nerve or vessel leakage (Figure 4). Histocompatibility leukocyte antigen (HLA)-A29 testing was negative and angiotensin-converting enzyme was within normal limits.

Given the unusual course and poor response to treatment, the patient was scheduled for a biopsy of the temporal subconjunctival nodule. In the operating room, removal of the conjunctiva revealed a subconjunctival orange-colored vascular tissue that was friable upon dissection from the bare sclera (**Figure 5**). The exposed sclera was covered with amniotic membrane and the specimen was sent fresh to pathology.

Pathology results indicated extranodal marginal zone lymphoma of mucosal-associated lymphoid tissue (MALT lymphoma) (**Figure 6**). Positron-emission tomography (PET) scan was negative for dissemination and therefore disease was localized to the right globe. The patient was co-managed with ocular oncology with a final diagnosis of conjunctival and uveal MALT lymphoma.

This case represents an example of lymphoma as a masquerade syndrome. His presentation and past medical history raised suspicion for an inflammatory etiology given that scleritis can present with co-existing uveitis and trabeculitis. One key feature to consider in our patient was the absence of pain at initial presentation. A severe dull or boring type pain is usually present made worse by eye movements with scleritis (1).

When he failed to respond to appropriate treatment, additional diagnoses were considered. Although his anterior segment findings were easily viewed at the slit lamp, this case highlights

how a complete examination can aid in the diagnosis of anterior segment cases. Thorough and repeat comprehensive examination led to the collaboration of anterior and posterior segment physicians to provide this patient the correct plan of action, obtain fresh tissue, and ultimately yield a diagnosis.

Adnexal lymphoma of the ocular region is a rare condition comprising just two percent of all non-Hodgkin lymphoma (2, 3). It typically involves the mucosa-associated lymphoid tissue (MALT) affecting the conjunctiva, lacrimal gland, orbital tissue, and the choroid. Overall it is considered to be a low grade lymphoma with a favorable diagnosis with an average delay of presentation to diagnosis of eight months (3, 4). Known as “the great masquerader,” the diagnosis of MALT lymphoma in the eye is a challenging dilemma for clinicians. Presentation often reveals non-specific exam findings, or those that are typical of other more common ophthalmic diseases. This presents an interesting situation in which a clinician may be fooled by the non-specificity or specificity of the patient’s presenting findings. Making matters more complicated, patients tend to present with non-specific complaints which may include vision out of focus, floaters, and red eye. Despite the rare occurrence of MALT lymphoma affecting the adnexal tissue, suspicion should be high especially in the setting of non-resolving or recurrent ocular disease.

Treatment of ocular lymphoma first and foremost is dependent on whether disease is localized or disseminated to other locations throughout the body (3). The current options for treatment include chemotherapy, radiotherapy, immunotherapy, and surgery (5). Surgery and chemotherapy particularly place patients at high risk for relapse. Radiotherapy is a very effective modality and may be the most common treatment type for lymphoma of the ocular region. Side effects of radiation are common and include dry eye syndrome, keratitis, cataract, and radiation retinopathy (5). Immunotherapy is an ever more popular treatment as most lymphoma cells express CD20 antigen on their cell surface, making anti-CD20 treatment options such as Rituximab favorable. There is also a high rate of recurrence reported with immunotherapy and varying treatment regimens have been proposed. Given the local extent of our patient’s disease, initial treatment with systemic rituximab was chosen with the option for additional radiotherapy if incomplete response to treatment occurred.

Conclusion

This case presents a diagnostic dilemma for the anterior segment specialists. The presentation, non-specific symptoms, history of inflammatory disorder, atypical exam features and incomplete response to treatment all prompted continued investigation for this patient. Masquerade syndromes including cancer must be kept in the differential in the face of poor response to treatment. Examination of the anterior segment as well as the posterior segment is essential. This case demonstrates the importance of comprehensive examination when appropriate, as it can make the difference in saving the patient’s life.



Figure 1: Slit lamp examination of the right eye reveals a subconjunctival elevated nodule with overlying conjunctival injection and chemosis.

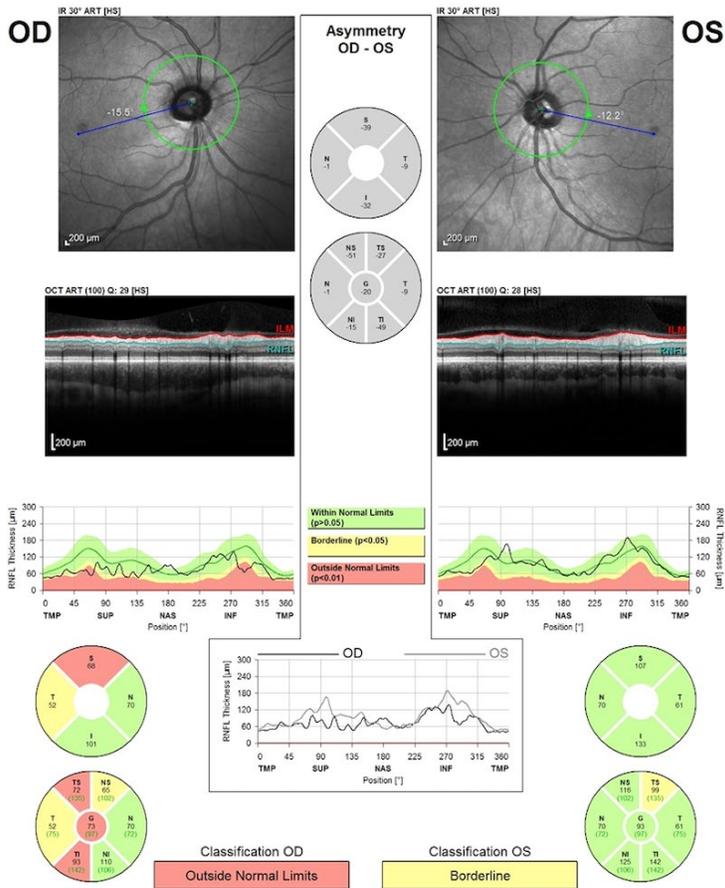


Figure 2: OCT Retinal Nerve Fiber Layer (RNFL) shows increased cup to disc ratio of the right eye on infrared imaging with atrophy of the RNFL superior and temporal.



Figure 3: Fundus photo of the right eye reveals evidence of multifocal yellow deposits in the post-equatorial region in a birdshot-like pattern.

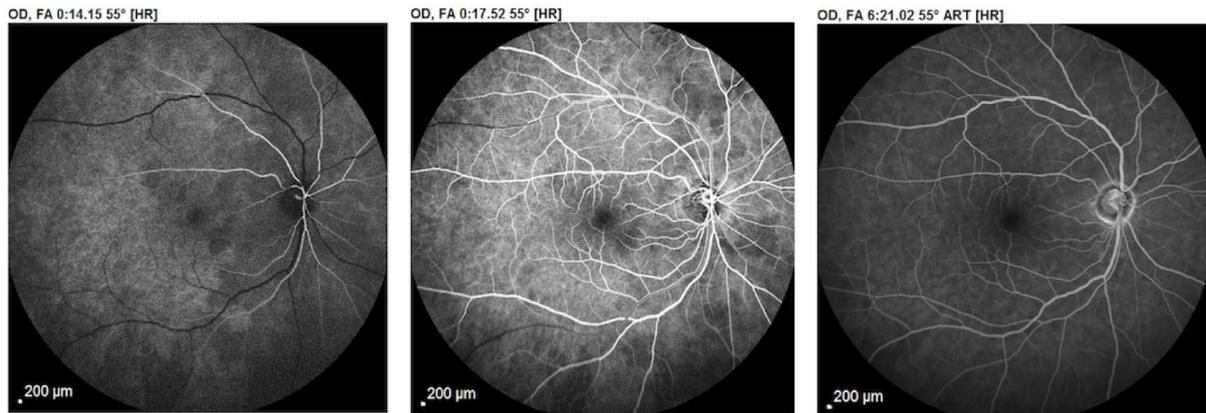


Figure 4: Fluorescein angiography shows patchy choroidal filling with hypofluorescent choroidal lesions in the mid periphery without optic nerve or vessel leakage in the late phase.

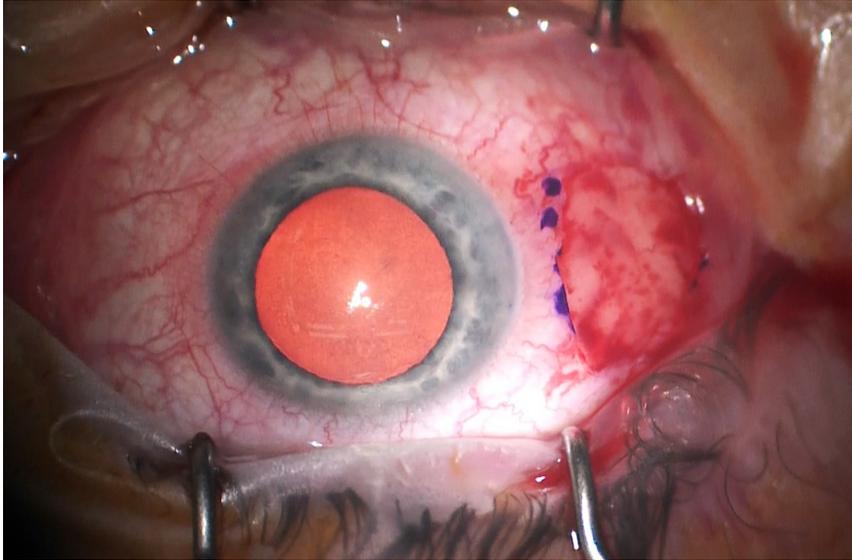


Figure 5: Intra-operatively, after submission of the superficial conjunctiva for immunohistology, a subconjunctival orange-colored vascular tissue was revealed. This specimen was dissected from the bare sclera and also sent for immunohistology as a fresh specimen.

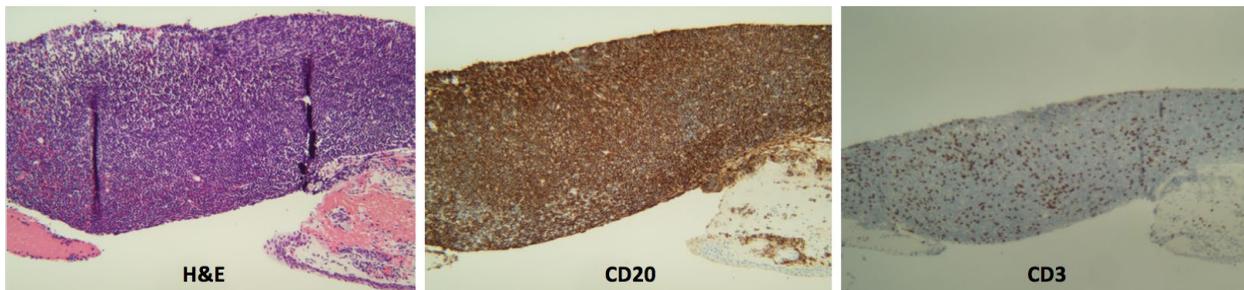


Figure 6: Hematoxylin and eosin staining shows the biopsied subconjunctival specimen with a paucity of lymphocytes. Immunohistochemistry staining shows a predominance of CD20 staining and lack of CD3 staining.

References:

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