cation of basement membrane was seen throughout the specimen (Figure 4).

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Financial Disclosure: None.
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Systemic Non-Hodgkin B-Cell Lymphoma
Encountered as a Vanishing Choroidal Mass

Intraocular lymphomas may be subclassified as primary ocular/central nervous system lymphoma and systemic non-Hodgkin lymphoma. Systemic non-Hodgkin lymphomas are usually B-cell lymphomas but may also be of T cell origin. Although ocular/central nervous system lymphomas may commonly be encountered with ocular involvement, it is rare for systemic non-Hodgkin lymphomas to be seen initially as ocular lesions.1-6 We report the case of a systemic large B-cell, non-Hodgkin lymphoma encountered as a choroidal mass with resolution of the ocular lesion after fine-needle aspiration biopsy.

Report of a Case. A 47-year-old woman sought treatment for sudden decreased vision in her left eye. Best-corrected visual acuity was 20/30 OD and hand movements OS. Intraocular pressure was 18 mm Hg in each eye. A left relative afferent pupillary defect was present. Results of an anterior segment examination were unremarkable in both eyes. Dilated ophthalmoscopic examination was unremarkable in the right eye, but disclosed a total, bulbar serous retinal detachment in the left eye. A choroidal mass was visualized, although details could not be appreciated owing to the overlying retinal detachment. Standardized A- and B-scan echography demonstrated an extensive, irregularly shaped, regularly structured, low-reflective lesion with maximal elevation of 8.9 mm (Figure 1). Marked vascularity was noted on dynamic echography and confirmed by color Doppler imaging (Figure 2).

Figure 1. Standardized A- and B-scan echography findings at initial examination. A, Transverse B-scan shows the extensive, solid, low-reflective mass lesion (large arrow). B, Longitudinal B-scan demonstrates the radial extent of the tumor (large arrow) and the total retinal detachment (small arrow). C, Standardized A-scan illustrates the surface of the solid mass (thin arrow) and the regular structure and low reflectivity (thick arrow).

Figure 2. Color Doppler image shows marked internal vasculature of the solid tumor (arrow).
The echography findings were consistent with a metastatic tumor such as lymphoma or small cell carcinoma. Systemic work-up results, including those of a whole-body computed tomographic scan, abdominal ultrasonography, and a chest x-ray, were negative. After a detailed discussion of the treatment options, including enucleation or a diagnostic biopsy, the patient underwent a transscleral fine-needle aspiration biopsy of the choroidal mass. The biopsy sample size was limited. No tissue fragments were identified. A small drop of the biopsy sample was placed on 4 slides and the remaining specimen was run through Millipore filters (Millipore Corp, Billerica, Mass). Microscopic examination disclosed rare clumps of cells with large hyperchromatic nuclei and a high nuclear-cytoplasmic ratio (Figure 3). Immunohistochemical staining was intensely positive for CD56, showed intermediate intensity for CD45, and was negative for HMB45. The limited biopsy sample size precluded staining for CD20. Cytopathologic analysis results were consistent with a malignant lesion, but classification was limited by the sample size.

Systemic examination results, including findings of a positron emission tomographic scan, were negative. One month after the biopsy, best-corrected visual acuity was 20/250 OS. The superior retina was attached and showed peripheral pigmentary changes of the retinal pigment epithelium. The inferior retina including the macula remained detached, but the mass lesion had vanished (Figure 4).
Echography confirmed the retinal detachment, but showed no evidence of the mass lesion in any quadrant (Figure 5). Given the spontaneous resolution of the mass lesion following a choroidal biopsy, no further intervention was recommended. Two months later, the retina was completely attached, with persistent pigmentary alterations and mild peripapillary hemorrhage (Figure 6).

Six months after the choroidal biopsy, the patient returned with left-sided maxillary pressure and left perioral numbness. Palpation of the malar eminence revealed a 4-cm mass occupying the soft tissue just below the orbital rim. A computed tomographic scan demonstrated a mass centered anterior to the bony portion of the maxillary sinus that extended into the maxillary sinus and into the soft tissue of the cheek (Figure 7). A positron emission tomographic scan showed uptake along the left paratracheal region in addition to the maxillary findings. Visual acuity was 20/400OS. Dilated funduscopic examination and ultrasonography findings showed no evidence of a retinal detachment or recurrent tumors in either eye. A trucut biopsy of the maxillary sinus lesion was performed through a sublabial approach, which disclosed a diffuse, large B-cell lymphoma (Figure 8) that was positive for Bcl-2, CD20, and CD45, but negative for CD3 and CD56. Ki-67 immunostaining showed a high proliferative index. The patient was
refractory to CHOP and EPOCH chemotherapy (cyclophosphamide, doxorubicin, vincristine sulfate, and prednisone and etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin, respectively). The maxillary mass showed further enlargement despite chemotherapy, and the patient was placed on palliative treatment including pain management.

Comment. Systemic non-Hodgkin lymphomas, unlike primary ocular/central nervous system lymphomas, are rarely seen at first examination with the eye as the primary site. Our patient came to us with a choroidal lesion and exudative retinal detachment, but without evidence of systemic disease after extensive evaluation that included whole-body imaging. Six months later, she developed an aggressive maxillary sinus lesion that led to the diagnosis of a diffuse, large B-cell lymphoma. This case illustrates that systemic non-Hodgkin lymphoma can manifest in the eye before overt systemic involvement and, therefore, should be entertained in the differential diagnosis of an unexplained choroidal mass and serous retinal detachment.

Cytopathologic analysis findings of the choroidal lesion were consistent with those of an undifferentiated malignancy. CD45 staining suggests either a T- or B-cell lymphoma, while CD56 is a marker for either a T-cell lymphoma or activated T or natural killer cells. B-cell-specific evaluation (ie, CD20) was not included in the immunophenotypic characterization, because the incidence of the eye as the initial site with B-cell lymphomas is low and the biopsy sample size was rate-limiting. The larger maxillary biopsy sample enabled characterization of a B-cell lymphoma with CD20 and CD45 immunostaining, and a relative lack of immunostaining for CD56 and CD3, which are designators of T-cell lymphoma. The lack of CD56 staining in the maxillary sinus biopsy specimen and positive CD56 staining in the choroidal biopsy specimen are consistent with a B-cell lymphoma, because CD56-stained T or natural killer cells can be present in B-cell lymphomas. Alternatively, Braylan et al report that lymphomas are complex disorders that require a large array of antibodies for their complete immunophenotypic characterization. Hence, we presume that the limited sample size of both biopsies explains the difference in CD56 labeling.

This case is particularly interesting given the resolution of the choroidal mass and retinal detachment after the fine-needle aspiration biopsy. Subretinal pigment epithelial detachments due to lymphoma have been reported to resolve spontaneously, possibly by an immune re-

Figure 7. A computed tomographic scan 6 months after the choroidal biopsy demonstrates a mass involving the left maxillary sinus and extending into the soft tissue of the cheek.

Figure 8. Hematoxylin-eosin-stained (A) and CD20-immunostained (B) sections of the biopsied maxillary mass. A, Hematoxylin-eosin staining shows a diffuse, large B-cell lymphoma that tested positive for Bcl-2, CD20, and CD45 (original magnification ×160). B, CD20-immunostained cells are evident (original magnification ×400).


**Chemoreduction With Topical Mitomycin C Prior to Resection of Extensive Squamous Cell Carcinoma of the Conjunctiva**

Topical mitomycin C (MMC) is effective for treatment of superficial or invasive squamous cell carcinoma (SCC) of the conjunctiva. In most instances, the chemotherapy agent is delivered 4 times daily in topical eyedrop form directly on the affected ocular surface. The medication is continued generally for 3 or 4 weeks, at which time the tumor is usually completely regressed.

Published results have shown that thin tumors, typically those that are less than 4 mm in thickness, show complete regression with MMC. Complete regression can be found with thin tumors even if they are extensive over most of the conjunctival and corneal surface. Thick tumors (≥4 mm in thickness), however, may show only partial regression with MMC, and there is the temptation to continue the medication for a prolonged period. Nevertheless, some patients do not show a complete response despite several chemotherapies cycles, and in such cases, prolonged therapy with this toxic medication could lead to serious vision-threatening and globe-threatening complications. Additionally, patient intolerance of the medication generally increases with multiple treatment cycles. In these cases with thick, extensive conjunctival SCC, we have used topical MMC as a neoadjuvant chemotherapy for tumor reduction (chemoreduction) prior to resection of the residual conjunctival mass. In this report, we describe 3 cases in which this strategy was used.

Following patient examination and pathologic confirmation of the diagnosis of SCC, the patients were given options for management, including the use of topical MMC. Advantages and disadvantages of this therapy were discussed with the patient. Investigational review board approval and patient consent was obtained. Temporary punctal plugs were placed in the upper and lower ipsilateral punctum to minimize systemic absorption of the drug and prevent punctal stenosis. Mitomycin C 0.04% was delivered in cycles that consisted of medication 4 times daily for 7 consecutive days followed by 7 consecutive days of no medication. The treatment cycles were repeated until the epithelial malignancy was judged to be clinically regressed. The medication protocol was designed to be continued until complete regression of the mass was achieved. If incomplete regression was noted, the medication was used until no further regression was evident or patient intolerance or toxic effects of the medication were unacceptable. The tumor response and toxic effects on the eye were recorded. Following MMC administration, the tumor residua was treated surgically as needed with conjunctival resection using the “no touch” technique, alcohol corneal epitheliectomy, and cryotherapy to the clinically unaffected surrounding conjunctival margin. The surgery was performed at least 2 weeks or more following discontinuation of MMC to allow for recovery of the conjunctiva and adequate wound healing.

**Report of Cases.** A summary of these cases is provided in the Table and Figure 1. They are described below.

**Case 1.** A 52-year-old woman was referred to us with extensive conjunctival SCC in the left eye, confirmed on previous incisional biopsy results. Her visual acuity was 20/100 OU from myopic chorioretinal degeneration. There was a gelatinous, extensively leukoplakic conjunctival tumor involving the entire inferior bulbar and tarsal conjunctiva from medial to lateral canthus plus 4 clock hours of limbal and 1 clock hour of corneal involvement (Figure 2). The entire mass measured 40 mm × 32 mm in basal dimension and 12 mm in thickness. Following 3 weeks of chemoreduction using topical MMC, the tumor showed gradual reduction in size to 24 mm × 20 mm in basal dimension and 8 mm in thickness and the corneoscleral limbus was free of