Intraocular Lymphoma

Dear Editor:

The vitreoretinal form of intraocular lymphoma is non-Hodgkin’s B-cell lymphoma, which commonly occurs in conjunction with CNS lymphoma. Treatment protocols currently suggest the use of systemic chemotherapy, which fails to obtain significant intravitreal cytotoxic doses, or external radiation, which initially eradicates the tumor, but recurrence and ocular complications are frequent. More recently, in an attempt to obtain high local concentrations of chemotherapy, intravitreal methotrexate has been used. Although initial reports of this therapeutic approach are very encouraging, with almost 100% tumor eradication, this treatment, also, is not without complications. The side effects, however, are usually transient and include mainly conjunctival irritation and corneal epitheliopathy. In this letter, we describe a previously unreported complication, the development of neovascular glaucoma, in 2 patients.

The first patient is a 79-year-old diabetic and hypertensive woman with known B-cell CNS lymphoma diagnosed 2 years earlier and successfully treated with intravenous methotrexate. She presented to our clinic with a complaint of decreased vision and was found to have visual acuity (VA) of 20/50 (both eyes) and intraocular pressure (IOP) of 14 mmHg. Two months later, she was noted to have vitreous cells bilaterally, which in diagnostic vitrectomy were found to be lymphomatous. The patient was started on intravitreal methotrexate injections of 400 μg/0.1 ml to both eyes according to our standard protocol of biweekly injections for 4 weeks, weekly injections for 8 weeks, and monthly injections for 9 months. The vitreous was clear after 6 injections. After the 17th injection, a dramatic rise in IOP to 64 mmHg (right eye) and 55 mmHg (left eye) was noted. The intraocular injections of methotrexate were stopped. Topical and hypotensive treatment failed to bring down the pressure. Slit-lamp examination and gonioscopy revealed neovascularization of the anterior chamber angle (ACA). The central iris was clear of ruberosis. Funduscopy and fluorescein angiography did not show any retinal pathology. The patient underwent Ahmed valve placement in both eyes, with successful reduction of IOP to normal without antiglaucoma medication. In follow-up, the neovascularization was clinically resolved, and 3 years after her initial intravitreal injections, there was no evidence of recurrence of the intraocular lymphoma.

The second patient is a 52-year-old diabetic and hypertensive man with CNS lymphoma diagnosed and successfully treated 5 years before his presentation to our eye clinic, complaining of decrease in VA of several months’ duration in both eyes. On initial presentation, the patient’s VAs were 20/40 (right eye) and counting fingers (left eye); IOP was 14 mmHg in both eyes. Bilateral posterior subcapsular cataract and cells in the vitreous were noted. In diagnostic vitrectomy, B-cell lymphoma was found. Intravitreal methotrexate injections were initiated in both eyes according to the protocol outlined above. After the fifth injection, the vitreous in both eyes was noted to be free of cells. After the 17th injection, IOP rose to 40 mmHg (right eye) and 50 mmHg (left eye). Bilateral neovascularization was evident on both direct and gonioscopic views, covering the ACA and the peripheral third of the iris. Funduscopy and retinal imaging showed no retinal pathology. Topical antiglaucoma medication was initiated in both eyes but only transiently reduced the pressure, and Ahmed valves were therefore placed bilaterally, resulting in adequate pressure control. Nine months after the diagnosis of neovascular glaucoma, IOPs were normal with antiglaucoma medication, with persistent neovascularization in both eyes and without recurrence of the intraocular lymphoma.

Neovascular glaucoma has been reported previously in intraocular lymphoma, as well as other tumors, in association with advanced intraocular disease or as a sequel of radiation. In addition, the tumor itself may induce vasculitis, which may in turn stimulate endothelial growth factor secretion and subsequent neovascularization. There was no evidence of such disease processes in our patients. On the other hand, both of our patients suffered from diabetes, and thus, their threshold for neovascularization may have been reduced.

One must consider the possibility of the neovascularization arising not from the patients’ diseases, but rather from the methotrexate injection itself, as may happen after injection of gentamycin, which causes retinal vascular nonperfusion. However, in our cases there was no evidence of retinal or choroidal pathology.

Thus, although the exact mechanism of the iris and angle neovascularization is unclear, this bilateral finding in 2 of our patients after intravitreal methotrexate should lead cli-
nicians to examine their patients closely for evidence of this complication. Prompt diagnosis is critical, as immediate surgical treatment of the glaucoma appears to result in adequate IOP control.

SHARON GOLDBERG, MD
SHAHAR FRENKEL, MD, PhD
ETYAN Z. BLUMENTHAL, MD
ABRAHAM SOLOMON, MD
JACOB PE’ER, MD
Jerusalem, Israel

References


Orbital Lymphoma, Amyloid, and Bone

Dear Editor:

The association of lymphoma of the mucosa-associated lymphoid tissue type with localized amyloidosis in the small bowel was first reported in 1995. Since that initial case report, low-grade B-cell lymphomas (most of which are marginal zone lymphomas, which include mucosa-associated lymphoid tissue-type lymphoma) and localized amyloidosis have been described in the lung, breast, and large bowel. We describe a patient with a marginal zone lymphoma of the orbit with localized amyloidosis and osseous metaplasia. A 74-year-old woman was referred with a 6-month history of painless protrusion of her left eye. She complained of mild blurred vision in both eyes. Her general health was good, and she had no significant medical history. Visual acuities (VAs) were 20/60 and 20/40 in the right and left eyes, respectively. There was 4 mm of left proptosis. The remainder of the eye examination was normal, except for age-related cataracts. On a CT scan, orbital lymphomas typically have a homogeneous electron density with distinct edges. Tumors usually conform to the shape of the globe or orbit. These same features also characterize an amyloid tumor of the orbit, with one exception: amyloidosis tends to calcify. A CT scan has documented the presence of dense calcification within amyloid tumors of the orbit (similar to the pattern in our case). In none of the reported cases, however, was there any histological correlation of the calcified tissue. Biopsies of calcified amyloidosis from a variety of tissues, including the lung, breast, female genital tract, and tarsus of the eyelid, have revealed osseous metaplasia.

The association of lymphoma with systemic amyloidosis has been recognized for some time but is not nearly as common as the association between multiple myeloma and amyloidosis. There have been 2 patients with lymphoplasmacytic lymphoma of the orbit and serum paraproteinemia who developed systemic amyloidosis. Neither patient had evidence of orbital amyloidosis.

We are not aware of another reported case in which both amyloidosis and bone developed within an orbital lymphoma.

BRIAN D. HAAS, MD, FACS
Orlando, Florida

CURTIS E. MARGO, MD, MPH
Tampa, Florida