correct number of patients is 101, not 102. This changes our data slightly in that the sensitivity of the ESR using either of the formulas described in the text becomes 101/119 (84.9%) rather than 102/119 (85.7%), and the sensitivity of the ESR using both formulas becomes 90/119 (75.6%) rather than 91/119 (76.4%); however, sensitivities of CRP assay alone and the combination of the ESR and CRP assay together remain the same: 97.5% and 99.2%, respectively. In addition, the difference pointed out by Jain et al in the calculated sensitivity of 88.1% for PV in their study of 42 biopsy-positive patients (37/42) compared with the sensitivity of 84.9% (101/119) in our study may not differ significantly, considering the number of patients enrolled in the 2 studies and the measurement variability of PV and ESR prevalence. In any event, correction of the discrepancy does not change any of our final conclusions: (1) the combination of an elevated ESR and a normal CRP assay, although rare, is not inconsistent with a diagnosis of GCA, and this combination should not be taken to indicate that another diagnosis is responsible, and (2) the use of both tests together will identify the vast majority of patients with GCA with a higher sensitivity than the use of either test alone.

Neil R. Miller, MD
Mona Parikh, MD
Baltimore, Maryland

Andrew G. Lee, MD
Randy H. Kardon, MD, PhD
Iowa City, Iowa

Peter J. Savino, MD
Philadelphia, Pennsylvania

Wayne T. Cornblath, MD
Ann Arbor, Michigan

Eric Eggenberger, MD
East Lansing, Michigan

Karl C. Golnik, MD
Cincinnati, Ohio

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.[1,2] Treatment protocols currently suggest the use of systemic chemotherapy,[3] which fails to obtain significant intravitreal cytotoxic doses, or external radiation,[4] 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.[5] 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 rubeosis. 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.[2] 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 gentamicin, 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
Eytan Z. Blumenthal, MD
Abraham Solomon, MD
Jacob Pe'er, MD
Jerusalem, Israel

References

1. Chan CC, Wallace DJ. Intraocular lymphoma: update on diagnosis and management. Cancer Control 2004;11:285–95.
2. Coupland SE, Heimann H, Bechrakis NE. Primary intraocular lymphoma: a review of the clinical, histopathological and molecular biological features. Graefes Arch Clin Exp Ophthalmol 2004;242:901–13.
3. Levy-Clarke GA, Chan CC, Nussenblatt RB. Diagnosis and management of primary intraocular lymphoma. Hematol Oncol Clin North Am 2005;19:739–49, viii.
4. Hoffman PM, McKelvie P, Hall AJ, et al. Intraocular lymphoma: a series of 14 patients with clinicopathological features and treatment outcomes. Eye 2003;17:513–21.
5. Smith JR, Rosenbaum JT, Wilson DJ, et al. Role of intravitreal methotrexate in the management of primary central nervous system lymphoma with ocular involvement. Ophthalmology 2002;109:1709–16.

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.[1] 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.[2] 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. A computed tomography (CT) scan of the left orbit showed a 3.6×2.3-cm well-demarcated irregularly shaped mass situated predominantly within the intraconal space (Fig 1 [all figures available at http://aaojournal.org]). There were multiple discrete radio-dense deposits within the lesion (Hounsfield units consistent with bone) and moderate enhancement of the soft tissue component with contrast. The nonencapsulated lesion was removed piecemeal at surgery. Postoperatively, the patient did well, retaining 20/40 VA.

On histological examination, the tumor consisted of a proliferation of small lymphocytes mixed with lymphoplasmacytic cells and plasma cells (Fig 2). The lymphocytes were positive for CD19, CD20, CD22, CD79a, and λ-light chain and negative for CD5 and CD10. A subset of cells with plasmacellular differentiation stained positive for CD138. Extracellular deposits of amorphous eosinophilic material formed sheets and thickened the walls of blood vessels. The material stained positive with Congo red and showed green birefringence when viewed under polarized light (Fig 3). Congo red positivity remained after pretreatment with potassium permanganate, indicating amyloid-light chains. Metaplastic bone was present within the amyloid deposits (Fig 4).

A postoperative evaluation guided by the diagnosis of extranodal marginal zone B-cell lymphoma revealed no evidence of systemic lymphoma or of amyloidosis elsewhere. A serum protein electrophoresis was normal and urine was negative for Bence Jones protein. Radiotherapy to the left orbit was recommended, but the patient declined further treatment.

Evidence of dense calcification within the soft-tissue tumor of the orbit on a CT scan was a pivotal finding in this case. In radiological parlance, *calcification* is used to describe 3 different forms of soft-tissue mineralization: dystrophic calcification, metastatic calcification, and osseous metaplasia. Each condition is demonstrable on a CT scan when mineral salt deposits attain a threshold density and size (calcified tissue or bone typically measures >80–100 Hounsfield units). The vast number of entities that present with radiological calcification of soft tissue can be pruned substantially when anatomic location, size, and pattern of deposit are assessed in a clinical context.

Soft-tissue osseous metaplasia is not nearly as common or ubiquitous as dystrophic or metastatic calcification. Perhaps the single most common predisposing condition that leads to osseous metaplasia is phthisis bulbi. We were unable to identify a case of osseous metaplasia occurring within a lymphoma.

On a CT scan, orbital lymphomas typically have a homogenous 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.[3] A CT scan has documented the presence of dense calcification within amyloid tumors of the orbit (similar to the pattern in our case).[3] 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.[4]

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.[5] 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