Intravitreal Melphalan for Treatment of Primary Vitreoretinal Lymphoma: A New Indication for an Old Drug.

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Europe, this practice is less consistently used in the United States. However, these studies do not constitute level I evidence, and thus, there is no worldwide consensus regarding endophthalmitis prophylaxis with cataract surgery.\textsuperscript{6}

Limitations. This study is limited by its retrospective nature and the possibility of selection bias. The mechanism of this increasing nonsusceptibility to fluoroquinolones is not fully understood, but it may be associated with widespread use of fluoroquinolones, use of antibiotics outside of the health care sector, and emergence of intrinsic genetic factors promoting resistance. Although this study involves only in vitro testing, the clinical implications of this laboratory data requires further investigations.

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Intravitreal Melphalan for Treatment of Primary Vitreoretinal Lymphoma: A New Indication for an Old Drug

Primary vitreoretinal lymphoma (PVRL) is a malignant large B-cell lymphoma affecting the eye and brain, with 5-year cumulative survival rate of 35% in those with brain involvement (68% in those without).\textsuperscript{1} Ocular involvement manifests with aggregated tumor cells in the vitreous, retina, optic disc, and subretinal pigment epithelial space. Management involves treatment of both eyes and brain, and treatment options for the eye(s) include systemic chemotherapy, external radiotherapy, or intravitreal injection of chemotherapy.

The most commonly used intravitreal medication for PVRL is methotrexate.\textsuperscript{2,3} Others have investigated intravitreal rituximab.\textsuperscript{4} Herein, we report our experience with melphalan, a medication commonly used for treatment of vitreous seeding from retinoblastoma.\textsuperscript{5,6} In 3 eyes of 2 patients with PVRL, both methotrexate and melphalan have been used for retinoblastoma, and methotrexate requires approximately 25 injections/y, whereas melphalan needs fewer at 4 to 6 injections/y, the latter achieving retinoblastoma seed control in up to 100% of cases.\textsuperscript{5,6}

Melphalan is a well-established alkylating agent, developed in 1953 and used to treat several hematologic malignancies, including lymphoma, leukemia, and multiple myeloma, as well as solid tumors including breast, ovarian, and neural cancers.\textsuperscript{5} When used in the vitreous for retinoblastoma, filtered preparation of 20 μg/0.1 mL is sufficient for tumor control.\textsuperscript{6} Owing to its effect on lymphoma and our experience with this medication, we challenged PVRL with melphalan.

Methods | This retrospective investigation was approved by the institutional review board of Wills Eye Hospital. Three eyes of 2 patients with biopsy-confirmed PVRL were offered standard treatment or intravitreal melphalan (low dose [10 μg/0.1 mL]). Following written consent, the medication was injected into the vitreous using sterile technique. Clinical features and outcomes were recorded.

Results | Case 1. A 92-year-old woman with vitrectomy-proven bilateral PVRL (large B-cell lymphoma cytology) demonstrated severe vitreous tumor infiltration in the right eye and mild infiltration in the left eye, with subretinal pigment epithelial tumor in the left eye (Figure 1). Visual acuity was 20/30 OD and 20/40 OS. She was treated with low-dose intravitreal melphalan (10 μg/0.1 mL) to both eyes. Following initial injection, complete clearance of vitreous tumor in both eyes was noted within 3 weeks. During the 19-month follow-up, the right eye required 6 bimonthly injections for minor seed recurrence, and the left eye remained stable without recurrence. There were no toxicities in either eye, but the left eye showed stable focal subfoveal fluid, with mild macular edema at presentation and throughout her course. Final visual acuity was 20/50 OU.
Case 2. A 65-year-old man with chronic uveitis in both eyes and vitrectomy-proven PVRL (large B-cell lymphoma cytology) demonstrated moderate vitreous tumor in both eyes (Figure 2). At treatment, visual acuity was 20/150 OD and 20/400 OS. The right eye was treated with intravitreal melphalan and the left eye with intravitreal methotrexate. The right eye demonstrated rapid improvement of visual acuity within 2 days (per patient observation) and measured 20/50 at 1 month, requiring no further melphalan injections over 16 months follow-up, whereas the left eye showed slower response and a total of 19 injections of methotrexate over 11 months follow-up. Both eyes showed intermittent cystoid macular edema from uveitis, and final visual acuity was 20/50 OD and 20/70 OS.

A summary of the 3 eyes with PVRL revealed rapid response to low-dose intravitreal melphalan, with complete vitreous tumor clearance in 2 cases following a single injection and tumor control following multiple injections in one case. There was no retinal toxicity.
Discussion | These 3 eyes with PVRL demonstrate that intravitreal melphalan, currently used for vitreous seeds from retinoblastoma, can result in vitreous lymphoma control with few injections. Given the limited number of cases and relatively short follow-up, further investigation seems warranted to determine efficacy, safety, and appropriate treatment regimen.

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I was the physician who conducted the medical encounters for patients with a prehistory and I can attest to the improvement in medical record accuracy. I was able to enter the examination room, greet the patient, and then read the patient’s narrative, all of which was documented in the record. I finished the history with specific questions and then performed a pertinent examination. Any medical decision making occurring readily transformed to shared decision making because the patients were engaged and I was relieved of clerical burdens.

After seeing the physician, each patient was given a paper copy of the encounter note at the checkout window. Patients were instructed to go home, read their record, and score it with an anonymous survey. Patients who completed a prehistory form in preparation for a medical encounter reported feeling better heard and understood.

Medical record inaccuracy could adversely affect patient safety and data analytics. These comments suggest that a prehistory form potentially may be a means of improving health record accuracy.

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Editorial Note: This letter was shown to the corresponding author of the original article, who declined to reply on behalf of the authors.


Incorporating Clinical, Histological, and Genetic Parameters for Choroidal Melanoma Prognostication

Walter et al recently reported that tumor diameter measurement enhances the prediction of metastatic disease from class 2 uveal melanoma (UM), as classified with gene expression profiling. They advocate combining these 2 predictors when estimating prognoses.

We agree with this recommendation. Since 2007, we have published several articles emphasizing the importance of combining clinical, histologic, and genetic survival predictors when estimating a prognosis for UM posttreatment. We developed an online prognostic tool predicting survival using multivariable analyses, also accounting for age and sex. Walter et al have not cited these articles, so their Discussion does not interpret their results by taking into consideration all other relevant evidence in the literature.