

## Out of Breath and Under Pressure

BY TAREK ALASIL, MD, AND DANIEL KIM, MD, MBA  
EDITED BY THOMAS A. DETTING, MD

**M**ary Green\* is a 56-year-old woman with a history of acute myelogenous leukemia (AML). This had been in remission, but she became concerned when she started feeling weak and short of breath. At the emergency room, her fears were confirmed and she was admitted to the hospital for relapse of her AML. Her white cell count was  $88,000/\text{mm}^3$ , hemoglobin was 9.2 g/dl and platelet count was  $35,000/\text{mm}^3$ . Ms. Green underwent reinduction chemotherapy with mitoxantrone hydrochloride and etoposide, which led to neutropenic fever. She was started on wide-spectrum antibiotics. In the interim, she complained of acute onset pressure-like pain in the right eye, which was exacerbated by eye movements. She also reported blurry vision and photophobia in the right eye.

### We Get a Look

Ms. Green was referred to us one month after her hospital admission. At this point, lab tests showed white cell

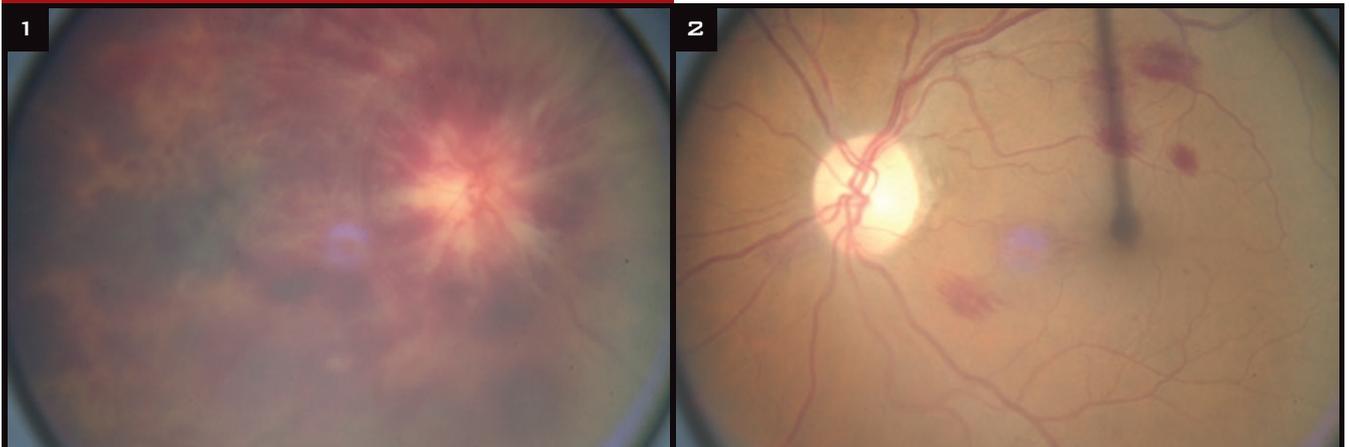
count of  $900/\text{mm}^3$ , hemoglobin of 9 g/dl and platelet count of  $14,000/\text{mm}^3$ . BCVA was 20/200 in the right eye and 20/40 in the left. Pressures by applanation tonometry were 15 mmHg

bilaterally. The right pupil was mildly reactive to light, and a right relative afferent pupillary defect was present. The left pupil was reactive to light. There was mild proptosis and upward gaze limitation in the right eye. Slit-lamp exam revealed mild conjunctival hyperemia in the right eye and cataracts bilaterally.

Dilated fundus exam of the right eye showed extensive preretinal and intraretinal hemorrhages in all four quadrants, macular edema and disc edema (Fig. 1). In the left eye, we noted scattered flame-shaped intraretinal hemorrhages (Fig. 2).

Fluorescein angiography (FA) of the right eye revealed extensive blockage of choroidal fluorescence by intraretinal hemorrhages, leakage correlating with areas of retinal edema, venous

### What's Your Diagnosis?



**WE GET A LOOK.** In the right eye, we noted extensive preretinal and intraretinal hemorrhages in all four quadrants, macular edema and disc edema (1). In the left eye, we noted scattered flame-shaped intraretinal hemorrhages (2).



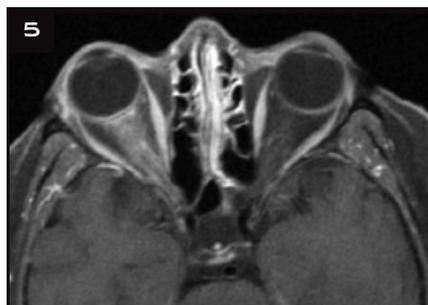
**FLUORESCHEIN.** Note blockage of choroidal fluorescence by intraretinal hemorrhages in the right (3) and left (4A, 4B) eyes.

engorgement and tortuosity, and florid disc edema (Fig. 3). FA of the left eye revealed focal blockage of choroidal fluorescence by intraretinal hemorrhages (Figs. 4A and 4B).

Contrast-enhanced MRI showed enhancement and thickening of the right optic nerve (Fig. 5).

**We Make a Diagnosis**

Mrs. Green was diagnosed with leukemic retinal and optic nerve infiltrates. She was emergently started on ocular radiation therapy focused to the right eye. The pain in the right eye gradually subsided. The patient was afebrile for 72 hours and got discharged with a close follow-up with oncology and ophthalmology clinics. Unfortunately, the visual acuity worsened to no light perception over the next two weeks.



**MRI.** Contrast-enhanced MRI reveals mildly enlarged right optic nerve with central and peripheral enhancement, which extends along the intraorbital length of the right optic nerve into the optic canal. The eye globes are otherwise normal in size, shape and signal intensity. There is no evidence of an intra- or extraconal mass. The left optic nerve is normal in signal intensity. No other focal area of abnormal contrast enhancement is identified.

**Discussion**

Thanks to continuing advances in diagnosis and treatment of acute leukemia, patient survival has improved considerably. As a result, physicians are seeing a greater variety of ocular manifestations among their patients. In some patients, for example, these ocular presentations are the side effects of treatment; in others, they indicate relapse of the leukemia.<sup>1</sup>

**Ocular involvement.** Ocular structures have been found to be involved in patients with various types of leukemia (estimates vary from 9 to 64 percent).<sup>2</sup> Leukemia may involve many ocular tissues by direct infiltration, hemorrhage, ischemia, hyperviscosity or toxicity due to various chemotherapy agents.<sup>1</sup> In a study of 113 cases of AML, Reddy and colleagues found ocular involvement in 47 patients (42 percent) including retinal changes in 44 patients (39 percent), infiltration of ocular tissues in two patients (1.8 percent) and neuro-ophthalmic signs in one patient (0.9 percent).<sup>3</sup>

**Treatment.** Leukemic infiltration of the optic nerve represents an emergency because vision might rapidly decline.<sup>4</sup> The blood-brain barrier shields the optic nerve from any systemically administered chemotherapeutic drugs, necessitating direct intrathecal injection for effective chemotherapy treatment.<sup>5</sup> Emergent radiation therapy combined with both intrathecal and continuing systemic chemotherapy is the most effective strategy if applied early and has been shown to improve vision that is impaired but is not yet lost.<sup>6</sup> Radiation therapy reduces the number of leukemic cells in the optic canal, which improves the flow of

cerebrospinal fluid around the nerve, and allows more effective action of cytotoxic drugs.<sup>5</sup>

Previous studies have demonstrated that leukemia patients with orbital and ocular infiltrations have a significantly lower survival rate than those who lack ophthalmic manifestations.

**Ms. Green's Case**

Ms. Green underwent local radiation therapy. However, she was no longer a candidate for systemic or intrathecal chemotherapy because of her neutropenic status and the increased risk of opportunistic infections. She was subsequently lost to follow-up.

Cases like this show the value of full collaboration among oncologists, ophthalmologists and other physicians. Prompt ophthalmic assessment of leukemia patients suspected to have eye manifestations is crucial.

\* Patient name is fictitious.

1 Sharma, T. et al. *Eye* 2004;18:663–672.

2 Schachat, A. P. et al. *Arch Ophthalmol* 1989;107:697–700.

3 Reddy, S. C. et al. *Ophthalmologica* 2003;217:441–445.

4 Esmaeli, B. et al. *Arch Ophthalmol* 2001; 119:443–446.

5 De Fatima Soares, et al. *Pediatr Radiol* 2005;35:799–802.

6 Wallace, R. T. et al. *Arch Ophthalmol* 1991; 109:1027.

*Dr. Alasil is a third-year resident in internal medicine at the Loma Linda University Medical Center in Loma Linda, Calif. Dr. Kim is director of that residency program. The patient was seen at Riverside County Regional Medical Center.*