

LETTER TO THE EDITOR**To THE EDITOR****Complete Recovery of Vision after Optic Nerve Relapse of Acute Lymphoblastic Leukemia****Keywords:** Leukemia, Optic neuropathy, Radiation therapy

As the survival rate of leukemia increases, a growing number of atypical complications have emerged. Acute lymphoblastic leukemia (ALL) is a proliferative disorder caused by abnormal growth of immature lymphocytes, typically resulting in anemia, neutropenia, and thrombocytopenia. ALL is classified into B-cell and T-cell types according to lymphocyte lineage. The incidence rate of ALL worldwide is approximately 1–5 per 100,000¹ and it follows a bimodal distribution, peaking at 1–4 years of age and rising significantly again with age greater than 60 years.² ALL can induce ocular manifestations directly through infiltration of neoplastic cells, or indirectly with hemorrhaging, opportunistic infections, central nervous system (CNS) complications, or complications of treatment.³ However, ocular involvement is often silent⁴ and it is rare for ocular manifestation to be the first presentation of ALL or its relapse. Here, we report a case of adult B-cell ALL with vision loss as the first sign of ALL relapse and with complete and rapid recovery of vision after radiation therapy.

A 70-year-old man presented with a 1-week history of painless, progressive vision loss in his left eye. He had a past medical history of B-ALL, diagnosed 3 years prior to presentation after a routine complete blood count showed evidence of pancytopenia and elevated blast count. He had received induction chemotherapy and intensification/maintenance phases of the Dana–Farber protocol (medications used include Vincristine, Doxorubicin, Methotrexate, Leucovorin, Asparaginase, 6-Mercaptopurine, and Prednisone), which were completed 1 year prior to vision loss. Lumbar punctures before initiation of chemotherapy did not demonstrate any evidence of CNS involvement. He had seen his oncologist 6 months prior to vision loss and had normal complete blood counts and a 6-month follow-up was arranged. His medical history was also significant for hypertension, coronary artery disease, and benign prostatic hypertrophy for which he took metoprolol, aspirin, finasteride, and tamsulosin.

On examination, he had a visual acuity of 20/20 (right eye) and light perception (left eye). There was a left relative afferent pupillary defect and dilated fundus examination showed left optic disk edema with a mild amount of subretinal fluid and a few retinal hemorrhages (Figure 1). Given the concern for an infiltrative optic neuropathy related to his history of ALL, he had urgent magnetic resonance imaging (MRI) of the brain and orbits with contrast that showed irregular bulky nodularity and enhancement of the left optic nerve highly concerning for leukemic infiltration (Figure 2). He received stereotactic radiotherapy to the left orbit (20 Gy in five fractions). On the last day of treatment, he noticed that his vision started to gradually improve and returned back to normal within 2 weeks. He underwent workup for recurrence of ALL with a lumbar puncture and bone marrow biopsy that showed blast cells in the cerebrospinal fluid and approximately 40% blasts in

the bone marrow. He underwent induction therapy with blinatumomab. At a 1-month neuro-ophthalmology follow-up visit, his visual acuity was 20/20 in both eyes with a normal visual field in the left eye. His examination remained stable at 6 months.

There are a number of mechanisms through which ALL can cause ocular symptoms directly or indirectly and almost every part of the eye could potentially be implicated. Hemorrhages can occur in any of the vascularized locations due to thrombocytopenia and infections can occur due to neutropenia. In this case, however, the culprit was primary leukemic infiltration of the optic nerve. A 2015 study based in India revealed that ocular involvement, even though often asymptomatic, is more frequently detected in adult, acute and myeloid leukemia.⁵ This case stood out due to the atypical lineage, timing, and severity of the symptoms and complete and rapid recovery of vision. The consideration of leukemic infiltration as a cause of optic neuropathy even in the absence of other indicators of leukemia during remission was crucial. MRI was of high diagnostic value in this case as it showed clear signs of nodularity and enhancement of the optic nerve, further strengthening the suspicion for leukemic infiltration. Other causes of optic disk edema to consider in this context are infection or raised intracranial pressure.

There have been several case reports worldwide of leukemic infiltration in the optic nerve, but the type of leukemia, presentation time, treatment, and patient response varied. To the best of the authors' ability, 11 complete case reports of leukemic infiltration in the optic nerve in adults in English were identified. Three of these cases were of chronic leukemia that eventually infiltrated the optic nerve at some point of the disease process. Four cases had a history of ALL and in three of these ALL case reports, optic nerve infiltration presented as the first sign of relapse.^{6–8} Despite treatment, two of these three patients succumbed to the leukemia without significant recovery. The other patient achieved regression of infiltration and full vision recovery at 1-year follow-up after receiving three-dimensional cranial radiotherapy. All three patients were decades younger than the patient in this case report. To the authors' knowledge, this case is the only report of ALL infiltration of optic nerve in a senior patient over 65 years of age. Published treatments typically consist of chemotherapy, steroid administration, localized radiation, or a combination thereof.^{7–10} One report of using radiation alone was shown to be effective in bringing the infiltration to regression and regaining vision, but this case was isolated to the optic nerve head and a 1-year time course was reported for complete recovery.⁸ Another report showed that Dasatinib alone can also be effective in treating optic nerve infiltration in a Philadelphia chromosome positive patient.¹¹ In the majority of cases, radiation was used in conjunction with at least one chemotherapeutic agent and the visual outcome varied from rapid deterioration to full recovery.

In summary, this report illustrates that optic nerve infiltration can be the first presentation of relapse of ALL in adults. It is possible to reverse vision loss with prompt treatment and a multidisciplinary approach. Clinicians should have a low threshold of suspicion for optic nerve infiltration in patients with a prior history of leukemia.

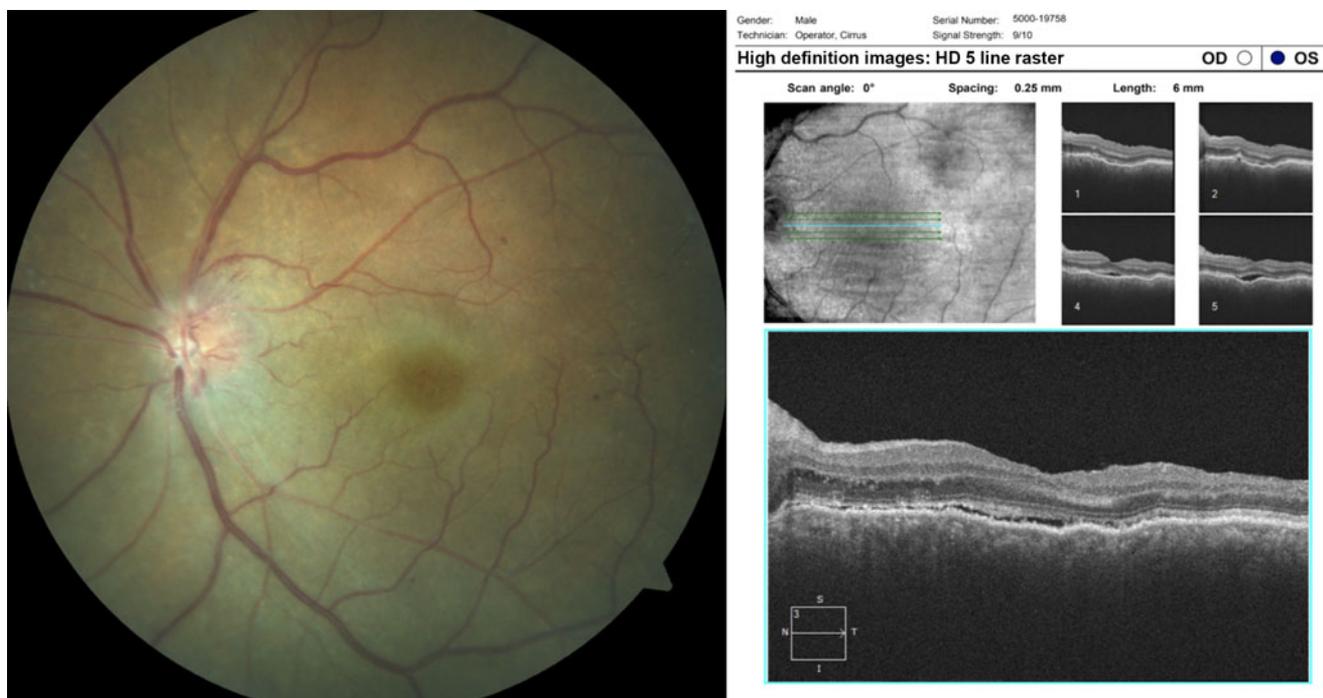


Figure 1: Fundus photography of the left eye (left) demonstrating optic disk edema, optic disk hemorrhages, and subretinal fluid adjacent to the optic nerve. Optical coherence tomography of the macula (right) demonstrates subretinal fluid and irregularity of the choroidal contour.

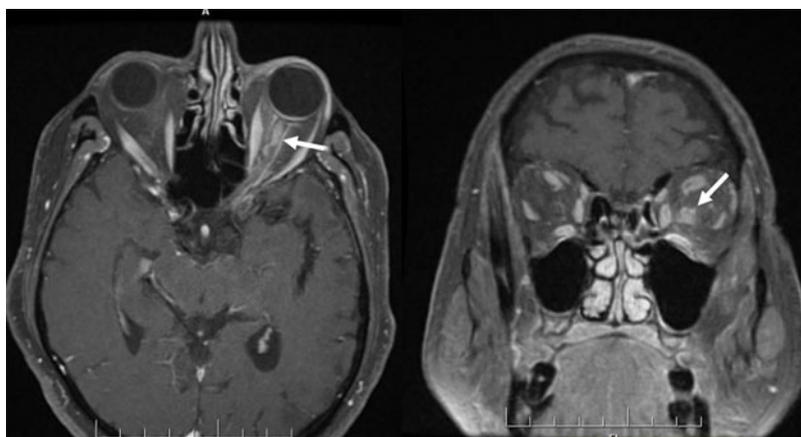


Figure 2: MRI T1 post-contrast demonstrating nodularity and enhancement of the optic nerve.

DISCLOSURES

AH, ATC, and JAM report no conflicts of interest.

STATEMENT OF AUTHORSHIP

Conception and design (AH, ATC, JAM), data collection (AH, ATC), drafting of manuscript (AH), critical revision (ATC, JAM), final approval (JAM).

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