LEUKEMIC OPTIC NERVE INFILTRATION IN A PATIENT WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Purpose: To describe the clinical presentation and imaging features of a patient with acute lymphoblastic leukemia that was complicated by optic nerve leukemic infiltration.

Methods: A 36-year-old man with history of acute lymphoblastic leukemia on treatment presented with decreased vision and optic nerve leukemic infiltrates.

Results: At presentation, ocular examination revealed decreased visual acuity at hand movement close to face in his right eye and 20/120 in his left eye. Fundus examination showed a pale optic disk with blurred margins and multiple flame-shaped and dot and blot retinal hemorrhages in his right eye and disk edema with whitish leukemic infiltrates over it with few dot and blot retinal hemorrhages in his left eye. The patient was referred to the treating oncologist, and curative orbital radiotherapy was administered. Vision improved dramatically to 20/40 in the right eye and to 20/20 in the left eye. He again reported with complaints of blurring of vision in the left eye after 1 month. Visual acuity was 20/20, but fundus revealed severe disk edema with whitish leukemic infiltrates. We diagnosed as relapse of leukemic optic nerve infiltration and referred to the treating oncologist for further management.

Conclusion: Isolated optic nerve relapse of leukemic infiltration is of paramount importance to early diagnosis, as vision can be saved if treatment is initiated promptly.

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Acute lymphocytic leukemia (ALL) is the most common malignancy in children, representing 11% of leukemias, and results in monoclonal proliferation of bone marrow (BM) lymphopoietic precursors lacking the potential for maturation.[1] The prognosis for children with ALL is often good, with 90% achieving complete remission and over 50% with >5-year survival. Adults with ALL have poorer outcomes, with 60% to 80% achieving remission and <35% with long-term survival.[1,2] Although 70% to 80% of children with ALL are cured with modern chemotherapy protocols, 20% to 30% experience disease relapse, particularly in the central nervous system after achievement of disease remission.[3,4] Therefore, cranial irradiation and intrathecal chemotherapy are required to prevent recurrence of ALL after conventional induction chemotherapy and the attainment of complete remission. Nevertheless, the orbital cavity and optic nerve are potential sanctuaries for leukemic relapse after conventional central nervous system prophylaxis because these structures are shielded during brain irradiation.[5] Additionally, relapse in ocular structures without systemic or BM involvement is extremely rare.

Case Report

A 36-year-old man presented to our hospital with painless loss of vision in his right eye (RE) for 20 days and left eye (LE) for 3 days. Intravenous methylprednisolone 1 g once a day for 2 consecutive days was given the day before the presentation. On examination, the patient was able to appreciate hand movements close to face in his RE and had visual acuity of 20/120 in his LE. Fundoscopic examination showed a pale optic disk with blurred margins with multiple flame-shaped and dot and blot peripapillary and retinal hemorrhages in his RE and disk edema with creamy white

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infiltrates over it and few dot and blot retinal hemorrhages in his LE (Figures 1 and 2). A complete blood count showed a leukocyte count of 97,720 per cubic millimeter (41% blasts, 47% neutrophils), a hemoglobin level of 17.1 g/dL, and a platelet count of 128,000 per cubic millimeter. T-cell ALL was documented upon ensuing immunophenotypic studies (positive staining for CD45 and negative staining for CD19, CD20, TdT, CD1a, and CD30), and BM examination revealed 90% blast cells. Induction chemotherapy with the conventional protocol (vincristine 2 mg/m^2, daunomycin 40 mg/m^2, prednisone 60 mg/m^2, and L-asparaginase 6,000 U/m^2) was instituted. Subsequent peripheral blood smears and examination of his BM documented the achievement of complete remission 7 weeks after induction chemotherapy. Intrathecal chemotherapy with methotrexate and cranial irradiation (15 Gy) was then administered. Magnetic resonance imaging of the brain revealed few small foci of demyelination in left frontal and right parietal white matter and a small focus of chronic bleed in the right posterior frontal region. Meanwhile, the BM remained cytologically and immunophenotypically negative for leukemic involvement. The patient was referred to the treating oncologist, and curative orbital radiotherapy (24 Gy) was administered. After 1 month of curative orbital radiotherapy, vision improved to 20/40 in his RE and to 20/20 in his LE. Fundoscopic examination of the RE showed resolving retinal hemorrhages with pale optic disk and almost resolved hemorrhages with normal disk in his LE (Figures 3A and 4A). Optical coherence tomography of the RE showed infiltrates nasal to the fovea (Figure 3B) and of the LE was normal (Figure 4B). Consolidation chemotherapy was continued. The patient remained stable for 1 month. He again came back with complaints of blurring of vision in the LE for 1 day. Visual acuity was 20/30 in the RE and 20/20 in the LE. Right eye fundus showed pale disk with clear margins (Figure 5). Left eye fundus revealed severe disk edema (Figure 6A), and optical coherence tomography showed peripapillary thickening (Figure 6B). We diagnosed as relapse of leukemic optic nerve infiltration and advised magnetic resonance imaging of the brain and orbit. The patient was referred to the treating oncologist for further management. However, the patient developed systemic complications in the form of pneumonia and could not survive.

Discussion

A variety of neuroophthalmic complications may develop in patients with leukemia. The incidence of ocular leukemic involvement varies between postmortem studies, and no distinction has been made between leukemic cell infiltration of the eye and secondary ocular changes in various studies.

Optic nerve infiltration has been reported in 5% to 13% of patients with leukemia.[6] Camera et al[7] noted that leukemic optic nerve infiltration occurs in 1.4% of pediatric cases of ALL. Infiltration of the optic nerve by leukemic cells has rarely been reported in adult patients with ALL, and they may present with

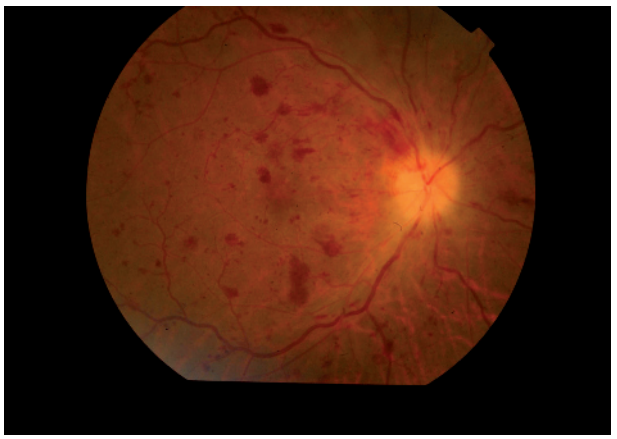

Fig. 1. Fundus photograph of the RE showing pale optic disk with blurred margins and multiple flame-shaped and dot and blot peripapillary and retinal hemorrhages in all four quadrants.

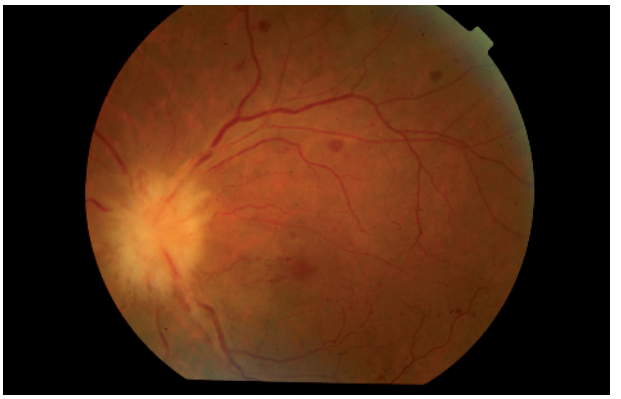

Fig. 2. Fundus photograph of the LE showing optic disk edema with creamy white leukemic infiltrates over it and few dot and blot retinal hemorrhages.

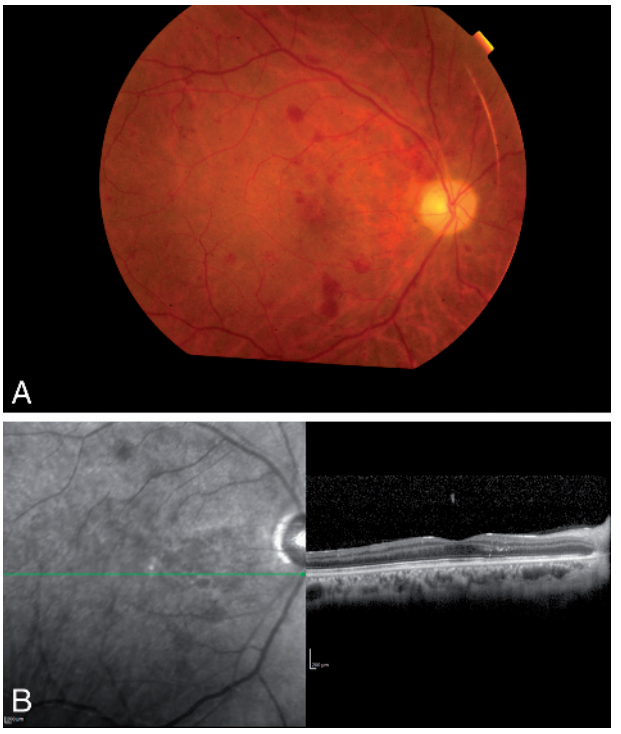

Fig. 3. A. Fundus photograph of the RE after 1 month of curative radiotherapy showing pale optic disk with clear margins and resolving retinal hemorrhages. **B.** Optical coherence tomography of the RE showing infiltrates nasal to the fovea.

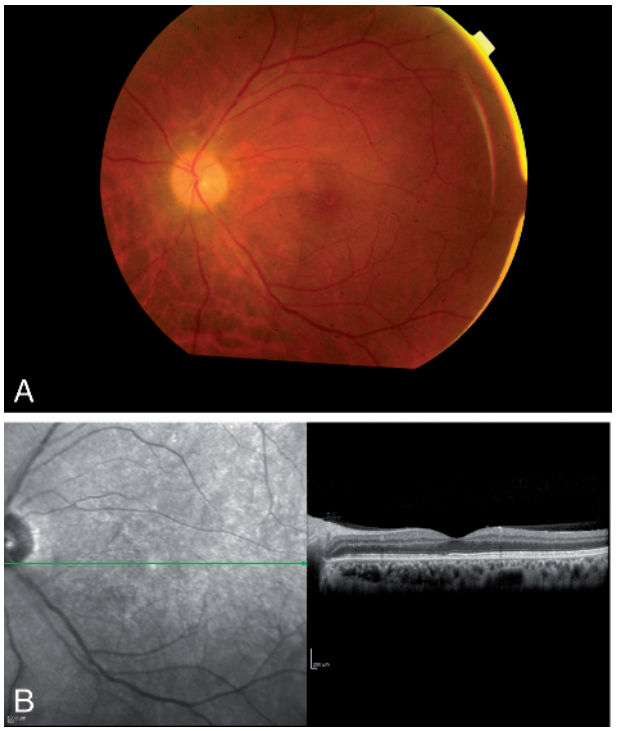

Fig. 4. A. Fundus photograph of the LE after 1 month of curative radiotherapy showing normal optic disk with almost resolved retinal hemorrhages. **B.** Optical coherence tomography of the LE showing a normal study.

insidious onset and progressive deterioration of visual acuity. Direct infiltration of the optic nerve has been described as a prelaminar fluffy white infiltrate superficial to the lamina cribrosa on the optic nerve head or as a retrolaminar infiltrate visible on neuroimaging in association with profound visual loss.[8] Brown et al[9] had described similar fundus findings of optic nerve involvement in a child with acute undifferentiated leukemia. Sudden loss of vision with unilateral optic nerve invasion is extremely rare, and

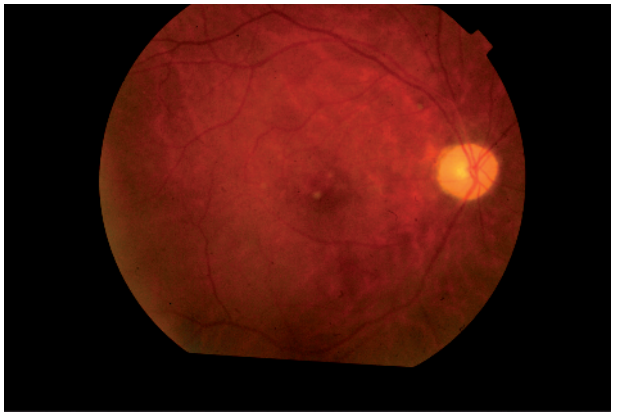

Fig. 5. Fundus photograph of the RE showing pale optic disk with clear margins.

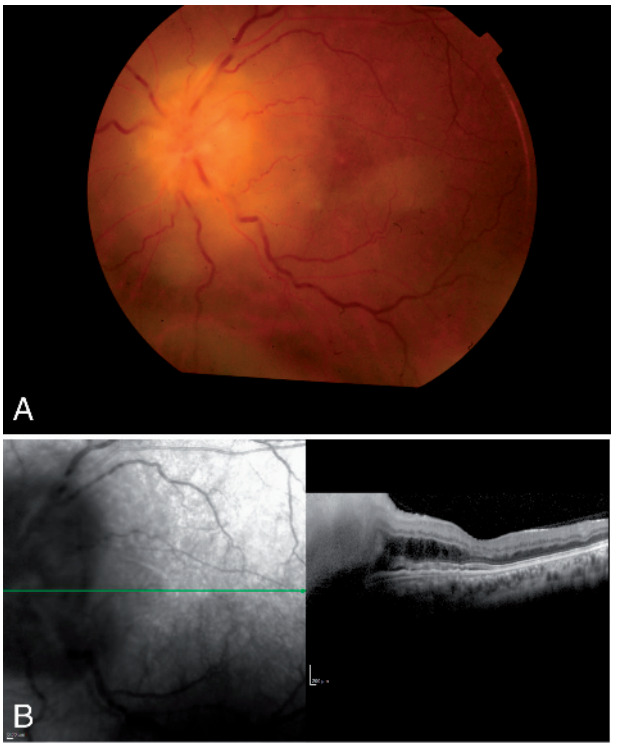

Fig. 6. A. Fundus photograph of the LE showing relapse of leukemic optic nerve infiltrates as evidenced by severe disk edema with creamy white infiltrates. **B.** Optical coherence tomography of the LE showing peripapillary thickening.

it should be promptly managed even after completion of central nervous system prophylaxis. Impairment of visual acuity might be the sole symptom of ocular involvement by leukemic cells. Clinicians should be aware of these possible manifestations and possible etiologies in patients with ALL, even if they have achieved disease remission. Moreover, other causes for vision loss in ALL during clinical remission, such as infection, vasculitis, radiotherapy-induced artifacts, or adverse effects of chemotherapeutic agents, should be carefully excluded. For a previously relapse-free patient, relapse in an isolated site suggests that the area must have been a sanctuary for leukemic cells during treatment. The optic nerve is usually shielded during brain irradiation, when this is used as a standard strategy. Early limited relapse without systemic involvement, such as in our case, is still a challenging issue for clinical management. Orbital radiation is an accepted treatment modality for optic nerve infiltration in leukemia. For both prelaminar and retrolaminar optic nerve involvement, a typical course of 2000 cGy to the orbit over a 1- to 2-week period may result in significant return of vision and resolution of clinical abnormalities. However, the efficacy and outcome vary in few reports. Adverse risk factors seen more commonly in adults have lessened the success of

treatment for ALL in comparison with what has been achieved in children. Early institution of more aggressive chemoradiotherapy or hematopoietic stem cell transplantation should be considered when cranial neuropathy heralds a systemic relapse. Despite optimal prophylaxis and salvage treatment, the outcome for adults with ALL with recurrence of the central nervous system is grave. Future studies should investigate better approaches for early diagnosis of relapsed disease and more intensive strategies to improve patient survival.

Key words: ALL, CNS relapse, leukemic infiltration, optic neuropathy, vision loss.

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