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Unilateral isolated optic nerve infiltration combined with central retinal artery occlusion in a patient with acute myeloid leukemia

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ABSTRACT

Purpose: To report a case of unilateral isolated optic nerve infiltration combined with central retinal artery occlusion in a patient with acute myeloid leukemia.

Observations: A 28-year-old acute myeloid leukemia patient with systemic remission after hematopoietic stem cell transplantation presented with optic nerve infiltration combined with central retinal artery occlusion. Fundus examination showed diffuse papillary swelling with blurred margins and whitening macular with cherry-red spot. CBFβ-MYH11 fusion transcript analysis revealed central nervous system relapse of acute myeloid leukemia and optic nerve infiltration.

Conclusions and importance: Isolated optic nerve infiltration combined with central retinal artery occlusion is an extremely rare presentation in acute myeloid leukemia. Even in the absence of cytological and radiographic evidence from cerebrospinal fluid, optic nerve infiltration should not be ignored.

1. Introduction

Acute myeloid leukemia (AML) is a clonal hematopoietic disorder with generally better clinical outcomes in younger patients.[1,2] Leukemic infiltration of the optic nerve is relatively rare and often occurs in acute lymphocytic leukemia. Isolated optic nerve infiltration in AMLs is an extremely rare initial presentation. We reported the case of a 28-year-old man presented with unilateral isolated optic nerve infiltration combined with central retinal artery occlusion (CRAO), which was the initial manifestation of central nervous system (CNS) involvement with AML recurrence after remission.

2. Case report

A 28-year-old man presented with blurred vision in his left eye for 1 week. The patient had a medical history of AML for 2 years. Hematopoietic stem cell transplantation performed. Systemic remission was achieved following chemotherapy.

On ophthalmic examination, the best-corrected visual acuity (BCVA) was 20/20 in both the eyes. Slit-lamp examination revealed no remarkable abnormality in the anterior segment. Fundus examination revealed diffuse papillary swelling with blurred margins, and the engorged retinal vessels with dot-shaped hemorrhages in the left eye (Fig. 1A, A_1). Optical coherence tomography (OCT) of the left eye showed no abnormality (Fig. A_2). Examination of the right eye revealed no abnormality. Bone marrow aspiration revealed complete remission of the leukemia in this patient. Magnetic resonance imaging (MRI) of the brain and orbit did not reveal clear evidence of leukemic cell infiltration of the left optic nerve. Though evaluation of lumbar puncture specimen showed no evidence of leukemic cells in the cerebrospinal fluid (CSF) as well, prophylactic intrathecal chemotherapy was performed.

After 13 days, the patient complained of sudden loss of vision in the left eye. The visual acuity was no light perception. Fundus examination revealed papillary swelling, creamy infiltration, tortuosity of the retinal vessels, aggravated dot and blot hemorrhages, and whitening macular with cherry-red spot (Fig. 1B, B_1). OCT of the left eye showed thickening and hyperreflectivity of the inner and middle retinal layers (Fig. 1B_2). Optic nerve infiltration combined with CRAO and mild CRVO was suspected. The patient was referred to a treating oncologist for further treatment. Although bone marrow and CSF cytology evaluations showed

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no signs of relapse, quantification of the CBFβ-MYH11 fusion transcript yielded a result of 12.64%. Furthermore, MRI of the lumbar spine and sacrococcygeal vertebrae showed enhancement of the spinal dura mater and sacral plexus, revealing AML CNS relapse. Salvage with additional chemotherapy and cranial radiotherapy was initiated. The patient is currently on maintenance therapy and remains in complete remission. At the last follow-up, fundus evaluation revealed old exudative lesions around the optic disc and inner retinal atrophy. (Fig. 2A, A_1, 2B).

3. Discussion

With an increase in the survival of patients with leukemia, CNS relapses are on the rise. The incidence of CNS involvement in AML in pediatric patients ranges from 6% to 29%, whereas it is not well known in adult patients.[3] Leukemic infiltration of the optic nerve is relatively rare and indicative of CNS involvement. Isolated optic nerve infiltration as the initial presentation of disease recurrence in adults is extremely rare. Very few cases have reported retinal artery/vein occlusions in acute leukemia patients with CNS relapse.[4–6] In our case, a patient with AML developed unilateral CRAO combined with CRVO caused by neoplastic infiltration of the optic nerve. Bone marrow and CNS cytology evidence and clear radiographic findings were insufficient.

Optic nerve infiltration occurs relatively rarely in acute leukemia and usually reveals CNS involvement. Few studies have reported that optic nerve infiltration is the only sign of CNS involvement even in complete remission.[7,8] This often presents a clinical dilemma when cytologic or radiographic evidence is negative, and diagnosis may be difficult, as in our case. *Shyam* et al. described a patient with AML who had optic nerve involvement presented with complete monocular vision loss.[2] *Shenoy* et al. reported a patient with acute lymphoblastic leukemia with normal CSF cytology findings, diagnosed by vitreous biopsy.[9] In this case, CNS involvement was highly suspected, while repeated CSF analysis showed inconclusive evidence. CSF CBFβ-MYH11 fusion transcript analysis was used to confirm the diagnosis of AML recurrence. In addition, tortuosity of the retinal veins and hemorrhage were observed when the CRAO occurred. These clinical characteristics suggest the possibility of retinal venous occlusion. *Ishikawa* et al. reported a patient with AML who presented with unilateral severe CRAO and mild CRVO.[6] Edema and leukemic infiltration of the optic nerve cause vascular compression, leading to CRAO. Atypic retinal venous occlusion might be the result of a reduction of retinal blood flow caused by CRAO.[10]

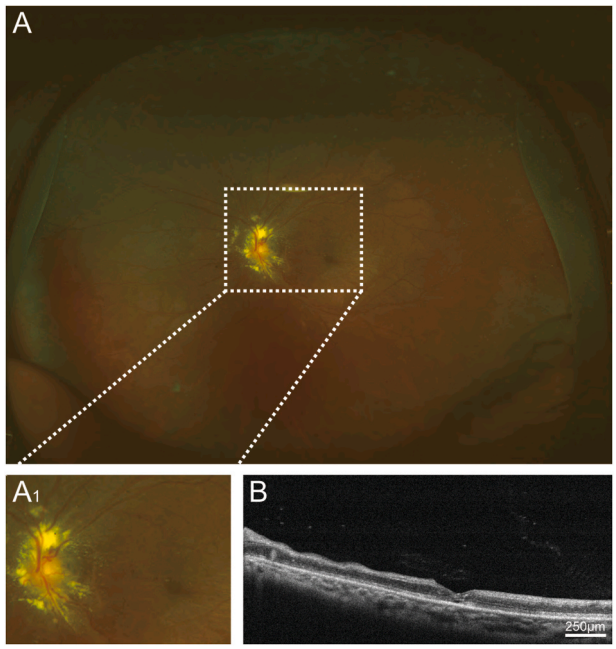

Fig. 2. Ocular coherence tomography demonstrating inner retinal atrophy. **A and A1.** Fundus photographs of the left eye demonstrate old exudative lesions around the optic disc. **B.** OCT shows inner retinal atrophy.

The optic nerve is recognized as a "pharmacologic sanctuary" due to the existence of a barrier between the optic nerve and the remainder of the CNS in patients with leukemic infiltration.[7] Thus, leukemic cells in the perineural space of the optic nerve may not be completely eradicated by intrathecal chemotherapy. In our case, prophylactic intrathecal

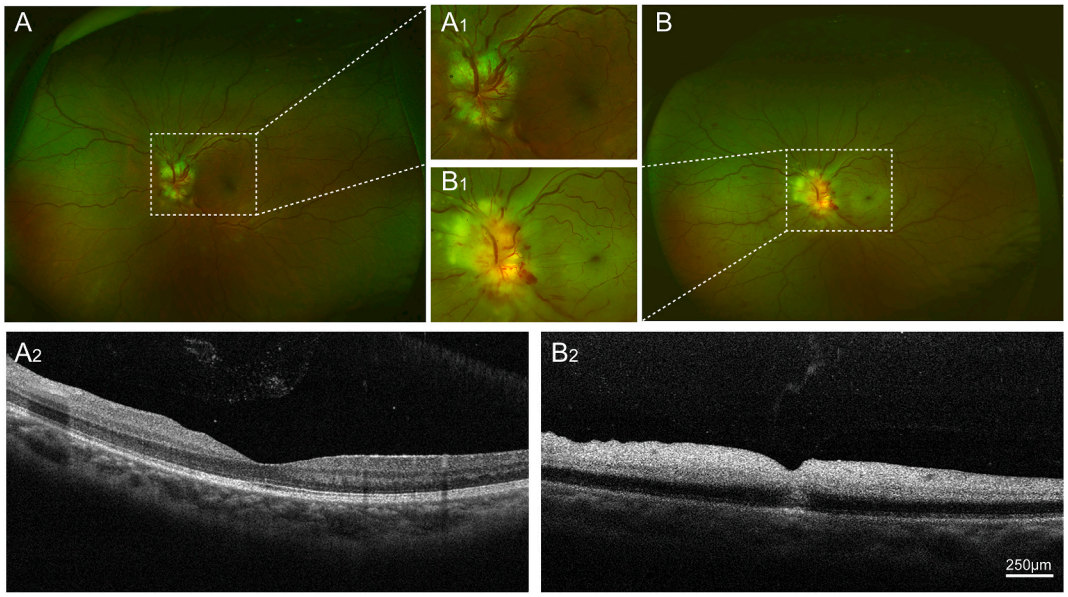

Fig. 1. Imaging on presentation demonstrating optic nerve infiltration and CRAO in AML.
A and A1. Fundus photographs of the left eye demonstrate diffuse papillary swelling with blurred margins. The retinal vessels are engorged with dot-shaped hemorrhages. **A2.** The OCT of the left eye demonstrates normal macular structure. **B and B1.** Fundus photographs of the left eye demonstrate worse papillary swelling, creamy exudation, tortuosity of the retinal vessels, dot and blot hemorrhages, retinal whitening, and a macular cherry-red spot. **B2.** OCT of the left eye demonstrates thickening and hyperreflectivity of the inner and middle retinal layers. . (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

chemoth. erapy was administered when the patient first presented with the only sign of optic disc edema; nevertheless, CRAO still occurred subsequently. Focal irradiation effectively reduces leukemic cells and allows cytotoxic drugs to reach the optic canal to attack leukemic cells. Furthermore, the optic nerve is less sensitive to radiotherapy than leukemic cells.[9] Our patient received intrathecal MTX, cytarabine, and focal radiotherapy after CRAO. Unfortunately, the treatment was too late to prevent vision loss. Our case suggests that a clinical diagnosis of optic nerve infiltration should be considered when a biopsy is not feasible or without high-risk cytogenetics, so that the initial treatment can be delivered promptly enough to rescue vision loss.

4. Conclusions

In conclusion, to the best of our knowledge, this is the first report of a patient with AML recurrence presented with unilateral optic nerve infiltration combined with CRAO in the absence of leukemic blasts in the bone marrow and CSF, but confirmed by CBFβ-MYH11 fusion transcripts. This case emphasizes that optic nerve infiltration should not be ignored in AML patients even in the absence of CNS involvement. Early diagnosis and timely treatment may help to rescue the vision.

Patient consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

Author declaration

[Instructions: Please check all applicable boxes and provide additional information as requested.]

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Intellectual property

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

Research ethics

We further confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

Written consent to publish potentially identifying information, such as details or the case and photographs, was obtained from the patient(s) or their legal guardian(s).

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Declaration of competing interest

No conflict of interest exists.

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