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Case report

Bilateral optic nerve and retinal infiltration as an initial site of relapse in a child with T-cell acute lymphoblastic leukemia

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ABSTRACT

Purpose: To describe a case of leukemic infiltration of bilateral optic nerves and retina as a site of relapse in a child with T-Cell Acute Lymphoblastic Leukemia (ALL).

Observations: We report a 7 year old female who presented one year following initial treatment for T-Cell ALL with visual acuity impairment, bilateral optic nerve infiltration and infiltration of the retina of both eyes. OCT demonstrated subretinal fluid in both eyes, which eventually resolved, and perivascular hyperreflectivity within the inner retinal layers. She was treated with systemic and intrathecal chemotherapy, total body and orbital radiation and eventual bone marrow transplantation with notable improvement in vision and regression of retinal and optic nerve findings. With continued remission, there was notable outer retinal thinning, specifically of the photoreceptors in the right eye.

Conclusions and importance: Leukemic abnormalities of the eye are not uncommon, however optic nerve and retinal infiltration are rare manifestations. Leukemic infiltrates of the retina can be detected by OCT despite normal funduscopic examination and monitored for improvement. The optic nerve and other ocular tissues are considered a pharmacologic sanctuary and thus, the optic nerve can be a site of relapse in leukemia. The use of radiation therapy is a helpful adjunct with systemic, intrathecal chemotherapy and stem cell transplantation in obtaining clinical remission and visual acuity improvement.

1. Introduction

Ocular abnormalities are commonly found in patients with leukemia.[1,2] Cases of optic nerve infiltration have been previously reported,[1–11] however infiltration of the optic nerve, retina and uveal tract are rare.[3,11,12] We report a case of bilateral optic nerve infiltration and right eye retinal perivascular infiltration, followed longitudinally by serial optical coherence tomography (OCT), as the initial presentation of disease relapse of T-cell acute lymphoblastic leukemia.

2. Case report

A seven year old female initially presented with an anterior mediastinal mass, leukocytosis and hepatosplenomegaly. She was subsequently diagnosed with T cell acute lymphoblastic leukemia with cytogenetics showing deletion of 11q23, partial deletion of 13. Fluorescence in situ hybridization (FISH) testing noted trisomy 9 and monosomy 8. Treatment was initiated with daunorubicin, pegaspargase, vincristine, dexamethasone, bortezomib and intrathecal cytarabine and methotrexate. Intrathecal chemotherapy was administered due to presence of leukemic cells in the initial cerebrospinal fluid analysis. She had complete remission after consolidation therapy. She was subsequently placed on maintenance therapy consisting of vincristine, intrathecal methotrexate, oral methotrexate and dexamethasone.

Twelve months after initial presentation, she complained of blurry vision of the right eye. She was seen in the ophthalmology clinic and noted to have count fingers vision in the right eye and 20/30 + 3 visual acuity of the left eye. Examination was significant for a right relative afferent pupillary defect and bilateral opacification of the retinal nerve fiber layer (RNFL) with suspicion for bilateral leukemic infiltration of the optic nerves with foveal involvement of the right eye (Fig. 1, Fig. 2).

She was admitted for reinduction chemotherapy and radiation therapy. Her admission complete blood count was notable for the following: Hgb 9.9 g/dL (reference range 13.3–17.2 g/dL), WBC 2.5 × 109/L (reference range 4.5–10 × 109/L), and PLT 279 × 109/L (reference range 179 × 109/L–373 × 109/L). A MRI scan was obtained, which indicated enhancement of the right optic nerve (Fig. 3). A lumbar puncture was performed, however no malignant cells were detected on cytology. She began intrathecal chemotherapy consisting of

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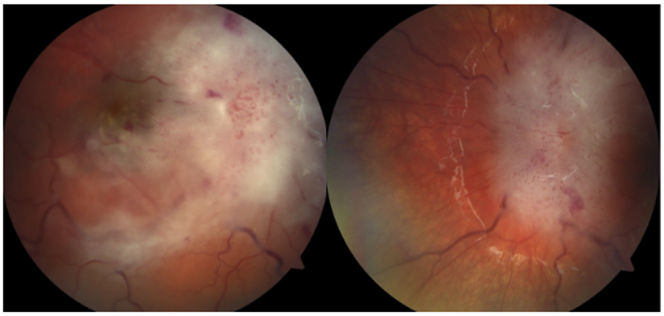

Fig. 1. Initial presentation fundus photographs. Right eye, Left eye respectively. Note optic nerve and retina infiltration, right more than left eye.

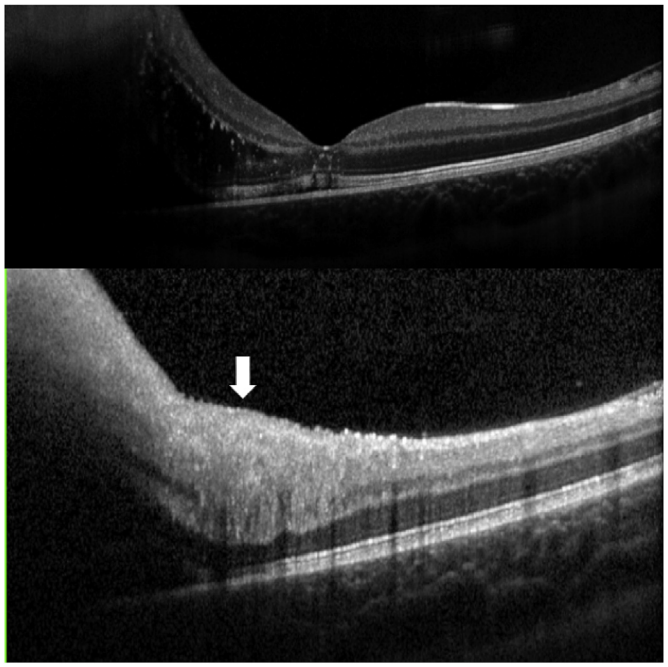

Fig. 2. Initial spectral domain optical coherence tomography, left eye. Note intraretinal edema nasal to fovea and retina nerve fiber layer hyperreflectivity indicating area of leukemic infiltration/nerve fiber layer edema (arrow) in the bottom image. Right eye images were unable to be captured.

methotrexate, hydrocortisone and cytarabine. The intrathecal chemotherapy was completed concurrently with systemic chemotherapy consisting of cyclophosphamide, etoposide and nelarabine. She received total body irradiation (TBI) with bilateral orbit radiation for a total dose of 12 Gy TBI, and 9 Gy to each orbit.

Following re-induction chemotherapy, her vision improved to 20/50 in the right eye and 20/25 in the left eye with a stable right relative afferent pupillary defect. OCT demonstrated resolving RNFL reflectivity, perivascular reflectivity, and improved sub-retinal fluid (Figs. 4–6). She underwent allogeneic bone marrow transplant 36 days after presentation, and achieved remission. One month after bone marrow transplant, her visual acuity had improved to 20/40 right eye and 20/25 left eye. Subsequently, her best corrected visual acuity was 20/25 in the right eye, 20/25 in the left eye with a relative afferent pupillary defect on the right; these measurements were taken three months after bone marrow transplant. After completion of therapy, she had a significant improvement in bilateral optic nerve and RNFL infiltration with residual thinning of photoreceptor outer segments in the right eye. She demonstrated clinical improvement of perivascular infiltration of the right eye (Fig. 4). However, there were persistent changes present on OCT despite resolution clinically (Fig. 5). Two years

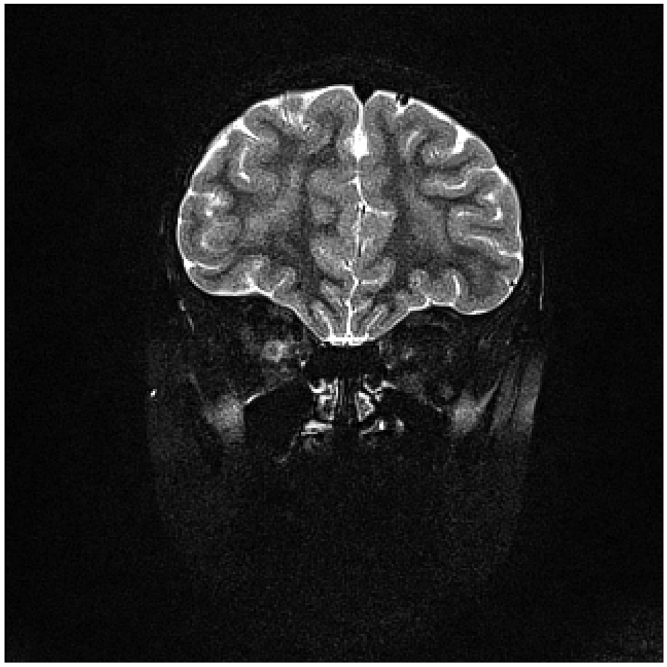

Fig. 3. T2 MRI with fat suppression, coronal view. Attention to area of enhancement of the right optic nerve.

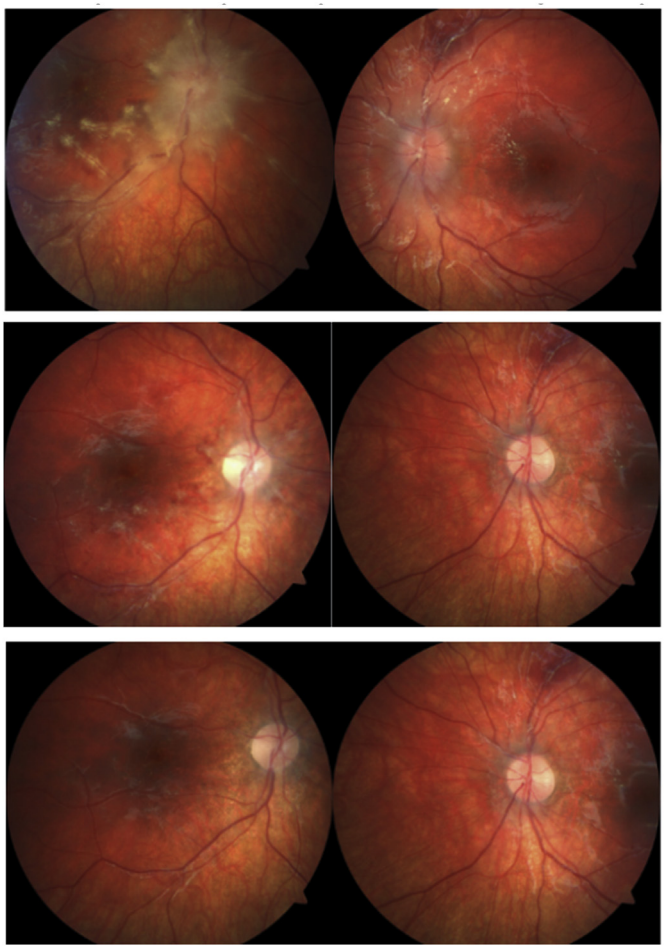

Fig. 4. Serial fundus photographs. From top to bottom, images denote the right and left eye respectively 3 weeks following presentation, one month following bone marrow transplant and 3 months following bone marrow transplant. Note the improvement in perivascular involvement throughout follow up.

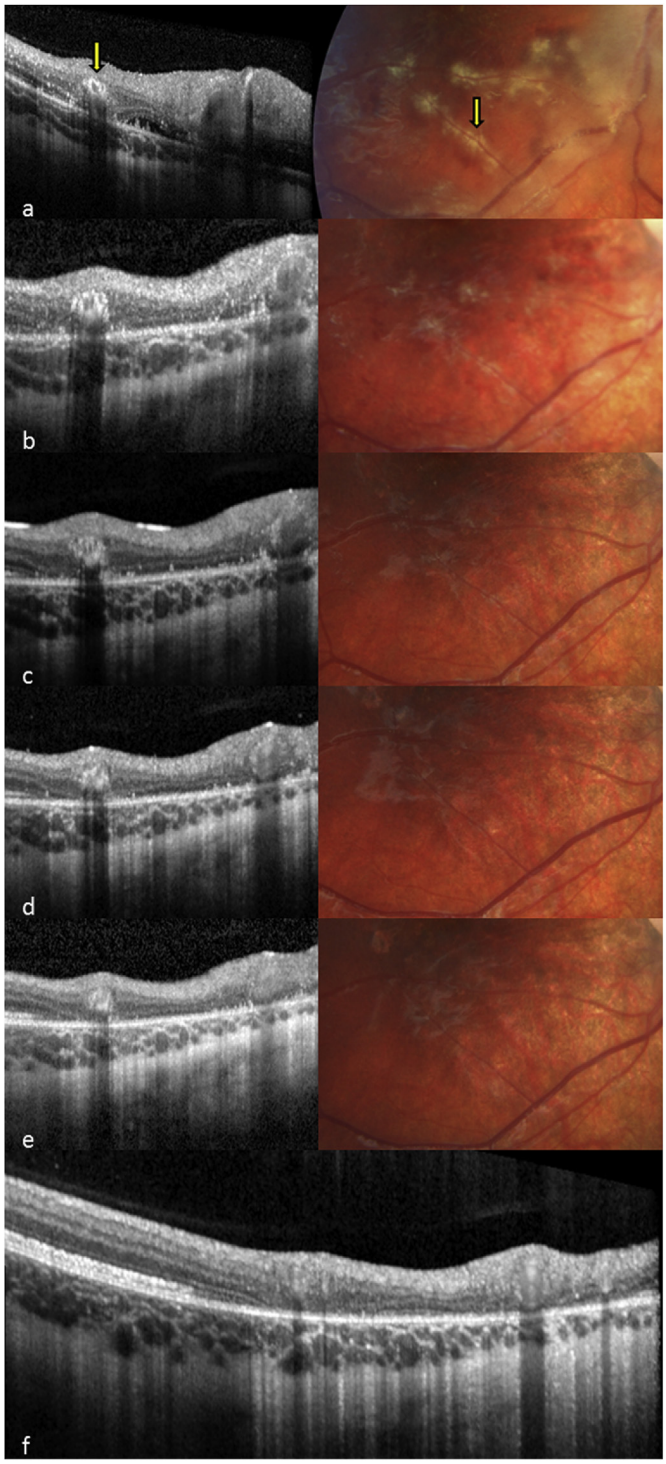

Fig. 5. Serial SD-OCT and fundus photographs of the right eye longitudinally following perivascular retinal infiltration (arrows) and retinal nerve fiber layer infiltration. Images represent 3 weeks (a), 2 months (b), 4 months (c), 6 months (d), and 7 months (e) after presentation. Note the persistence of perivascular hyper-reflectivity even after resolution on fundus photographs. There is complete resolution of the perivascular hyper-reflectivity by 18 months after presentation (f).

following her bone marrow transplant, her best corrected visual acuity was 20/25 right eye and 20/30 left eye with a right afferent pupillary defect.

Initial, RNFL analysis was not possible due to the extent of the edema limiting accurate automatic and manual segmentation. At 3 months from presentation the first RNFL analysis was able to be performed which demonstrated bilateral thickening: Global Score- 156 and 121 respectively. Overtime as the edema resolved, there was consecutive thinning right > left eye, with the Global Score stabilizing at 67 and 90 respectively.

She remains without subretinal fluid bilaterally, however there is thinning of the photoreceptors at the interdigitation zone which has remained stable upon serial examinations in the right eye (Figs. 6 and 7).

3. Discussion

Leukemic ocular abnormalities may be seen in up to 53% of patients.[1,2] Optic nerve infiltration occurs more commonly in children, in acute leukemia and in acute lymphoblastic leukemia.[11] The optic nerve is recognized as a “pharmacologic sanctuary” secondary to the inadequate penetration of systemic chemotherapies to ocular tissues.[1–5,8,10] Thus, many adjuvant therapies are often required to achieve complete remission.[4,8–10] Additionally, there is little association between the presence of malignant cells on cerebrospinal fluid cytology and involvement of the optic nerve.[1,3,10]

In our case, the WBC count was low due to maintenance therapy and the subsequent lumbar puncture did not reveal CSF involvement. This highlights the importance of the ocular findings, as they were the sole indication of relapse in a patient otherwise felt to be in remission.

Few reports have documented the optic nerve as a site of initial relapse following documented remission, and fewer note leukemic retinal infiltration. Lin et al., presented a case series of patients with optic nerve involvement at the time of relapse of their leukemia.[8] In all 3 cases, ophthalmoscopic findings of leukemia were limited to disc edema with one case also having retinal venous engorgement. Our case demonstrates diffuse nerve fiber layer edema and infiltration with involvement of the surrounding retina. Additionally, we provide longitudinal findings of this condition which have not been reported before.

There was consecutive atrophy of the right optic nerve following resolution of the infiltration and edema. This was visible clinically and was also documented with serial RNFL thickness measurements. The left eye also demonstrated relative thinning of the RNFL following resolution, however not to the extent of the right eye. This is consistent with relative involvement between the two eyes at presentation. She also received bilateral orbital radiation, which could also affect RNFL thickness over time, though no signs of radiation retinopathy developed over the follow up period. Leukemic infiltration of the retina has a hyperreflective quality which can be monitored with serial OCT, andis present even in the absence of clinical findings on examination.

4. Conclusion

This case highlights the clinical and imaging findings of bilateral optic nerve and retinal leukemic infiltration as the only site of initial relapse of T-cell ALL in a child. Leukemic retinal infiltrates may be followed with serial OCT images as leukemic retinal infiltrates may be present on OCT imaging despite absence of clinical findings.

Patient consent

Written consent was obtained from the patient's guardian to use ophthalmic imaging and data in the publication of this case report.

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None.

Authorship

All authors attest to satisfying the ICMJE criteria for authorship.

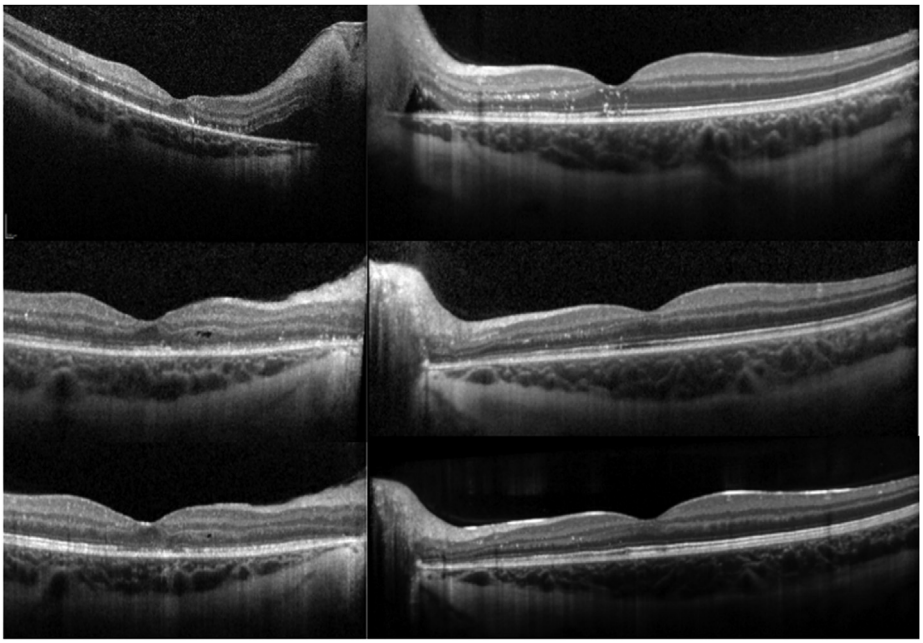

Fig. 6. Serial SD-OCT. From top to bottom, images denote the right and left eye respectively 3 weeks following presentation, one month following bone marrow transplant and 3 months following bone marrow transplant.

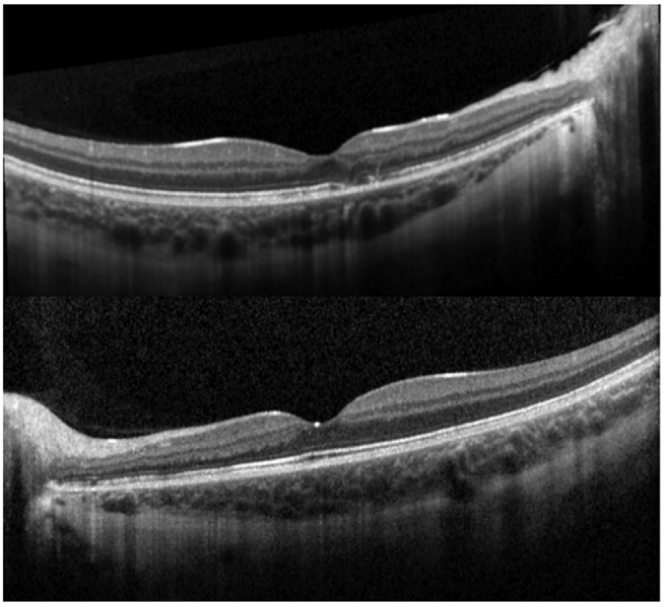

Fig. 7. SD-OCT image of right eye (top) and left eye (bottom) 2 years after bone marrow transplant. Note absence of subretinal fluid, however there is persistent thinning of the photoreceptors at the interdigitation zone.

Declaration of competing interest

The authors have no financial disclosures or conflicts of interest.

Acknowledgments

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajoc.2020.100695.

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