Bilateral proliferative retinopathy in B-cell acute lymphoblastic leukemia

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A 4-year-old child with B-cell acute lymphoblastic leukemia presented with vitreous hemorrhage due to proliferative retinopathy in both eyes. Pars plana vitrectomy was performed in both eyes to clear nonresolving vitreous hemorrhage after systemic stabilization. Visual recovery was limited by the disc drag in the right eye and subfoveal exudation in the left eye. Etiopathogenesis and management of proliferative retinopathy in acute leukemias are discussed.

Key words: Acute lymphoblastic leukemia, leukemic retinopathy, proliferative retinopathy

Acute leukemias usually present with ocular features of anemia and thrombocytopenia (in the form of retinal and preretinal

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hemorrhages, Roth spots, hard exudates, and cotton wool spots). On the other hand, chronic leukemias present with features of venous stasis and ischemia because of high blood viscosity resulting from increased cell counts.[1] Peripheral retinal nonperfusion and retinal neovascularization are known complications of chronic leukemia, particularly in patients with chronic myeloid leukemia.[2-4]

Proliferative retinopathy in acute leukemias has been rarely reported. Only two such case reports exist in literature where T-cell acute lymphoblastic leukemia (ALL) patients had proliferative retinopathy.[5,6] Here, we present a case of bilateral proliferative retinopathy in a child with B-cell ALL. This is the first such report, to the best of our knowledge (searched on PubMed and Google Scholar using keywords proliferative retinopathy, acute ALL, vitreous hemorrhage, retinal neovascularization, vitrectomy, and leukemic retinopathy)

Case Report

A 4-year-old girl presented to the retina clinic with complaints of sudden painless diminution of vision in both eyes associated with floaters over the past 1 week. She had been diagnosed as a case of high-risk B-cell acute ALL 1 month back at hematology department and was on induction chemotherapy with vincristine, L-asparaginase, daunorubicin, and intrathecal methotrexate at the time of presentation.

Visual acuity in both eyes was restricted to hand movements close to the face with projection of light accurate in all quadrants. Anterior segment examination was unremarkable in both eyes. Vitreous hemorrhage obscuring fundus view was present in both eyes. Ultrasonography B scans revealed vitreous hemorrhage in both eyes without any evidence of retinal detachment.

After obtaining informed consent from the parents, the patient underwent 25-gauge pars plana vitrectomy (PPV) in the left eye. Vascular attenuation, pallid edema of the retina, and a six-disc diameter area of subretinal exudation along with hemorrhage along the inferotemporal arcade were noted intraoperatively [Fig. 1]. Focal exudates were also noted at the macula. Vitreous biopsy was taken and sent for cytopathology. Laser photocoagulation was done to the avascular retina in the inferior quadrants. Cytopathology of the vitreous sample showed red blood cells, occasional macrophages, and mature lymphocytes; however, no malignant cells were seen. The patient was prescribed standard postoperative treatment consisting of topical antibiotic, cycloplegic, and steroids.

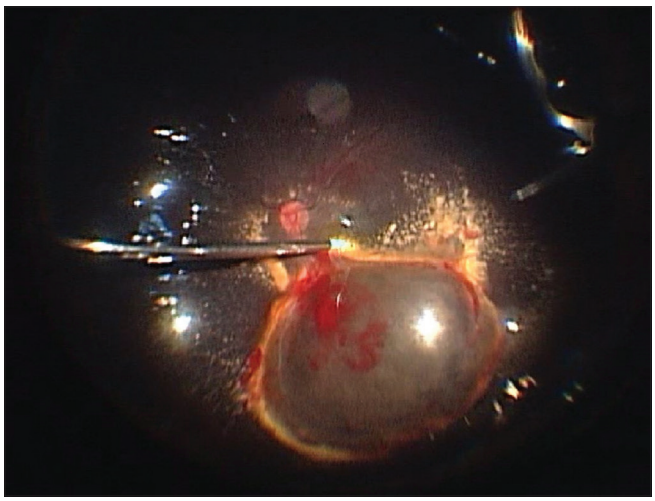

Figure 1: Intraoperative photograph of the left eye of a patient with B-cell acute lymphoblastic leukemia with proliferative retinopathy. After clearing the vitreous hemorrhage, fluid-air exchange is being done. Inferotemporal large area of subretinal exudation can be noted

The child was not systemically stable during consolidation phase and interim maintenance phase of chemotherapy, so right eye surgery was postponed.

Subretinal exudation and hemorrhage decreased in the left eye over time and visual acuity improved to 20/120 [Fig. 2a and b]. Swept source optical coherence tomography (OCT, Topcon Inc.,) showed macular thickening with inner retinal hyperreflectivity suggestive of edema [Fig. 2c]. Optically clear sub-internal limiting membrane (ILM) cavity was seen near the inferior arcade at the site of previous hemorrhage and exudation. Ultra-wide-field fundus fluorescein angiography (Optos Inc.,) done in the left eye 2 months after the PPV did not show active neovascularization at disc or elsewhere [Fig. 2d].

Six months later, once the child was stable systemically after completion of the maintenance phase, right eye 25-gauge PPV was performed. Fibrovascular proliferation leading to tractional retinal detachment and peripheral subretinal exudation was noted in the nasal area [Fig. 3a and b]. Membrane peeling, traction release, and nasal scatter laser photocoagulation were done. 20% Sulfur hexafluoride gas was used for endotamponade, and the patient was prescribed standard postoperative treatment as before.

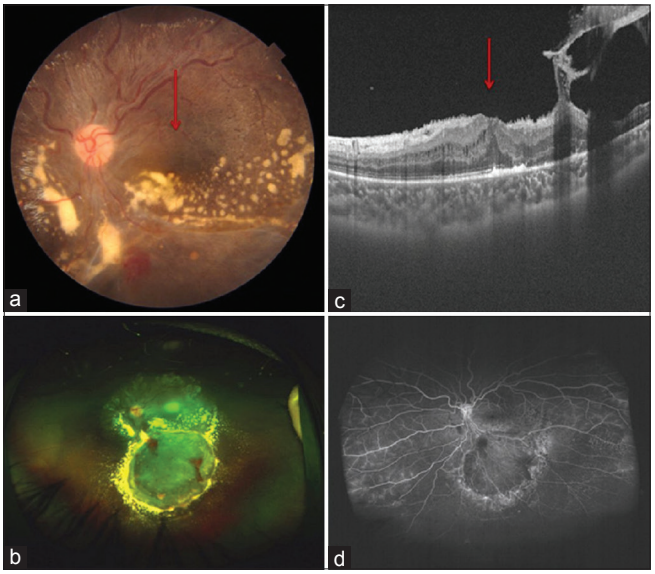

Figure 2: Two-month postoperative condition of the left eye. (a) 45° fundus photograph showing vascular attenuation, resolving subretinal exudates at macula and inferotemporal area of retinal traction with overlying fibrous proliferation. (b) Inferotemporal area of resolving subretinal infiltrates and hemorrhage is evident on ultra-wide-field photography. (c) Swept source optical coherence tomography vertical line scans at fovea show inner retinal edema along with subinternal limiting membrane clear cavity inferiorly. (d) Absence of neovascularization on wide-field fluorescein angiography with window defects of laser scars inferotemporally

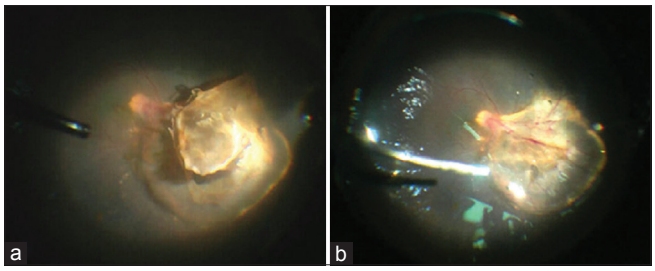

Figure 3: Intraoperative photographs of pars plana vitrectomy in the right eye. (a) Nasal fibrous proliferation with underlying tractional retinal detachment can be seen. Membrane peeling was done. (b) Shows the condition after fluid-air exchange with relieved retinal traction

Meanwhile, the child had completed delayed intensification phase of chemotherapy and was shifted to maintenance therapy. Following surgery and chemotherapy, proliferative retinopathy regressed in both eyes over time [Fig. 4]. Best-corrected visual acuity was 20/120 in the right eye and 20/40 in the left eye at last follow-up 3 months after last surgery. The child was advised to continue treatment for ALL and undergo regular ophthalmic follow-up.

Discussion

Various mechanisms can independently or simultaneously lead to sluggish blood flow, vascular stasis, capillary dropout, retinal ischemia, neovascularization, and its sequelae in a case of leukemia. These include anemia, leukocytosis, hyperviscosity, leukoemboli, endothelial damage by toxins released from leukemic cells, and thrombocytopenia.[1]

Proliferative leukemic retinopathy occurs due to chronic nonperfusion of large areas of the retina that predisposes to retinal neovascularization and creation of fibrovascular membranes that eventually create traction and bleed. Chronic leukemia develops proliferative retinopathy due to long-standing retinal nonperfusion. On the other hand, acute leukemias due to their short duration of presentation do not develop proliferative retinal changes. However, in this case, the ocular presenting feature was vitreous hemorrhage with underlying fibrovascular membranes and tractional retinal detachment. In a large series of vitreous hemorrhage in pediatric patients (261 eyes of 246 patients studied over 10 years) by Rishi *et al*., acute leukemia was not found to be a causative factor highlighting the rarity of this occurrence.[7] Chemotherapeutic agents in addition to the disease process itself could have worsened microangiopathy leading to much severe ischemia.[5]

Leukemic retinal infiltrates have a predilection for inner retinal layers. ILM generally acts as an impermeable membrane for leukemic cell infiltration.[8] Our case had an optically empty sub-ILM cavity visible in the left eye on OCT, which was suggestive of sub-ILM collection of infiltrates and hemorrhage. This character of ILM could also account for the absence of malignant cells on cytopathological analysis of vitreous biopsy.

Prognosis in leukemic retinopathy depends on the macular involvement (presence of ischemia or hemorrhage or infiltrate) and phase of the disease (nonproliferative or proliferative).

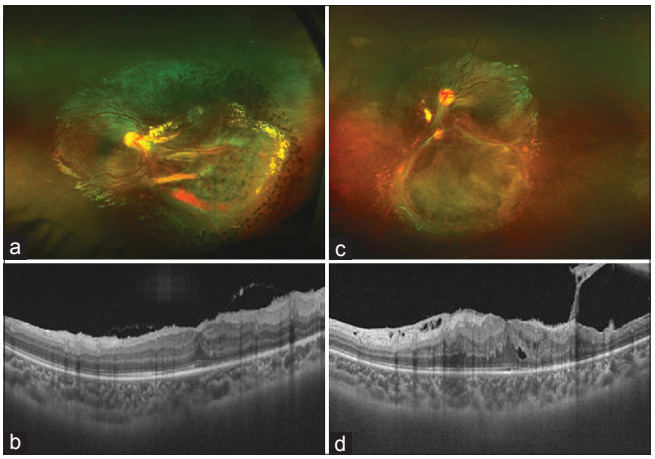

Figure 4: Color photograph at final follow-up in the right eye (a) shows nasal disc drag and scatter laser photocoagulation scars. Swept source optical coherence tomography through the fovea (b) shows a near normal foveal contour in the right eye. Color picture of the left eye (c) shows resolved subretinal exudates and hemorrhage inferotemporally. (d) Shows persistent subinternal limiting membrane cavity on swept source optical coherence tomography inferiorly with retinal edema

Retinopathy typically resolves with treatment of underlying disease, i.e., with chemotherapy. However, once proliferative stage ensues, laser photocoagulation of the peripheral capillary nonperfusion (CNP) areas becomes necessary. Some authors have suggested prophylactic treatment of significant CNP areas even in the absence of retinal neovascularization given the poorer visual outcomes because of increased vasculopathy in such eyes with chemotherapy.[5] Vitrectomy is needed if traction sets in, which is threatening or involving the macula or if vitreous hemorrhage occurs. Vitrectomy in leukemic retinopathy cases is reported to be safe as seen in previous case reports.[9,10]

Our patient did not undergo baseline retinal screening after diagnosis of hematological malignancy. Visual improvement was limited by the presence of macular infiltrates in both eyes initially and disc drag in the left eye with likely damage to the retinal nerve fibers. Although macular exudates resolve completely over time with chemotherapy in leukemic retinopathy, photoreceptor outer segment atrophy usually ensues and limits the visual recovery.[11]

Conclusion

This case highlights the rare occurrence of proliferative retinopathy in B-cell ALL and its management. Early screening, diagnosis, and treatment of ocular involvement is necessary in these cases to prevent visual morbidity.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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