https://doi.org/10.3329/cbmj.v13i2.75322

# Severe Leukemic Retinopathy due to Acute Lymphoblastic leukemia

Hossain I[1], Rahman NA[2], *Kadir SMU[3]

## Abstract

Leukaemia is a myeloproliferative disorder which commonly affects the eye. The retina is most commonly affected by leukaemia. Both acute and chronic leukaemia can develop retinopathy. Patients can develop anaemia and thrombocytopenia. The ophthalmic features include white-centred retinal haemorrhages (Roth spot), cotton wool spots, macular haemorrhages and vitreous haemorrhages. CNS involvement through the optic nerve can cause papillo-oedema and cranial nerve palsy. Opportunistic infection can occur after chemotherapy. A young female patient was diagnosed with Acute Lymphoblastic leukaemia (ALL); she presented with pain and blurred vision in both her eyes. In coloured fundus photograph (CFP) shows dilated, tortuous blood vessels and grey-white streaks along vessels due to perivascular infiltrate. Large whitish opacity all over the fundus. Optic nerve infiltration is also present. Vascular occlusion like CRVO occurs due to hyperviscosity. OCT shows leukaemic infiltration of the retina, causing detachment. The modalities of the Management of leukaemia involve chemotherapy, immunotherapy or radiotherapy, but the Management of leukaemic retinopathy is symptomatic. ALL is treated with vincristine, prednisolone and L-asparagine. Eye treatment was done by intravitreal injection of methotrexate. Patients with acute lymphoblastic leukaemia (ALL) may be asymptomatic and develop vision loss (VL).

CBMJ 2024 July: vol. 13 no. 02 P: 277-281

**Keywords:** Acute lymphoblastic leukemia; Ocular manifestations, Roth spot, Chemotherapy

## Introduction

Leukaemia is blood cancer usually begin in bone marrow due to abnormal blood cells. The clinical presentation of leukaemia includes bleeding, bruising, bone pain, fatigue, fever and infection. The complete blood count usually confirms the diagnosis, and peripheral blood film (PBF) and bone marrow biopsy ensure leukaemia diagnosis.[1,2] The Cause of leukaemia is idiopathic. Genetic and environmental factors may play the most important role.[3] There are four types of leukaemia found in the literature: Acute lymphoblastic leukaemia (ALL), acute myeloid leukaemia (AML), chronic myeloid leukaemia (CML), and chronic lymphocytic leukaemia (CLL). In acute leukaemia, immature blood cells increase, resulting in low production of mature blood cells and low production of haemoglobin and platelets. In chronic leukaemia, there is excessive production of mature blood cells, but it is still abnormal.[4]

1. *Dr. Ireen Hossain, Consultant, Bangladesh Eye Hospital and Institute, Dhaka, Bangladesh.*
2. *Dr. Niaz Abdur Rahman, Consultant, Vitreo-Retina Services and Managing Director. Bangladesh Eye Hospital & Institute, Dhaka, Bangladesh.*
3. **Dr. Syeed Mehbub Ul Kadir, Assistant Professor; Sheikh Fazilatunnesa Mujib Eye Hospital and Training Institute, Gopalganj.*

***Address of Correspondence:***
*Email: mehbubkadir@gmail.com*

Acute lymphoblastic leukaemia mostly occurs in children but can occur in adults older than 65 years. The main treatment modalities are chemotherapy and radiotherapy. Chronic lymphoblastic leukaemia occurs in adults over 55 years but rarely occurs in children.[5,6]

Leukaemia is diagnosed by complete blood counts, bone marrow examination, MRI, CT scan, and ultrasound. It is treated with medication, mainly multidrug chemotherapy. Radiation therapy can also be used. In a few cases, bone marrow transplantation can cure it. Leukaemic retinopathy can occur in both acute and chronic cases. The retina is the most ocular tissue involved in leukaemia. It can be involved directly by leukaemic cells in orbit, iris, choroid, optic nerve and other tissue. Indirect effects by anaemia and thrombocytopenia leading to intraretinal haemorrhage, white-centred retinal haemorrhage, cotton wool spots, macular haemorrhage, subhyloid haemorrhage and vitreous haemorrhage. Signs of CNS involvement are papillo-oedema and cranial nerve palsies. Opportunistic infections can occur as a complication of chemotherapy such as ocular hypertension, cataracts, diplopia and other disorders. Treatment is chemotherapy, immunotherapy and radiotherapy. The survival rate is lower than five years in those patients who present with leukemic retinopathy than in those without ophthalmic involvement.[5] Here we attempt to evaluate the ophthalmological findings in a patient with acute lymphoblastic leukemia (ALL) in a tertiary eye hospital of Bangladesh.

## Case Summary

A teenage female patient was diagnosed with Acute Lymphoblastic Leukaemia. She had complaints of pain and blurred vision in her eyes for the last three months. She also had headaches, nausea, fever, joint pain, fatigue, and loss of weight. On systemic examination, we found pale skin, bleeding from gum, Joint pain and bone pain, mild shortness of breath, weakness of limbs, and ophthalmic features include loss of vision due to leukemic infiltration of the optic nerve and central retinal vein occlusion (CRVO).

Laboratory Examination revealed a total leucocyte count of -17,550 cells/ml, Hb%—6.9 gm/dl, Platelet count—89000/L, and Peripheral Blood Film showing acute Leukaemia. On bone examination, we found that the left superior iliac spine shows acute Leukaemia, probably ALL. The Flow Cytometry report showed negative B cell markers like CD10, CD19, CD20, and CD4.

T cell marker (CD3, CD5, CD7) was positive. All Myeloid/monocyte markers (CD13, CD14, CD33, CD64, CD71, CD79a, MPO) was negative. CD34 was positive. Other markers like cyCD3, CD117, TdT, and HLA-DR were negative. Peripheral Smear morphology showed Acute Leukaemia. Bone marrow Morphology showed acute Lymphoblastic Leukaemia and Impression – T cell acute lymphoblastic Leukaemia. Opportunistic Infection CMV IgG – 153.1 AU/ml (Reactive)

She was treated with chemotherapy (Inj vincristine, inj cyclophosphamide, inj cytarabine) for acute lymphoblastic leukaemia. intra-vitreal injection of methotrexate was given.

**On ophthalmic examination**

| Parameter | RE | LE |
|---|---|---|
| Visual acuity | 6/60 | Close to face |
| IOP | 17 mm Hg | 18 mm Hg |
| Ocular motility | Normal | Normal |
| Ant. segment | Corneal opacity | Corneal opacity |
| Fundus | Leukaemic infiltration of optic disc, dilated tortuous blood vessels, cotton wool spot, grey white streaks along blood vessels due to perivascular infiltrate (Fig. 1). | Leukaemic infiltration of optic disc, dilated tortuous blood vessels, cotton wool spot, grey white streaks along blood vessels due to perivascular infiltrate. (Fig. 2). |

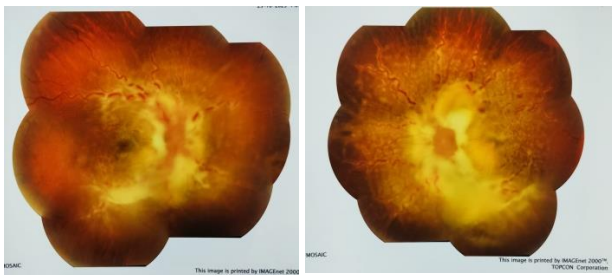
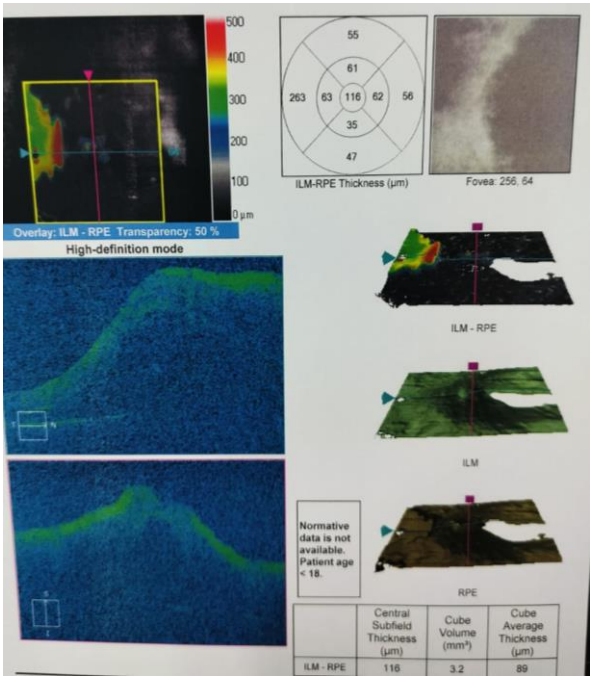
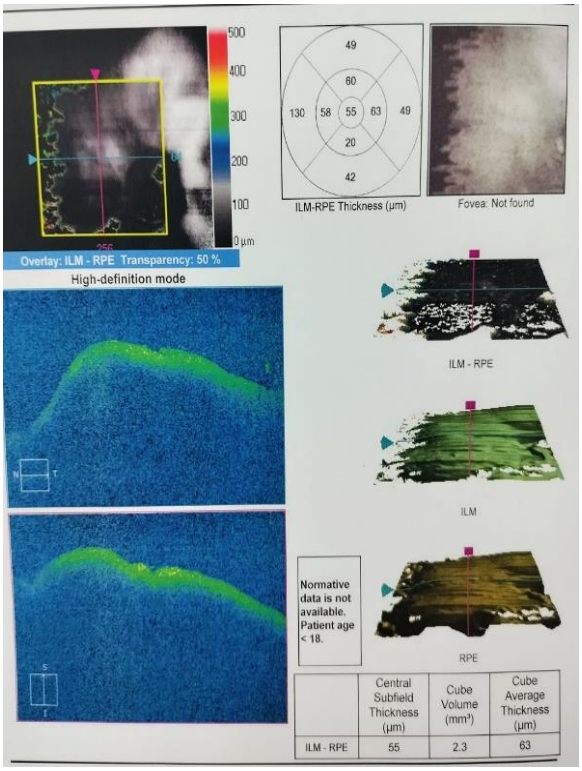


**Figure 1 and 2:** Colour fundus photograph (CFP) of right and left eyes showed dilated tortuous vessel (CRVO due to hyperviscocity), cotton wool spot, grey white streaks along blood vessels due to perivascular infiltrate and leukaemic infiltration of disc




(3)




(4)

**Figure 3 and 4:** OCT of the right and left eyes shows leukaemic infiltration in retina causing detachment and disorganized retinal layers

## Discussion

Leukaemia is a blood cell disorder that affects many organs, including the eyes. The causes of leukaemia are unknown. Genetic and environmental factors are most important.[3] ALL-cure rates are 80% in children and 40% in adults. The most conventional drug works by Either targeting DNA or inhibiting nucleic acid synthesis. Treatment of acute lymphoblastic leukaemia falls into separate phases.[7]

1. **Induction therapy**- The purpose is to kill the leukaemic cells in blood and bone marrow to restore normal cells
2. **Consolidation therapy/post-remission therapy-** The aim is to destroy remaining leukaemic cells
3. **Maintenance therapy-** The purpose is to prevent leukemic cells from regrowing
4. **Prevented treatment of spinal cord-** Phases of treatment of acute lymphoblastic leukemia can take two to three years

-Chemotherapy is the main treatment of acute lymphoblastic leukemia
-Immunotherapy is used to help the immune system to kill cancer cell
-Radiotherapy - X-ray or proton can kill cancer cells
-Stem cells or bone marrow transplants can replace damaged cells.

All the patients with acute leukaemia presented anaemia, leukocytopenia and thrombocytopenia on the blood examination.[6,7] Our patient showed anaemia and thrombocytopenia. Ocular manifestations may be found in both acute and chronic leukemia. The ocular manifestations occur in about 23% to 33%in acute Leukaemia.[6,7]

The ocular features are ocular hypertension (61.1%), white-centered retinal hemorrhage known as Roth spot (22.2%), cotton wool spots, macular hemorrhage, and vitreous haemorrhage.[7] If it affects the optic disc, papilla-oedema and cranial nerve palsy can develop.[7] The vision loss may be found in about 23% of cases.[8] We found the leukemic infiltration of optic disc, dilated tortuous blood vessels, cotton wool spot, grey white streaks along blood vessels due to perivascular infiltrate in the posterior segment of our patient. Ophthalmic features were more common in AML (24%) than in ALL (22%), especially papilledema with central nervous system compromise in ALL (5%) and AML (11%).[7]

Ocular infiltration is treated with specific systemic chemotherapy guided by a pediatric oncologist and regular ophthalmologic consultations to monitor the local response.[7] Research showed the presented ocular manifestations of traditional systemic treatment can reduce penetration in the vitreous. Intravitreal Injection of methotrexate showed improvement of inflammatory cells and tumor cells.[5] Intravitreal Injection Anti-VEGF & injection steroids can be used. The survival rate is five years or lower for those who present with leukemic retinopathy.[5,6]

## Conclusion and Recommendation

Leukemic retinopathy in ocular involvement is a worse prognosis. Any leukemic patient who complains of visual symptoms needs an urgent ocular evaluation, including a colored fundus photograph and OCT in both eyes. Systemic treatment is very important to prevent ocular

penetration, and intravitreal methotrexate may be used as a treatment modality to improve vision.

## Reference:


1. *Miranda-Filho A, Piñeros M, Ferlay J, Soerjomataram I, Monnereau A, Bray F. Epidemiological patterns of leukaemia in 184 countries: a population-based study. Lancet Haematol. 2018;5(1):e14-e24.*
2. *Chennamadhavuni A, Lyengar V, Mukkamalla SKR, Shimanovsky A. Leukemia. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK560490*
3. *Hutter JJ. Childhood leukemia. Pediatr Rev. 2010;31(6):234-41.*
4. *Arber DA, Orazi A, Hasserjian R, Thiele J, Borowitz MJ, Le Beau MM, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood. 2016;127(20):2391-405.*
5. *Hafeez MU, Ali MH, Najib N, Ayub MH, Shafi K, Munir M, et al. Ophthalmic manifestations of acute leukemia. Cureus. 2019 Jan 7;11(1):e3837.*
6. *Chakroborty KD, Hasan MM, Hasanuzzaman M, Sultana Z, Khaleque SA. Ophthalmic manifestations of leukemia and their management. Mugda Med Coll J. 2024;7(1):36-41.*
7. *Benvenuto F, Sgroi M, Guillen SS, Ancona D, Fandiño A. Ocular findings in children with acute leukemia at a tertiary care center in South America. Oman J Ophthalmol. n2022;15(2):159-62.*
8. *de Queiroz Mendonca C, Freire MV, Viana SS, Silva Tavares MKG, Almeida Silva WM, Cipolotti R. Ocular manifestations in acute lymphoblastic leukemia: A five-year cohort study of pediatric patients. Leuk Res. 2019;76:24-8.*