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Indian Journal of Clinical and Experimental Ophthalmology

Journal homepage: www.ijceo.org

Case Series

Clinical profile of ocular manifestations associated with acute leukemia

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ARTICLE INFO

Article history:
Received 05-09-2023
Accepted 14-05-2024
Available online 30-12-2024

Keywords:
Ophthalmological manifestations
Leukemia
Pseudo- hypopyon
Retinal haemorrhages

ABSTRACT

Background: Ocular manifestations in acute lymphoblastic leukemia (ALL) are not uncommon but rarely present as the sole symptom. They usually arise secondary to anemia, thrombocytopenia, and hyperviscosity. However, atypical features like optic disc edema and pseudo-hypopyon may indicate relapse. This case series of 9 ALL patients identified potential relapse markers. We advocate for routine ophthalmological referrals for all leukemic children to assess for atypical features during follow-up. Notably, there is a dearth of epidemiological and clinical studies on this topic in northeastern India.

Materials and Methods: This prospective, descriptive hospital based study was conducted on 9 nos of patients with Acute Leukemia whose duration were over 1 year and whose diagnosis were already confirmed by the paediatrics oncology outpatient department physicians; based on the peripheral blood smear and bone marrow biopsy. These patients were underwent a comprehensive ophthalmological clinical evaluation, dilated fundus examination, optical coherence tomography and other tailored investigations.

Results: Among 9 pediatric patients, 66.67% were from rural areas, 33.33% from semi-urban areas, and none from urban areas. Ocular involvement was observed in 22.22% of patients unilaterally, 22.22% had no ocular signs, and 55.55% exhibited bilateral involvement (representing 55.55% of all eyes). Conjunctival involvement was seen in 27.77% of eyes, with subconjunctival hemorrhage (16.66%) being the most common. Conjunctival congestion occurred in 11.11% of eyes. Anterior chamber involvement included uveitis (16.66%), hyphema (5.55%), and pseudo-hypopyon (5.55%). Iris bombe, a form of posterior synechiae, was observed in 16.66% of uveitic eyes. Elevated intraocular pressure was found in 16.66% of eyes. 72.22% of eyes showed no other anterior chamber involvement. Vitritis was the most common vitreous involvement, observed in 16.67% of eyes. 83.33% of eyes had no vitreous involvement. Retinal involvement included hemorrhages (16.67%) and edema (11.11%), while 72.22% of eyes had no retinal involvement. Epiretinal membrane was found in 5.56% of eyes, with 94.44% showing no macular involvement. Elevated LDH levels were present in 33.33% of patients.

Conclusion: Ocular involvement in leukemia can be primary or secondary to hematological abnormalities. Relapse should be suspected in any patient with ocular signs, especially after remission. Retinal hemorrhages are the most common manifestation of leukemic retinopathy. Atypical features like pseudo-hypopyon, hyphema, and optic disc swelling with elevated LDH warrant immediate investigation for relapse. Thorough oncological evaluation is crucial during follow-up. We recommend ophthalmological referral for all leukemic patients for comprehensive assessment.

1. Introduction

The Leukemias are a group of hematopoietic neoplasia characterized by abnormal proliferation of white blood

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https://doi.org/10.18231/j.ijceo.2024.136

cells.[1] Ocular manifestations are more common in acute leukemia. These involvements are either due to primary or due to secondary causes associated with anaemia, thrombocytopenia and hyperviscocity of the blood circulation.[1] Primary ocular involvement is usually rare and it is basically due to the direct infiltration of ocular tissues by the leukemic cells. Primary involvement of the tumor cells might manifest as Uveitis, vitritis, choroiditis or retinitis.[2] Uveitis sometimes should be considered as a masquerading presentation. Infiltrations to the other ocular structures like optic nerve in the form of papilloedema are also seen in some patients.[3] Posterior segment involvements are the most commonly seen findings and of these, retinal haemorrhages are frequently seen in fundus examinations. Other posterior segment findings are macular edema, papilloedema, epiretinal membrane; cotton wool spots and vitreous haemorrhages etc. Retinal haemorrhages are more commonly attributed to the haematological changes rather than direct ocular infiltration.

This study has been aimed to carry out to find out the ocular manifestations in acute leukemic patients in the paediatric age group. The findings were obtained at the first visit from the patients referred from the paediatric oncology department diagnosed with leukemia; after fulfilling the inclusion criteria. The Patients were referred on the basis of ocular complains. The ocular complains were decreased vision, watering, redness, ocular pain and photophobia.

1.1. Case 1

An 8 year old male child presented to the department of ophthalmology with pain, redness, watering and photophobia in both the eyes for the last 20 days. He was already diagnosed in the department of paediatric oncology as a known case of Acute Lymphocytic Leukemia. The boy was already undergone 10 cycles of Maintenance Chemotherapy. His ocular examination revealed a fixed, irregular, non- reactive pupil of the Right Eye. Anterior chamber was Shallow, and there was presence of a blood mixed hypopyon of 2 mm height. Other findings were: AC cells 4+ and iris had a typical sectoral forward bowing around the temporal region which might be indicative of Iris-bombe formation. His Intra ocular pressure was elevated (40 mm hg) in his right eye. (Figure 1) The child was managed conservatively with topical 1% prednisolone acetate, topical 1% atropine sulphate along with anti- glaucoma medications. Gonioscopy revealed no occludable angle. Fundus examination revealed no signs of neo-vascularization. On subsequent follow up, his intra ocular pressure came down to normal limit. Though he completed 10 cycles of maintenance therapy, his peripheral blood smear examination findings revealed few atypical lymphocytes. He was then considered as a potential candidate of relapse after remission on the basis of ocular findings and referred for bone marrow examinations.

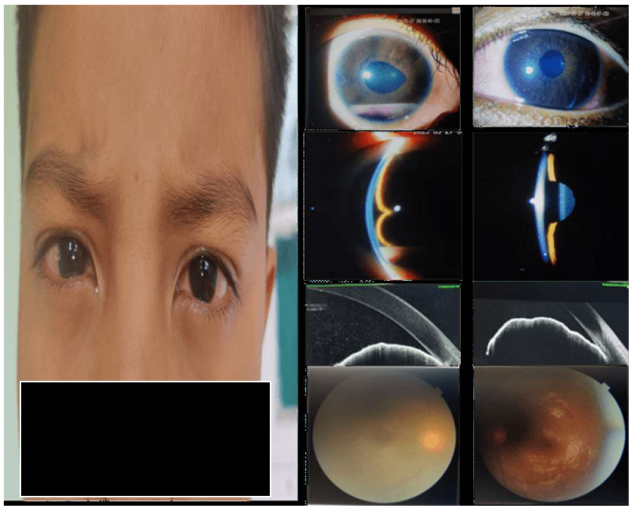

Figure 1:

1.2. Case 2

An 11 year old male child, diagnosed case of acute pro-myelocytic leukemia (AML-M3), referred from the department of paediatrics with the complains of recent onset diminution of vision. Ophthalmological evaluation revealed bilateral eyelid swelling, subconjunctival hemorrhage and dot blot haemorrhages with vessel tortuosity. A 1 DD of pre-retinal haemorrhage was found, involving the superior aspect of the optic disc extending up to the superior-temporal quadrant of the left eye. Apart from the hematological findings of myelocytic leukemia, his LDH level was found elevated. (Figure 2)

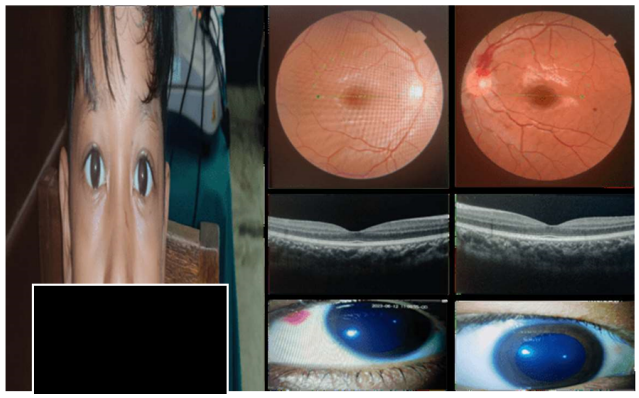

Figure 2:

1.3. Case 3

An 11 year female child with already a known case of B type of ALL referred from the department of paediatrics for the complaints of visual acuity impairment of both eyes. Her present complaints was started with sudden onset

diminution of vision, lower limb weakness followed by fright sided facial palsy. She was disoriented and her best corrected visual acuity was hand movement close to the face in both the eyes. She had already completed her maintenance therapy and presented to Paediatric department with the symptoms suggestive of recurrence. Pediatrician had positively evaluated her for central nervous system involvement and referred her to evaluate ophthalmological signs. She was hypertensive. LDH value was found to be elevated to about 817 U/L. On Slit lamp examination, we found that the anterior segments of both the eyes were within normal limit. Fundus examination revealed bilateral optic nerve head swelling, vessel tortuousity and engorgement. Though the findings were was suggestive of raised intracranial tension, optic nerve head leukemic infiltration must be born in mind. (Figure 3)

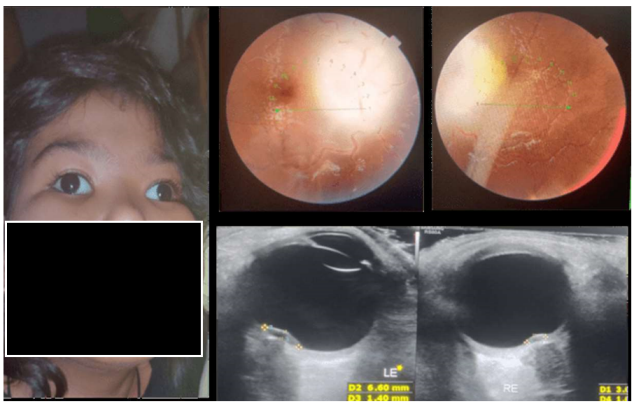

Figure 3:

1.4. Case 4

A 4 year old male child was referred to our department from the department of paediatric for routine eye check-up who was a known case of with B-ALL. The patient was on his 4^{th} cycle of maintenance therapy during the time of presentation. Ocular examination revealed a fleshy mass swelling of the left eye near the lateral fornix. His best corrected visual acuity was found to be 6/6 in both the eyes. Other ocular examinations were performed and it was found that there was no obvious abnormality except the fleshy mass which was suggestive of dermolipoma.(Figure 4)

1.5. Case 5

A 9 year old male child with a diagnosis of B-Acute Lymphocytic Leukemia was referred from the department of pediatrics for the ocular examination. His best corrected visual acuity was found to be 6/6 in both eyes. On fundus examination, pre-retinal haemorrhages were found on the inferior-temporal quadrant of his left eye. Ocular Coherence Tomography of the macula was done and epi-

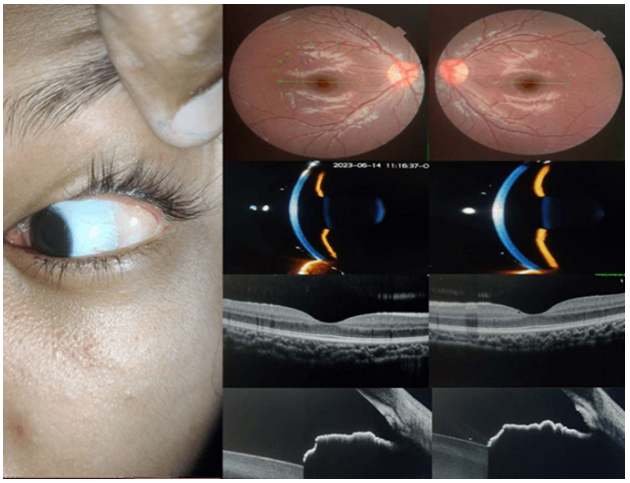

Figure 4:

retinal membrane over the left macula was seen. LDH value was also found to be elevated to about 383 u/L. (Figure 5)

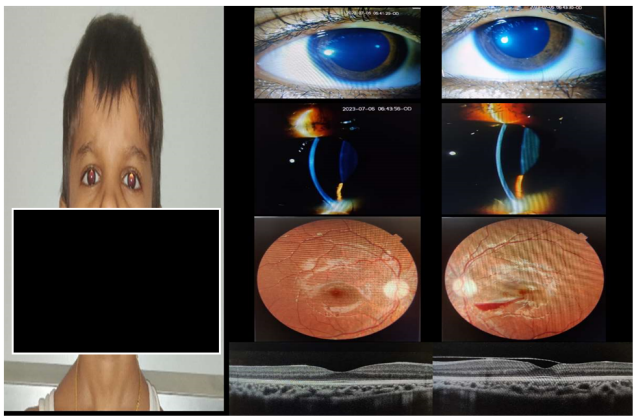

Figure 5:

1.6. Case 6

A 12 year old male child already a known case of B-ALL, receiving chemotherapy, referred with the chief complain of ocular irritation. On examination, ecchymosis, characteristics forward bowing of peripheral iris have been noticed with shallow anterior chamber. There was no posterior synechiae. Fundus was normal. (Figure 6)

1.7. Case 7

A 9 year old female child known case of B-ALL presented with multiple joint pain and rashes all over the body in centrifugal pattern. Patient was referred to department of ophthalmology for the complaints of diminution of vision B/L eyes from the past 2 months. All findings were normal, except for tessellated fundus and little bit of perifoveal

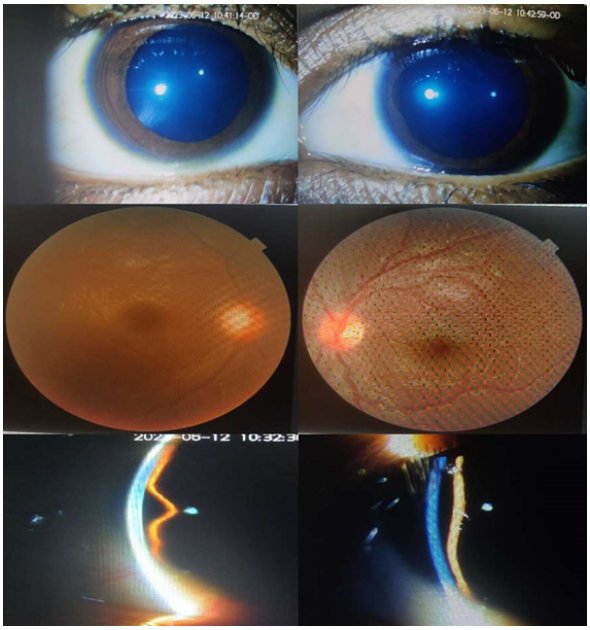

Figure 6:

thickening in OCT. (Figure 7)

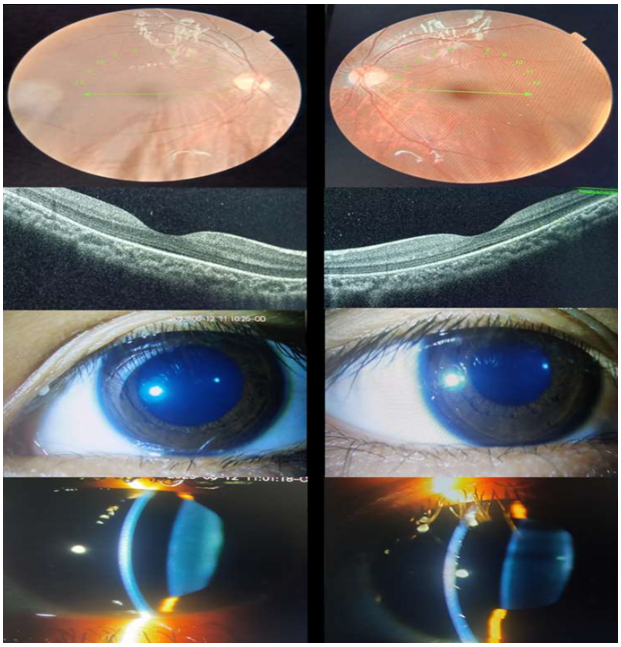

Figure 7:

1.8. Case 8

A 6 year old male child pre-diagnosed with B-ALL referred from the Department of Paediatrics for diminution of vision of Left Eye for the past 10 days. There were petechial hemorrhages over the right lower palpebral conjunctiva. It was found that there was subconjunctival haemorrhage in the left eye. Fundus examination revealed flame shaped hemorrhages on the border of the optic nerve head, extending towards the superior- temporal quadrant. (Figure 8)

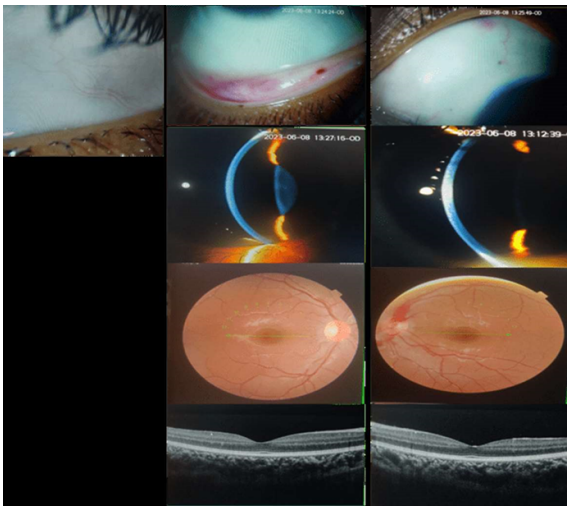

Figure 8:

1.9. Case 9

A 5 year old female child diagnosed with Acute Leukemia presented with icterus along with periorbital swelling of B/L eye for 3 days. Her ophthalmological findings were found normal. (Figure 9)

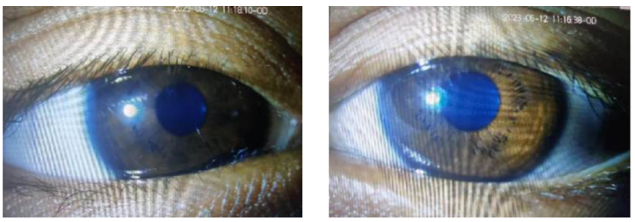

Figure 9:

2. Results and Observation

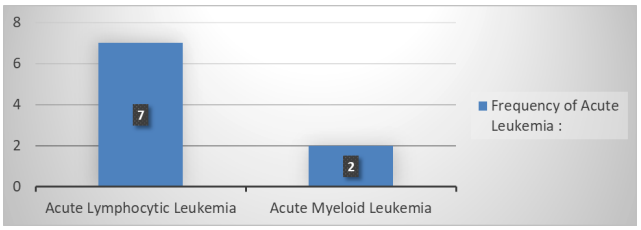

Chart 1: Frequency of acute leukemia

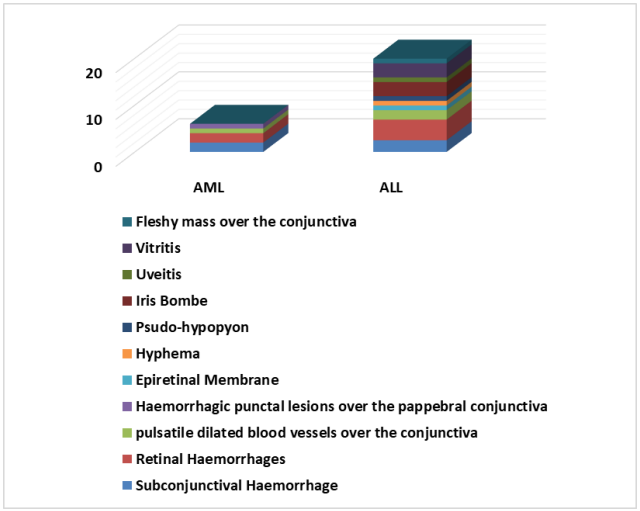

Chart 2:

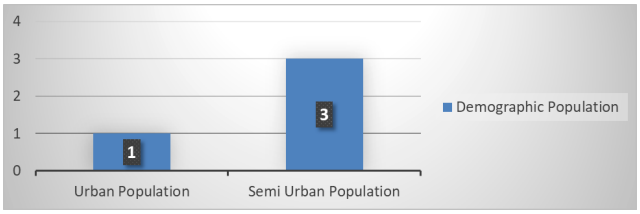

Chart 3: Demographic population

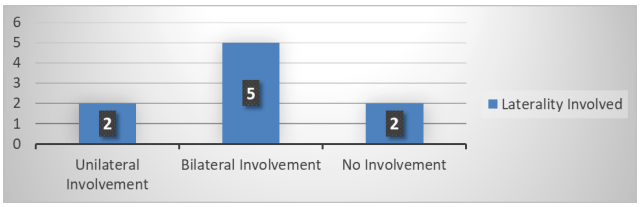

Chart 4: Laterality involved

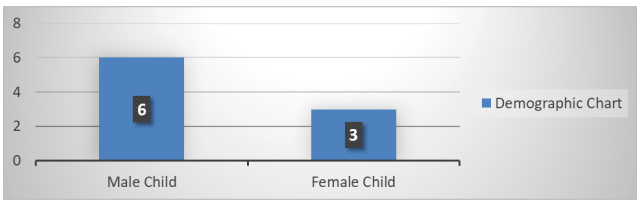

Chart 5: Demographic chart

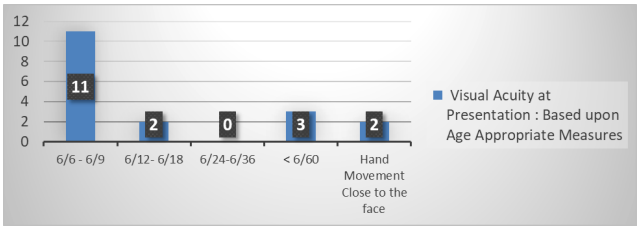

Chart 6: Visual acuity at presentation: Based upon age appropriate measures

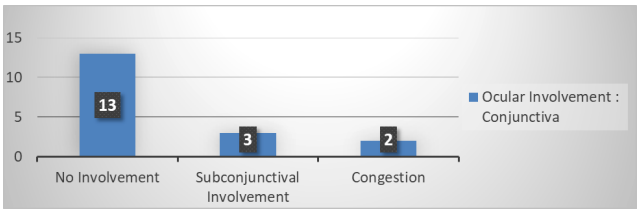

Chart 7: Ocular involvement: Conjunctiva

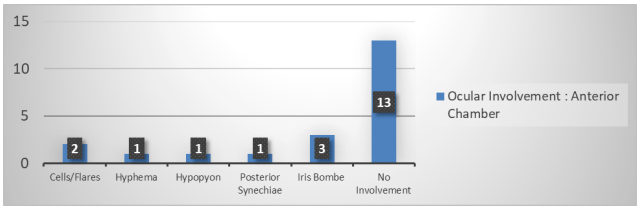

Chart 8: Ocular involvement: Anterior chamber

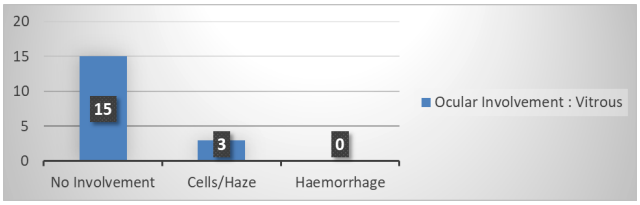

Chart 9: Ocular involvement: Vitrous

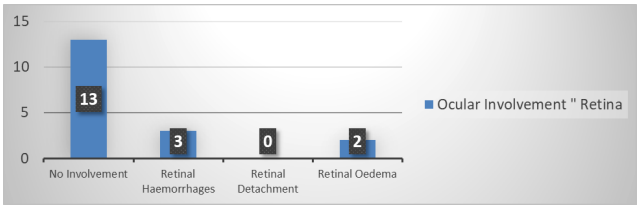

Chart 10: Ocular involvement: Retina

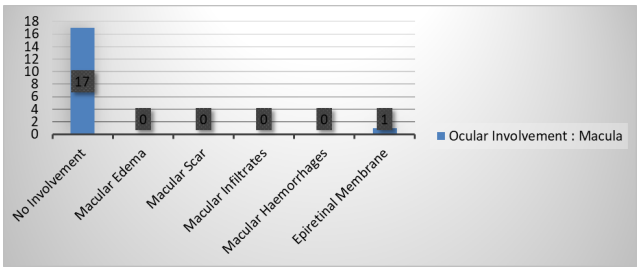

Chart 11:

3. Discussion

The Leukemias are a group of hematopoietic neoplasia characterized by abnormal proliferation of white blood cells.[1] Ocular manifestations are more common in acute leukemia. These involvements are either due to primary or due to secondary causes associated with anaemia, thrombocytopenia and hyperviscocity of the blood circulation.[1] Primary ocular involvement is usually rare and it is basically due to the direct infiltration of ocular tissues by the leukemic cells. Primary involvement of the tumor cells might manifest as Uveitis, vitritis, choroiditis or retinitis.[2] Uveitis sometimes should be considered as a masquerading presentation. Infiltrations to the other ocular structures like optic nerve in the form of papilloedema are also seen in some patients.[3] Posterior segment involvements are the most commonly seen findings and of these, retinal haemorrhages are frequently seen in fundus examinations. Other posterior segment findings are macular edema, papilloedema, epiretinal membrane; cotton wool spots and vitreous haemorrhages etc. Retinal haemorrhages are more commonly attributed to the haematological changes rather than direct ocular infiltration. Retinal haemorrhages are quite common in acute leukemia, But increased LDH were correlated with remission and relapse. So posterior segment findings and LDH level might be a topic of interest, if found after remission of leukemia for further investigations to rule out relapse.[4] Retinal haemorrhages are quite common in acute leukemia, but increased LDH level was correlated with remission and relapse. So posterior segment findings and LDH level might be a topic of interest, if found after remission of leukemia for further investigations to rule out relapse.[4] Dini G et al also stated that the optic nerve head involvement by the leukemic cells is an ophthalmic emergency and need to be treated as the earliest. Radiation therapy and systemic chemotherapy has shown promising effects in the remission of the disease.[5] El salloukh et al aslo reported leukemic retinopathy of epi retinal membrane in acute myeloid leukemia and they expressed that it correlated with low platelet count.[6] They also mentioned that ophthalmological manifestation should be treated as a sign of relapse after remission. Diffuse iris infiltration can be caused by leukemic cells and in this scenario; micro-hyphema must be evaluated. Anguita R et al reported a case of acute lymphoblastic leukemia with diffuse iris infiltrates.[7]

In a case report Decker EB et al reported relapse of a 16 year old girl diagnosed with acute lymphocytic leukemia with no evidence of active central nervous system involvement but with a unilateral hypopyon.[8] They had the opinion that the anterior chamber would serve as a sanctuary for cancer cells. In another report by Charif CM et al presented that hypopyon could be the initial presentation in leukemia or might reveal a relapse.[9] Wadhwa N et al also reported a case of unilateral hypopyon as an initial presentation of relapse in acute lymphocytic leukemia.[10] So, atypical hypopyon should always be considered as an indicator of relapse and proper and prompt oncological evaluation must be carried out to rule out relapse of episodes of acute leukemia. Tyagi M et al and Thulasidas M et al also reported similar findings.[2,11] In our cases, conservative management with topical corticosteroids and cycloplegics subsided the signs the uveitis in few weeks. There might be the need of anterior chamber tapping for the demonstration of tumor cells in the hypopyon, but peripheral blood smear examination and bone marrow examination usually seemed to be more conclusive.

4. Conclusion

Ocular manifestations of leukemia may be the primary involvement of the leukemic cells or it may be secondary to haematological de-arranged profile. Occasionally, the only sign of a leukemic process recurrence may be ophthalmologic involvement. Every ocular signs should be seen with the suspicion of relapse after remission. Retinal hemorrhages is a most common manifesttations of leukemic retinopathy. Atypical features such as pseudo-hypopyon, hyphema, optic nerve head swelling with elevated LDH level should be always treated as a signs of relapse. And further oncological evaluation must be considered in each follow up. We have the opinion that each leukemic patients should be referred to the ophthalmological ward for the comprehensive eye evaluation which can further be re-evaluated by paediatric oncologist.

5. Source of Funding

None.

6. Conflict of Interest

None.

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Cite this article: Das RK, Rabha J, Bharali P, Sunny. Clinical profile of ocular manifestations associated with acute leukemia. *Indian J Clin Exp Ophthalmol* 2024;10(4):789-795.