CASE REPORT ASIAN JOURNAL OF MEDICAL SCIENCES

Leukemic retinopathy, a rare entity: A case report

Aman Kumar Gupta[1], Rakshya Basnet[2], Roshan Dev Yadav[3], Sweta Singh[4]

[1,3]Ophthalmologist, Lumbini Eye Institute and Research Center, Bhairahawa, Nepal, [2]Resident, Department of Ophthalmology, Lumbini Eye Institute and Research Center, Bhairahawa, Nepal, [4]Assistant Professor and Consultant Vitero-Retinal Surgeon, Lumbini Eye Institute and Research Center, Bhairahawa, Nepal

Submission: 10-05-2021 Revision: 06-08-2021 Publication: 01-09-2021

ABSTRACT

Chronic myelogenous leukemia (CML), also known as chronic myeloid leukemia, is a myeloproliferative disorder characterized by increased proliferation of the granulocytic cell line without the loss of their capacity to differentiate. Consequently, the peripheral blood cell profile shows an increased number of granulocytes and their immature precursors, including occasional blast cells. CML accounts for 20% of all leukemias affecting adults. Retinal lesions are the most common ocular manifestation of leukemia. They are found most often in adults and in patients with myeloid leukemia. Despite the significant efforts made by different groups to optimize treatment and outcome, there are still unmet needs and unanswered questions. Ophthalmologic manifestations are among the therapeutic challenge. Here we present a case of CML (chronic phase) with ophthalmologic manifestations as initial presentation, trying to shed light on this important type of presentation.

Key words: Chronic myelogenous leukemia; leukemic retinopathy

Access this article online

Website: http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v12i9.37021

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

Leukemias are a group of heterogeneous neoplastic disorders of white blood cells. Based on their origin, myeloid or lymphoid, they can be divided into two types. Leukemias traditionally have been designated as acute or chronic, based on their untreated course.[1] In 2016, the WHO revised the classifications for hematopoietic and lymphoid tissue. With regards to myeloproliferative neoplasm, minimal changes were made (prefibrotic myelofibrosis was added as distinct entity and mastocytosis was removed from the list of myeloproliferative neoplasm), the chronic leukemias (chronic neutrophilic leukemia CSF3R mutation identified as oncogene and for chronic myeloid leukemia [CML] and chronic eosinophilic leukemia) remain unchanged in comparison to previous classifications (WHO 2008).[2]

CML is a myeloproliferative neoplasm that can present in different ways; it varies from incidental finding in routine complete blood count to symptomatic presentations such as splenomegaly. Among the uncommon presentations of CML are ophthalmologic manifestations, which can vary from incidental finding during eye examination to blurred vision and partial/total loss of vision.[2]

CASE REPORT

A 18 years old male student, from Kapilvastu, Nepal who was previously healthy, presented on 20th Aug, 2020, with a condition that started with a history of sudden painless loss of vision in temporal half of Right eye (RE) since 5 days which was progressive in nature, deterioration of vision was for both near and distance, equal in both day and night, not

Address for Correspondence:
Dr. Aman Kumar Gupta, Ophthalmologist, Lumbini Eye Institute and Research Center, Siddharthanagar-3, Bhairahawa, Nepal.
Mobile: +977-9848054091. **E-mail:** amankrg007@gmail.com

associated with pain, redness, discharge. He gave history of abdominal swelling since last 7 months associated with hardening of abdominal wall, mild pain, loss of appetite and fatigue. He lost 4kgs over the last 4 months. General examination showed thin and cachexic built (Image. 1). Vitals: Pulse was 140/min palpated over radial artery, with normal volume, with no radio-radial and no radio-femoral delay. His BP was 90/60 mm Hg, his respiration was abdominal-thoracic with 16 breaths/min. The patient showed pallor of 4+ (Image. 2 and 3). Cardiovascular examination showed increase in JVP with pulsations over right upper chest and right arm (Image. 4). Auscultation had gallop rhythm. His abdominal examination showed abdominal fullness with splenomegaly 6 cms below left costal margin (Image. 5) with Castell's sign positive on percussion over splenic area. His visual acuity in RE was 6/6p and in Left eye (LE) it was 6/6. His pinhole vision was 6/6 for bilateral eye (BE). His near visual acuity was N/6 at 33cm. Confrontation test showed visual field defect over the temporal half of RE. Ocular examination had round, regular and reactive pupil with 3mm on slit lamp examination. Fundus of the RE showed media haze of grade 2+ with round, sharp optic disc margin. Cup-disc ratio (CDR) and neuro-retinal rim (NRR) of optic disc could not be commented on properly. Dull foveal reflex was

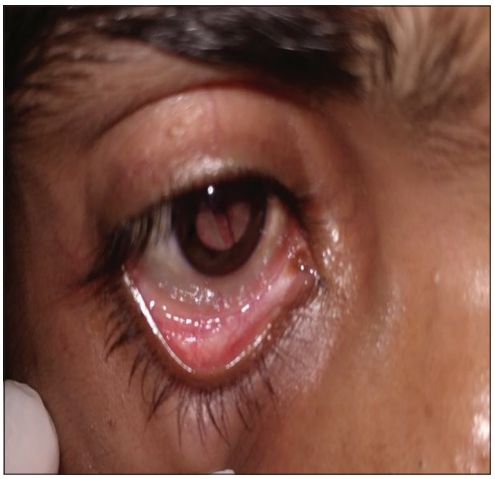

Image 3: Anemic, conjunctival pallor

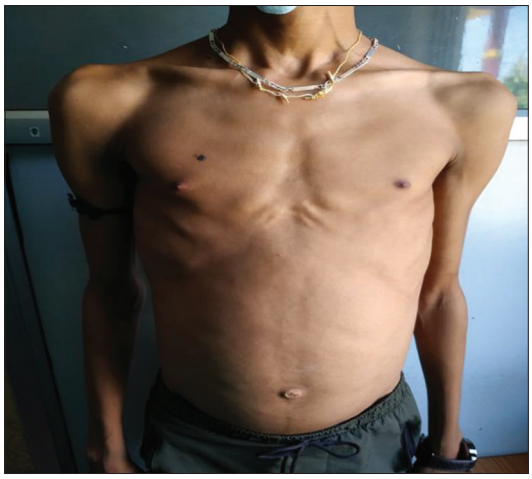

Image 1: Cachexic with weight loss

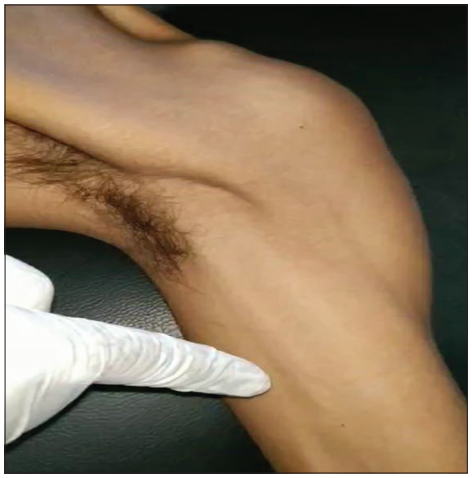

Image 4: Abnormal Pulsations

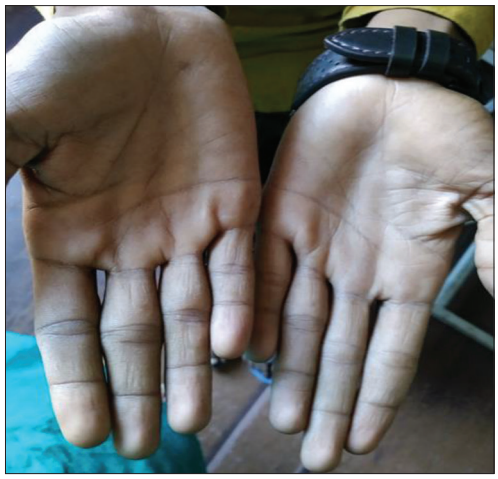

Image 2: Sign of pallor over the palms

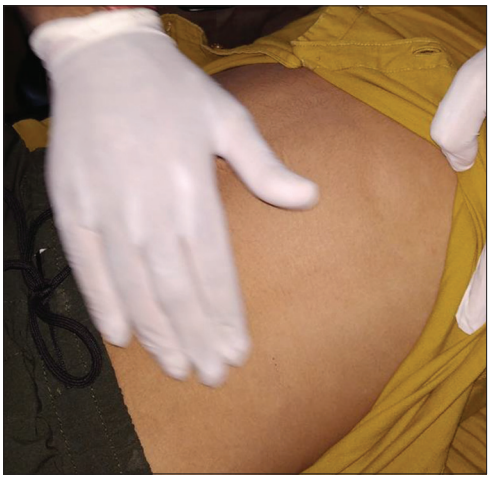

Image 5: Abdominal fullness with palpable spleen

seen on macular area. Superior-temporal vessels were of large caliber, dilated, very tortuous following curvy pattern.

Globular bulging type of lesion was noted in the inferior quadrant touching the inferior disc margin which was convex and solid in appearance most likely of choroidal pathology (Image. 6). Fundus examination of LE had clear media with round and sharp optic disc margin. CDR was about 0.1, with healthy NRR. Foveal reflex was seen on the macular area. All the vessels including superior and inferior vessels were of large caliber, dilated, very tortuous following curvy pattern (Image. 7). Gray-white streaks along vessels were seen and may have been caused by local perivascular leukemic infiltrate in the periphery. Multiple, yellow, creamy, flat sub-retinal lesions were noted in mid peripheral retina. An ultrasonography (USG) of RE was done. A and B scan of the patients RE in which the A-scan showed multiple low to medium reflectivity in the vitreous cavity area which were thicker than the normal. This thick spike was present even behind the retinal spike indicating likelihood of choroidal pathology and on lowering of the gain to 77 Db spikes were more likely double peaked which was further suggestive of choroidal lesions. B-scan of this patients RE showed hyperechoic lesion which was homogenously spread, diffuse, irregular, smooth and flat in configuration present in the cavity especially upper side of cavity and more hyperechoic lesion posterior to retina was seen suggesting choroidal pathology (Image. 8 and 9). There was no after movement on eye movement. A provisional diagnosis of Vascular Occlusive Disease with Choroidal Detachment was made. Patient was urgently asked to consult a physician and was asked to follow-up with Complete Blood Count (CBC), Erythrocyte Sedimentation Rate (ESR), Random Blood Sugar (RBS), Liver Function Test (LFT), Renal Function Test (RFT),

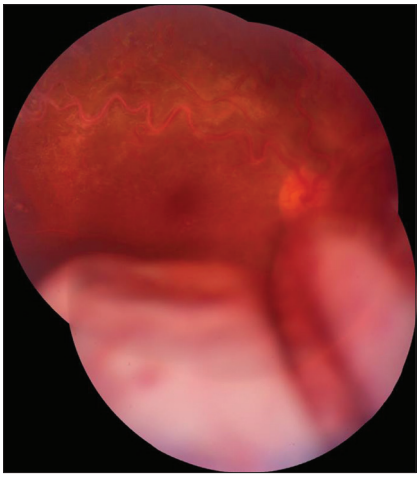

Image 6: RE Fundus photo on first presentation: dilated and tortuous superior-temporal vessels with whitish inferior mass

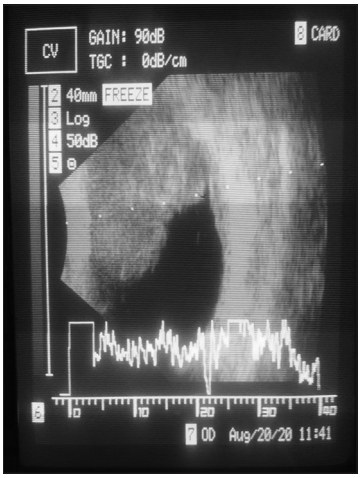

Image 8: A and B scan of RE with low to medium reflectivity with choroidal pathology with persistence of hyperechoic shadows despite reduction in gain

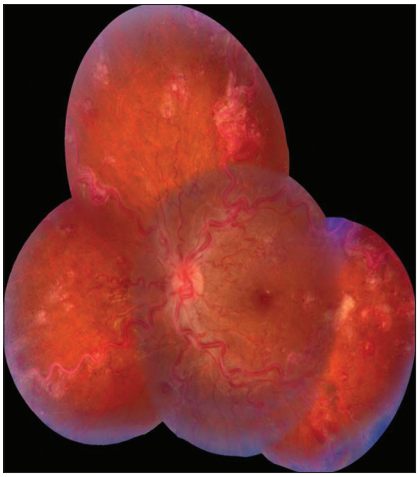

Image 7: LE Fundus photo on first presentation: dilated and tortuous vessels with exudates and cotton wool spots with relatively healthy macula

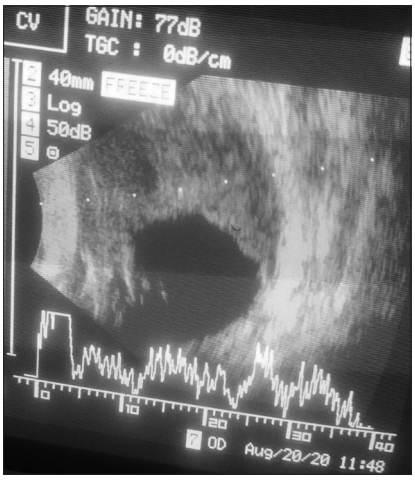

Image 9: A and B scan of RE with low to medium reflectivity with choroidal pathology with persistence of hyperechoic shadows despite reduction in gain

C - reactive protein (CRP), Mantoux test, chest x-ray-PA view, USG –Abdomen reports.

Patient returned back on 27th Aug, 2020; with complains of sudden loss of vision in right eye since 4 days and stated that he had the investigations done only after his vision loss and came immediately to our hospital after the reports came in hand. CBC showed: Hb: 8.6mg/dl, TLC: 128000 cells/mm^3, Neutrophils: 68%, Lymphocytes: 27%, Eosinophil: 4%, Basophil:0%, Monocyte:1%; RBC: 2.15million/mm^3, Platelets: 225000 cells/mm^3; RBS:65.3mg/dl; SGOT:59U/L; SGPT:72U/L. USG Abdomen and Pelvis showed massive splenomegaly, mild hepatomegaly, mild left sided hydronephrosis. His VA this time was no perception of light (NPL) in RE, and 6/18 in LE. His fundus examination this time showed hazy media with poor fundus visibility over RE. LE fundus show similar picture to the previous with more tortuosity of vessel with plenty of exudate and this time with some macular involvement. An urgent Oncology consultation was sent.

Patient came back on 27th Dec 2020, and this time his VA was still NPL in RE, where as it was 6/6 in LE. RE showed poor pupillary reaction with some whitish pupillary light reflex, whereas the LE was round regular and reacting with good pupillary reflex. RE fundus examination still had poor visibility (Image. 10) whereas the LE fundus examination showed complete resolution of previous lesion with a healthy macula (Image. 11). His hemoglobin (Hb) during oncology consultation had dropped to 6.9mg/dl with TLC being 666000cells/mm^3. Blood biochemistry showed Na: 133mmol/L, K: 3.1mmol/L, LDH 703U/L, Protein: 8.3g/dl, Uric Acid: 7.4mg/dl. Bone Marrow Aspiration showed Myeloproliferative Neoplasm with 3% Blast cells. A BCR-ABL quantification was advised to rule out CML. Quantitative RT-PCR showed an International standardization (IS) ratio of 53% in Cytogenetic study. Qualitative reverse transcriptase polymerase chain reaction (RT-PCR) for BCR-ABL1 translocation showed fusion transcript of b2a2 encoding for major transcript p210 and quantitative RT-PCR showed an International standardization (IS) ratio of 53% in Chromosomal study. A diagnosis of Chronic Myeloid Leukemia with associated Retinopathy BE was therefore made. Patient was treated with Imatinib that progressively lead to resolution of splenomegaly and hepatomegaly (Image. 13 and 14). The abdomen was soft and there was no more abdominal fullness (Image. 14). The patient was no more pallid and had gained weight. There was no abnormal pulsation or raised JVP (Image. 15). The VA in LE had improved to 6/6 with an absolutely normal fundus with normal caliber vessels (Image 12), but the RE was still NPL with dense vitreous haze and poor fundus visibility.

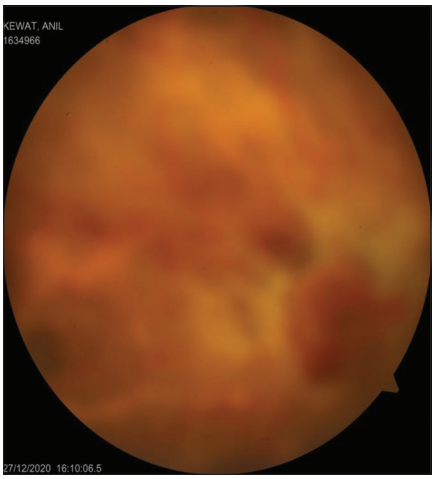

Image 10: RE fundus photo after treatment with Imatinib

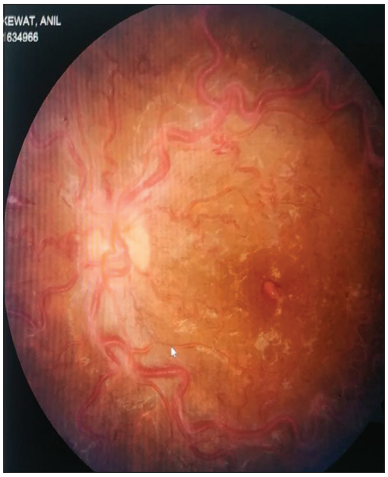

Image 11: LE fundus photo before treatment

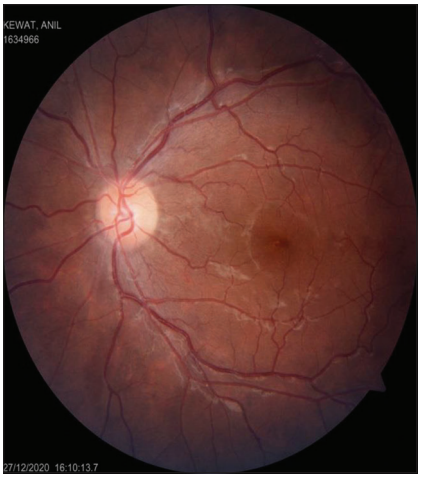

Image 12: LE fundus photo after treatment with Imatinib

DISCUSSION

Ophthalmic manifestations are uncommon presentations of CML with a paucity of literature, and little is known

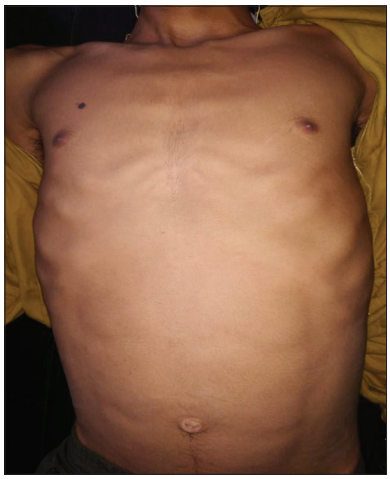

Image 13: Showing abdominal fullness with splenomegaly before treatment with Imatinib

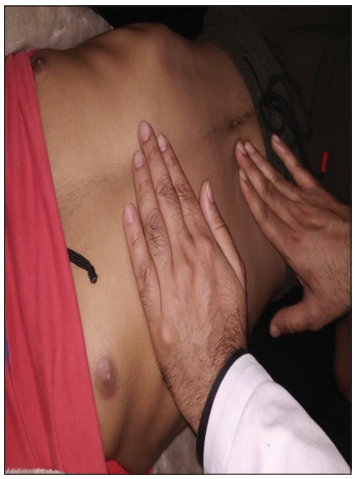

Image 14: Resolved splenomegaly with soft abdomen post Imatinib treatment

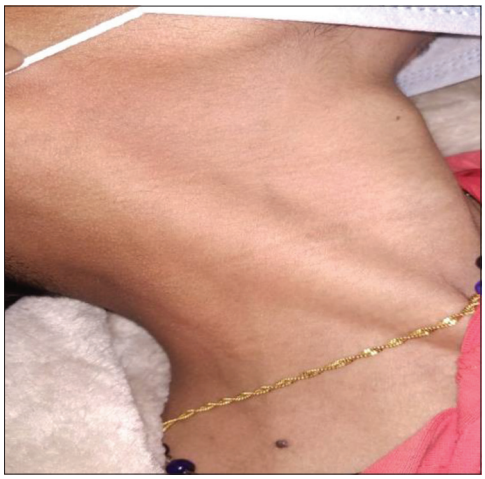

Image 15: Normalization of JVP post treatment with Imatinib

about it.[2] CML is a myeloproliferative disorder that results from expression of the fusion gene BCR–ABL following a chromosomal translocation in the hematopoietic stem cell. The diagnosis of CML is established by increased bone marrow cellularity and identifying a reciprocal translocation between chromosomes 9 and 22 in a hematopoietic stem cell.[3] Ophthalmologic manifestations have a wide range of presentations and findings upon fundoscopy and eye examination. The optic nerve or retina might be affected. The pathological complications on the eye could be reversible or irreversible. The irreversible could be urgent like retinal hemorrhage or non-urgent like cotton wool spots, infections, or proptosis. Blurring of vision or blindness could be the first presentation of CML; in other scenarios, it could also be the first presentation of blast crisis. Patients with ophthalmic manifestation of CML have been reported to have a lower 5-year survival rate.[2] Hyperleukocytosis is the crucial clinical manifestation of CML, which can result in local circulatory stasis. It has been reported that ocular complications are related to retinal ischemia caused by leukostasis in CML. All of these complications were collectively referred to "Leukostasis Retinopathy".[4] Cotton-wool spots are known to represent nerve fiber layer infarcts. Retinal vein tortuosity and dilation are thought to be secondary to hyperviscosity. Peripheral retinal microaneurysms and retinal neovascularization may be seen, particularly in patients with CML. Neovascularization of the disc has been reported in a case where no apparent ischemia was present. It was recognized that angiogenic factors secreted from the tumor may play a role in the pathogenesis of retinal and optic nerve head neovascularization. The choroid is the most commonly affected ocular structure in pathological studies. However, choroidal involvement is difficult to detect clinically owing to the subtle choroidal changes. Occasionally, serous retinal detachments and retinal pigment epithelium (RPE) changes have been reported. In rare cases, they can be the first sign of relapsing leukemia.[1] Treatment options for patients with CML are varied and include a potential cure with allogeneic hematopoietic cell transplantation, disease control without a cure using TKIs (Tyrosine Kinase Inhibitors) or palliative therapy with cytotoxic agents.[3] Leukemic infiltration of the eye is best treated with systemic chemotherapy appropriate for the type and stage of the leukemia. Adjunct radiation may be applied to lesions of the optic nerve or orbit. Of note, the various chemotherapeutic agents used to treat leukemia may cause ocular toxicity such as cataract development, cranial nerve palsies, optic atrophy, and intraocular inflammation.[2]

CONCLUSION

As an ophthalmologist we may be the first one to come across a case of CML as patient may simply present with diminution of vision to no perception of light. Sudden visual loss could be a common presentation with

asymmetrical involvement. Patients presenting complain, his cachexic look, abdominal fullness, associated blood evaluation with high TLC count and a baseline fundoscopy examination could very much help us clinch to the diagnosis; because as an ophthalmologist we can salvage the patients vision and a prompt referral to an oncologist could help save life of a patient. A timely intervention can save the patients sight.

REFERENCES

1. Ophthalmologic Manifestations of Leukemias: Background, Pathophysiology, Epidemiology. 2020 Jul 27 [cited 2021 May 4]; Available from: https://emedicine.medscape.com/article/1201870-overview#a5
2. Mohamed SF, Qatami A, Nashwan A, Abdulla MA and Yassin MA. Ophthalmologic Manifestations as Initial Presentation of Patients with Chronic Myeloid Leukemia: Report of Two Cases. Case Reports in Oncology. Case Rep Oncol. 2020;13:7–11.
   https://doi.org/10.1159/000504928
3. Buzaid AN and Al-Amri AM. Sudden visual loss as an initial manifestation of chronic myeloid leukemia. Saudi Journal of Medicine and Medical Sciences. 2017; 5(3):278-280.
   https://doi.org/10.4103/sjmms.sjmms_35_16
4. Chen B, Yan X, Zhang X and Yang H. Leukostasis retinopathy: An uncommon visual threatening complication of chronic myeloid leukemia with severe hyperleukocytosis – A case report and review of the literature. Indian J Ophthalmology. 2018; 66(12): 1871-1874.
   https://doi.org/10.4103/ijo.IJO_627_18

Author's contribution:
AKG- Concept of the study, reviewed literature, preparation and revision of manuscript; **SS-** Reviewed literature and revision of manuscript; **RDY-** Revision of manuscript; **RB-** Revision of manuscript

Work attributed to:
Lumbini Eye Institute and Research Center, Bhairahawa, Nepal

ORCID ID:
Dr. Aman Kumar Gupta- https://orcid.org/0000-0003-3064-2779
Dr. Rakshya Basnet- https://orcid.org/0000-0003-4404-6361
Dr. Roshan Dev Yadav- https://orcid.org/0000-0002-8356-3436
Dr. Sweta Singh- https://orcid.org/0000-0001-6716-9757

Source of Funding: None, **Conflict of Interest:** None.