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Ocular Manifestations in Leukemias and Their Correlation with Hematologic Parameters at a Tertiary Care Setting in South India

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Purpose: To determine the prevalence of ocular manifestations and the association of these manifestations with hematologic parameters among patients with leukemia attending a hemato-oncology unit at a tertiary care government hospital in South India.

Design: This was a cross-sectional observational study.

Participants: All patients attending a hemato-oncology unit at a tertiary care government hospital in South India who were diagnosed with acute or chronic leukemia that was confirmed by a bone marrow biopsy.

Methods: Consecutive patients with leukemia presenting at the hematology clinic underwent standardized leukemia blood workup and comprehensive ophthalmic evaluation. Patient demographics, the type of leukemia, ophthalmic features, and hematological parameters such as hemoglobin level, white blood cell count, and platelet counts were recorded. The association between ophthalmic manifestations and blood counts was analyzed using multivariable regression analysis.

Main outcome measures: The study measured the prevalence of various ocular manifestations in different types of leukemias and their association with hematologic parameters.

Results: In total, 133 eyes of 133 patients were examined during the study period. The prevalence of leukemic ophthalmopathy was found to be 68% in cases of acute myeloid leukemia, 42% in cases of acute lymphoid leukemia, 33% in cases of chronic lymphoid leukemia, and 13% in cases of chronic myeloid leukemia. Vision-threatening complications such as subhyaloid hemorrhage involving the posterior pole (20%) and vitreous hemorrhage (10%) were seen exclusively in patients with acute leukemias. Multivariable logistic regression after adjusting for the type of leukemia, patient age, and white blood cell and platelet counts showed that the hemoglobin level was the only factor predictive of developing subhyaloid hemorrhage (every 1-g/L increment increase in hemoglobin level led to a 30% reduction in the likelihood of developing subhyaloid hemorrhage; 95% confidence interval 0.5−0.9; $P = 0.02$). The probability of developing subhyaloid hemorrhage was reduced by >50% when hemoglobin level improved from 5 to 7 g/L and when platelet count improved from 10 000 to 50 000 cells/mm^3 for both types of acute leukemia. There was no association between white blood cell counts and ophthalmic manifestations.

Conclusion: Leukemic ophthalmopathy is more common in acute and myeloid cases and less common in chronic and lymphoid subtypes. It is predominantly due to secondary rheological changes. Blood transfusion should be considered when hemoglobin level and platelet count decrease below 7 g/L and 50 000 cells/mm^3, respectively, to prevent vision-threatening complications. Patients with acute leukemias should undergo ophthalmic screening at baseline and then periodically to prevent visual morbidity. *Ophthalmology Retina 2017;■ :1−7 © 2017 by the American Academy of Ophthalmology*

Leukemias are traditionally divided into acute and chronic forms. The acute leukemias are characterized by the presence of immature white blood cells called *blasts* in the bone marrow, whereas chronic leukemias are associated with abnormal proliferation of mature white blood cells. Acute and chronic leukemias are further broadly classified as myeloid and lymphoid leukemias.[1]

Ocular involvement in leukemia is predominantly due to accompanying hematologic or rheological abnormalities such as anemia, thrombocytopenia, or hyperviscosity. These secondary manifestations range from milder conjunctival ecchymosis to retinal hemorrhages that can lead to severe vision loss.[2−4] Occasionally, primary invasion of ocular tissue by the leukemic cells can lead to proptosis, cranial nerve palsies, optic nerve infiltration, massive choroidal infiltration, and exudative retinal detachment.[5−7] Rarely, opportunistic infections associated with immunosuppression from disease or its therapy, such as chemotherapy and bone marrow transplantation, can also affect the eye.[8] Ophthalmic manifestations are usually proportional to the disease severity but may sometimes be the presenting manifestation in leukemia or may signal an isolated focal relapse after complete recovery from systemic leukemia.[9]

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Many publications describe the entire spectrum of ophthalmic manifestations of the different varieties of leukemia.[10–14] However, few studies have looked at the associations between the primary and secondary ophthalmic manifestations and blood counts and how these metrics influence the eye.[15–17] Predictive analytics for vision-threatening complications such as macular hemorrhages can be derived from such association studies. Further, it may be possible to make recommendations for blood transfusion to prevent such vision-threatening complications based on associations between blood counts and ophthalmic manifestations. We performed a cross-sectional study to identify ophthalmic manifestations and correlate them with blood parameters in patients with leukemia.

Methods

The study was approved by the ethics committee of the parent institution and followed the tenets of the Declaration of Helsinki. Informed consent was obtained from all participants at the time of ophthalmic evaluation. A total of 133 patients, comprising both newly diagnosed and known cases of leukemia undergoing treatment, who attended the hemato-oncology unit at a tertiary care government hospital in South India between September 2014 and April 2016 were recruited for the study. Several patients were missed from the outpatient clinic because of either lack of time on the part of the principal investigator or poor patient cooperation (Table 1). Leukemia was diagnosed by a hemato-oncologist based on the complete hemogram, including total white blood cell (WBC) counts, peripheral smear cellular morphology, bone marrow aspiration results, and supportive immunohistochemical evidence. Patients with coexisting ocular or systemic disease with leukemia-like ocular manifestations, including human immunodeficiency virus, diabetes mellitus, hypertension, sickle cell anemia, and dense cataracts that precluded posterior segment examination, and severely ill patients who were unable to consent to examination were excluded. Patients were examined immediately after obtaining consent from the outpatient clinic and within a few days after admission for the inpatients. We obtained details including demographic parameters, specifics of the leukemia including the type of leukemia (i.e., acute myeloid leukemia [AML], acute lymphoid leukemia [ALL], chronic myeloid leukemia [CML] and chronic lymphoid leukemia [CLL]), duration of the disease in known cases, and hematological parameters such as hemoglobin (Hb) level, total WBC count, and platelet count.

Table 1. Comparison of Demographics, Ophthalmic Manifestations, and Blood Counts Among the Different Types of Leukemia

Variable	Acute Leukemia		Chronic Leukemia		*P* value
	AML (n = 70)	*ALL (n = 138)*	*CML (n = 161)*	*CLL (n = 32)*	
Total no. of patients included in our study	AML (n = 40)	ALL (n = 52)	CML (n = 38)	CLL (n = 3)	
New cases	8 (20)	11 (21)	4 (11)	0	0.49
Median age at diagnosis (y), n (IQR)	32 (18–42)	20 (12–30)	43 (36–55)	55 (45–70)	<0.001
Pediatric patients (<18 y)	10 (25)	23 (44)	1 (3)	0	<0.001
Male	23 (57)	38 (73)	20 (53)	1 (33)	0.14
Ocular involvement	27 (68)	22 (42)	5 (13)	1 (33)	<0.001
BCVA (logMAR), mean ± SD	0.4±0.4	0.4±0.5	0.3±0.3	0.7±0.3	0.23
Primary ophthalmic involvement					
Leukemic retinal infiltrates	0 (0)	0 (0)	1 (3)	0	0.78
Optic nerve infiltration	0 (0)	1 (2)	2 (6)	0	0.67
Lateral rectus palsy	2 (5)	0 (0)	0 (0)	0	0.57
Secondary: Anterior segment changes					
Ecchymosis	2 (5)	0 (0)	0 (0)	0	0.77
Subconjunctival hemorrhages	1 (2.5)	0 (0)	0 (0)	1 (33)	0.13
Corkscrew conjunctival vessels	0 (0)	0 (0)	0 (0)	1 (33)	0.44
Periorbital edema, mechanical ptosis	1 (2.5)	0 (0)	0 (0)	0	0.91
Secondary: Posterior segment changes					
Disc edema	2 (5)	1 (2)	2 (6)	0	0.80
Dot/blot hemorrhages	7 (18)	5 (10)	2 (5)	0	0.31
Splinter hemorrhages	4 (10)	1 (2)	0 (0)	0	0.09
Roth spots	12 (30)	7 (13)	1 (3)	0	0.007
Cotton-wool spots	5 (13)	2 (4)	0 (0)	0	0.10
Dilated/tortuous veins	3 (8)	2 (4)	2 (5)	0	0.85
Subhyaloid hemorrhage	8 (20)	10 (19)	0 (0)	0	0.03
Vitreous hemorrhage	3 (8)	6 (12)	0 (0)	0	0.18
Tractional retinal detachment	0 (0)	1 (2)	0 (0)	0	0.91
Neovascularization of retina and disc	0 (0)	0 (0)	1 (3)	0	0.87
Macular edema	0 (0)	0 (0)	1 (3)	0	0.69
Blood counts					
Mean hemoglobin level (g/dL), mean ± SD	6.8±2.1	6.8±2.5	10.2±1.9	8.1±3.1	<0.001
Mean platelet count (cells/mm^3), mean ± SD	83 372±147 760	63 943±93 520	157 851±128 957	246 333±213 657	<0.001
Mean total leucocyte count (cells/mm^3), mean ± SD	124 845±206 514	146 229±221 737	40 772±59 511	85 033±83 081	0.006

Data are no. (%) unless otherwise indicated.
ALL = acute lymphoid leukemia; AML = acute myeloid leukemia; BCVA = best-corrected visual acuity; CLL = chronic lymphoid leukemia; CML = chronic myeloid leukemia; IQR = interquartile range; logMAR = logarithm of the minimum angle of resolution; SD = standard deviation.