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Original Research Article

Orbital and Ocular Manifestations of Acute and Chronic Leukemia

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ABSTRACT

Introduction: Ocular disorders have been reported in 30-90% of cases of leukemia. Ophthalmic involvement in leukemia is associated with significant ocular morbidity and vision loss and has critical implications for the natural course and survival prognosis of systemic leukemia.
Materials and methods: The present prospective study was conducted at department of Ophthalmology of tertiary Cancer care center from September 2014 to May 2016. All patients ≥ 18 years age diagnosed with leukemia, in spite of chemotherapy status and not underwent bone marrow transplant therapy were included in this study. Each included patient was subjected to ophthalmological evaluation and leukemia related and non-leukemic ophthalmic findings were documented. The data was analyzed by using SPSS version 23 and applying chi square test.
Results and Conclusions: Out of 67 patients diagnosed with leukemia ocular lesions were found in 35 (52.23%) leukemic patients with no significant intersex difference. The distribution of leukemic ophthalmopathy by type of leukemia was AML- 19/29 (65.51%), ALL- 10/17 (58.82%), CML- 4/12 (33.33%) and CLL- 2/9 (22.22%) subjects. Ocular involvement is more commonly seen in acute leukemias (29/46, 63.04%) and myeloid leukemias (23/41, 56.09%) with preponderance of secondary or indirect ophthalmic manifestations (28/35, 80%). The common ophthalmic manifestation was proptosis (42.85%) in primary ophthalmopathy and retinal hemorrhages with cotton wool spots (28.57%) in secondary ophthalmopathy. All leukemia patients should have an ophthalmic assessment mandatory at diagnosis and periodically.

Key words: Leukemia, Ophthalmopathy, Retinal hemorrhages, Proptosis, Cotton wool spots.

INTRODUCTION

Leukemia is a malignant proliferative disorder of leucopoietic bone marrow stem cells and widespread infiltration of other organs, tissues and peripheral blood by immature neoplastic leucocytes. [1] Ocular disorders have been reported in 30-90% of cases of leukemia. [2-3] Orbital and ocular lesions have also been reported to be the third most frequent extramedullary location of acute leukemias after the meninges and testicles. [3] Ophthalmic involvement can be classified into primary or direct in the form of anterior segment, uveal infiltration, orbital infiltration, optic nerve infiltration, cranial nerve palsies, papilledema and secondary or indirect manifestations such as retinal or vitreous haemorrhage, infections, vascular occlusion. [4] In the era before effective antileukemic therapy, retinopathy was believed to be of no prognostic significance in acute leukemia. Now a day, although high proportion of patients achieve initial bone marrow remission with combination chemotherapy, it is important to take a closer look at sites of extramedullary leukemic infiltration, both because of their

local morbidity and that these sites may act as a reservoir for proliferation of leukemic cells which may eventually result in systemic relapse.[5] Ophthalmic involvement in leukemia is associated with significant ocular morbidity and vision loss, and has critical implications for the natural course and survival prognosis of systemic leukemia. Recent reports have demonstrated that the presence of ocular involvement is associated with poor prognosis in acute childhood leukaemias.[3] Therefore, the present study was undertaken to consider an ophthalmic evaluation in all cases of leukemia in adults.

MATERIALS AND METHODS

The present prospective study was conducted at department of Ophthalmology of tertiary Cancer care center in Aurangabad, India from September 2014 to May 2016. Informed consent was obtained from patients. All patients ≥18 years age diagnosed with leukemia, in spite of chemotherapy status and not underwent bone marrow transplant therapy were included in this study. Those patients with coexisting ocular or systemic disease with leukemia like ocular manifestations e.g. HIV/AIDS, diabetes mellitus, systemic hypertension, sickle cell disease, retinal vascular disease, fund us with obscuring media opacity and severely ill patients were excluded from the study. After history taking, each included patient was subjected to ophthalmological evaluation including visual acuity by Snellen charts, anterior segment examination by flashlight and slit-lamp and fundus examination by binocular indirect ophthalmoscopy. Leukemia related and non-leukemic ophthalmic findings were documented for each subject. The data was analyzed by using SPSS version 23 and applying chi square test.

RESULTS

Out of 67 adults diagnosed with leukemia at the Medical oncology clinic and referred for ophthalmological evaluation during the study period, 41 (61%) were males and 26 (38%) were females (male to female ratio = 1.6:1). Mean age of the cohort was 60.21 years with range of 18 years to 78 years. There were 25 newly diagnosed and 42 follow up leukemic patients. Among all diagnosed leukemic patients, 46 were acute leukemia, 21 with chronic leukemia and 41 were myeloid leukemia, 26 with lymphoid leukemia. Their distribution by leukemia subtype was acute myeloid leukemia (AML) - 29 (43.28%), acute lymphocytic leukemia (ALL) - 17 (25.37%), chronic myelogenous leukemia (CML) - 12 (17.91%) and chronic lymphocytic leukemia (CLL) - 09 (13.43%) subjects. Ocular lesions were found in 35 (52.23%) leukemic patients. There was no significant intersex difference in the involvement of leukemic ophthalmopathy. The leukemic ophthalmopathy was significantly associated with acute leukemia (29/46, 63.04%) rather than chronic leukemia (6/21, 28.57%), (P = 0.009). The distribution of leukemic ophthalmopathy by type of leukemia was AML 19/29 (65.51%), ALL 10/17 (58.82%), CML 4/12 (33.33%) and CLL 2/9 (22.22%) subjects. Myeloid leukemias were more commonly observed to have ocular manifestations, 23/41 (56.09%) as compared to lymphoid leukemias, 12/26 (46.15%). These findings were not found significant statistically. Ocular findings were more common in acute myeloid leukemia (65.51%) as compared to other leukemias. This comparison was found insignificant statistically. Primary or direct leukemic ophthalmic infiltration was seen in 7/35 (20%) patients. Of the 7 patients with primary leukemic ophthalmopathy, 5 (71.42%) had AML and 2 (28.5%) had CML. Among all patients with primary ophthalmic involvement, 3 had relapse of leukemia, 1 shown bilateral lacrimal gland involvement, 1 had proptosis due to orbital mass and 1 had optic nerve infiltration. Secondary or indirect ophthalmic involvement was seen in 28/35 (80%) patients. The posterior segment involvement of the eye more than the anterior segment was found statistically

significant ($p<0.05$). Some patients had more than one manifestation in one or both eyes. The preponderance of secondary ophthalmic manifestations over the primary manifestations seen in this study was statistically significant ($p<0.05$). Of the 35 subjects with leukemic ophthalmopathy, 8 (22.85%) had blindness (vision less than 3 meters), and 5 (14.28%) were visually impaired. The common ophthalmic manifestation was proptosis (42.85%) in primary ophthalmopathy and retinal hemorrhages with cotton wool spots (28.57%) in secondary ophthalmopathy (table 2 & 3). These findings were not found significant statistically.

Table 1: Type of leukemia with ophthalmopathy

Type of leukemia	Total no.	Ophthalmopathy n (%)
Acute myeloblastic leukemia (AML)	29	19 (65.51)
Acute lymphoblastic leukemia (ALL)	17	10 (58.82)
Chronic myelocytic leukemia (CML)	12	04 (33.33)
Chronic lymphocytic leukemia (CLL)	09	02 (22.22)
Total	**67**	**35 (52.23)**

Table 2: Primary leukemic ophthalmopathy (n=7)

Primary / Direct	No (%)
Proptosis	3 (42.85)
Optic nerve infiltration	2 (28.57)
Papilledema	1 (14.28)
Cranial nerve palsies	1 (14.28)

Table 3: Secondary leukemic ophthalmopathy (n=28)

Secondary / Indirect	No (%)
Retinal hemorrhages with Cotton wool spots	08 (28.57)
White centered hemorrhages	07 (25.00)
Premacular / subhyaloid hemorrhages	03 (10.71)
Vitreous hemorrhages	03 (10.71)
Sub conjunctival hemorrhages	05 (17.85)
Iris infiltration and pseudohypopyon	02 (7.14)

DISCUSSION

The demographic characteristics of our study cohort showed a preponderance of males, however, there were no statistically significant gender based differences in the prevalences of leukemia and leukemic ophthalmopathy. This demographic trend is similar to reports of Reddy et al. [4] The prevalence of ocular involvement in leukemic patients has been reported to be between 9% and 90% in various studies. [4] This divergent variation in results may imply the transient nature of leukemic ocular findings, which may wax and wane with time and treatment. It may also be due to the varied study designs being used. The leukemic ophthalmopathy (52.23%) documented in the present study was comparable to 69.00% reported by Alemayehu et al [6] but differed markedly from 35.4 % reported by Reddy et al [4] and 39.0% in by Schachat et al. [7] Acute leukemia patients in this study had significantly more ocular manifestations than chronic patients (63.04% vs. 28.57%). This was similar to the findings of Reddy et al [4] Omoti et al. [8] However, studies by Eze et al [9] and Nelson et al [10] found chronic leukemias to have more ocular findings than acute ones. This discrepancy could be either because of different study designs or may be an actual reflection of the disease. Myeloid leukemias were more commonly observed to have ocular manifestations (56.09%) as compared to lymphoid leukemias (46.15%). This was similar to the findings of the other major studies. [4,9] The patients with AML had the highest incidence of ocular manifestations (65.51%). This was similar to studies by Reddy et al [4] and Omoti et al. [8] The significant preponderance of secondary ophthalmic manifestations (80%) over the primary manifestations (20%) in leukemic patients in this study was in agreement with the study of Koshy J et al. [11] In the present study, the spectrum of leukemic ophthalmopathy showed a preponderance of posterior over anterior segment manifestations. These resulted predominantly from secondary hematologic complications caused either by the systemic leukemia or its treatment rather than primary leukemic ocular infiltration. These findings were similar to that reported in the study of Eze et al. [9] The common ophthalmic manifestations as proptosis (42.85%) in primary ophthalmopathy and

retinal hemorrhages with cotton wool spots (28.57%) in secondary ophthalmopathy reported in current study were similar to documented in the study of Jacob Koshy et al [11] and Eze et al. [9]

CONCLUSION

In the current study, ocular involvement is more commonly seen in acute leukemias and myeloid leukemias with preponderance of secondary or indirect ophthalmic manifestations. All leukemia patients should have an ophthalmic assessment at diagnosis and periodically at least every 6 months thereafter because of the poorer prognosis associated with ocular involvement and to identify possible extramedullary disease.

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