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OCULAR MANIFESTATIONS IN HEMATOLOGICAL MALIGNANCIES: AN OBSERVATIONAL STUDY IN A MEDICAL COLLEGE & CANCER HOSPITAL IN WEST BENGAL

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ABSTRACT

Background: Haematological malignancies like Leukemia, Lymphoma & Myeloma can cause ocular manifestations which can be vision threatening sometimes. This study aims to evaluate the ocular manifestations in haematological malignancies in a medical college & cancer hospital in West Bengal.

Methods: In this hospital-based cross-sectional study conducted in the Department of Ophthalmology of Sri Ramkrishna Institute of Medical Sciences & Sanaka cancer Hospital in Durgapur, West Bengal, we examined total of 121 patients having hematological malignancies in between July 2023 to June 2024.

Results: Among 121 patients ocular manifestations were noted in 59 patients.Most common Anterior segment finding was subconjunctival haemorrhage (5.08%), whereas most common posterior segment manifestation was intra retinal haemorrhage. Vision threatening complications like sub hyaloid haemorrhage, exudative RD & mcular edema were noted in 19 patients.

Conclusions: Ocular involvement specially retinal involvement is common in hematological malignancies.So ocular examination specially fundus examination should be done in each & every patient of hematological malignancies.

Keywords: Hematological malignancies, Intra retinal Haemorrhages, sub conjunctival haemorrhages, fundus examination.

INTRODUCTION

Hematological malignancies include disorders of erythrocytes, leukocytes, platelets, and diseases of coagulation and plasma proteins. They are called Leukemia, Lymphoma & Myeloma according to the cell affected.[1] The ocular manifestations of these diseases could result from direct neoplastic infiltration of ocular tissues or indirect ocular involvement as associated with hematological abnormalities and treatment complications.[2] The involvement can be intraocular, adnexal, orbital& neuro-ophthalmic.

Among all the ocular manifestations, the most clinically significant manifestation is leukemic retinopathy which was first described byLiebreich in the 1860s.[3] Ocular manifestations in lymphoma are relatively rare. Most of these occur due to direct infiltration of the adnexa, orbit & intraocular tissue which present as proptosis or conjunctival mass, uveitis, retinitis& vasculitis.[3] Multiple myeloma affects the orbital and ocular tissue by direct infiltration or extramedullary plasmacytoma and manifests as proptosis, compressive mass lesions, corneal deposits& ciliary body cysts. Another mechanism of ocular involvement is hyperviscosity syndrome due to increased monoclonal immunoglobulins leading to hyperviscosity retinopathy, retinal microaneurysm, choroidal infiltrate& retinal venous occlusion.[4]

Ocular manifestations are usually proportional to the disease severity but it may be the presenting feature of an underlying hematological disorder and may occur before the presentation of systemic disease.[5] Ocular manifestations may also signal an isolated focal relapse after complete recovery from the systemic disease.[6] Therefore all patients with hematological malignancy will need ophthalmological evaluation for the disease's diagnosis, relapse & prognosis. In this study our aim was to evaluate the spectrum of ocular manifestations of hematological malignancies presenting in a medical college & cancer hospital in West Bengal.

METHODS

This is a hospital-based cross-sectional study conducted in the Department of Ophthalmology of Sri Ramkrishna Institute of Medical Sciences & Sanaka cancer Hospital in Durgapur, West Bengal from July 2023 to June 2024. All new and previously (on treatment) diagnosed cases of leukemia, lymphoma, multiple myeloma, and plasma cell dyscrasia attending the Department of Ophthalmology from July 2023 to June 2024 were included in the study. Diagnosis of hematological malignancy was based on complete blood count (CBC), microscopic examination (blood film), bone marrow biopsy/aspirate, cytochemistry, histology, immunohistochemistry& flow cytometry (immuno-phenotyping).[7] Ocular manifestations due to direct tumor infiltration were considered primary manifestations of hematological malignancies. Manifestations due to abnormal blood parameters were considered secondary ocular manifestations. Patients with systemic disorders such as diabetes, hypertension, autoimmune disease, significant cataract obstructing the fundus view were excluded from the study. The study ultimately included 121 patients for statistical analysis.

A brief history and demographic details were obtained from each patient. Visual acuity was tested using Snellen's chart. Anterior segment evaluation was done by slit lamp. Dilated fundus examination was done on a slit lamp with a 90D lens. The peripheral fundus examination was done by indirect ophthalmoscope. Anterior and posterior segment photographs were taken.

RESULTS

This study included 121 patients diagnosed with hematological malignancy, either newly diagnosed or under treatment. The study included 56 (46.3%) newly diagnosed and 65 (53.7%) previously diagnosed patients on treatment for hematological malignancy. The mean age of the patients was 35.30 ± 14.61 years (range: 8–72 years). There were 79 (65.3%) males and 42 (34.7%) females. Maximum patients were aged 20–40 years [Table 1]. Types of hematological malignancies noted were leukemia (96 patients, 79.33%), multiple myeloma (14 patients, 11.57%), and lymphoma (11 patients, 9.09%). The majority of the patients were referred from the Department of Hematology for an ophthalmic assessment irrespective of the presence or absence of ocular symptoms. Only 5 patients (4.13%) presented directly to the Ophthalmology department with vision complaints. These 5 patients, on the basis of their ophthalmic findings, were later referred to the Hematology department and then diagnosed with a hematological malignancy.

Loss of vision was the most common complaint seen in 27 (22.31%) cases. Headache and redness of the eyes were noted in 8 (6.61%) and 6 (4.95%) cases, respectively.

Ocular manifestations were noted in 59 cases (48.76%), among which 54 patients (44.62%) were of leukemia, 3 cases (2.47%) were of lymphoma, and 2 case (1.65%) was of multiple myeloma. 62

patients (50.81%) did not have ocular manifestations during the examination. Unilateral involvement was noted in 8(13.55%) cases, and bilateral involvement was noted in 51 (86.44%) cases. Vision-threatening complications were noted in 19 patients, presenting as subhyaloidhemorrhage in 13 (10.74%) cases, exudative retinal detachment in 4 cases, and macular edema in 2 cases.

Anterior segment manifestations were noted in 9 cases (15.25%), while posterior segment manifestations were seen in all 59 patients (100%) with ocular manifestations. The most common anterior segment manifestation was subconjunctival hemorrhage (5.08%), followed by a relative afferent pupillary defect (1.6%). The most common posterior segment manifestation was intraretinal hemorrhage (76.27%), followed by preretinal hemorrhage (23.72%).

A statistically significant association was found between total red blood cell count (TRBC) with posterior segment manifestations ($p = 0.001$). Similarly, a statistically significant association was notedbetween low total platelet count (TPC) and posterior segment manifestations ($p < 0.001$).

Figure 1: Fundus photograph shows widespread intraretinal hemorrhages in both the eyes with preretinal hemorrhage in left eye

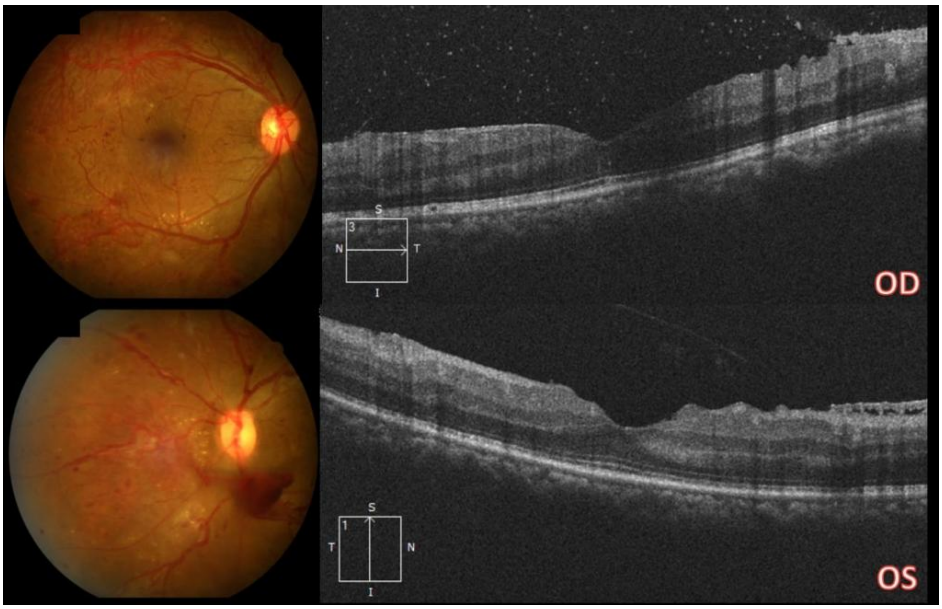

Figure 2: Fundus photograph shows gross NVE in both the eyes with preretinal hemorrhage in left eye. OCT Macula shows no macular edema in both the eyes

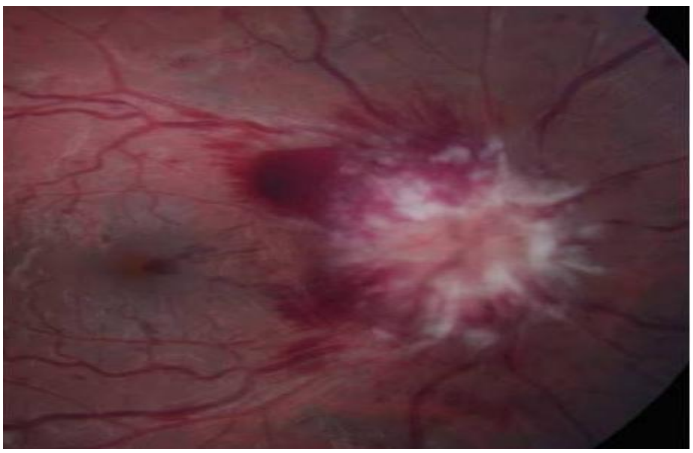

Figure 3: Fundus photograph shows Optic nerve head infiltration

DISCUSSION

Ocular manifestations in hematological malignancies have been reported in the literature, ranging from 24% to 70%.[8] This wide variation in prevalence may be due to the transient nature of ocular findings associated with hematological malignancies. The wide variance reported can also be due to the setting in which previous studies have been conducted. Results are expected to be different if the study is conducted in a primary oncology referral center as compared to angeneral hospital. Hematological malignancies may present with or be associated with ocular disorders. Therefore, recognizing the various ocular manifestations of hematological malignancy is essential to assess the course and prognosis of the disease. During the study period, 121 patients diagnosed with hematological malignancies were examined for the presence or absence of ocular manifestations and their association with blood parameters. We found this sample size adequate for evaluating the study at 95% confidence intervals. The sample size of this study is comparable with the 102 patients in a study conducted by Dhasmana R et al.,[9] 111 patients in a study conducted by Omoti AE et al.,[10] and 100 patients studied by Menon LM et al.[11]

Leukemia was the most common hematological malignancy seen in our study, followed by multiple myeloma and lymphoma, similar to the study by Eze et al.,[12] who reported the findings in 72 subjects of leukemia, and Bukhari Z et al.,[13] who also reported ALL predominance. In our study population, 13.4% of patients had BCVA less than 6/18, associated with severe posterior segment involvement and vision-threatening complications. Similar visual loss in 13.7% of patients was reported by Dhasmana R et al.,[9] which differed from Eze et al.,[12] in which visual loss was reported in 32.1% of cases. This variation is because of the transient nature of ocular findings associated with hematological malignancies.

The prevalence of ocular manifestations in the present study is 49.48%. This is comparable to the 43.8% prevalence reported in the study by Koshy J et al.[14] from Northern India and 35.4% reported in a study by Reddy SC et al.[2] from Malaysia. However, our results differ from the study by Eze B et al.[12] from Nigeria, which reported a prevalence of 77.8%. This difference may be because they have exclusively included only leukemia patients in their study.

Anterior segment manifestations were noted in six cases (12.5%), while posterior segment manifestations were seen in all 48 patients (100%) with ocular manifestations. Some subjects had more than one manifestation in one or both eyes. Anterior segment manifestations were noted in acute leukemia only. Anterior segment manifestation in subconjunctival hemorrhage was noted in 4.1% of patients. Bukhari et al.[13] reported subconjunctival hemorrhage in 11.1% of cases. This difference is because they considered only leukemia patients in their study. Posterior segment manifestations were most prominent in our study, particularly in leukemia. We noted different manifestations, with retinal hemorrhages being the most common finding, followed by cotton wool spots. [Figure 1]In 1 Patient with Chronic myeloid leukemia (CME), gross neovascularisation elsewhere (NVE) was seen in both the eyes.[Figure 2] Pan retinal photocoagulation (PRP) was done

alongwith systemic stabilisation to prevent vitreous hemorrhage. Cystoid macular edema was noted in 1 patient that resolved completely after systemic control. Neuro-ophthalmic manifestations like disc edema, optic atrophy, and optic nerve head infiltration were noted in nine cases. [Figure 3] Central retinal vein occlusion was seen in one patient each with AML and lymphoma. Similar findings were seen in various other studies as well.[11,13]

Ocular lesions are proportional to the severity of hematological malignancy and sometimes can be the presenting sign of the illness or an isolated focal relapse after complete recovery. Similarly, our study revealed one refractory ALL revealed by optic nerve head infiltration and exudative retinal detachment. Patients with multiple myeloma may present with infiltration of orbit, conjunctiva, uvea, lacrimal sac, lacrimal gland, chorioretinopathy, neuro-ophthalmic abnormalities, corneal deposits, and opportunistic infections.[15] However, none of these findings were noted in our study, possibly due to the small sample size. There is sufficient literature on ocular manifestations in hematological malignancy but minimal studies on the association of blood parameters with ocular manifestations in hematological malignancy. Some studies have shown a direct relationship between blood parameters and ocular manifestation.[9,16] Lower values of TPC, hemoglobin, TRBC, and high TLC have been associated with a higher incidence of ocular manifestations.

Retinal hemorrhages and cotton wool spots are hematological malignancy's most striking posterior segment features. Retinal hemorrhages are associated with anemia and thrombocytopenia, and venous tortuosity or occlusions are related to hyperviscosity syndrome. Development of cotton wool spots occurs due to occlusion of precapillary arterioles, which results in retinal ischemia. In this study, reduced hemoglobin ($p < 0.001$) and TRBC ($p < 0.05$) had a significant association with retinal hemorrhages and cotton wool spots while showing no association with disc edema ($p > 0.05$). Similar results were noted in the studies by Suresh K et al.,[17] Dhasmana R et al.,[9] Soman S et al.,[16] and Bukhari Z et al.[13]

The present study has a few limitations. This is a single-center hospital-based cross-sectional study. We considered a small number of patients with hematological malignancy. So the results may not reflect the exact prevalence of ocular manifestations in the general population of West Bengal. This study did not take the stage or severity of the systemic disease into consideration. The correlation of the stage of the disease with the blood parameters could have increased the clinical significance of the study. Dry eye disease has been reported to be the most common ocular manifestation in the study by Bouazza M et al.[18] The present study is not designed to evaluate dry eye disease, and this is a shortcoming of this study.

CONCLUSION

In conclusion we can say that indirect involvement of the retina is the most common ocular pathology in hematological malignancies, with intraretinal hemorrhages being the most common finding. In addition, according to our study, TLC and TPC were significant predictors of ocular manifestations in hematological malignancies. Many patients with ocular manifestations do not complain about eye symptoms.So ocular examination is highly recommended as a part of the routine examination at the time of diagnosis of hematological malignancies and during each & every follow up to diagnose any ocular manifestation.

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