OCULAR MANIFESTATIONS IN HEMATOLOGICAL DISORDERS

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ABSTRACT:

Background & Objectives: *To analyse the incidence of ocular involvement in systemic haematological disorders.*

Methods: *This was a prospective non-interventional study done on 40 patients with blood disorders diagnosed from June 2009 to August 2010. Patients with diabetes, hypertension or dense cataracts were excluded. A complete haematological work up and ocular examination was done.*

Results: *Spectrum of diseases identified included anaemia, paraproteinemia, acute lymphocytic leukaemia, acute myeloid leukaemia, chronic lymphoid leukaemia, Hodgkin's lymphoma, non-Hodgkins lymphoma. Bilateral retinopathy in the form of retinal haemorrhages was noted in 62.5% of patients, anterior segment changes and venous changes were found in 7.5% and 56.25% respectively.*

Conclusion: *Flame shaped haemorrhages was the commonest presentation(100%). Reduction in platelet count with associated endothelial hypoxic damage due to anaemia increases the presence of retinal haemorrhages.*

Key words : *anemic retinopathy, haematological disorders, ocular manifestations.*

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INTRODUCTION:

Haematological diseases encompass a wide spectrum of disorders that can present with ocular manifestations. Indeed, ocular manifestations may be the initial indication of an underlying haematological disorder. Blood disorders are one of the major health problems presenting with variable clinical manifestations. Nutritional anemia remains the common haematological abnormality especially in third world nations. The retinal metabolism is unable to tolerate this deprivation of its essential supplies with impunity for too long in anemia, falling prey to hypoxic damage in the end. Anaemic changes can thus be an indicator for the retinal damage manifesting either as haemorrhage or pallor.[1,2] Leukaemia while less prevalent, shows ocular manifestations such as roths spots, arteriolar pallor, proptosis 9-90% of the time due to direct infiltration of ocular tissue or due to an opportunistic infection or as an associated haematological abnormality.[3,4,5] Sub conjunctival and retinal haemorrhages may occur with thrombocytopenia irrespective of any aetiology. Previous reports indicate that their indeed exists a link between haematological abnormality and ocular manifestations.[6,7,8] This study was designed to evaluate the ocular abnormalities in anaemia, platelet disorders and haematological malignancies.

MATERIALS & METHODS

This prospective non-interventional descriptive study was conducted from June 2009 to August 2010 in the Department of Ophthalmology, Sri Ramachandra University (SRU). 40 patients suffering from haematological disorders were evaluated in the ophthalmology department. Exclusion criteria were patients having diabetes, hypertension, dense cataractous changes and other media opacities which prevented posterior segment examination. A proforma was devised to include patients demographical data, a brief medical history, ophthalmic history, anterior and posterior segment examinations with a haematological profile. All patients underwent detailed examination of the anterior and posterior segment which included best corrected visual acuity, slit lamp evaluation of anterior segment, intraocular pressure measurement, dilated retinal examination using direct, indirect ophthalmoscope and slit lamp biomicroscopy using volk 78 D lens. Fundus photography documentation was done in cases with positive findings. Complete haematological profile including haemoglobin levels, total leucocyte count, differential count, erythrocyte sedimentation rate, platelet count, peripheral blood smear, bone marrow study (for leukaemia and paraproteinemias) and lymph node biopsy (in case of lymphoma) was obtained and recorded.

RESULTS

Among the forty patients enrolled, the spectrum of diseases included - Leukaemia (40 %) Acute lymphocytic leukaemia (ALL) - 7 (43.75%), Acute myeloid leukaemia (AML) -7 (43.75%), Chronic lymphoid leukaemia (CLL) - 2 (12.5%), Anaemia (20 %), lymphoma (17.5%) (Hodgkins - 2, Non-Hodgkins lymphoma (NHL) - 5), paraproteinemias (12.5 %) and Idiopathic thrombocytopenic purpura(ITP)(10%). (Fig.1).

Blood disorders were more prevalent in the age group of 21-40 years (37.5%) followed by 41-60 years (32.5%).

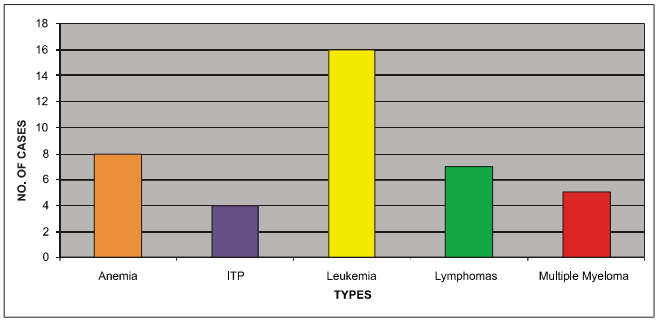

Fig. 1: Spectrum of diseases of study subjects

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Majority were males 62.5% as shown in fig. 2. Females with ocular manifestations predominated in the age group of 61-80 years.

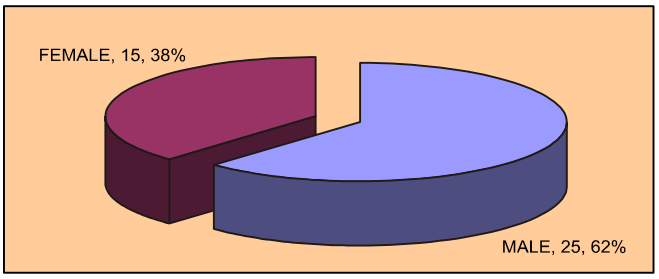

Fig. 2 – Gender related distribution of study subjects

Among the forty patients, 25 (62.5%) had retinopathy, which was mostly bilateral. Of these 58.82 % (20/34) had normocytic normochromic anaemia while 41.17% (14/34) had microcytic hypochromic anaemia on peripheral smear. Among the 8 patients with isolated anaemia and no other additional haematological abnormality was noted. Arterial pallor was found in 5 (62.5%) and background pallor in 5 (62.5%) cases. Of these 60% had Hb < 4 gm % and 40% with Hb between 4 –8 gm %. Venous pallor was present in 5 (62.5%) and dilatation of vessels in 4 (50%). Disc pallor was found in 3 cases (37.5%) of which 66.6% had Hb < 4 gm%. We also encountered anterior segment manifestations in (7.5%) of patients.

Patients who had severe anaemia with a Hb level < 4 g % had 100% venous changes, which reduced to over $^{1}/_{3}^{rd}$ when Hb was above 8g% (25%). Seven cases of anaemia (87.5%) showed retinopathic changes. Among these 57.14% had Hb levels < 4g%, 28.57 % had Hb levels between 4-8 g% and 14.28 % had levels > 8g%. Superficial haemorrhages such as flame shaped haemorrhages (5/7) were found to be most common (77.42%) followed by deep haemorrhages in 57.14% (4/7) and white centred haemorrhages in 42.85 %(3/7).(Fig.3). Among these 28.57% had a Hb level < 4g/dL. Pre-retinal haemorrhage was present in 28.57% (2/7) and sub hyaloid haemorrhage in 14.28 % (1/7) of cases. It was noted that among patients with Hb level < 4g%, all types of haemorrhages were present while deep (28.57%) and flame shaped haemorrhages were more common in cases with Hb range of 4-8 g% and > 8 g % respectively as shown in Table 1.

Variable retinal changes were seen among the 16 patients with leukaemia. Arterial pallor was noted in 56.2% of patients.[8] Among these 75% (6/8) belonged to a Hb range between 4-8g%. Retinal haemorrhages (Fig.4) were present in 50 %. A subset of this showed haemorrhages to be superficial in 100% and deep in 75%. Roth's spots (Fig.4) were found in 50% of cases among which 75% had TLC count of < 4000cells/ mm^3. Venous dilatation was found in 56.25%, background pallor in 5 (31.25%). Majority of these cases 3/5 (60%) had Hb range between 4-8g%. Retinal oedema was present in 25%, optic disc pallor in 3 (18.75%) and hard exudates in 12.5%. About 71.42% of ALL and 42.85% of AML cases showed retinal haemorrhages.

Table 1 : Types of retinal haemorrhage among study subjects

Types of Hge	In Leukemia's n = 16	In Anemia's n = 8
Flame	100%	71.42%
Roth spots	50%	42.85%
Deep	75%	57.14%
Pre-retinal	12.50%	28.57%
Subhyaloid	12.50%	14.28%

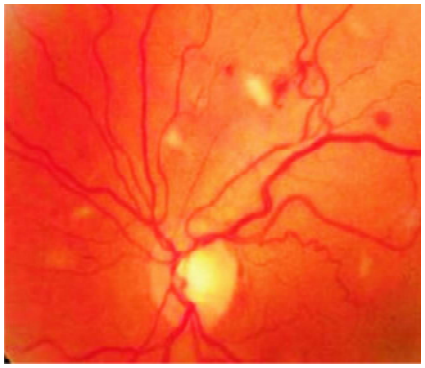

Fig. 3: Retinal haemorrhages and cotton wool spots in anaemia

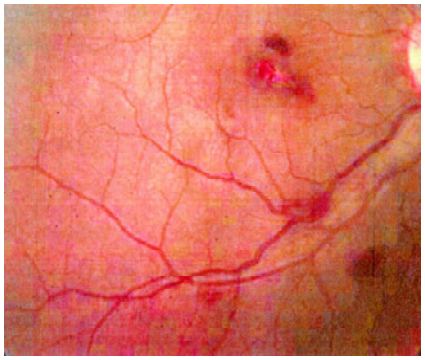

Fig. 4: Flame shaped retinal haemorrhages with Roth spots in leukaemia

Among the 4 cases of ITP background retinal findings predominated with pallor in 50%, hard exudates in 50% and retinal haemorrhage in 50%. A subset of this showed presence of sub-hyaloid haemorrhages in all cases (100%), deep and pre-retinal haemorrhages in 50 % and 75% respectively. Retinal oedema was detected in 25% of cases. Fifty percent of the haemorrhages were associated with a platelet count between 10000-20000 cells/mm^3, 25% with a count < 10000 cells/mm^3 and > 20000 cells/ mm^3 each.

All 5 patients with paraproteinemias were diagnosed with multiple myeloma wherein 40% showed retinal haemorrhages and arterial pallor in 20%.

Among the 7 cases of lymphoma, anterior and posterior segment findings were equally prevalent which included conjunctival congestion (14.28%), anterior chamber reaction (14.28%) and background retinal haemorrhage (14.28%). Patients with non Hodgkins lymphoma had a male predominance with 60 % of the tumors in males.

DISCUSSION

Hematological disease includes disorders of erythrocytes, leukocytes and platelets as well as disorders of coagulation and plasma proteins. These diseases may affect the eye either as local ocular involvement or as ophthalmic manifestations arising in the disease process. Quite often, ocular manifestations can be the presenting symptom of hematological diseases. Most patients with ocular manifestations are symptomatic requiring an ophthalmic consultation. Hematological disorders can affect any part of the eye and manifestations may vary with disease. Common manifestations include conjunctival pallor and hemorrhages, intraretinal hemorrhages and cotton wool spots. Retinal infiltrates, bleeding manifestations in eyelids, anterior segment, optic nerve, and orbit are relatively uncommon.

Majority of our patients showed a leukemic predominance (40%) followed by anaemia (20%), lymphomas (17.5%), paraproteinemias (12.5%) and ITP (10%). Male showed a greater predisposition (75:25), possibly due to the protective effect of oestrogen in women against retinopathy.

Among 34 diagnosed to have anaemia, 8 had findings of anaemia exclusively without an association with any other haematological disorder. The highest percentage of patients had normocytic, normochromic anaemia (58.82%). This was not consistent with other studies which may probably be due to small sample size. It was observed that it is the decreased amount of Hb in the blood, which leads to the subjective impression of 'pallor'. The critical Hb level was found to be 7g/dl, which was consistent with other studies.[9] The categorisation of anaemia was done as mild, moderate and severe. There was no appreciable difference in patients with disc oedema in severe versus moderate anaemia. The prevalence of pallor was found in all grades of anaemia. Arterial pallor was present in 62.5% of cases.

Flame shape haemorrhages were most frequently documented (100%) followed by deep haemorrhages (75%). Pre retinal haemorrhages were found to be more prevalent in severe anaemia (28.57%). There was no evidence of vitreous haemorrhage in our study. Either the internal limiting membrane halts the forward progress of a pre retinal haemorrhage or the formed posterior vitreous phase prevents the ingress of blood into vitreous in a sub-hyaloid haemorrhage. The prevalence of haemorrhage was found to be 41.17% for microcytic hypochromic anaemia and 58.82% for normochromic, normocytic anaemia.

Venous dilatation was the most common finding (56.25%) in acute leukemias in our study. Literature documents venous dilatation and tortuosity as the initial retinal change in leukaemias.[10] Although it may simply be an evidence of associated anaemia, the entity of anaemia in leukaemia predisposes to haemorrhage than just anaemia due to any other cause.[4,11,12]

Flame shaped haemorrhages (100%) followed by white centred haemorrhages (75%) were prevalent in all patients with anaemia or leukaemia. In most cases of leukaemia , roth spots and superficial flame shaped haemorrhages were seen.[5] However, deep haemorrhages and white centred haemorrhages occur more frequently in anaemia. Males have 3-fold greater chance of developing haemorrhages[5]. The highest prevalence of white centred haemorrhages occurs in patients with total WBC counts < 4000 cell/mm^3 and upto 25% are associated with counts in between 4000-11000. An increased prevalence is found in the group with platelet counts < 1.5 lakh.[13,14] This shows that white centred haemorrhages are linked to the severity of anaemia and lack of platelets. A finding that is inconsistent with previous studies.[11,12]

Ophthalmic manifestations of multiple myeloma can affect equally almost all ocular structures. They may be the first manifestation of the disease. In our study retinal haemorrhages predominated (40%). In Lymphoma, both anterior and posterior segment changes are equally prevalent.[10] Uveitis and extraocular muscle involvement are characteristic ocular features.[15,16] Presence of uveitis in the absence of neurological signs indicates a possibility of intra-ocular lymphoma. Review of literatures reveals non-Hodgkins lymphoma (71.42%) to be found more prevalent than Hodgkins lymphoma.[10] An anterior chamber reaction combined with restriction of extraocular movements are characteristic features to suggest an intraocular lymphoma.

This study was a onetime analysis and patients were referred to us by the concerned experts for their ophthalmic manifestations. Therefore, details of response to therapy could not be documented, a limitation of the present study. The treatment of the underlying haematological disorders was under the direct purview of the primary treating physician and could not be accessed.

CONCLUSION

This study concludes that males have greater predisposition to ocular haemorrhages as compared to females in setting of haematological abnormalities . Flame shaped haemorrhages is commonest pattern of ocular haemorrhage in hematological disorders. Thrombocytopenia of less than 1,50,000/mm^3 increases the propensity for ocular haemorrhages..

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