Original Research Article

Ocular manifestations in hemorrhagic disorders and haemoglobinopathies

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Abstract

Background: To study ocular manifestations in Hemorrhagic disorders and Haemoglobinopathies **Methods and Material:** This study was undertaken from in the department of ophthalmology. 40 cases admitted and diagnosed with various Hemorrhagic disorders and Haemoglobinopathies in Medicine, Paediatrics, wards were studied for ocular manifestations related to it. All the cases were examined for ocular manifestations in the respective wards, where the patients were admitted. Whenever general condition permitted, patients were examined in more details in the Ophthalmology O.P.D **Results:** In this study we studied 10 cases of idiopathic thrombocytopenic purpura and 10 case of Henoch-Schonlein purpura Out of these 20 cases, flame shaped haemorrhages were present in 10 cases (50%), papilloedema and dilated tortuous vessels in 5 cases (25%) and subconjuctival haemorrhage was present in 5 cases (25%) In haemoglobinopathy , we studied 20 cases 15 were of thalassemia 5 was of sickle cell disease We studied 15 cases of thalassemia major and 5 cases of sickle cell disease. Out of these 20 cases, conjunctival pallor was observed in 15 cases and fundal pallor in 10 cases .Out of 20 cases, 15 cases (75%) showed ocular manifestations **Conclusions:** To conclude Hemorrhagic disorders and Haemoglobinopathies affect thousands of people worldwide, with the potential for significant morbidity and mortality. The ocular manifestations may be the initial indication of the underlying disease. Because prompt diagnosis and treatment is critical in management of these disorders, it is essential to be aware of these changes as well as the important clinical findings associated with this disorders

Key Words: Hemorrhagic disorders, Haemoglobinopathies, purpura, Sickle cell disease

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INTRODUCTION

The blood is common to every tissue and its disease may be present in any part of body. The columns of arterial and venous blood lie exposed in the fundus of eye, so that they can be observed through the ophthalmoscope during any time of life. The ophthalmic symptoms may be initial mode of presentation so the ophthalmologist is often the first witness before the patient reaches the haematologist for final diagnosis. Haematological disorders often have ophthalmic features. There are situations where patient presents with ocular symptoms like dimunition of vision due to haemorrhage at macula, vein occlusion and many a time a leukemic child may present with proptosis. Hemorrhagic disorders such as Purpuras may present with haemorrhages involving whole of the retina and vitreous in young girls especially who suffer from Idiopathic thrombocytopnic purpura. Idiopathic thrombocytopenic purpura (ITP) is a bleeding condition in which the blood doesn't clot as it should. Haemorrhages may also occur in the lids, conjunctiva, iris and choroid. Thrombocytopenic purpura should be included as one of risk factors of expulsive choroidal haemorrhage.[1] Haemoglobinopathies

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such as Sickle cell disease which is an inherited blood disorder that affects red blood cells. People with sickle cell disease have red blood cells that contain mostly hemoglobin- S, an abnormal type of hemoglobin. Sometimes these red blood cells become sickle-shaped (crescent shaped) have difficulty passing through small blood vessels. It may present with lid edema, conjunctival sickling sign, iris atrophy, and iris neovascularisation and angioid streaks. In sickle cell thalassemia exudative and haemorrhagic changes have been found in the retina.[2] Because of the ocular symptoms and signs predominating many Hemorrhagic disorders and Haemoglobinopathies, it is important to examine the patient thoroughly, especially after mydriasis. A timely suspicion of the causative factor will enable early, prompt diagnosis and treatment of the serious haematological disorder

AIMS AND OBJECTIVES

Knowledge of ocular manifestations in Hemorrhagic disorders and Haemoglobinopathies is important not only because of frequency with which changes are seen but because eye often reflects the disease state of body . The retina is great meeting point between ophthalmology and general medicine . This study describes ocular changes in patients with haematological disorders The study was carried out with following aims

1. To study complete clinical profile of ocular manifestations in Hemorrhagic disorders and Haemoglobinopathies
2. To find out incidence of ocular manifestations in Hemorrhagic disorders and Haemoglobinopathies

REVIEW OF LITERATURE

Haemorrhagic Disorders –

Fundamentally there are three broad categories of hemorrhagic disorders.[3]

1. Biochemical defects of blood coagulation: e.g. hemophilia and Christmas disease.
2. The diseases of inadequate blood platelets: e.g. idiopathic thrombocytopenic purpura (ITP) and thrombotic thrombocytopenic purpura (TTP).
3. Vascular abnormalities: e.g Henoch - Schonlein purpura, scurvy and hereditary haemorrhagic telangiectasia. All these disorders are of concern to the ophthalmologist because even mild bleeding may be catastrophic when it occurs in or around the eye and because such bleeding may easily be induced in the course of ocular surgery. Ocular manifestations of hemophilia are primarily neurologic, resulting from central nervous system haemorrhage. Pupillary abnormalities, cranial nerve palsies, blurred vision and papilloedema have been described following intracranial bleeding.[4] Repeated retinal haemorrhages were noted in one patient with Factor XI deficiency.[5]

Purpuras are conditions characterized by multiple spontaneous capillary haemorrhages all over the body especially in the skin and mucous membrane.[6] Ophthalmologically, haemorrhages may occur in the lids, conjunctiva, iris, choroid and retina. In thrombocytopenic purpura, due to a fall in the number of blood platelets , in addition to the conjunctival haemorrhages , those in the retina , may extend into the vitreous or cause a retinal detachment. There also may be cotton wool spots, a star figure at the macula and papilloedema as well as signs of cerebral haemorrhage such as aphasia and homonymous hemianopia. Donald Lewellen and Lawrence Singerman (1980)[7] has reported a 33 year old woman of thrombotic thrombocytopenic purpura (TTP) who developed optic atrophy and bilateral neovascularization of the disc with extensive vitreous haemorrhage that progressed to traction and rhegmatogenous retinal detachment. In the vascular (nonthrombocytopenic) purpuras which may be hereditary or due to nutritional, infective or allergic factors including sensitivity to drugs and serum (Henoch-Schonlein purpura), Hemorrhages are seen in conjunctiva but retinal haemorrhages are rare (Hawthorne, 1922). Haemoglobinopathies:- This term includes a number of conditions depending on an inherited disorder of the synthesis of haemoglobin whereby mutants are formed involving haemoglobin-S (Glutamic acid replaced by Valine at β-6 globin chain position) and haemoglobin-C (Glutamic acid replaced by Lysine at β -6 globin chain position) which act as multiple alleles.[6] If a person receives a normal gene(A) from one parent and an abnormal gene from the other such as S or C, he has a heterozygous sickling trait (such as AS, AC) but rarely shows signs of disease but should two abnormal genes be transmitted the result is the development of one of the sickling disease. In the mild heterozygous forms (AS), tortuosity of the retinal vessels and vitreous haemorrhages have been noted as well as uveitis and secondary glaucoma. Sickle cell anaemia (SS) is characterized by sludging of the blood column and segmentation of the capillary flow. This may be very evident in the conjunctiva wherein the retarded flow and increased viscosity are clinically apparent. In the retina the changes are generally confined to tortuosity and engorgement of the retinal veins, together with the appearance of angioid streaks. In sickle cell haemoglobin C disease (SC), all these changes are more marked. Sickle cell thalassemia (S-thal) is an inherited abnormality of haemoglobin synthesis with a high level of foetal form (HbF). In heterozygotes (thalassemia minor) the changes are

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minimal and ocular findings are rare. In homozygotes (thalassemia major, Colley's anaemia) a severe microcytic anaemia develops characterized by the presence of target cells with systemic changes including osteoporosis, splenomegaly and cranial deformities. In thalassemia, exudative and haemorrhagic changes have been found in retina. The anterior segment of the eye may be the initial site of the sickling process. A reliable sign of sickle cell disease is the comma shaped or curlicue capillary segment that can be observed on the bulbar conjunctiva, especially in the inferior temporal quadrant. This sign has been graded according to severity, with the mildest change consisting of a long linear dilatation of an apparently continuous conjunctival vessel and the most severe consisting of multiple short , truncated vessel segments apparently isolated from the afferent and efferent vasculature.[8] Light and electron microscopic studies have demonstrated these corkscrew like vessel segments to be capillary microaneurysms tightly packed with normocytic or sickled red blood cells. In several series of cases, this sign was observed in 97 % of patients will sickle cell anaemia, in 80 % with sickle C disease and in 64 % with sickle |3-thalassemia.[3] Patrik Condon and Graham Serjeant (1972)[9] had carried out a study of ocular manifestations of homozygous sickle cell disease in Jamaican patients. Out of 76 patients, 74 i.e. 97.4% showed the conjunctival vessel anomalies like comma or corkscrew shaped vascular dilatations on the bulbar conjunctiva. Spiros Galinos *et al..* (1973)[10] have described iris atrophy in haemoglobin SC disease. Jerre Chambers *et al..* (1974)[11] have described a case of 26 years old black woman with haemoglobin SC disease who showed bilateral iris atrophy, pigment accumulation in the angles, loss of iris processes, anterior subcapsular cataract, posterior synechiae, vitreous haemorrhage, retinitis proliferans with seafan formation, retinal ghost vessels and areas of retinal capillary non perfusion. Patrik Condon and Graham Serjeant (1972)[9] in their study of 76 patients of homozygous sickle cell disease observed following ocular lesions: -

- Conjunctival vessel anomalies (19.74%),
- peripheral retinal whitening (93.4%),
- peripheral vessel disease (93.4%),
- Central retinal capillary tortuosity and dilatation with microaneurysmal formation (39.5%),
- pigmented chorioretinal lesions (32.9%),
- peripheral arterio-venous anomalies (27.6%),
- Browri mottled areas and iridescent glistening spots (13.2%),

other changes like retinal haemorrhages, retinal detachment, retinitis proliferans (1-3% cases.)

Angioid Streaks are lesions due to focal degeneration of the elastic lamina of Bruch's membrane. Angioid Streaks have been found in 1% to 10% of patients, with the incidence increasing with age.1 In study of 22 sickle cell anaemia patients done by Ghosh K. *et al..* (1998)[12], 36% of the eyes showed angioid streaks and 32% of the eyes showed evidence of arteriovenous changes in the form of beading of the veins, breaking in blood columns and no flow areas. Alan Penman *et al..* (1994)[13] gives new classification of peripheral retinal vascular changes in sickle cell disease as: -

Type I: Qualitatively normal Continuous arteriolar - venular loops with thinned capillary bed.

Type II: Qualitatively abnormal a) Capillary stumps extending into non perfused retina b) Irregular capillary border without arterior venular loops or capillary stumps,

Type III: Indeterminant

Focal areas of retinal pigment epithelial hyperplasia and migration may occur at the site of deep retinal or subretinal haemorrhages, giving rise to the distinctive "black sunburst" sign that is readily observed ophthalmoscopically.68 Fundus photography and fluorescein angiography have demonstrated that there is a complex recurrent process of closure and recanalization of the retinal vessels as the focal impactions of sickled red blood cell develop and disintegrate.[14.15]

MATERIALS AND METHODS

This study was undertaken from in the department of ophthalmology . 40 cases admitted and diagnosed with various Hemorrhagic disorders and Haemoglobinopathies in Medicine, Paediatrics, wards were studied for ocular manifestations related to it . All the cases were examined for ocular manifestations in the respective wards, where the patients were admitted. Whenever general condition permitted, patients were examined in more details in the Ophthalmology O.P.D. For the record of visual acuity, a standard Snellen's chart was used. Detailed fundus examination was done in every case after full mydriasis of both eyes. Fundus photography and Fundus Fluorescein Angiography (F.F.A.) was done in selected cases showing posterior segment lesions. Ultrasonographic study (A-scan, B-scan) was done in selected cases where media were opaque. When patients were called by respective departments for review, simultaneous ophthalmic examination and evaluation was done in the cases which presented with ocular symptoms and signs. All patients were subjected to detailed history, thorough clinical examination, routine and specific lab investigations

RESULTS

Table 1: Distribution of cases according to haematological disorder

Haematological disorder	No. of cases	Percentage
Haemorrhagic disorders	20	50 %
Haemoglobinopathies	20	50%
Total	**40**	**100%**

Out of total 40cases, 20 cases (50%) of haemorrhagic disorders**,** 20 cases (50%) of haemoglobinopathies .

Table 2: Distribution of cases according to Haemmorhagic disorder

Haemmorhagic disorders	Idiopathic thrombocytopenic purpura	Henoch-Schonlein purpura	Total
	10 cases	10 cases	20 cases

In haemmorhagic disorder, we studied 20 cases 10 were, Idiopathic thrombocytopenic purpura 10 were, Henoch-schonlein purpura

Table 3: Percentage of haemorrhagic disorders with ocular Manifestations

Total no. of cases	No. of cases with ocular manifestations	Percentage
20	16	80%

Ocular manifestations were present in 20 out of 16 cases (80%) of purpura

Table 4: Distribution of ocular manifestations in Haemorrhagic disorders (Total cases : 20)

Ocular manifestations	Idiopathic Thrombocytopenic Purpura (10 cases)	Henoch-Schonlein purpura (10 cases)	Total(20 cases)	Percentage
Subconjunctival haemorrhage	-	5	5	25%
Papilloedema	5	-	5	25%
Dilated and tortuous vessels	5	-	5	25%
Flame shaped haemorrhages	5	5	10	50%

Out of these 20 cases, flame shaped haemorrhages were present in 10 cases (50%), papilloedema and dilated tortuous vessels in 5 cases (25%) and subconjuctival haemorrhage was present in 5 cases (25%)

Table 5: Distribution of cases according to haemoglobinopathy (Total 20 cases)

Haemoglobinopathy	Thalassemia	Sickle cell disease	Total
	15 cases	5 cases	20 cases

In haemoglobinopathy , we studied 20 cases,15 were of thalassemia, 5 was of sickle cell disease

Table 6: Percentage of haemoglobinopathies with ocular manifestations

Total no. of cases	No. of cases with ocular manifestations	Percentage
20	15	75%

Out of 20 cases, 15 cases (75%) showed ocular manifestations

Table 7: Distribution of ocular manifestations in haemogiobinopathies(Total cases : 20)

Ocular manifestation	Thalassemia(15 cases)	Sickle cell disease(5 case)	Total
Conjunctival pallor	15	-	15
Fundal pallor	10	-	10

We studied 15 cases of thalassemia major and 5 cases of sickle cell disease. Out of these 20 cases, conjunctival pallor was observed in 15 cases and fundal pallor in 10 cases.

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DISCUSSION

HAEMORRHAGIC DISORDERS

We studied 10 cases of idiopathic thrombocytopenic purpura and 10 case of Henoch-Schonlein purpura.(Table 2) Out of these 20 cases, flame shaped haemorrhages were present in 10 cases (50%), papilloedema and dilated tortuous vessels in 5 cases (25%) and subconjuctival haemorrhage was present in 5 cases (25%) (Table 4). Thus Ocular manifestations were present in 20 out of 16 cases (80%) of purpura (Table 3) Rubenstein *et al.*. (1968)[16] found in their study that in thrombocytopenia with associated anaemia, the incidence of ocular haemorrhages is as high as 70% if both are severe. In thrombocytopenia alone it was 0% .(they studied 6 cases) and in anaemia alone 10% in their study. 2 cases (50%) which showed haemorrhages in our study were having associated anaemia, one with haemoglobin level 7 gm% and other with 10.8 gm%. Foster Moore (1925), Kyrieleis (1926) and others[17] have stated that, in purpura haemorrhages are usually small, superficial and near the disc. Our 2 cases also showed superficial flame shaped haemorrhages near the disc.

AEMOGLOBINOPATHIES

In haemoglobinopathy , we studied 20 cases 15 were of thalassemia 5 was of sickle cell disease (Table 5) We studied 15 cases of thalassemia major and 5 cases of sickle cell disease. Out of these 20 cases, conjunctival pallor was observed in 15 cases and fundal pallor in 10 cases (Table 7). Out of 20 cases, 15 cases (75%) showed ocular manifestations (Table 6). These changes perhaps are not specific of thalassemia major and depend more on the degree of anaemia. None of these patients showed retinal haemorrhages. These patients were all previously diagnosed cases of thalassemia major and had reported to the hospital for blood transfusions. This indicates that the disease was not freshly diagnosed and other retinal findings, if any, may have regressed.

SUMMARY AND CONCLUSIONS

This study of ocular manifestations of Hemorrhagic disorders and Haemoglobinopathies was undertaken in which 40 cases of various Hemorrhagic disorders and Haemoglobinopathies were studied for ocular manifestations. In total 40 cases, 20 cases of haemorrhagic disorders and 20 cases of haemoglobinopathies were studied. From this study, following conclusions were drawn: We studied 10 cases of idiopathic thrombocytopenic purpura and 10 case of Henoch-Schonlein purpura.

1. Out of these 20 cases, flame shaped haemorrhages were present in 10 cases (50%), papilloedema and dilated tortuous vessels in 5 cases (25%) and subconjuctival haemorrhage was present in 5 cases (25%)
2. Thus Ocular manifestations were present in 16 out of 20 cases (80%) of purpura
3. 10 cases (50%) which showed haemorrhages in our study were having associated anaemia, one with haemoglobin level 7 gm% and other with 10.8 gm% In haemoglobinopathy , we studied 20 cases 15 were of thalassemia 5 was of sickle cell disease.We studied 15 cases of thalassemia major and 5 cases of sickle cell disease. Out of these 20 cases, conjunctival pallor was observed in 15 cases and fundal pallor in 10 cases Out of 20 cases, 15 cases (75%) showed ocular manifestation.

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