RETINAL FINDINGS IN SEVERE ANEMIA

by

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Introduction

The association of ocular changes, particularly retinal changes, and anemia has been well documented.^{1,2} However, the pathogenesis of these pathologic changes are not well understood. In many areas of the world there is little opportunity to study the eye in a large group of patients with severe anemia except for those with an associated malignant disease. And consequently the number of published studies on this subject is small and most of these deal with those anemias related to leukemia or other malignancies.³

The purpose of this paper is to present a series of anemic patients and their fundus findings and correlate the findings with sex, age, severity of anemia, hookworm findings in the stool and etiology of the anemia.

Selection of Patients and Methods

The fundi of 100 patients with hemoglobin values of 9.4 gms% or less who were admitted in the Shanta Bhawan Hospital or the United Mission Bhaktapur Hospital were examined. This group ranged in age from three years to eighty two years old and included 25 patients fourteen years old or less. Examination was done with direct ophthalmoscopy after dilating the pupils with 1 percent or 2 percent homatropine or cyclopentolate hydrochloride 1 percent, phenylephrine hydrochloride 10 percent. Drawings were made of the fundi which showed retinal haemorrhages and/or exudates. These patients were diagnosed as having "anemic retinopathy." Disc pallor, vessel size etc. were not noted. Patients with diabetes or hypertension were excluded from the study. Hemoglobin values were obtained by the cyanmethemoglobin or acid-hematin methods. Many of these patients had several hemoglobin determinations and those listed are the mean values.

The etiology of the anemia was determined by clinical and laboratory methods. Many patients had multiple diagnoses, frequently of which more than one may be partially responsible for the anemia. In cases where this was felt to be the situation more than one etiology is noted. It should be noted that although tuberculosis does not usually cause more than a mild anemia,⁴ it is felt to be a contributing factor here in that if the patient's nutritional status is, at best, borderline then the anorexia secondary to tuberculosis further compromises the nutritional status and therefore becomes a factor in the etiology of the

anemia. If the patient had hookworms in his stool and no other etiology could be found for his anemia the diagnosis was anemia due to hookworm. Patients with tuberculosis and in whom no other obvious cause could be found for the anemia, the diagnosis was said to be secondary to tuberculosis although as noted above, inadequate nutrition was probably a factor in many of these patients.

Results

The study results are shown in table 1 which shows the group of patients with retinopathy, their age, sex, hemoglobin value, diagnosis and fundus findings. Tables 2 through 6 relate the anemic retinopathy with severity of anemia, age and sex of the patients, etiology of the anemia and the hookworm findings in the stool.

TABLE I

Retinal findings in 13 patients with anemic retinopathy

No.	Age	Sex	Hemoglobin gms per cent	Diagnosis	Retinal findings
1.	8	f	1.5	Aplastic anemia	bilateral hemorrhages and exudates
2.	27	m	3.4	Aplastic anemia	bilateral hemorrhages
3.	61	m	4.4	Tbc	one hard exudate
4.	25	f	4.5	Amebiasis	bilateral hemorrhages
5.	12	f	4.6	Hookworm anemia	multiple small exudates
6.	43	f	5.0	Tbc	one hard exudate
7.	61	m	6.7	Hepatic cirrhosis	one hard exudate
8.	40	f	7.0	Tbc	one soft exudate
9.	35	f	7.2	Tbc	one soft exudate
10.	62	m	7.9	Cancer of bladder	bilateral hemorrhages and exudates
11.	40	m	8.0	Hookworm anemia	one hard exudate
12.	35	f	8.0	Tbc	hemorrhages and exudates
13.	27	m	8.3	Staphylococcal septicemia and cavernous sinus thrombosis	bilateral hemorrhages

TABLE 2

Anemic retinopathy and severity of anemia

Hb gms. per cent	1-1.9	2-2.9	3-3.9	4-4.9	5-5.9	6-6.9	7-7.9	8-8.9	9-9.4
Retinopathy	1	0	1	3	1	1	3	3	0
All cases	2	2	2	4	8	9	20	40	13

TABLE 2a

Anemic retinopathy and severity of anemia

Hb. gms. per cent	less than 9.4	less than 8.0	less than 6.0
Retinopathy	13	10	6
All cases	100	47	18
Per cent with anemic retinopathy	13 per cent	21 per cent	33 per cent

TABLE 3

Anemic retinopathy and age of patients

Age	0-4	5-9	10-14	15-19	20-29	30-39	40-49	50-59	60+
Retinopathy	0	1	1	0	3	2	3	0	3
All cases	3	12	10	9	29	11	10	8	8

TABLE 3a

Anemic retinopathy and age of patients

Age	0-19	20-39	40-59	60+
Retinopathy	2	5	3	3
All cases	34	40	18	8
Per cent with anemic retinopathy	5.9 per cent	12.5 per cent	16.7 per cent	37.5 per cent

TABLE 4

Anemic retinopathy and sex of patients		
	male	female
Retinopathy	6	7
All cases	53	47

TABLE 5

Anemic retinopathy and etiology of anemia						
Diagnosis	Hookworms			and Aplastic		
	Hookworms	Tuberculosis	Tuberculosis	anemia	Other☆	Unknown
Retinopathy	3 (1)☆☆	2 (0)	3 (0)	2 (1)	3 (0)	0 (0)
All cases	37 (8)	17 (5)	23 (5)	2 (1)	6 (2)	15 (4)

☆ Amebiasis, hepatic cirrhosis, cancer of bladder, staphylococcal septicemia and cavernous sinus thrombosis, Hodgkin's disease, thalassemia.

☆☆ In brackets are the number of children under the age of 14 years old.

TABLE 6

Anemic retinopathy and hookworm findings in the stools		
Stool examinations	Hookworms present	Hookworms absent
Retinopathy	7	7
All cases	61	39

13 per cent of the patients with anemia of 9.4 gms. per cent or less had anemic retinopathy. However, 21 per cent had anemic retinopathy when the anemia was of hemoglobin values of less than 8 gms. per cent and 33 per cent had anemic retinopathy with hemoglobins of less than 6 gms. per cent. This would seem to indicate that with increased severity of anemia the greater is the percentage of cases with retinopathy. (see Table 2a)

The hemorrhages took various forms; splinter, round, punctate, flameshaped and those with white centers. Exudates were both "soft" and "hard."

The highest hemoglobin in which retinopathy was detected was 8.3 gms. per cent in a patient with staphylococcal septicemia and cavernous sinus thrombosis.

Of the 25 cases of children 14 years old and younger, two cases had retinopathy. This is in contradistinction to Merin and Freund's series of 36 children none of whom had

retinopathy although 24 had hemoglobins of no more than 7 gms. per cent.³ However none of these children had aplastic anemia and it is not known from their study if any had thrombocytopenia. Both of the children in this study were very anemic. The child with aplastic anemia had a hemoglobin of 1.5 gms. per cent and a platelet count of 60,000/mm³. The second child had a hemoglobin of 4.6 gms. per cent secondary to hookworm anemia. The platelet count on this child was not done, but there was no cutaneous evidence of thrombocytopenia.

12 per cent (two patients) of the patients with tuberculosis and no hookworms in their stool had retinopathy which consisted of exudates only while 13 per cent (three patients) of the patients with tuberculosis and who had hookworms in their stools had retinopathy. One of three had hemorrhages and exudates and the other two patients had exudates only.

8 per cent of the patients with a diagnosis of hookworm anemia had anemic retinopathy.

In comparing the frequency of retinopathy with the various age groups there is a parallel increase in the incidence of retinopathy with the increase in age groups. Age group 0-19 years old showed 5.9 per cent of the patients with retinopathy, 20-39 years old 12.5 per cent had retinopathy, 40-59 years old 16.7 per cent had retinopathy and in the 60+ age group 37.5 per cent had retinopathy. (see Table 3a)

Discussion

The manifestations of anemic retinopathy are non-specific and may closely simulate hypertensive, uremic and diabetic changes. The most frequent lesions seen are hemorrhages and exudates. However, disc pallor, optic atrophy, optic neuritis, retinal detachment and papilledema may be found.⁵ One may also see a change in the color of the arteries to approximate the color of the veins, venous engorgement and perivascular sheathing.³

The retinal hemorrhages take various forms: flameshaped, punctate, splinter, subhyaloid or intravitreal if they break through the internal limiting membrane of the retina. Occasionally the hemorrhages have white centers.^{3,6}

Exudates may occur after chronic intermittent blood loss and hemorrhages may occur more commonly after acute blood loss.⁷

There are several suggestions as to the pathogenesis of anemic retinopathy.

Rubenstein has found that when either anemia or thrombocytopenia alone is found, retinal hemorrhage is unlikely. (0 per cent in thrombocytopenia alone, 0 per cent in Cooley's anemia and hemophilia and 10 per cent in anemia alone). When the two are combined, retinal hemorrhage was found in 44 per cent of the patients. When there was severe anemia i.e., hemoglobins of less than 8 gms. per cent and a platelet count of less than 50,000/mm³ 70 per cent of the patients had ocular hemorrhage.⁶ Both of the patients in the present series who had anemia and thrombocytopenia had retinal hemorrhages.

Rubenstein suggests that as long as a sufficient number of platelets are present to ensure the integrity of the endothelial lining, ocular hemorrhages do not frequently occur even in the presence of anemia.⁶ However in this present series, 25 per cent of the patients with anemia of less than 6 gms. per cent hemoglobin and no known thrombocytopenia had anemic retinopathy. Conversely even in thrombocytopenia, retinal hemorrhages do not occur unless an anoxic anemic environment is present. Since skin hemorrhages occur in patients with thrombocytopenia without anemia, trauma is probably also a factor in the production of skin hemorrhages whereas the retina is relatively protected.⁶ Holt and Gorden-Smith also note that retinal hemorrhages do not occur when the sole abnormality in the peripheral blood is thrombocytopenia.⁷

In Merin and Freund's series there were 36 children up to and including age 14, none of which showed any anemic retinopathy, although there was no significant difference in the severity of the anemia between the children and the adults. The etiologies of the anemias were also similar. They therefore suggest that the aging of the retinal blood vessels predisposes to the deleterious effect of the anemia.³ This is also suggested in the present study where with increased age there is an increase in the incidence of retinopathy (see Table 3a).

Holt and Gorden-Smith suggest that the presence of retinal hemorrhages are related to the degree of anemia which may be a reflection of vascular damage caused by anemic hypoxia -- although retinal hemorrhages are usually not associated with other diseases causing hypoxia such as cyanotic heart disease.⁷ The present series appears to support this in that as the hemoglobin values decrease the incidence of retinopathy increases. (see Table 2a).

Holt and Gorden-Smith also suggest that leukemic tissue may infiltrate the retina and give rise to hemorrhage. And that abnormal serum proteins may disturb the integrity of the endothelial lining of the small blood vessels thereby increasing the threshold of hemoglobin concentration at which hemorrhage occur. Or that this arteriolar endothelial damage combined with a high central retinal vein pressure may produce the hemorrhages. They suggest that severe anemia may produce spasm of the retinal arterioles which causes ischemic infarct of the retina followed by exudates.⁷

Summary

In this study 100 patients with hemoglobin values of 9.4 gms. per cent or less have been examined for fundus hemorrhages and/or exudates -- "anemic retinopath." The relationship of anemic retinopathy with sex, age, severity of anemia, hookworm in the stool and the etiology of the anemia has been noted. A discussion of the various theories of the pathogenesis of anemic retinopathy is presented. This study tends to support the theories that aging of the blood vessels, severe anemia (anoxia), and thrombocytopenia with anemia are factors in the production of anemic retinopathy.

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