Ocular Findings in Children with Homozygous Sickle Cell Anemia in Nigeria

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Sickle cell anemia (SS) is characterized by both hemolysis and a tendency to vascular occlusion due to the increase in blood viscosity caused by sickled erythrocytes. The sickling of erythrocytes results in a variety of clinical signs and symptoms affecting several organs but easily observed in the eyes. Serjeant, Serjeant, and Condon,1 have shown that there is a significant relationship between the grade of conjunctival vascular abnormality and the number of irreversibly sickled cells, suggesting that these cells may be related to the genesis of the vascular anomalies. Reversible sickling also occurs in decreased oxygen tension and acidosis.2 The circulation time in the retina of patients with sickle cell hemoglobin has been shown to be longer than normal and this may also contribute to intravascular sickling.3

All these factors constitute a vicious cycle of erythrosis which lead to peripheral retinal vascular changes which have been documented by several authors.4-6 in adults. Condon, Gray, and Serjeant7 studied the retinal vascular pathology in children with SC disease before age 15 years. The present study was designed to observe the pattern of conjunctival and retinal vessel disease in children with homozygous SS disease between the ages of 5 and 14 years and to observe the evolution of the disease in a longitudinal study. The first part of the study is reported here.

MATERIAL AND METHODS

Children with routine clinical appointments at the Paediatric Sickle Cell Anaemia Clinic of the Lagos University Teaching Hospital were referred for ocular examination. The first 29 patients were examined from June to October 1975 and were invited for another examination in 1977. The remaining 73 patients were examined from April to June 1977. A total of 102 children with ages ranging from 5 to 14 years were examined but 11 children were excluded from the study because they failed to cooperate. The age and sex distribution of the remaining 91 children is shown in Table I.

The diagnosis of homozygous sickle cell anemia was based on the presence of one band in the position Hb S on starch gel electrophoresis and positive metabisulphite sickling tests.

The conjunctival vasculature was examined through a Carl-Zeiss 69 slit lamp and classified into five grades of severity on the basis of slip lamp appearance as described by Serjeant, Serjeant, and Condon.1 Examination of the fundus was performed with a Hamblin direct ophthalmoscope, Fison binocular indirect ophthalmoscope, and where indicated, with a three-mirror contact lens. Fundus photographs were taken using the Zeiss Retinophot camera.

Seven children examined in 1975 attended for re-examination in 1977.

RESULTS

There were no ocular symptoms but the conjunctival vessels were found to be abnormal in 81.3 percent of all the children as shown in Table I. Similarly, the fundus was abnormal in 58.2 percent of them as shown in Table II. The pathological retinal findings are summarized in Table III.

Conjunctival Abnormalities

This was seen in 81.3 percent of all the children but in 91.4 percent of children aged 10 years and above. All those with normal conjunctival vasculature except five were seen in the early part of the study before it was realized that the intensity of the heat from the slit lamp

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reversed the abnormality in young children. Grade 1 changes were seen in 29 children, grade 2 in 20 children, grade 3 in eight children and grade 4 in 11 children. There was a preponderance of grades 3 and 4 in the 10 to 14 year olds. Although the irreversibly sickled cells were not determined in this group of children, another study by one of us (Professor F.E.A. Lesi) has demonstrated that the ISC varies with age in a positive manner as shown by the coefficient correlation (Table IV).

**Vascular Abnormalities**

Abnormal tortuosity of the major vessels at the disc and posterior pole was seen in 25 patients (27%). Peripheral arteriolar occlusion occurred in six eyes of five patients (5%), the youngest being a five-year-old female. One boy of eight had a localized cluster of abnormal new vessels, flat on the retinal surface at the 3 o'clock position in the periphery of the left eye. As fluorescein angiography was not carried out, it is not possible to say if leakage of dye into the vitreous would have occurred.

**Whitening of the Peripheral Retina**

This was seen in 22 patients (24%) and consisted of palor of the extreme retinal periphery and was often associated with peripheral venous tortuosity. Only one quadrant was involved in 14 patients but two quadrants or more of both eyes were involved in eight patients; all except one being older than nine years.

**Pigmented Chorioretinal Lesions**

These chorioretinal scars called black sunbursts by Welch and Goldberg were seen in ten children (11%). They were usually circular lesions with scattered pigmentation often in a spiculated manner and did not interfere with vision. Condon and Serjeant state that the etiology of the lesion is doubtful but Goldberg suggests that they represent the presence of melanin and blood breakdown products. Two patients seem to confirm the latter view. In the first patient, an intraretinal hemorrhage seen two years previously had converted to a black sunburst while the center of another hemorrhage was occupied by a black sunburst in the second patient.

**Refractile Retinal Deposits**

These were seen in 11 patients (12%). Some consisted of isolated colored iridescent spots scattered in the retinal periphery while others were found in the center of circular mottled lesions.

**Retinal Hemorrhage**

Round, flat hemorrhages with well defined borders were seen peripherally in four eyes of

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**TABLE I**

AGE AND SEX DISTRIBUTION AND CONJUNCTIVAL VESSEL ABNORMALITY

<table>
<thead>
<tr>
<th>Age Group (Years)</th>
<th>Sex</th>
<th>Total Cases</th>
<th>Conjunctival Vessel Abnormality</th>
<th>No. Affected</th>
<th>Percentage Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>5-9</td>
<td>34</td>
<td>22</td>
<td>56</td>
<td>28</td>
<td>14</td>
</tr>
<tr>
<td>10-14</td>
<td>20</td>
<td>15</td>
<td>35</td>
<td>18</td>
<td>14</td>
</tr>
<tr>
<td>Total</td>
<td>54</td>
<td>37</td>
<td>91</td>
<td>46</td>
<td>28</td>
</tr>
</tbody>
</table>

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**TABLE II**

AGE AND SEX DISTRIBUTION AND RETINAL LESIONS

<table>
<thead>
<tr>
<th>Age Group (Years)</th>
<th>Sex</th>
<th>Total Cases</th>
<th>Retinal Lesions</th>
<th>No. Affected</th>
<th>Percentage Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>5-9</td>
<td>34</td>
<td>22</td>
<td>56</td>
<td>15</td>
<td>13</td>
</tr>
<tr>
<td>10-14</td>
<td>20</td>
<td>15</td>
<td>35</td>
<td>14</td>
<td>11</td>
</tr>
<tr>
<td>Total</td>
<td>54</td>
<td>37</td>
<td>91</td>
<td>29</td>
<td>24</td>
</tr>
</tbody>
</table>
TABLE III
PREVALENCE OF RETINAL LESIONS IN 91 CHILDREN WITH SS DISEASE

<table>
<thead>
<tr>
<th>Retinal Lesions</th>
<th>No. of Patients</th>
<th>No. of Eyes</th>
<th>Percentage of Patients Involved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tortuosity of major vessels</td>
<td>25</td>
<td>50</td>
<td>27</td>
</tr>
<tr>
<td>Whitening of the peripheral retina</td>
<td>22</td>
<td>31</td>
<td>24</td>
</tr>
<tr>
<td>Refractile retinal deposits</td>
<td>11</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Pigmented chorioretinal lesions</td>
<td>10</td>
<td>14</td>
<td>11</td>
</tr>
<tr>
<td>Peripheral arteriolar occlusion</td>
<td>5</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Retinal hemorrhage</td>
<td>4</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Peripheral neovascularization</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Microaneurysmal formation on optic disc</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

four patients. The second eye of one of these patients also contained a large intraretinal hemorrhage occupying almost one quadrant of the retinal periphery. At its center was a black sunburst. While one of the round hemorrhages has been noticed to evolve into a black sunburst, the others are still being watched.

Angioid streaks were not seen in this series.

DISCUSSION

In this study, selection based on ocular symptoms was avoided. Abnormalities in the conjunctival vasculature was the most frequent finding confirming the constancy of the sign in homozygous sickle cell disease. The more severe grades of conjunctival vascular abnormality were found in the older children. While these anomalies are of limited importance in the conjunctiva, they are probably representative of a generalized small vessel disease.

Severe retinal disease was very uncommon in this study. Only one patient had peripheral new vessels in one eye and peripheral arteriolar occlusion was seen in six eyes of five patients. This is in marked contrast to the findings in children with sickle cell hemoglobin C disease in whom severe changes with arteriolar occlusions were noted in 17 out of 54 patients.

The most frequent findings were abnormal tortuosity of the major vessels at the disc and posterior pole which occurred in 25 (27%) patients. The next most common finding was whitening of the retinal periphery seen in 22 (24%) patients. First described by Paton, the pallor has been attributed to retinal ischemia, and Goldberg suggested that the absence of typical cloudy swelling may result from the paucity of ganglion cells and the thinness of the retina at the extreme periphery. Condon and Serjeant, however, felt that if reflected peripheral retinal hypoxia rather than complete ischemia since it was more commonly associated with mild peripheral retinal vessel disease.

Black sunbursts were present in 11 percent of the patients. Condon and Serjeant reported this sign in 6.6 percent of their patients with homozygous sickle cell anemia even though 47 out of their 76 patients were aged 20 years and above. The same authors found the lesion in four children with sickle cell hemoglobin C disease, but three of them were 15 years old. Although black sunbursts occur in homozygous SS disease and sickle cell hemoglobin C disease, they occur more frequently in the former and possibly also have an earlier onset. It would be necessary to examine adult patients with homozygous sickle cell disease in this

TABLE IV
IRREVERSIBLY SICKLED CELLS ESTIMATIONS ACCORDINGLY TO AGE, IN Hb SS DISEASE PATIENTS

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean %</td>
<td>2.9</td>
<td>4.3</td>
<td>5.3</td>
<td>6.0</td>
<td>6.3</td>
<td>11.1</td>
<td>9.4</td>
<td>9.0</td>
<td>11.9</td>
<td>5.7</td>
</tr>
<tr>
<td>S.D.</td>
<td>1.9</td>
<td>2.5</td>
<td>3.3</td>
<td>4.0</td>
<td>4.8</td>
<td>10.6</td>
<td>2.9</td>
<td>5.3</td>
<td>6.2</td>
<td>2.5</td>
</tr>
</tbody>
</table>

Correlation coefficient = 0.5
Irreversibly sickled cells increases with age.
environment before it can be concluded that black sunbursts occur more commonly in Nigerians than Jamaicans.

A categorical statement cannot be made on the frequency of peripheral retinal vessel disease or on the macular vasculature since fluorescein studies were not carried out. However, the presence of peripheral arteriolar occlusion in six eyes of five patients and the peripheral new vessels in an eight-year-old boy show that severe vascular disease can occur even in these very young patients. The presence of intraretinal hemorrhages in five eyes which in most cases is said to be due to sudden occlusion of an adjacent arteriole is further evidence of vascular disease.

While 29 out of 54 (54%) boys had retinal disease, 24 out of 37 (65%) of the girls were thus affected suggesting a female preponderance; but the difference is not statistically significant. The average hemoglobin value for the males was 46.5 percent (6.8G) and for the females 49.7 percent (7.3G) with a range of 27 to 67 percent. It was not possible to relate the hemoglobin level with the severity of the ocular disease.

**SUMMARY**

The ophthalmological findings in 91 Nigerian children with homozygous sickle cell anemia is reported. While the most constant sign was abnormality of the conjunctival vasculature, seen in 74 (81%) of the patients, retinal lesions were found in a total of 53 (58%) patients. Only tortuosity of major vessels was seen in some patients but several others had more than one type of retinal lesion.

**REFERENCES**