CASE REPORT

CONGENITAL HEMOLYTIC ICTERUS IN A NEGRO FAMILY

By E. G. GOODMAN, M.D., and B. R. CATES, M.D.

IN a recent article by Stragnell and Smith a Negro family was studied in which three members showed definite evidence of chronic hemolysis and the presence of spherocytes in the blood. Sickling preparations were negative. This stimulated us to check the hospital records and review the literature on the subject. According to the standard textbooks of hematology, congenital hemolytic jaundice in the Negro is extremely rare. Wintrobe mentions 1 case in a Negress of "undoubtedly mixed blood." In 1945 Scherer and Cecil described a 14 year old Negro girl with hemolytic anemia. The family was investigated. A maternal uncle and maternal grandmother, both tan in color, showed microspherocytes in blood smears. Her father and paternal uncle showed no anemia and had normal fragility tests, but a slightly increased icteric index and a low grade reticulocytosis were present.

The congenital hemolytic anemias usually show a racial predilection. In general, the Mediterranean races are subject to anemia with target and oval cells, the Negro race to sickle cell anemia, and the white race (exclusive of the Mediterranean group) to hemolytic anemia with spherocytosis. Whenever any of these diseases appears in a racial group other than that in which it is usually described, the question of racial admixture must always be considered.

Recently we had the opportunity of studying a Negro family with pure Negroid features that showed all of the characteristics necessary for a diagnosis of congenital hemolytic icterus with spherocytosis as usually seen in the white race. We believe it is worth while to report such cases, especially since splenectomy is of definite value in this disease whereas in Mediterranean target-oval cell anemia and sickle cell anemia removal of the spleen does not appreciably alter the course of the disease.

CASE REPORT

G. T., a 22 year old colored married female, was seen in the Duke Hospital Dispensary on August 8, 1946, complaining of cramp-like upper abdominal pain of one week's duration. The initial episode of abdominal pain occurred seven months before her visit, when she had sharp right upper quadrant pain which lasted for about an hour and was relieved by nausea and vomiting. At that time her local physician discovered that she was anemic and that the spleen was enlarged. She was admitted to another hospital, where two transfusions of blood together with antianemic treatment were given. The upper abdominal pain was quite typical of gallbladder colic and occurred at irregular intervals up to the time of the severe episode which brought her to this hospital.

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The family history was interesting in that the patient's father died of "anemia," one sister died of "malaria" at the age of 15 years, and another sister had been anemic most of her life and had required several transfusions. One sister gave a history of gallbladder colic and another was asymptomatic but when studied here was found to have anemia, jaundice, and an enlarged spleen.

The general physical examination revealed nutrition and development to be adequate. Complexion was black (see fig. 1). Superficial lymph nodes were not palpable. The head was symmetrical, without exostosis or other bone deformities. There was definite icterus of the sclerae. There was a cardiac systolic murmur heard best over the pulmonic area. The blood pressure was 120/68. On abdominal examination, the spleen was both visible and easily palpable, the tip being felt just to the left of the umbilicus. The liver border could not be palpated. The extremities showed no ulcerations, cyanosis, or edema.

Examination of the blood showed a hemoglobin of 8.4 Gm., or 54 per cent. R.B.C. 3,250,000 per cu. mm. W.B.C. 7,000 per cu. mm. Differential formula revealed mature polymorphonuclears 67 per cent, band forms 5 per cent, eosinophils 1 per cent, basophils 1 per cent, small lymphocytes 8 per cent, large lymphocytes 9 per cent, and monocytes 8 per cent. The reticulocytes numbered 4.7 per cent. The M.C.V. was 75 cu. micra, M.C.H. 25 micromicrograms. The fresh blood showed a marked degree of hemagglutination at room temperature. There was no evidence of sickling. There were many small, dense red cells, quite typical of spherocytes. A fragility test showed the patient's cells to begin hemolyzing at 0.66 per cent saline and to be complete at 0.36 with a control showing hemolysis to begin at 0.46 and to be complete at 0.34. Bone marrow was aspirated from the sternum by puncture. There was a marked erythroblastic hyperplasia with 117 nucleated red cells to 100 leukocytes.
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Spleenic Puncture: A small amount of material was aspirated from the spleen through a No. 16 needle. This showed a mixture of small, large, and early lymphocytes. No abnormal cells were found.

The blood Kahn, Kline, Wassermann, and Mazzini tests were all strongly positive. The Van den Berg reaction was indirect with a total bilirubin of 3.2 mg per cent. The total serum protein was 8.1 Gm., albumin 4.2 Gm. per cent, globulin 3.9 Gm. per cent, giving an A/g ratio of 1.1. Urine examination was negative, the urobilinogen value (Wallace-Diamond) being 1:10. Oral cholecystogram showed the gall-bladder to concentrate the dye well. There were small areas indicative of nonopaque stones.

**Table 1.—Blood Values Before and After Splenectomy**

<table>
<thead>
<tr>
<th>Date</th>
<th>Hgb.</th>
<th>R.B.C.</th>
<th>W.B.C.</th>
<th>Ret. %</th>
<th>Serum Bilirubin</th>
<th>Mth. %</th>
<th>Fraility</th>
<th>Spherocytes</th>
</tr>
</thead>
<tbody>
<tr>
<td>8-20-46</td>
<td>8.4</td>
<td>3.25</td>
<td>7,000</td>
<td>4.7</td>
<td>3.3</td>
<td>.66-.36</td>
<td>Present</td>
<td></td>
</tr>
<tr>
<td>8-23-46</td>
<td>7.8</td>
<td>3.06</td>
<td>9,000</td>
<td>9.1</td>
<td>.62-.42</td>
<td>Present</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-27-46</td>
<td>8.8</td>
<td>3.36</td>
<td>7,700</td>
<td>11.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-28-46</td>
<td>Given 4 500 cc. transfusions preoperatively and postoperatively.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-30-46</td>
<td>15.0</td>
<td>5.77</td>
<td>16,600</td>
<td>2.4</td>
<td>.64-.28</td>
<td>Present</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9-3-46</td>
<td>14.1</td>
<td>5.31</td>
<td>10,900</td>
<td>2.9</td>
<td>.64-.28</td>
<td>Present</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9-6-46</td>
<td>14.2</td>
<td>4.59</td>
<td>5,800</td>
<td>1.5</td>
<td>.61-.62</td>
<td>Present</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10-1-46</td>
<td>12.3</td>
<td>4.70</td>
<td>8,000</td>
<td>1.5</td>
<td>.64-.28</td>
<td>Present</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 2.—Investigation of Family**

<table>
<thead>
<tr>
<th>Name</th>
<th>Relationship</th>
<th>Hgb.</th>
<th>R.B.C.</th>
<th>W.B.C.</th>
<th>Ret.</th>
<th>Serum Bilirubin</th>
<th>Urine Urobilinogen</th>
<th>Fraility</th>
<th>Spherocytes</th>
<th>Spleen</th>
<th>Gall-stones</th>
</tr>
</thead>
<tbody>
<tr>
<td>G. T.</td>
<td>Patient</td>
<td>8.4</td>
<td>3.25</td>
<td>7,000</td>
<td>4.7</td>
<td>3.3</td>
<td>Increased</td>
<td>.66-.36</td>
<td>Present</td>
<td>Enlarged</td>
<td>Present</td>
</tr>
<tr>
<td>L. G.</td>
<td>Sister</td>
<td>13.0</td>
<td>4.37</td>
<td>14,500</td>
<td>10.0</td>
<td>3.38</td>
<td>Increased</td>
<td>.50-.38</td>
<td>Present</td>
<td>Enlarged</td>
<td>None</td>
</tr>
<tr>
<td>E. B.</td>
<td>Sister</td>
<td>11.1</td>
<td>4.31</td>
<td>10,400</td>
<td>11.7</td>
<td>1.94</td>
<td>Increased</td>
<td>.70-.40</td>
<td>Present</td>
<td>Enlarged</td>
<td>Present</td>
</tr>
<tr>
<td>Mat. niece</td>
<td></td>
<td>14.4</td>
<td>4.80</td>
<td>6,450</td>
<td>1.0</td>
<td>&lt;5%</td>
<td>Normal</td>
<td>.46-.32</td>
<td>None</td>
<td>Neg.</td>
<td>None</td>
</tr>
<tr>
<td>M. A.</td>
<td>Age 32</td>
<td>17.2</td>
<td>5.28</td>
<td>6,650</td>
<td>2.7</td>
<td>&lt;5%</td>
<td>Normal</td>
<td>.46-.32</td>
<td>None</td>
<td>Neg.</td>
<td>None</td>
</tr>
<tr>
<td>L. G.</td>
<td>Age 28</td>
<td>15.8</td>
<td>5.23</td>
<td>5,150</td>
<td>1.5</td>
<td>&lt;5%</td>
<td>Normal</td>
<td>.46-.32</td>
<td>None</td>
<td>Neg.</td>
<td>None</td>
</tr>
<tr>
<td>J. B.</td>
<td>Brother</td>
<td>15.8</td>
<td>5.23</td>
<td>5,150</td>
<td>1.5</td>
<td>&lt;5%</td>
<td>Normal</td>
<td>.46-.32</td>
<td>None</td>
<td>Neg.</td>
<td>None</td>
</tr>
<tr>
<td>Sister</td>
<td>Unable to contact=&quot;asemic most of life.&quot; Has had several transfusions.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Father</td>
<td>Died of &quot;anemia.&quot;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mother</td>
<td>Living and supposedly well.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sister</td>
<td>Died of &quot;malaria&quot; at the age of 15 years.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Course in the Hospital: Spinal fluid examination showed no evidence of central nervous system syphilis. Quantitative serologic studies on the peripheral blood showed a titer high enough to rule out a false positive reaction. The patient was, therefore, given an intensive course of penicillin treatment. On August 18, 1946, a splenectomy and a cholecystectomy were done. An accessory spleen, measuring about 4 cm. in diameter, was discovered in the transverse mesocolon and removed. Before, during, and after operation the patient was given a total of 2,000 cc. of citrated blood.

Pathologic Report: Gross examination.—The spleen weighed 610 Gm. and measured 2 1 x 1 2 x 4 cm. The capsule was somewhat thickened and was covered by a fresh organizing fibrinous exudate. The cut surface of the spleen presented a congested appearance. The Malpighian bodies were particularly prominent. There was an increased amount of fibrous tissue in the trabeculations. On microscopic examination
the splenic pulp was markedly engorged by the erythrocytes, but conversely the sinusoids were empty
and stood out very prominently. The reticulo-endothelial cells showed a great deal of hemosiderin pig-
ment. The Malpighian bodies were widely separated and appeared to be reduced in number because of
the great engorgement of the splenic pulp. The findings were thought to be characteristic of those seen
in congenital hemolytic icterus. The gallbladder was distended by dark green bile and contained approxi-
mately ten small pigmented calculi.

The patient's postoperative course was uneventful and she was discharged from the hospital September
7, 1946. On a return visit she was doing quite well and her blood values were relatively normal (table 1).

Investigation of Family: Five members of the family were brought to the hospital for study. The results
are shown in table 2. Two sisters were found to have anemia, reticulocytosis, spherocytosis, jaundice,
increased fragility of erythrocytes, and enlarged spleens. One had gallstones. Two brothers and a maternal
niece showed no evidence of disease. One sister who could not be located was said to be anemic and had
been transfused on several occasions. A sister died of "malaria" at the age of 15 years and this could have
been a hemolytic crisis. The father died of "anemia." No more definite information could be obtained.
The mother is living and supposedly well.

DISCUSSION

Three members of a Negro family, all females, were studied and showed all the
criteria necessary to make the diagnosis of congenital hemolytic icterus with
spherocytosis. After the diagnosis was established in the first case, splenectomy was
performed, following which all evidence of increased hemolysis disappeared,
although the spherocytes remained in the blood and the erythrocyte fragility
remained about the same as before splenectomy. The gallbladder was also removed
as it contained stones and gallbladder colic was the primary complaint on admission.
The marked hemagglutination, which was present at room temperature when the
patient was first seen, disappeared after several days; but the cells still showed auto-
agglutination when the blood was cooled to 4°C.

Congenital hemolytic icterus with spherocytosis occurs in the Negro race, al-
though it is rare. The hospital records were examined carefully and no previous
cases in the Negro were found. From the reported cases, the disease seems to be
more common in the female. The disease itself may be quite benign and give no
symptoms unless complications occur. Cholelithiasis is one of the common com-
plications which cause the patient to seek medical advice.

Geographically, the family reported here was from South Carolina, the one re-
ported by Stragnell and Smith from "Carolina," and the family studied by Scherer
and Cecil from Virginia. The sexes of the reported cases in the Negro are as follows:
Wintrobe—female; Scherer and Cecil—female; Stragnell and Smith—one male and 2
females (brother and sisters); Goodman and Cates—3 females, giving a total of 8
cases with 7 females to 1 male.

SUMMARY

1. A Negro family is reported in which 3 sisters were found to have congenital
hemolytic icterus.
2. All members of the family observed showed strong Negroid characteristics.
   There was nothing to suggest an admixture of white blood.
3. The literature was reviewed. Including the 3 reported in this paper, 8 cases
   have been reported. The disease may be more common in the female as the reported
cases show 7 females to 1 male.
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4. Congenital hemolytic icterus, on rare occasions, occurs in the Negro race and recognizing it as such is helpful since splenectomy is of distinct value.

REFERENCES


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