Haemoglobin H disease in 2 Filipino families

McDONALD K. HORNE, III, CAROL WALTERS, AND JERRY D. REEVES

From the Department of Internal Medicine and the Department of Pediatrics, David Grant USAF Medical Center, Travis AFB, California 74535, USA

SUMMARY Haemoglobin H disease is described in successive generations of 2 Filipino families. The condition was asymptomatic. The inheritance pattern of haemoglobin H disease in these families appeared to be like that described for Thais.

Haemoglobin H disease is a form of α-thalassaemia characterised by the presence of β-chain tetramers (Hb-H) in the red cells of affected individuals. The incidence and clinical severity of the disease vary in different parts of the world. In Thailand, where haemoglobin H disease is most commonly recognised, it causes a moderately severe microcytic anaemia with hepatosplenomegaly (Wasi et al., 1969). Among American negroes, in contrast, the disease is rare and apparently is benign when it does occur (Schwartz and Atwater, 1972). The clinical features and genetics of haemoglobin H disease among Filipinos have not been well described, though evidence of an α-thalassaemic gene has been found in 5-4% of American-born Filipino infants (Koenig and Vedvick, 1975). We have recently had an opportunity to study 2 American Filipino families with haemoglobin H disease in successive generations. Our findings are reported here.

Clinical summary

All members of the families were of pure Filipino descent. In Family 1, the proposita (I.2) was gravida 3, para 3, abortus 0. She denied complications with her pregnancies and claimed to have been always in good health. Her husband (I.1) and 3 children (II.1, II.2, II.3) had similarly never been seriously ill. All the family members were of small stature. However, there was no pallor, jaundice, frontal bossing, or hepatosplenomegaly.

In Family 2, the proposita (I.2) was gravida 2, para 2, abortus 0. She had always been healthy. Her son (II.2) was completely asymptomatic, participating in competitive athletics. Only the tip of the mother’s spleen was palpable, whereas the son’s spleen extended 3 cm below the left costal margin. He also had mild frontal bossing. The husband (I.1) and the other child (II.1) from Family 2 were not available for study but were said to be in good health.

LABORATORY METHODS

Blood counts and red cell indices were obtained for the families with a Coulter-S counter. Reticulocyte counts were performed by standard methods. Red cells from each family member were stained with brilliant cresyl blue (BCB) for Hb-H inclusions (Atwater and Schwartz, 1972). Hb-A2 was quantified by microchromatography (normal, 1.5 to 3.5%) (Huisman et al., 1975). Haemoglobin electrophoresis was done by standard techniques. A bone marrow aspirate was obtained from the proposita of Family 1.

Results

FAMILY 1

The haematological data for Family 1 are presented in Table 1. The same morphological changes in the proposita (I.2) were present in the red cells of one of her sons (II.3). The blood of the other children (II.1 and II.2) contained occasional target cells and microcytes. Blood from the father (I.1) of Family 1 contained only rare target cells. A fast-moving band was found when haemoglobin from the proposita (I.2) or her son (II.3) was electrophoresed at pH 8.4 on cellulose acetate. BCB staining of the red cells from the proposita (I.2) and her son (II.3) showed plentiful inclusion bodies. Marrow from the proposita showed erythroid hyperplasia and normal iron stores. Serum iron and iron-binding capacity from all of the children were normal with saturations of 35%, 31%, and 27%.

FAMILY 2

The haematological data for Family 2 are shown in Table 2. Red cell morphological changes were similar
Haemoglobin H disease in 2 Filipino families

Table 1  Haematological data for Family 1

<table>
<thead>
<tr>
<th></th>
<th>I.1</th>
<th>I.2</th>
<th>II.1</th>
<th>II.2</th>
<th>II.3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>50</td>
<td>46</td>
<td>18</td>
<td>16</td>
<td>8</td>
</tr>
<tr>
<td>Sex</td>
<td>M</td>
<td>F</td>
<td>F</td>
<td>M</td>
<td>M</td>
</tr>
<tr>
<td>Haemoglobin (g/dl)</td>
<td>14-6</td>
<td>9-6</td>
<td>11-7</td>
<td>14-8</td>
<td>10-0</td>
</tr>
<tr>
<td>RBC (10^6/mm³)</td>
<td>4-95</td>
<td>5-44</td>
<td>5-49</td>
<td>6-35</td>
<td>5-29</td>
</tr>
<tr>
<td>MCV (µ³)</td>
<td>85</td>
<td>59</td>
<td>63</td>
<td>69</td>
<td>58</td>
</tr>
<tr>
<td>Reticulocyte count (%)</td>
<td>*</td>
<td>6-0</td>
<td>0-9</td>
<td>1-3</td>
<td>5-8</td>
</tr>
<tr>
<td>RBC morphological abnormality</td>
<td>±</td>
<td>+++</td>
<td>+</td>
<td>+++++</td>
<td>*</td>
</tr>
<tr>
<td>Hb A₂ (%)</td>
<td>0-8</td>
<td>1-4</td>
<td></td>
<td></td>
<td>1-0</td>
</tr>
<tr>
<td>RBC with BCB inclusions (%)</td>
<td>*</td>
<td>44</td>
<td>*</td>
<td>*</td>
<td>75</td>
</tr>
<tr>
<td>'Fast' haemoglobin (%)</td>
<td>*</td>
<td>8</td>
<td>*</td>
<td>*</td>
<td>12</td>
</tr>
</tbody>
</table>

* Not performed.

to those observed in I.2 and II.3 of Family 1. BCB staining revealed many red cell inclusions. Iron-binding capacity saturation for the mother was 19% and for the son 28%.

Discussion

Haemoglobin H disease was diagnosed in the mother and one son in each of these Filipino families by identification of typical changes in red cell morphology and characteristic inclusion bodies in red cells stained with BCB. Furthermore, an electrophoretically fast band of haemoglobin was found in both families. Nevertheless, the physical stigmata of thalassaemia were absent in Family 1, and limited to mild splenomegaly and frontal bossing in Family 2. None of the affected individuals had suffered unusual medical problems. Haemoglobin H disease in these families, therefore, appeared to be a benign condition.

Two other children (II.1 and II.2) in Family 1 had only subjective laboratory evidence of thalassaemia, typical of thalassaemia minor. The son (II.2) was not even anaemic. However, his red cells were microcytic, and his red cell count was raised. Both of these children had occasional target cells in their peripheral blood. The father (I.1) had no evidence of thalassaemia except a low Hb A₂.

Haemoglobin H disease has apparently never been described in successive generations in Filipinos. However, the inheritance pattern observed in the families reported here can be explained by the hypothesis proposed for the inheritance of haemoglobin H disease in Thais (Wasi et al., 1964). It is postulated that 2 thalassaenic genes exist: one allele, α-thalassaemia-1 (α-thal-1), produces thalassaemia minor in the heterozygote, and the other, α-thalassaemia-2 (α-thal-2), produces a 'silent carrier' state with no discernible disease. Haemoglobin H disease occurs in the individual who has inherited both an α-thal-1 and an α-thal-2 gene. According to this hypothesis the father (I.1) in our Family 1 is a silent carrier of the α-thal-2 gene, and his 2 children with α-thalassaemia minor (II.1 and II.2) have the α-thal-1 gene. The child with haemoglobin H disease (II.3) must have inherited an α-thal-1 gene from his mother (I.2) and an α-thal-2 gene from his father (I.1).

Similarly, the father in Family 2 must be postulated to carry either an α-thal-1 gene or an α-thal-2 gene, and the mother to be a double heterozygote (α-thal-1 + α-thal-2) with clinical haemoglobin H disease. According to this hypothesis, their offspring (II.2) received a different thalassaenic gene from each parent to develop haemoglobin H disease himself.

References


Requests for reprints to Dr M. K. Horne, Sammons Cancer Center, Baylor University Medical Center, 3500 Gaston Avenue, Dallas, Texas 75246, USA.
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M K Horne, 3rd, C Walters and J D Reeves

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