Medicine in the Elderly

Haemoglobin-H disease presenting with microcytic hypochromic anaemia in an 81 year old woman

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Summary: Over an 11 year period, the diagnosis of haemoglobin-H (Hb-H) disease was missed in a Caucasian woman of British stock who first presented with microcytic hypochromic anaemia at the age of 81. The diagnosis was confirmed at the age of 92, when the typical inclusions of Hb-H disease were demonstrated in erythrocytes stained with brilliant cresyl blue, and the presence of Hb-H was documented by haemoglobin electrophoresis. She subsequently developed biliary obstruction due either to an inflammatory polyp associated with choledocholithiasis or ampullary carcinoma.

Introduction

Haemoglobin-H (Hb-H) disease is a variant of α-thalassaemia characterized by typical inclusion bodies in the erythrocytes, and a natural history which is compatible with survival into the eighth decade. I report the case of a Caucasian woman of British stock who was 81 when she first presented with hypochromic microcytic haemolytic anaemia complicated, 11 years later, by biliary obstruction.

Case report (Table I)

In April 1979, a full blood count (FBC) from an 81 year old British Caucasian woman showed a haemoglobin (Hb) of 9.9 g/dl, mean corpuscular volume (MCV) 62 fl, mean corpuscular haemoglobin (MCH) 18.2 pg, reticulocyte count 10%, together with target cells and numerous red cell fragments in the blood film. The serum bilirubin was 49 μmol/l and serum alkaline phosphatase 66 IU/l. The significance of the stigmata of haemolysis was overshadowed by the belief that the microcytic hypochromic blood picture signified iron deficiency, especially in a woman of her age and racial stock.

In spite of iron supplements, however, she had persistent microcytosis and hypochromia, and this prompted a review of all her haematological results with the consequence that, in February 1989, the direct Coomb’s test was performed. The negative results of this test were not pursued until she presented with biochemical stigmata of obstructive jaundice the following year. Her serum bilirubin was now 57.8 μmol/l, with a serum alkaline phosphatase of 600 IU/l and gamma glutamyl transpeptidase (GGT) of 1,098 IU/l. The serum haptoglobin was 70 g/l, signifying continuing haemolysis, and the reticulocyte count varied between 2% and 4%. A blood film stained with brilliant cresyl blue showed typical inclusions of haemoglobin-H (Hb-H) disease (Figure 1). Haemoglobin electrophoresis confirmed the presence of haemoglobin-H, and further tests showed that she had α-thalassaemia with a single deletion.

The ultrasound scan showed a polypoidal filling defect at the lower end of the common bile duct which was dilated. Her serum bilirubin, alkaline phosphatase and GGT levels subsequently rose, but three weeks later had spontaneously fallen. She felt better and was discharged home, but she died unexpectedly. Postmortem showed evidence of coronary heart disease and left ventricular failure. The common bile duct was moderately dilated with no evidence of calculus in the common bile duct or malignancy in the pancreas or ampulla.

Comment

This patient showed typical haematological features of Hb-H disease: namely, characteristic inclusion bodies in the red blood cells, in association with the presence of Hb-H on haemoglobin electrophoresis. Phenotypic correlates of Hb-H disease include α-thalassaemia-1/α-thalassaemia-2 and α-thalassaemia-1/Hb CS, respectively, and also concurrence of hereditary spherocytosis and α-thalassaemia. A normal life span, with survival

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Table I  Haematological and biochemical results

<table>
<thead>
<tr>
<th>Date</th>
<th>Hb (g/dl)</th>
<th>MCV (fl)</th>
<th>MCH (pg)</th>
<th>Retics (%)</th>
<th>Bilirubin (μmol/l)</th>
<th>Alk. phos. (IU/l)</th>
<th>GGT (IU/l)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>30/4/79</td>
<td>9.9</td>
<td>62.0</td>
<td>18.2</td>
<td>10</td>
<td>49.0</td>
<td>66</td>
<td></td>
<td>LDH = 512 IU/l</td>
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<tr>
<td>14/3/84</td>
<td>11.0</td>
<td>60.0</td>
<td>18.8</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18/2/89</td>
<td>10.9</td>
<td>67.5</td>
<td>19.1</td>
<td>15</td>
<td>25.9</td>
<td>86</td>
<td>26</td>
<td>Direct Coombs test negative</td>
</tr>
<tr>
<td>4/5/90</td>
<td>9.8</td>
<td>62.4</td>
<td>17.2</td>
<td>2</td>
<td>57.8</td>
<td>600</td>
<td>1,098</td>
<td>Haptoglobin 70 g/l</td>
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<tr>
<td>13/6/90</td>
<td>10.2</td>
<td>65.0</td>
<td>17.2</td>
<td>4</td>
<td>123.9</td>
<td>637</td>
<td>792</td>
<td>Hb-H electrophoresis</td>
</tr>
<tr>
<td>4/7/90</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Died at home</td>
</tr>
<tr>
<td>19/7/90</td>
<td></td>
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</tr>
</tbody>
</table>

Retics = reticulocytes count (normal = 1–2%); serum bilirubin = 3.0–21.0 μmol/l; alkaline phosphatase (Alk. phos.) = 25–125 IU/l; gamma glutamyl transpeptidase (GGT) = 0–45 IU/l; serum lactic dehydrogenase (LDH) = 100–190 IU/l; serum haptoglobin = 50–200 g/l.

Figure 1  Multiple inclusion bodies in erythrocytes stained with brilliant cresyl blue, × 5,500.

into old age\(^2\) can be expected in patients with milder forms of this disorder, but this is not widely known, hence the perception that old age is incompatible with the diagnosis of congenital haemolytic anaemia. Hb-H disease is most prevalent in South East Asia, but has also been reported in patients of British stock.\(^5\)

In this particular instance, the subsequent development of obstructive jaundice must have been the result of impaction of a pigment stone in the lower end of the common bile duct, the polypoidal mass perhaps being an associated inflammatory polyp.\(^7\) Partial remission of biliary obstruction probably resulted from spontaneous expulsion of the pigment stone, perhaps with associated sloughing of the inflammatory polyp. In conclusion, the differential diagnosis of medical conditions presenting in old age should always include those congenital diseases which are compatible with full life expectancy.

Acknowledgement

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References

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