banding had developed in all fingernails and increased to two to three bands in each. The toenails were normal. Plasma specimens taken before, during, and after a 5-day course of combination therapy showed that ACTH levels were 55, 94, and 40 pg/ml, respectively, and β-MSH was undetectable (<50 pg/ml).

Discussion

ACTH and MSH are known to have the potential to induce darkening of human skin. It has also been shown that both hormones are capable of forming pigmented banding in fingernails (Lerner and McGuire, 1964). Bondy and Harwick (1969) reported a case of longitudinal nail banding with a markedly raised plasma MSH which appeared after bilateral adrenalectomy. This evidence indicates that the nail changes in patients with tumours could be due to an increased release of ACTH and/or MSH from the pituitary following hypoadrenalism, which is caused through some undetermined mechanism by anticancer agents. However, plasma levels of these hormones in our case do not support this. We therefore believe that an alternative hypothesis may be necessary to explain the appearance of the nail pigmentation.

Summary

In order to elucidate the mechanism of the pigmented banding in the fingernails in patients with malignant disease, plasma ACTH and β-MSH levels were determined in a 10-year-old Japanese girl with non-Hodgkin's lymphoma. The pigmented banding appeared during treatment with a combination of doxorubicin, cyclophosphamide, vincristine, and prednisone. Specimens taken before, during, and after a 5-day course of therapy showed that ACTH was 55, 94, and 40 pg/ml, respectively, and β-MSH was <50 pg/ml in all 3 samples.

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References


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Early onset of homozygous β²-thalassaemia associated with neonatal jaundice

Thalassaemia major usually manifests itself only at 2 to 3 months of age (Weatherall and Clegg, 1972; Oski and Naiman, 1972). A defect of β-chain synthesis in fact would not be expected to reduce total haemoglobin concentration and lead to a high degree of α-chain precipitation until after the first few months of life when the synthesis of γ-chain has declined sufficiently and the synthesis of β-chain predominates. This paper concerns an infant with homozygous β²-thalassaemia with onset of severe anaemia at 5–6 weeks of age after exchange transfusions for hyperbilirubinaemia of unknown aetiology.

Methods

Haematological values were determined on a Coulter Counter model ZBI. Osmotic fragility was assessed by the Simmel method (Silvestroni and Bianco, 1945). HbA₂ was determined by DE-microchromatography (Huisman et al., 1975), and HbF by the method of Singer et al. (1951). Globin chain synthesis was measured in the peripheral blood reticulocytes by methods previously described (Kan et al., 1968).
Case report

The propositus, a 2-month-old girl, was the product of the fourth pregnancy of a 33-year-old mother. The father was aged 32 years. The union was not consanguineous. Both parents were of South Sardinian extraction. The first pregnancy terminated with the birth of a stillborn male. The first 2 children are healthy.

Gestation was full term; birthweight 3.7 kg (between the 50th and 75th centiles), length 50 cm (between the 25th and 50th centiles). She was admitted on day 5 of life because of increasing jaundice associated with haematemesis noted for the first time on the first day of life.

The liver and spleen were not enlarged. Bilirubin was 28 mg/100 ml (478.8 μmol/l) with 1 mg (17.1 μmol/l) in the conjugated form. Hb was 13 g/dl; haematocrit 39%; red cell count 3.51 × 10⁶/mm³ (×10¹²/l); MCV 111 μ³ (111 fl); MCH 37 pg; and MCHC 33 g/dl. The reticulocyte count was 5% and there were 2 nucleated red blood cells per 100 white blood cells. Her blood group phenotype was A-CcDee-kk. The mother’s blood group phenotype was O-CCDee-kk. Direct and indirect Coombs’s test were negative; G6PD activity normal.

She had two exchange transfusions, each of 600 ml of whole blood on days 5 and 10 of life. On day 4, the second exchange transfusion, Hb was 7 g/dl. She then had two transfusions each of 200 ml whole blood. At day 16 enlargement of liver and spleen was noted.

At the age of 40 days she was discharged with an Hb level of 10.2 g/dl. At 2 months she was admitted to the paediatric department because since discharge the parents had noticed pallor, failure to thrive, and poor feeding. Physical examination showed marked anaemia. Weight was 4.15 kg (between the 3rd and 10th centiles), length 57 cm (between the 25th and 50th centiles). The liver was palpable 3 cm and the spleen 2 cm below the costal margins. Follow-up showed that she had thalassaemia and was highly dependent on transfusion. The transfusion programme gave an annual mean Hb level of 10.5. Annual blood consumption was 300 ml/year; the rate of fall in Hb after transfusion was 1% (% of post-transfusion Hb/day) and the transfusion quotient (Modell, 1976) was 1.3.

Haematological data of the propositus and her parents are given in the Table. Bilirubin was 0.81 mg/100 ml (13.9 μmol/l); conjugated 0.24 mg/100 ml (4.1 μmol/l). Reticulocyte count was 6% and there were 77 nucleated RBC/100 WBC. Blood smears showed hypochromia, anisopoikilocytosis, polychromasia, and marked basophilic stippling.

Smears stained with methyl violet showed no inclusion bodies. Direct and indirect Coombs’s tests were negative. Serum iron was 28 μmol/l (156 μg/100 ml) and total iron binding capacity 60 μmol/l (335.2 μg/100 ml). Red cell osmotic fragility was slightly decreased. G6PD activity was 6 μmol/g Hb (normal value 4–9), and pyruvate kinase 150 mU/10⁶ RBC (normal value 60–220). HbF was 25·42% HbA₂ 1·90%. No abnormal haemoglobin variants were detected. The heat stability test and the isopropanol precipitation test showed no unstable Hb variants. The myeloid:erythroid ratio was 0.65.

β-globin-chain synthesis was found to be undetectable. Peripheral blood smears of both parents showed slight to moderate anisocytosis and occasional target and hypochromic cells. HbA₂ was raised and HbF levels were normal in both the mother and father (Table). These data showed that both parents are heterozygous for a β-thalassaemia gene.

<table>
<thead>
<tr>
<th>Table</th>
<th>Haematological data</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Infant, at age 5 w</td>
</tr>
<tr>
<td>Hb (g/dl)</td>
<td>5.8</td>
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<tr>
<td>Haematocrit (%)</td>
<td>20</td>
</tr>
<tr>
<td>Red blood cell (× 10⁶/mm³)</td>
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<tr>
<td>MCV (μ³)</td>
<td>83</td>
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<tr>
<td>MCH (pg)</td>
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<tr>
<td>MCHC (g/dl)</td>
<td>27·6</td>
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<tr>
<td>Hb A₂ (%)</td>
<td>1·9</td>
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<tr>
<td>Hb F (%)</td>
<td>25·42</td>
</tr>
<tr>
<td>a/y ratio</td>
<td>2·51</td>
</tr>
</tbody>
</table>

Discussion

β-thalassaemia usually develops so slowly and insidiously that considerable time elapses before it becomes noticeable. Most children with thalassaemia are diagnosed by the end of the first year of life. However, a careful examination of some infants at risk followed from birth showed significant anaemia at 7 to 8 weeks of age (Oski and Naiman, 1972). Our patient showed neonatal jaundice and an earlier onset of severe anaemia with a decrease in Hb concentration to 5-6 g/dl at 8 weeks of age.

Severe jaundice in the presence of a moderate Hb level and a moderate reticulocyte count suggest acute haemolysis of recent onset rather than long-standing red cell destruction. As all other common causes of neonatal jaundice had been excluded in our patient it is possible that thalassaemia itself was the cause of the jaundice. The very rapid fall in Hb, even for a newborn, indicating an excessive red cell destruction from birth which could exceptionally occur in
thallasaemia, adds validity to the above suggestion. As shown in the follow-up data this very rapid fall in Hb was essentially limited to the first 2 months of life. Alternatively, the early onset of the disease may have been caused by the exchange transfusion performed at birth for hyperbilirubinaemia of unknown aetiology.

Blood regeneration after exchange transfusion occurs at a time when the synthesis of γ-chain has declined and the synthesis of β-chain predominates. For this reason the genetic defect of β-chain synthesis would be expressed clinically earlier than usual. This hypothesis would be correct only if the exchange transfusion had lowered the infant’s Hb. However, the low Hb level observed after the exchange transfusion was quickly corrected by transfusion of 400 ml whole blood, which should have raised her Hb to at least 17 g/dl.

From a practical point of view this paper demonstrates the use of globin-chain synthesis measurements in the identification of homozygous β-thalassaemia when haematological data are inconclusive. This should also be considered in the differential diagnosis of hypochromic anaemia developing in the first 2 months of life after exchange transfusion at birth.

Summary

An infant with homozygous β°-thalassaemia developed neonatal jaundice and severe anaemia during the first few weeks of life. It is suggested that thalassaemia itself with excessive red cell destruction from birth could be the cause of neonatal jaundice and early presentation of the disease. Alternatively, this early onset may depend on exchange transfusion performed at birth for jaundice of unknown aetiology. Globin-chain synthesis measurement is useful in the identification of homozygous β°-thalassaemia when the haematological data are inconclusive.

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References


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Chronic myeloid leukaemia in a child

A closely observed case

Chronic myeloid leukaemia (CML) is occasionally manifest in adults by the finding of a persistent neutrophil leucocytosis with no apparent cause. Signs of CML then develop and the disease pursues its usual fatal course. Philadelphia chromosome (PH\textsuperscript{1}) positive ‘adult type’ CML is rare in childhood: the Manchester Children’s Tumour Register notes only 9 cases in 23 years. We here report the case of a 12-year-old boy who was found to have a persistent leucocytosis after an operation. The PH\textsuperscript{1} chromosome was found in the marrow and 2½ years later the disease transformed into an acute leukaemia, apparently lymphoblastic and with central nervous system (CNS) leukaemia.

Case report

A Pakistani boy was found to have an undescended left testis and was admitted for orchidopexy. Preoperative Hb level was 12·3 g/dl and physical examination unremarkable; the spleen was not palpable. After a routine, uncomplicated operation he became very ill with a toxic confusional state. White cell count was 76 × 10\textsuperscript{9}/l, with 99% neutrophils showing marked ‘toxic’ granulation. Platelet count was also high (410 × 10\textsuperscript{9}/l). His temperature rose to 40°C on the second postoperative day and a clinical diagnosis of septicaemia was made although no organism was grown from the blood. There was