Case Presentation
A child with Cyanosis

BY: DR. SHAHNAZ
Name: Yasir
Age: 11 Years
Residence: Gujar Khan
Mode of admission: OPD
Date of admission: 19-11-2007
CASE PRESENTATION

PRESENTING COMPLAINTS:
Fever 10 days
Shortness of breath 10 days
Bluish discolouration of nails 5 yrs
PAST HISTORY: insignificant

FAMILY HISTORY: insignificant

BIRTH HISTORY: SVD, hospital delivered with no complications.

DEVELOPMENTAL HISTORY:

IMMUNIZATION HISTORY:
EXAMINATION

G.P.E:

Temperature: 100° F
Respiratory rate : 38/min
Pulse : 100/min, regular
B.P. : 100/80 mm of Hg
Cyanosis : Peripheral
SYSTEMIC EXAMINATION

C.V.S:
- Tachycardia
- S1+S2+0
- No added sounds

RESPIRATORY SYSTEM:
- Trachea central
- Chest movements decreased on left side
- Occasional crepts in Lt middle & lower zones

GIT: NAD

C.N.S: NAD
PROVISIONAL DIAGNOSIS

Bronchopneumonia
Methaemoglobinemia
INVESTIGATIONS

- CBC
- Chest X-Ray
- Urine R/E
- Peripheral film
- ECG
- ECHO
- Hb Studies
- Hb electrophoresis
<table>
<thead>
<tr>
<th>Tests</th>
<th>Result</th>
<th>Reference Range/Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin Studies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood counts:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TLC</td>
<td>11.1</td>
<td>4.0 - 10.0 \times 10^{9} /L</td>
</tr>
<tr>
<td>TRBC</td>
<td>5.12</td>
<td>4.5 - 5.5 \times 10^{12} /L</td>
</tr>
<tr>
<td>Haemoglobin</td>
<td>13.6</td>
<td>14.0 - 18.0 g/dL</td>
</tr>
<tr>
<td>PCV</td>
<td>0.41</td>
<td>0.39 - 0.52 L/L</td>
</tr>
<tr>
<td>MCV</td>
<td>81.6</td>
<td>77 - 91 fl</td>
</tr>
<tr>
<td>MCH</td>
<td>26.6</td>
<td>26 - 32 pg</td>
</tr>
<tr>
<td>MCHC</td>
<td>32.2</td>
<td>32 - 36 g/dl</td>
</tr>
<tr>
<td>Platelet count</td>
<td>301</td>
<td>150 - 400 \times 10^{9} L</td>
</tr>
<tr>
<td>Reticulocytes</td>
<td>1.6</td>
<td>0.5 - 2.5 \times 10^{9} /L</td>
</tr>
<tr>
<td>Red cell distribution width - SD</td>
<td>41.8</td>
<td>39.0 - 46.0 fl</td>
</tr>
<tr>
<td>Differential leukocyte count:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neutrophils</td>
<td>63</td>
<td>40 - 80 %</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>27</td>
<td>20 - 40 %</td>
</tr>
<tr>
<td>Monocytes</td>
<td>05</td>
<td>2 - 10 %</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>05</td>
<td>1 - 6 %</td>
</tr>
<tr>
<td>RBC morphology:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type</td>
<td>Normochromic and normocytic</td>
<td></td>
</tr>
<tr>
<td>Haemoglobin studies:</td>
<td></td>
<td></td>
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<tr>
<td>Haemoglobin electrophoresis shows</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemoglobin F quantitation</td>
<td>1.2</td>
<td>Cellulose acetate electrophoresis</td>
</tr>
<tr>
<td>Haemoglobin A2 quantitation</td>
<td>2.7</td>
<td>%</td>
</tr>
</tbody>
</table>

**Opinion**

Haemoglobin M disease

**Comments**

Advised: Family screening

REPORTED BY: BRIG SUHAIB AHMED

Report authorised by Col Jaleel Anwar
MANAGEMENT

SUPPORTIVE:

SPECIFIC:
  I/V antibiotics
CASE DISCUSSION

STRUCTURE OF HAEMOGLOBIN

Hemoglobin

Heme

(Fe-protoporphyrin IX)
Methemoglobin is an oxidized form of hemoglobin, which is unable to carry oxygen and lead to cyanosis.

Methemoglobinemia is a situation in which the level of methemoglobin exceeds 1%. Normally, about 3% of the total hemoglobin is daily oxidized, but already reduced by the enzymatic cytochrome b5 reductase system.
Types of Methaemoglobinemia

Two types of methemoglobinemia need to be distinguished:

- **In the first one**: normal hemoglobin is oxidized into methemoglobin.

  This may result from an increased formation of methemoglobin through the action of a toxic agent a deficiency in cytochrome b5 reductase activity (recessive congenital methemoglobinemia -RCM- of type I or II),
Second type of methemoglobinemia

The presence of a hemoglobin variant with increased auto-oxidation rate.

The presence of a variant with abnormal spectral properties named Hb M. Hbs M, were the first hemoglobin variants described.

Mutations in the HBB gene cause methaemoglobinemia, beta-globin type.
The HBB gene produces one of the subunits of haemoglobin, called beta haemoglobin or the beta chain. Mutations in specific regions of the HBB gene lead to an abnormal version of beta haemoglobin known as haemoglobin M. Haemoglobin M disrupts the normal interaction between iron and haemoglobin, which interferes with the delivery of oxygen to cells.

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.
These variants are found worldwide, and result frequently from de-novo mutations.

<table>
<thead>
<tr>
<th>Name</th>
<th>Mutation</th>
<th>Clinical presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb M-Boston</td>
<td>α58 (E7) His-</td>
<td>cyanosis starts at birth and remains at a constant level. Well tolerated</td>
</tr>
<tr>
<td></td>
<td>&gt;Tyr (α 1 or 2)</td>
<td></td>
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<tr>
<td>Hb M-Iwate</td>
<td>α87 (F8) His-</td>
<td>cyanosis starts at birth and remains at a constant level. Well tolerated</td>
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<tr>
<td></td>
<td>&gt;Tyr (α 1 or 2)</td>
<td></td>
</tr>
<tr>
<td>Hb M-Saskatoon</td>
<td>β 63 (E7) His-</td>
<td>cyanosis develops after birth and reach its final level at 6 months. Well tolerated</td>
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<tr>
<td></td>
<td>&gt;Tyr</td>
<td></td>
</tr>
<tr>
<td>Hb M-Hyde Park</td>
<td>β 67 (E11) Val-</td>
<td>cyanosis develops after birth and reach its final level at 6 months. This Hb is also unstable and leads to some degree of hemolytic anemia</td>
</tr>
<tr>
<td></td>
<td>&gt;Glu</td>
<td></td>
</tr>
<tr>
<td>Hb M-Milwaukee</td>
<td>β 63 (E7) His-</td>
<td>cyanosis starts at birth and remains at a constant level. Well tolerated</td>
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<td>&gt;Tyr</td>
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<tr>
<td>Hb F-M-Osaka</td>
<td>G γ63 (E7) His-</td>
<td>Cyanosis is maximum at birth and deceases progressively with the switch from HbF to Hb A</td>
</tr>
<tr>
<td></td>
<td>&gt;Tyr</td>
<td></td>
</tr>
<tr>
<td>Hb F-M-Fort Riplev</td>
<td>G γ92 (F8) His-</td>
<td>Cyanosis is maximum at birth and deceases progressively with the switch from HbF to Hb A</td>
</tr>
<tr>
<td></td>
<td>&gt;Tyr</td>
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</tr>
</tbody>
</table>
In the abnormal, M forms of haemoglobin (Hb Ms) amino acid substitution in or near the haem pocket creates a propensity to form methaemoglobin instead of oxyhaemoglobin in the presence of molecular oxygen.
Hb M should be considered in all patients with chronic cyanosis, especially when their pulmonary and cardiac function is normal. The greatest hazard for carriers of Hb M is misdiagnosis with the risk of expensive and hazardous cardiovascular investigations and this is specially the case for newborn babies.
Hereditary methemoglobinemia with deficiency of NADH Cytochrome b5 reductase.
# Drug Reported to Be Capable of Inducing Haemolytic Anaemia in G6PD Deficient Subjects

## Aminoquinolines
- Primaquinine
- Pamaquin
- Chloroquine
- Pentaquine
- Quinacrine (Nepacrine)
- Quinocide
- Quinine
- Hydroxychloroquine

## Analgesics
- Acetylsalicylic Acid (Aspirin)
- Acetanilide
- Antipyrine (Phenazone)
- Phenacetine (Acetophenetidin)
- Aminopyrine

## Sulphonamides
- Sulphathiazole
- Sulphanilamide
- Sulphacetamide
- Sulphafurazole
- Sulphasalazine
- Salicylazosulphapyridin
- Sulphadiazine
- Sulphamethoxyypyridazine
- Sulphadimidine
- Sulphasoxazoic
- Sulphapyridine

## Sulphones
- Avlosulfon
- D.A.P.S.
- Dubranox
- Maloprim
- Dapsone
- Solfasone
- Sulphoxone
- Thiazosulphone

## Nitrofurans
- Nitrofurantion
- Furazolidone
- Nitrofurazone

## Miscellaneous
- Napthalene (Mothballs)
- Probenecid
- Dimercaprol (BAL)
- Methylene Blue
- Acetylphenylhydrazine
- Vitamin K (& water soluble analogues e.g. Synkavit, potassium monoophosphosphate, Menadid sodium diphasphate monazodine)
- Phenylhydrazine
- Paraminosalicylic Acid
- Nalidixic Acid
- Mebarsphenamine
- Quinine (Auchone)
- Diphenhydramine (as in cough mixtures)
- Quinidine (Alkaloids)
- Chloramphenicol
- Niridazole
- Pyramidine
- Fava Bean (Broad Bean)
- Isoniazide
DIAGNOSIS
Hb Electrophoresis
A more specific diagnosis is made through spectrophotometrical studies. As compared to normal methemoglobin the absorption peaks in the visible are shifted towards a shorter wavelength (610-620 nm instead of 630 nm for normal methemoglobin). This abnormal spectrum may be difficult to recognize in the case of an or chain variant, since it only affects the abnormally oxidized hemes - ca. 10% of the total heme here.
REFERENCES


^ A Syllabus of Human Hemoglobin Variants (1996)

^ Hemoglobin Variants

NELSON TEXTBOOK OF PAEDIATRICS
THANK YOU