Case Report

Congenital Methemoglobinemia

Asma Saadia, Mohammad Haroon Yusaf, Sajid Azeem Qureshi, Asim Mumtaz

Dept. of Pathology, Shalamar Institute of Health Sciences, Lahore, Pakistan

ABSTRACT

Congenital methemoglobinemia is a rare cause of cyanosis. We report a case of a girl, 17 years old with peripheral cyanosis and normal cardio-pulmonary system. She was diagnosed as a case of methemoglobinemia based on findings of polycythemia and HbM band on hemoglobin electrophoresis. We emphasize the importance of this rare entity in the differential diagnosis of cyanosis.

Keywords: Methemoglobinemia, Congenital, Hb M, Cyanosis

Introduction

Methemoglobinemia is a rare cause of cyanosis. Most of the cases reported in literature are of the acquired type from the effects of drugs or chemicals(1) including aniline, aminophenones, chlorates, Dapsone, Prilocaine, Nitrates, Nitrobenzene, phenazopyridine, Primaquine and related anti-malarials and sulfonamides. Congenital or hereditary methemoglobinemia is even a rarer variety (2). The clinical features and long-term outcome are poorly documented and there are no systematic reviews (3). Congenital methemoglobinemia is further categorized into two main types–one due to methemoglobin reductase enzyme deficiency and the other due to an abnormal oxygen affinity hemoglobin termed hemoglobin M (2).

Cyanosis caused by abnormal forms of hemoglobin can be life-threatening, and early recognition is necessary to prevent delay in management (4). Diagnosis of the variety with abnormal hemoglobin structure and function is based on clinical suspicion when cyanosis is present with normal oxygen saturation and in the absence of any cardiopulmonary abnormality and response to ascorbic acid therapy (5). Electrophoresis is a useful tool in the determination of abnormal hemoglobin such as hemoglobin M (4). The condition is generally
asymptomatic even when the methemoglobin level is as high as 40% of total hemoglobin (6). In the patient described herein, pulmonologic and cardiologic investigations failed to yield a diagnosis which was later based upon physical findings, arterial blood gas analysis and hemoglobin electrophoresis.

Case report

We report a case of a girl, 17 years old, resident of Lahore, Pakistan who presented with bluish dusky coloration of lips, hands and feet for the last 8-9 years. Her problem of occasional shortness of breath on exertion for about two years prompted consultation. Growth and development was apparently normal. She reported that a first cousin of her had similar symptoms. The discoloration of lips was persistent and not related to the intake of any drug, any particular food, any previous illness, or any season of the year. On examination, she had peripheral cyanosis, especially on the lips and tips of hands and feet. Other systems in particular cardiovascular and respiratory systems were essentially unremarkable. No splenomegaly or hepatomegaly was noted. Laboratory investigations revealed:

- Hb: 17.3 gm/dl (normal for her age is 11.0-16.0 gm/dl)
- RBC: 5.5 x 10^6/ul (normal for age 4.0 – 6.0)
- PCV: 52.3% (normal for age 36 – 48)
- MCV, MCH and MCHC were within normal limits.
- Platelets, leukocyte count and differential count were also within normal limits.
- Reticulocytes: 1% (0.2-2.0%)
- Red cell distribution width: 53 (39-46)
- RBC morphology was normocytic-normochromic.

Arterial blood gases revealed a normal pH with PO2 at 83% (normal range 80-100%) and O2 saturation (SO2) of 96.6% (normal range 96 – 100%).

Liver function tests and thyroid function tests done were essentially normal while antinuclear antibody and C-reactive protein were negative.

ECG and echocardiography were within normal limits. Based on the above clinical history and investigations, hemoglobin electrophoresis was requested, to rule out methemoglobinemia, which revealed band of Hb M in addition to normal HbA2 and HbF and lead to the diagnosis of congenital (Hb M) methemoglobinemia.

Hemoglobin electrophoresis revealed bands of HbA and HbM. Quantitation showed 50% HbA and 50% HbM (Fig. 1). The presence of HbM band confirmed the diagnosis of Congenital methemoglobinemia (HbM disease).

Fig. 1 - Hemoglobin Electrophoresis Pattern of Patient

Discussion

Causes of cyanosis include those with decreased PaO2 and SO2 including cardiac right-to-left shunts and respiratory disorders and those with normal PaO2 and SO2 including Methemoglobinemia (7-10). Our patient had cyanosis with normal PO2 and SO2 with no findings on ECG and Echocardiography ruling out cardiopulmonary causes and indicating the possibility of any rare etiology of cyanosis.

Moreover, our case had polycythemia, indicating some hematological abnormality. Hy-
poxic causes of polycythemia include high altitude, hypoxic lung disease, cyanotic heart disease, smoking, and abnormal hemoglobin with altered oxygen affinity including methemoglobin and sulfhemoglobin (11). Methemoglobinemia is a rare disorder of hemoglobin molecule with high oxygen affinity causing tissue hypoxia. Methemoglobin is present in small amounts in normal individuals (< 1.9 gm/dl) and up to 2.8 gm/dl in full-term neonates. The patient is cyanosed when the level is more than 10% and may not become symptomatic (breathlessness, headache) even when the level is more than 40% (6-10), while a level more than 75% is incompatible with life (9).

Hemoglobin M is an abnormal hemoglobin autosomal dominant condition usually due to spontaneous mutation (1). Majority of HbM cases have histidine replaced by tyrosine in the alpha or beta globin chain and tyrosine stabilizes iron in its ferric form (1) which alters oxygen affinity of the hemoglobin molecule. Alpha chain variants present at birth while beta chain variants present later in life (2) as is the possibility in our case which started to experience the bluish discoloration of lips and extremities at about 8 years of age. Ascorbic acid (which reduces methemoglobin) and methylene blue (that activates enzyme) are used to treat methemoglobinemia (7-10). In our case methylene blue could not be of use, so only ascorbic acid therapy was advised with fortnightly follow-up.

Although congenital methemoglobinemia has been rarely observed in Pakistan (5, 12, 13), all previous cases had cyanosis as the basic abnormality as also was seen in our case. Other presenting symptoms were not well elaborated and comparable in the previous reports as the type of methemoglobinemia in hemoglobin M runs a benign course and the patients are “more blue than sick”. Furthermore, most of the previous reports were of children in neonatal period or early childhood while our case became symptomatic in adolescence. Nevertheless, congenital methemoglobinemia is a very rare but treatable cause of cyanosis and it is important to consider it as a differential diagnosis in cyanosis with polycythemia.

References