A Rare Case of Familial Methemoglobinemia with Congenital Heart Disease

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Received: 4 December 2022

Accepted: 6 February 2023

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DOI 10.5001/omj.2024.16

Abstract

Dyshemoglobins are characterized by their functional redundancy. It's a rare condition with a wide clinical spectrum. There have been few cases of congenital methemoglobinemia. A 12-year girl presented with a fever & cough and was diagnosed with covid-19 with oxygen saturation (spO2) of 85%. She was diagnosed with large ASD with PAH. ABG revealed normal PaO2 and on 100% exposure to oxygen blood turned to chocolate brown color. After treatment, the patient underwent successful ASD repair.. It is important to diagnose dyshemoglobin disorders in acutely ill patients for the avoidance of oxidizing agents and for the timely intervention to prevent life-threatening insults.

Keywords: Methemoglobinemia, congenital methemoglobinemia, cyanosis, diagnosis, heart disease.

Introduction

Methemoglobinemia is a condition characterized by the oxidation of ferrous iron to ferric iron, thereby losing the functional capacity to bind to oxygen. It can be hereditary or acquired. Hereditary methemoglobinemia is a rare condition caused by enzyme deficiency cytochrome b5 reductase, which reduces the meth-hb to normal hb with the help of NADH[1,2]. Type I deficiency is seen only in erythrocytes and type II is due to a deficiency of the membrane- bound form of the enzyme in outer mitochondrial membrane and endoplasmic reticulum. Type II will have severe developmental delay and premature death. Hemoglobin M disease is autosomal dominant inheritance, in which tyrosine amino acid is replaced for histidine in the globin chain of hemoglobin causing decreased oxygen binding capacity[4]. In these conditions, the meth-hb levels will be less than 30% and present only with central cyanosis. Acquired methemoglobinemia is a life-threatening condition leading to hypoxia, cardiac dysfunction and mortality. Intravenous methylene blue, ascorbic acid and dextrose are commonly used for the treatment.

Case Report

A 12-year girl presented with fever and cough for 5 days with mild exercise intolerance. No PND, orthopnoea, pedal edema, or decreased urine output. Clinical examination showed central cyanosis with four limb oxygen saturation of 83-85% and normal blood pressure with grade 3/6 systolic murmur in the left second intercostal space with wide-fixed split-second heart sound. She was diagnosed to have COVID-19 and a large atrial septal defect (ASD) of 14 mm with the left to right shift with mild pulmonary arterial hypertension. Atrial blood gas showed normal paO2 & pCO2. Complete blood count showed hemoglobin of 10 g/dl with normal indices, total leucocyte counts of 7000/mm^3 and platelets -200x10^9/L. Despite starting supplemental oxygen, the patient's oxygen saturation has not improved. The patient's mother was operated on for symptomatic ASD at the age of 30 and was found to have low spo2 during the follow-up. The patient's father and sister's spo2 were normal. With the above clinical picture, we had a suspicion of abnormal hemoglobin along with familial congenital heart disease. The blood sample of the patient as well as the mother gave us the diagnosis of abnormal hemoglobin chocolate brown color as shown in (fig 1) and was further confirmed by the spectrophotometric meth-hb level of 22% with a total meth-hb concentration of 2.2g/dl. She was started on oral ascorbic acid 1500mg/day and on subsequent follow up had a significant fall in the meth-hb level of less than 5%. The patient was operated on for ASD with all necessary precautions and discharged successfully.

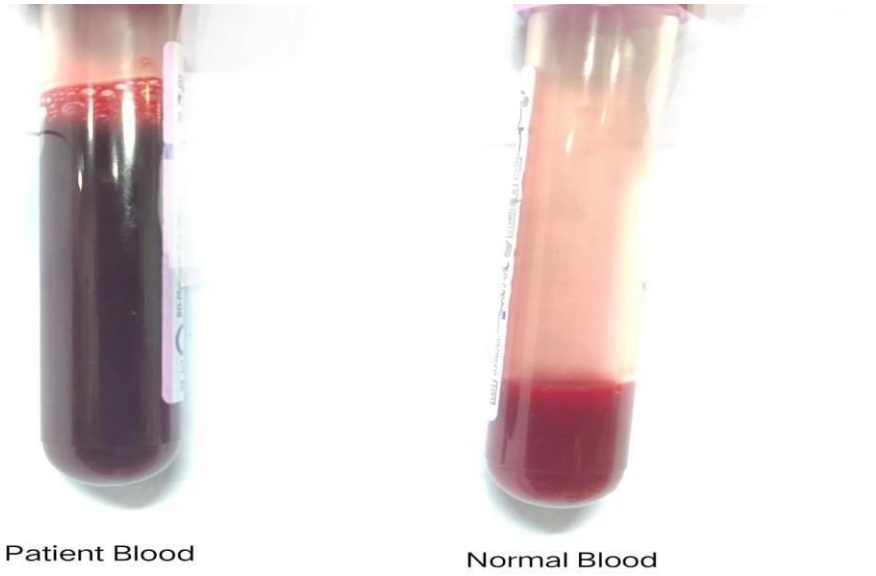

Figure 1: Patient blood depicting chocolate brown color on 100% exposure to oxygen as compared to normal blood.

Discussion

In methemoglobinemia, the oxidation of ferrous to ferric iron forms methemoglobin. The oxidation-reduction reaction always occurs in tandem with the amount of generation of free radicals by environmental exposure, dietary elements, or drug exposure. The normal range of meth-hb is 1-3%.

Methemoglobinemia can be either congenital or acquired. Congenital methemoglobinemia is a very rare condition with true incidence unknown. It can be autosomal recessive (cytochrome b5 reductase deficiency) or dominant (hemoglobin M disease) inheritance[5]. Congenital methemoglobinemia can occur

from infancy & presents with a meth-hb level of less than 30% and compensatory erythrocytosis. They predominantly manifest as central cyanosis and other signs & symptoms can be aggravated by stress & oxidant exposure[4]. On the other hand, acute toxic methemoglobinemia with levels, of more than 20% produces symptoms of hypoxia, and levels of more than 50% produce metabolic acidosis, coma, and cardiac arrhythmia. The presence of central cyanosis not improving with oxygen along with normal paO2 and SaO2 with chocolate brown color blood on exposure to 100% oxygen is diagnostic of methemoglobinemia. In the low-resource setting, the bedside quantitative color chart developed by shihana et al can be used to assess the concentration of

meth-hb. Methemoglobin levels can be measured by advanced ABG, co- oximetry, and spectrophotometry or gas chromatography-mass spectrometry. Treatment is only warranted for acquired methemoglobinemia with levels of more than 30% for asymptomatic and more than 20% for symptomatic patients. The treatment cut-off can be lowered for anemic and cardiac patients.

Congenital methemoglobinemia is a well-tolerated condition with only central cyanosis and the treatment needed in cases of oxidant stress. Methylene blue 5- 7 mg/kg 1-2 doses along with a high dose of ascorbic acid are given for symptomatic methemoglobinemia. Our patient findings (positive family history in immediate generation) point towards congenital methemoglobinemia.

Response to ascorbic acid in our case favors type 1 hereditary methemoglobinemia (autosomal recessive) -cytochrome b5 reductase deficiency[6]. However, genetic testing could not be done due to lack of facility & financial constraints.

Conclusion

We present this case to conclude that dyshemoglobin disorders are rare conditions and can manifests as a varied clinical spectrum from asymptomatic cyanosis to life-threatening cardiac dysfunction and can result in mortality if not timely recognized and intervened. Secondly, these dyshemoglobins can be masked in congenital heart disease, and if unrecognized during the surgery can get precipitated by oxidising anaesthetic agents. The treatment differs in both the type and the severity of the dyshemoglobins.

Authors' contributions

JK & KK drafted the manuscript, carried out the literature research, and prepared the illustrations. SS,GD,UK helped to draft the manuscript. All the above-mentioned authors read and approved the final manuscript.

Ethics approval and consent to participate

Written consent was obtained from the parents for the standard medical care given to their child as described in this case study.

Consent for publication

Written informed consent was obtained from the patient's parents for the publication of this case report, images, and all information contained in it.

Competing interests

The authors declare that they have no competing interests.

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