Case Report

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Methemoglobinemia & Hemolysis Secondary to Hematite (Geru Powder) Ingestion in a G6pd Deficient Patient

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Abstract

A 3 years old boy presented with h/o fever, gross hematuria and vomiting after ingesting some locally popular ayurvedic drug formulation called GERU which contains Ferric oxide. On investigations he was found to be G6PD deficient which lead to Intravascular hemolysis and Methemoglobinemia. He was aggressively and conservatively managed in a Paediatrics ICU and was discharged in stable condition after 5 days.

Keywords: G6PD Deficiency; Intravascular Hemolysis; Hemoglobinuria; Methemoglobinemia; Geru; Hematite; Toxicity; Ayurvedic Medication; Ferric Oxide; Hypoxia; Forced Alkaline Diuresis; Saturation Gap; Methylene Blue.

Introduction

Hematite is a silicate of alumina and iron oxide (ferric). It is a mineral, coloured black, brown, grey or red. In India it is popularly called as GERU and is widely used for multiple purposes. In some areas it is used for jewelry, earthen pot paints, medicinal use in allergy, headache, bleeding, constipation etc.

G6PD deficiency (Glucose-6-phosphate dehydrogenase deficiency) is an X-linked recessive genetic condition that predisposes to spontaneous destruction of red blood cells (hemolysis) and resultant jaundice in response to a number of triggers, such as certain foods, illness, or drugs.

It is commonly prevalent in people of Mediterranean and African origin but is not uncommon in Indian subcontinent as well.

It can manifest at any age when the trigerring factors come into play.

The condition is characterized by abnormally low levels of glucose-6-phosphate dehydrogenase, an enzyme involved in the pentose phosphate pathway that is especially important in the red blood cell.

There is no specific treatment, other than avoiding known triggers.

Methemoglobinemia is a disorder characterized by the presence of a high levels of methemoglobin (metHb, i.e., ferric [Fe^{3+}] rather than ferrous [Fe^{2+}] haemoglobin) in the blood.

The Ferric [Fe^{3+}] form in methemoglobin has a decreased ability to bind oxygen. However, the ferrous iron has an increased affinity for bound oxygen. The binding of oxygen to methemoglobin results in an increased affinity of oxygen to the three other heme sites (that are still ferrous) within the same tetrameric hemoglobin unit. This leads to an overall reduced ability of the red blood cell to release oxygen to tissues, with the associated oxygen–hemoglobin dissociation curve shifted to the left.

When methemoglobin concentration is elevated in red blood cells, tissue hypoxia can occurs.

Normally, methemoglobin levels are <1%, as measured by the co-oximetry test. Elevated levels of methemoglobin in the blood are caused when the mechanisms that defend against oxidative stress within the red blood cell are overwhelmed and the oxygen carrying ferrous ion (Fe^{2+}) of the heme group of the hemoglobin molecule is oxidized to the ferric state (Fe^{3+}). This converts hemoglobin to methemoglobin, resulting in a reduced ability to release oxygen to tissues and thereby hypoxia. This

can give the blood a bluish or chocolate-brown color. Spontaneously formed methemoglobin is normally reduced (regenerating normal hemoglobin) by protective enzyme systems, e.g., NADH methemoglobin reductase (cytochrome-b5 reductase) (major pathway), NADPH methemoglobin reductase (minor pathway) and to a lesser extent the ascorbic acid and glutathione enzyme systems. Disruptions with these enzyme systems lead to methemoglobinemia.

Hypoxia occurs due to the decreased oxygen-binding capacity of methemoglobin, as well as the increased oxygen-binding affinity of other subunits in the same hemoglobin molecule, which prevents them from releasing oxygen at normal tissue oxygen levels.

Here in our case, the 3 years old patient consumed Geru/Hematite powder containing Ferric oxide which lead to intravascular hemolysis and methemoglobinemia as he was a G6PD deficient patient.

Case History

GERU mineral stone

GERU in powder form

A 3 years old boy was brought to the emergency deptt at around 10pm by his parents with h/o passing grossly high coloured urine (hematuria) since 1 day, multiple episodes of vomiting and mild fever.

They also gave a h/o some allergic skin rash 2 days back for which he was given some ayurvedic drug formulation locally known as Geru powder, following which he developed the above symptoms.

He otherwise had no known medical or surgical conditions and was not allergic to any medications.

On examination, patient was conscious oriented and was in mild to moderate respiratory distress.

He had pallor (+) and icterus (+) but no cyanosis.

He had fever of 101 degree F.

Pulse was 100/min, regular. BP was 100/50 mmHg, SpO2 was only 75% at RA.

On Primary Survey

Airway

Patent

Breathing

Mild respiratory distress but equal chest rise; SpO2 75% at RA

Circulation

P 100/min, BP 100/50 mmHg, CRT <2 secs

Disability

GCS 15/15, RBS 120mg%, Pupils NSNR B/L

Exposure

No hypothermia/Rash/Deformity.

Patient was immediately taken on the monitored bed and O2 supplementation was started @15 LPM through face mask.

Two large bore IV lines were inserted and IV fluids started with (Dextrose 10% + Sodabicarb 35ml) @ 75ml/hr.

Initial ABG analysis showed

pH = 7.442,

PO2 = 32mmHg,

PCO2 = 27.9 mmHg,

Lactate = 1.23,

Methemoglobin levels = 21.3%,

Hb = 6.4gm%,

O_2 sat = 90%.

Blood samples were sent for CBC, LFT, KFT, G6PD DCT, Urine R/M, CXR.

On Secondary Survey

Neurological Exam: Conscious, oriented, No Focal Neurological deficit.

RS: AE B/L clear and equal; no adventitious sounds

CVS: S1 S2 normal; no murmur

PA: soft, non tender, BS+; No organomegaly/ guarding/rigidity.

Extremities: Normal finding; no rash.

Forced alkaline dieresis was started and Inj Frusemide was 20mg+10mg given. Blood transfusion was started with PRBC.

Nephrology and Hematology consultations were requested and the patient was shifted to PICU after 2 hrs of aggressive management in the ER.

Course in PICU

Investigations showed:

LFT was deranged – Indirect Hyperbilirubinemia.

CRP was raised.

CBC showed raised TLC 24,000/cmm

DCT was negative.

KFT was normal.

CXR was normal.

Total Iron levels 497 mcg/dl [Normal adult = 50-170, Children = 50-120]

G6PD report showed deficiency of the enzyme (1.36 Units/gm Hb) [5-20].

Blood Peripheral Smear examination showed Normocytic Normochromic Anemia with e/o *HAEMOLYSIS* with No e/o basophilic stippling.

In view of fever, raised TLC and CRP, Piperacillin+Tazobactum was started @1gm IV TDS.

Lasix infusion was started @ 0.2mg/kg/hr.

Vitamin C was started at 500mg/day orally.

After 12 hrs of presentation, patient's respiratory distress decreased and Urine output started improving and MethHb levels reduced to 7.1%

After 2 PRBC infusion, Hb was 12gm/dl.

Patient started maintaining SpO2 with minimal O2 requirement.

Sodabicarb infusion was stopped when the Bicarb levels started rising.

After 48 hrs, MethHb levels reduced to 2.6%.

After 72 hrs, urine colour started improving (became lighter coloured) and finally became normal coloured and

Bilirubin levels also normalized.

Total iron levels reduced to 120.

He was shifted to ward after 4 days of ICU stay and was discharged in stable condition after 5 days of hospitalization.

During the entire hospital stay, the pt was having normal higher mental functions and was on improving trend since the start of the treatment.

Discussion

This 3 yrs old boy with G6PD deficiency had Intravascular hemolysis with hemoglobinuria with methemoglobinermia.

He developed the symptoms after ingesting a locally popular ayurvedic medication formulation called GERU powder which is actually HEMATITE that contains Silicate of Aluminate and Ferric oxide.

This ferric oxide in G6PD deficient patient lead to intravascular hemolysis and methemoglobinemia.

The presence of met-Hb should be suspected when the oxygen saturation as measured by pulse oximetry is significantly different from the oxygen saturation calculated from arterial blood gas analysis (saturation gap),as evident in this case.

Methemoglobinemia was indicative when the Pulse oximetry SpO2 was 75% and the ABG O2 saturation was 90% . There was a significant gap between the 2 values.This was confirmed when the MethHb levels were shown to be raised.

The patient was managed conservatively and aggressively with supplemental oxygen, forced alkaline diuresis, blood transfusion, antibiotics, adequate hydration and he was treated successfully.

Met-Hb is usually treated with 100% oxygen and 1% methylene blue solution.

The methylene blue acts as an electron acceptor for NADPH met-Hb reductase. NADPH is then generated via the pentose phosphate pathway.

Methylene blue however, is contraindicated in G6PD deficiency since the reduction of met-Hb by

methylene blue is dependent upon NADPH generated by G6PD. As a result, methylene blue may not only be ineffective but is also potentially dangerous, since it has an oxidant potential that may induce hemolysis in G6PD deficient subjects.

If methylene blue is contraindicated, moderate doses of ascorbic acid (300 to 1000 mg/day orally in divided doses) should be given, as it may also cause oxidant hemolysis in G6PD-deficient patients when given in very high doses.

Conclusion

G6PD deficient patients can manifest symptoms any time in life especially when exposed to oxidative stress.

The can present with intravascular hemolysis and methemoglobinemia leading to hypoxia and death.

Methylene blue therapy, which is usually used for methhemoglobinemia, is contraindicated in G6PD deficient patients.

Removal of triggering factor and conservative management and treatment of the root cause of the disease are the mainstay of treating such patients.

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