

Phenol poisoning - Induced Acute Oxidative Haemolysis with Methemoglobinemia in Glucose-6- Phosphate Dehydrogenase (G6PD) Deficiency

Harsha G¹, Mohammad Shan Ansari², Gaurav Singh³, Jaivik patel⁴

¹PG 3rd Year MD Department of Medicine VMMC and Safdarjung Hospital, New Delhi

²Senior Resident Department of Medicine, VMMC and Safdarjung Hospital, New Delhi

³Senior Resident Department of Medicine, VMMC and Safdarjung Hospital, New Delhi

⁴PG 2nd Year Department of Medicine, VMMC and Safdarjung Hospital, New Delhi

Received: 18-04-2024 / Revised: 21-05-2024 / Accepted: 26-06-2024

Corresponding author: Harsha G

Conflict of interest: Nil

Abstract:

We Present a Patient of Phenol Poisoning Induced Acute Haemolysis with Methemoglobinemia with Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency. G6pd Deficiency Commonly Presents with Acute Intravascular Haemolysis Precipitated by Oxidative Stress Induced by Various Infections, Medications and Drugs. Additionally, We Discuss the Mandatory Requirement of G6pd Analysis Before Methylene Blue Injection.

Keywords: Glucose-6-phosphate-dehydrogenase, Phenol, Methanol poisoning, Hemolysis, Methaemoglobinemia, Methylene Blue.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Phenol Is an Organic Aromatic Compound Found in Phenyl Products Lavatory Disinfectant Solutions, Which Is a Household Item. It Is Commonly Used as Disinfectant in Households, Work Places, And Hospitals. Ingestion Of Phenyl with Intention of Self-Harm Is Very Common Which Mainly Causes Local Complications in Oral Cavity, Pharynx and Oesophagus but In Rare Cases Can Cause Oxidative Haemolysis in Patients with Glucose-6- Phosphate Dehydrogenase (G6PD) Deficiency¹. We Report A Case Who Developed, Intravascular Haemolysis with Methemoglobinemia Following Alleged Ingestion of Black Phenyl.

Case Presentation

A 22 Year Old Previously Healthy Male Presented With Throat Pain, Nausea And Vomiting, After Alleged Ingestion Of Black Phenyl Around 6 Hours Ago After Having Heated Argument With His Father. Patient Was Clinically Stable at Presentation with Normal Vitals, Systemic and General Examination Findings. Patient Had No History of Comorbidities, Or Addiction History. He Was Admitted Chest X Ray, Electrocardiogram, Arterial Blood Gas Analysis Were Unremarkable and Hemogram and Basic Biochemistry Blood Samples Were Un Remarkable with Haemoglobin Being 11 G/Dl and Surgical Advice Sought for Upper GI Endoscopy Which Was Done As Per The

Caustic Acid Ingestion Protocol And It Was Unremarkable, Patient Was Conservatively Managed With Vitals Monitoring. Day 2 Of Admission Patient Starts Complaining of Fatigue, Restlessness and Shortness of Breath. With 88% Oxygen Saturation On high flow mask 15 Litres pf O₂, RR 26/Min on Arterial Blood Gas Analysis Methaemoglobin Was 8% With Rest Unremarkable. Given His Poor Oximetry Reading and Increased Methaemoglobin Level, Methemoglobinemia Diagnosis Was Made and Injection Methylene Blue Was Given At 1g/Kg Infusion Over 2 hrs, But Patient's Clinical Status Starts Deteriorating and He Started Complaining Worsening of Shortness Of Breath, Jaundice And Black cola Coloured Urine and Serial Arterial Blood Gas Analysis Depicting Increasing Trends Of Methaemoglobin Level From 8 To 23%, Fall In Haemoglobin From 11g/Dl To 4g/Dl, Raising Levels Of Indirect Bilirubin From 1 Mg/Dl To 12 Mg/Dl, Other Markers Of Haemolysis Increased Lactate Dehydrogenase, Decreased Serum Haptoglobins, And Peripheral Smear Demonstrating Haemolysis. Haematology Advice was Sought and Methylene Blue Was Withheld, G6PD Levels Were Sent and It Was Noted That Patient Had Acute Intravascular Haemolysis. Patient Was Given with Serial Packed Red Blood Cell Transfusions for Maintaining Haemoglobin More Than 8g/Dl and Adequate Hydration Was

Maintained with Intravenous Fluids and Also Addition Of IV N Acetyl Cysteine And Oral Vitamin C Was Put In View Of Oxidative

Haemolysis, Patient Improved And Was Found To Have G6PD Deficiency.



Figure: 1



Figure: 2

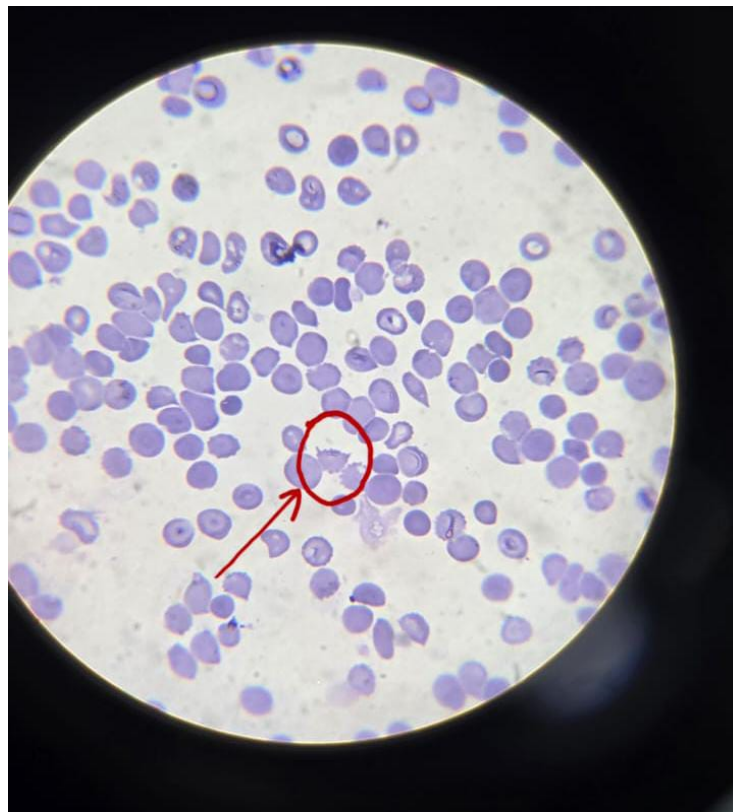


Figure: 3

Table 1:

	Day 1	Day 2	Day 3	Day 4	Day 4	Day 5	Day 6
SpO ₂ %	95	94	95	95	95	95	94
PO ₂	85 mm hg						
Meth Hb %	2	8	16	23	12	4	3
Haemoglobin g/dl	11	10	4	3	7	9	9
MCV cubic mm	85	98	112	114	113	110	106
Platelets cubic mm	105	110	145	158	155	210	323
Total counts Cubic mm	6	7	6	6	6	9	6
SGOT u/l	147	165	485	131	105	76	45
SGPT u/l	32	122	211	164	139	87	48
ALP u/l	67	111	178	189	102	88	79
Total bilirubin mg/dl	1.8	2.1	15.4	8.4	5.4	3.0	2.0
Direct	0.8	1	5	2.1	1.4	1.5	1
Indirect	1	1.1	10.4	6.3	4	1.5	1
Creatinine mg/dl	0.8	0.8	1.8	1.7	1.4	1.3	0.8
Lactate dehydrogenase u/l			1873	1600			200
Serum haptoglobin mg/dl				2.4 (40 – 280)			
G6PDU/G hb	3.9 (4.6 – 13.5)						
Peripheral smear	haemolysis						
ECG	normal						
Chest Xray	normal						

Discussion

G6PD Deficiency Should Be Considered in Patients Particularly Those of African, Asian, Or Mediterranean Descent Who Experience Haemolytic Anaemia After Exposure to Known Oxidative Stressors, Such as Oxidative Medications, infection, and fava beans[2,3,4]. The free radicals oxidize Fe²⁺ in the haemoglobin to Fe³⁺ leading to the production of methaemoglobin [5,6]. Methaemoglobin is unable to bind to oxygen, unlike regular haemoglobins. In our patient, we were alarmed by the SpO₂, which persistently showed 70%-80% under room air, improving to merely 90% under a high flow mask with 15L/min oxygen. This is due to methaemoglobin equally absorbing both the red and infrared lights emitted by the pulse oximetry probe, thus leading to oxygen saturation interpreted to be falsely low by the oximetry probe[7]. Methylene blue reduces methaemoglobin to haemoglobin by accepting electrons from NADPH (nicotinamide adenine dinucleotide phosphate hydrogen methaemoglobin), thus is also used for the treatment of methemoglobinemia, however, it should not be used in patients with G6PD deficiency. This is because NADPH production requires G6PD enzyme activity[8]. In our case methylene blue was given before evaluating G6PD level which worsened the oxidative haemolysis caused by phenol compounds where methylene blue acting as a second haemolytic agent. Similar methhaemoglobinemia and acute haemolysis after ingestion of naphthalene is also been reported[9].

Conclusions

Though local complications are ruled out it is imperative to monitor patients of phenol poisoning for possible intravascular haemolysis as in our case where patient had developed complications on day 2 of admission, Methaemoglobinemia and intravascular haemolysis requires high index of clinical suspicion, low pulse oximetry value and normal arterial blood gas analysis value should make one highly suspicious about methaemoglobinemia although methylene blue is the treatment of choice for methaemoglobinemia one as to mandatorily evaluate for if ongoing haemolysis and evaluate for g6pd levels before methylene blue injection.

References

1. Khatua CR. Intravascular hemolysis in black phenyl poisoning - two case reports. *Illustrated Case Rep Gastroenterol OPJ*. 2011; 7:59–61.
2. Mason PJ, Bautista JM, Gilsanz F. G6PD deficiency: the genotype phenotype association. *Blood Rev*. 2007; 21:267-83.
3. Cappellini MD, Fiorelli G. Glucose-6-phosphate dehydrogenase deficiency. *Lancet*. 2008; 371:64-74.
4. Luzzatto L, Seneca E. G6PD deficiency: a classic example of pharmacogenetics with ongoing clinical implications. *Br J Haematol*. 2014; 164:469-80.
5. Dela Cruz M, Khalid MM, Mostafa A, Ershad M, Vearrier D, McKeever R: Hemolytic crisis following naphthalene mothball ingestion in a 21-month-old patient with glucose-6-

- phosphate dehydrogenase (G6 PD) deficiency. *Case Rep Pediatr.* 2019, 2019:1092575.
6. Deo P, Sahu KK, Dhibar DP, Varma SC: Naphthalene ball poisoning: a rare cause of acquired methaemoglobinaemia. *BMJ Case Rep.* 2016.
 7. Chan ED, Chan MM, Chan MM: Pulse oximetry: understanding its basic principles facilitates appreciation of its limitations. *Respir Med.* 2013, 107:789-99.
 8. Liao YP, Hung DZ, Yang DY: Hemolytic anemia after methylene blue therapy for aniline-induced methemoglobinemia. *Vet Hum Toxicol.* 2002, 44:19-21.
 9. Thangatorai R. Naphthalene-Induced Acute Oxidative Hemolysis With Methemoglobinemia in Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency. *Cureus.* 2022 Mar 25;14(3):e23496.