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Middle-Aged male with acute respiratory arrest following brief illness: A Case Report

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Abstract

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is a common cause for hemolytic anemia which can precipitate acute hemolysis when exposed to oxidative agents. Acalypha indica, a medicinal plant known as "Kuppameniya," in Sri Lanka is used as herbal medication as well as a plant-based dish and it has been reported to induce oxidative hemolysis and methemoglobinemia in individuals who are susceptible. We report a case of a 44-year-old previously healthy male with well-controlled asthma who was having features of exacerbation of asthma presenting with acute onset dyspnea, and dark-colored urine after ingestion of Acalypha indica for the first time. Clinical and laboratory findings revealed acute intravascular hemolysis, indirect hyperbilirubinemia and acute kidney injury with possible methemoglobinemia. The patient required mechanical ventilation, blood transfusions, therapeutic plasma exchange, and oral vitamin C. Methylene blue was avoided due to risk of oxidative stress. He made a complete recovery after active management with multidisciplinary care.

This case emphasizes the importance of recognizing herbal-induced oxidative hemolysis and methemoglobinemia, especially in undiagnosed individuals with G6PD-deficiency, in regions where such traditional remedies are commonly used.

Keywords: *Acalypha indica, G6PD deficiency, hemolysis, methemoglobinemia, herbal medicine*

Introduction

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most common enzymopathy worldwide, affecting over 400 million individuals, particularly in regions such as Africa, the Middle East, Asia, and the Mediterranean, causing a spectrum of disease including neonatal hyperbilirubinemia, acute hemolysis and chronic hemolysis [1]. This X-linked recessive disorder affects the ability of red blood cells to withstand oxidative stress due to reduced nicotinamide adenine dinucleotide phosphate (NADPH) production, causing increased susceptibility of red blood cells for hemolysis when exposed to oxidative triggers such as certain drugs, infections, and dietary components like fava beans. Acute hemolysis usually self-limited although sometimes it can be severe enough requiring blood transfusion [1].

Acalypha indica, locally known in Sri Lanka as *Kuppameniya*, is a leafy plant widely used in traditional medicine and local plant-based dish. Although commonly perceived as harmless, or even beneficial with its use in traditional medicine there is a evidence to suggest that *Acalypha indica* can act as a potent oxidative agent in individuals with G6PD deficiency, leading to acute hemolytic crises and, in some cases, methemoglobinemia [2–6]. Case reports from Sri Lanka and other South Asian countries have reported this under-recognized cause of oxidative hemolysis in patients with G6PD deficiency, highlighting the clinical significance of cultural dietary practices in genetically predisposed individuals [2–5].

Methemoglobinemia, characterized by oxidation of hemoglobin iron from the ferrous (Fe^{2+}) to the ferric (Fe^{3+}) state, further complicates the clinical picture by impairing oxygen delivery to tissues as it has high affinity for oxygen when compared to hemoglobin causing impaired release of oxygen at the tissue level. This results in a characteristic saturation gap—where pulse oximetry readings are low despite normal arterial oxygen levels—a diagnostic clue that may be overlooked [3–5]. Importantly, standard treatments for methemoglobinemia such as methylene blue are contraindicated in G6PD-deficient patients, as they rely on NADPH for reduction and can exacerbate hemolysis [1,4]. In such cases, ascorbic acid serves as a safer alternative for reducing methemoglobin levels [3,4].

We present a case of a previously healthy middle-aged Sri Lankan male who developed acute hemolytic crisis with possible methemoglobinemia leading to severe hypoxia and respiratory arrest, and acute kidney injury after consumption of traditional dish containing *Acalypha indica*. This case highlights the importance of clinical suspicion for oxidative triggers in undiagnosed G6PD-deficient individuals and the need for increased awareness of traditional herbal agents as potential hemolytic precipitants in endemic regions where these plants are consumed as medication or as a local cuisine.

Case Presentation

A 44-year-old Sri Lankan male with a background of well-controlled intermittent bronchial asthma presented with brief mild viral lower respiratory tract infection over 1 week duration with fever, non-productive cough, and progressive dyspnea. Over the preceding 24 hours, his dyspnea worsened significantly which brought him to the medical consultation. On examination he was ill looking and clinically pale with peripheral saturation measured by pulse oximetry 66%, despite normal findings in the lungs. He was immediately admitted to the emergency care unit for stabilization where he went to respiratory arrest and regained consciousness following basic resuscitation with oxygen support.

After stabilization on direct questioning he revealed that he has noticed dark-colored urine without reduction in urine out put since same day morning hours, which was associated with acute worsening of lethargy, and fatigue. He denied jaundice, pruritus, steatorrhea or any other gastrointestinal symptoms, recent travel to foreign countries, or ingestion of unfamiliar foods or medications. Also he denied any past history or family history of similar episode. And he denied past history of hepatitis, tuberculosis, illicit drug use or high risk sexual behaviors. He denied history of exertion and cold exposure prior to this episode and he didn't have any other bleeding manifestations as well

Importantly, he reported consuming a traditional dish containing *Acalypha indica* (*Kuppameniya*) for the dinner first time a day prior to the worsening of symptoms with appearance of dark urine, but he denied similar episode among other family members who also consumed the same dish. On further examination, he despite being tachypneic, pale, and hypoxic with peripheral saturation of 66%, his other vital parameters and systemic examination was not significant. there was no jaundice, skin bleeding, lymphadenopathy or features of chronic anemia or hematological disease such as hepatosplenomegaly. Despite low saturation in the peripheral blood arterial blood gas revealed normal oxygenation (PaO_2 406.2 mmHg, SpO_2 99%) suggesting a saturation gap. After catheterization coca cola colored urine was noticed and after initial stabilization patient was transferred for ICU. During ICU admission he again went in to cardiorespiratory arrest where he was immediately

intubated and stabilized with mechanical ventilation. Clinically acute intravascular hemolysis was suspected and further investigations were sent for the diagnosis.

Laboratory investigations showed indirect hyperbilirubinemia (6.35 mg/dL), elevated LDH (3760 U/L), and an elevated reticulocyte count (4.79%) suggestive of acute hemolysis and the Coombs test was negative excluding autoimmune hemolytic anemia. The blood picture revealed Heinz bodies, burr cells, and polychromatic cells which is suggestive of G6PD deficiency. Urinalysis showed possible hemoglobinuria or myoglobinuria. Serum creatinine rose progressively from 1.08 to 5.23 mg/dL, indicating acute kidney injury possibly secondary to hemoglobinuria. His G6PD level and methemoglobin level were not measured due to poor resource availability at that time.



Figure 1



Figure 2



Figure 3

Table 1: Laboratory Findings of the Patient

Investigation	07/05	08/05	09/05	10/05
Hemoglobin (g/dL)	11.2	10.6	10.6	10.7
HCT (%)	33.4	31		
MCV(fL)	98	98		
MCHC(g/dL)	33.5	34		
WBC (x10⁹/L)				
Neutrophils(%)	25.4	30.1		
Lymphocytes(%)	72	84		
Eosinophils(%)	19.2	9.5	28.9	23.8
	1.2	0		

Investigation	07/05	08/05	09/05	10/05
Platelets ($\times 10^9/L$)	270	206	160	117
CRP (mg/L)	8.2	-	192	180.2
Creatinine (mg/dL)	1.08	1.44	3.28	5.23
Blood urea(mg/dL)	48.3			
Uric acid(mg/dL)	4.4			
Sodium (mmol/L)	138	140	137	136
Potassium (mmol/L)	3.8	3.9	4.1	4.2
Calcium (mmol/L)	-	1.17	1.17	2.25
Phosphorus(mg/dL)	3.0			
AST(U/L)	40.5	-	104	100.3
ALT(U/L)	64.5		49.6	62
Albumin(g/L)	41.1		38.8	37
Globulin(g/L)	24.5		25.4	25.6
ALP(U/L)	64.9			
Gamma GT(U/L)	29.6			
Direct bilirubin(mg/dL)		0.29		
Indirect bilirubin(mg/dL)		6.35		
LDH(U/L)		3760		
Retic count(%)		4.79		
PCT(ng/mL)	0.62		2.06	2.73
APTT(sec)		26.7	30.4	
PT/INR(ratio)		1.01	1.28	1.3
Direct cooms test		negative		
D- dimer(ng/mL)		9997		
ESR(mm/hour)	05			
Blood picture	Red cells- normochromic normocytic, many burr cells, henz bodies, polychromatic cells, occasional NRBC WBC- neutrophil leukocytosis Platelet- Normal			

Investigation	07/05	08/05	09/05	10/05
USS Abdomen	Horse -shoe kidney Rest of the USS normal			
Troponin (ng/L)	4.3	42.3		
ABG				
• pH	7.34			
• PaCO ₂ (mmHg)	29.7			
• PaO ₂ (mmHg)	406.2			
• SpO ₂ (%)	99			
•				
• Hb(mg/dL)	10.8			
• HCT(%)	37			
• Lactate(mmol/L)	1.3			
• Na ⁺ (mmol/L)	134			
• K ⁺ (mmol/L)	3.52			
• HCO ₃ ⁻ (mEq/L)	18.1			
• Base excess(mEq/L)	-7			
• PaO ₂ /FiO ₂ ratio	406.2			
Peripheral SpO ₂ measurement	66% on room air 88% with NRBM			
UFR				
• Color	Straw			
• pH	7.5			
• protein	3+			
• glucose	+			
• bilirubin	Nil			
• urobilinogen	Normal			
• pus cells(HPF)	6-8			
• red cells(HPF)	4-6			
• cast	Granular			
Urine dipstick		Positive for Hemoglobin or		

Investigation	07/05	08/05	09/05	10/05
		myoglobin		

Management and Outcome

The patient was managed in the ICU with mechanical ventilation, intravenous fluids, and alkaline diuresis to prevent AKI. His blood pressure was maintaining without inotropic support and initially saturation was 88 with SIMV mode. Empirical intravenous cefepime and ciprofloxacin was commenced and later on ciprofloxacin was omitted as it can worsen oxidative stress. Multi-disciplinary team was involved in managing the patient such as general physician, respiratory physician, nephrologist, and hematologist and intensivist. Despite mechanical ventilation initially his saturation was not improving for 2 days highlighting the possibility of severe hemolysis and with liaison with the hematologist it was decided to do TPE and he underwent 2 cycles of TPE and 8 pints of red cell concentration transfusion which increases and stabilizes the patient's saturation. While searching for the cause for ongoing hemolysis 3 days after ingestion of *acalypha indica*, he underwent UGIE where it was evident large undigested plant particles still stagnated in the stomach causing ongoing hemolysis despite medical management. Therapeutic lavage of the gastric content should have attributed to the improvement of saturation along with TPE. Despite proper hydration and alkaline diuresis his renal functions were deteriorated with time suggesting acute tubular necrosis and he underwent 1 cycle of acute hemodialysis where his renal functions were improved after that with gradual returning to baseline without necessitating further hemodialysis. Even though there is marked saturation gap with possibility of associated methemoglobinemia he was managed with oral vitamin C, while avoiding methylene blue as it can precipitate hemolysis in G6PD deficiency by worsening oxidative stress.

With above management and supportive care after 3 days of intubation his oxygenation parameters normalized, and the urine cleared by the third day. He was successfully extubated and made a gradual recovery with improvement in renal function. He was able to discharge on day 9 from admission without any long-term complications.

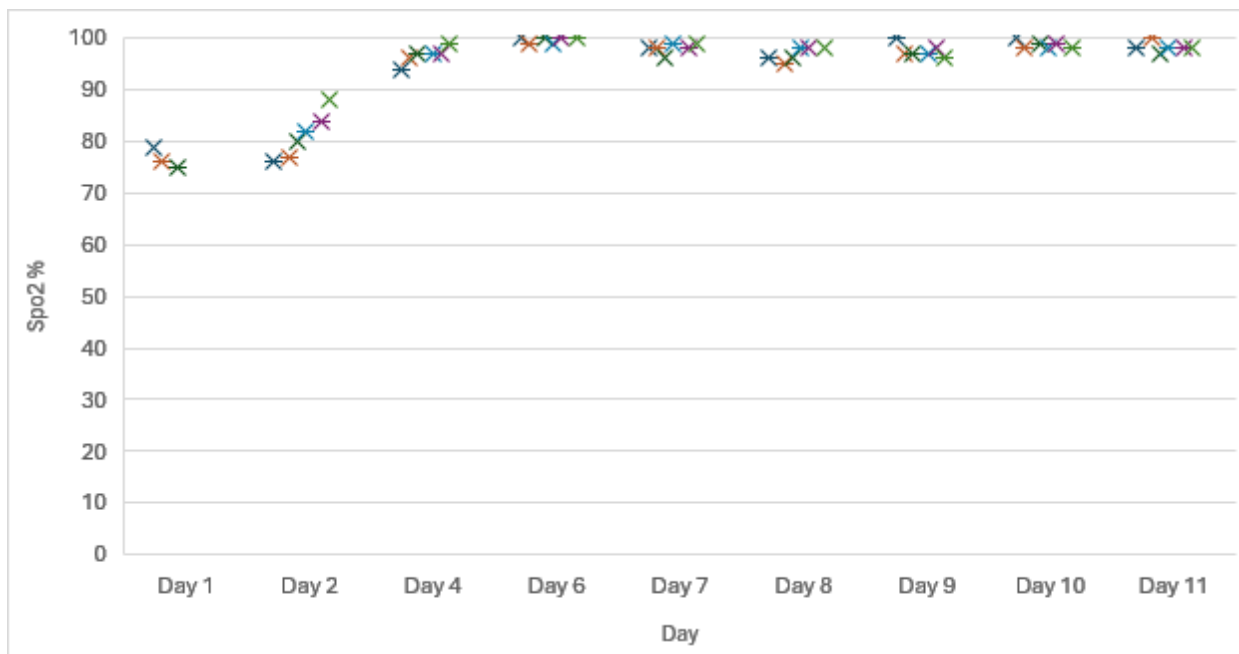


Figure 4: Oxygen Saturation Progression Over 11 Days.



Figure 5



Figure 6

Discussion

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is a common X-linked enzymatic disorder affecting millions worldwide, with a variable prevalence in different regions, including Sri Lanka [1]. The enzyme G6PD is important in producing NADPH which has a vital role in protecting erythrocytes from oxidative damage, and maintaining the redox balance within the cell. G6PD deficient red blood cells are vulnerable to oxidative stress from drugs such as dapsone and antimalarials, infections like certain viruses, and certain foods like fava beans or herbal substances such as *Acalypha indica* as well as situations with emotional stress.

Acalypha indica (locally known as “Kuppameniya”) is widely consumed in Sri Lanka both as a leafy vegetable and as a traditional herbal remedy. Although commonly regarded as safe, it has been increasingly recognized as a potent oxidant capable of triggering hemolytic crises and methemoglobinemia in individuals with G6PD deficiency [3–7]. Our case adds evidence of the oxidant potential of *Acalypha indica* in this vulnerable population with undiagnosed G6PD deficiency.

The relationship between ingestion of *Acalypha indica* and the onset of symptoms such as dark urine, fatigue, and worsening dyspnea in our patient strongly implicates the plant as the possible precipitant for the acute hemolytic crisis of this patient. Sharmika et al. documented a middle-aged Sri Lankan male who developed acute hemolysis and methemoglobinemia following consumption of *Acalypha indica*, presenting with anemia, elevated lactate dehydrogenase, and a saturation gap on pulse oximetry consistent with methemoglobinemia [3]. Earlier reports from Sri Lanka by Lamabadusuriya and Jayantha [6], as well as Sellahewa [7], similarly describe *Acalypha indica*-induced hemolysis in G6PD-deficient individuals, reinforcing the clinical significance of this association.

Methemoglobinemia occurs when hemoglobin iron is oxidized from the ferrous to the ferric state, which has a high affinity for oxygen compared to hemoglobin will impair oxygen delivery and release to the peripheral tissues causing tissue hypoxia. This will further aggravate the tissue hypoxia in the setting of ongoing hemolysis as in our patient. The presence of a saturation gap — low peripheral oxygen saturation despite normal arterial oxygen tension — is a useful diagnostic clue, as seen in our patient and others [3,5]. Treating methemoglobinemia in G6PD deficiency is challenging because the standard antidote, methylene blue, requires NADPH for its reduction and can exacerbate hemolysis in deficient individuals. Instead, ascorbic acid has been effectively used as a safer alternative, as demonstrated by Sharmika et al. and Pallapothu and Sankar [3,5].

Management of acute hemolysis in G6PD deficiency remains primarily supportive, including hydration and blood transfusions with close monitoring. Our patient also underwent therapeutic plasma exchange due to the severity of hemolysis as well as possible association of methemoglobinemia where standard care is not possible due to G6PD deficiency. Monitoring renal function is crucial, given the risk of hemoglobinuria-induced acute kidney injury, which has been reported in similar cases [3].

The collection of these cases in Sri Lanka suggests the presence of undetected G6PD deficient individuals within this population that show sensitivity to oxidative stressors such as *Acalypha indica* though it is not a common cause of precipitant. Further genetic and epidemiological studies are needed for identification of this population who are vulnerable for hemolytic crisis with possible exposure to a precipitant.

Despite the widespread use of *Acalypha indica* as a traditional remedy as well as a local dish, we have minimal awareness of it causing life-threatening hemolysis in G6PD-deficient individuals, its pathophysiology and chemical constituent which leads to oxidative stress. Our case, consistent with previous reports, emphasize the need for increased public education, early recognition by clinicians, and broader screening for G6PD deficiency, particularly in regions where traditional herbal remedies are commonly used.

Conflict of Interest

The author declares that there are no conflicts of interest regarding the publication of this case report.

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