RESEARCH PAPER

Severe Methemoglobinemia from a Suspected Adulterated Biostimulant Co-ingested with Chlorpyrifos-Cypermethrin: A Case Report

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ABSTRACT
Methemoglobinemia is an uncommon cause of refractory cyanosis in which haemoglobin iron is oxidised from the ferrous to the ferric form and is unable to bind oxygen. We report a 26-year-old previously healthy man who presented two hours after ingesting around 100 mL of a liquid biostimulant labelled as containing alginic acid and humic acid. He was drowsy, centrally cyanosed, hypotensive, with peripheral oxygen saturation of 80% on room air, rising only to 90% on 10 L of supplemental oxygen. The arterial blood was chocolate-brown on a blotting-paper test, and co-oximetry confirmed a methemoglobin level of 76.5%. He responded promptly to a single intravenous dose of methylene blue at 2 mg/kg, with methemoglobin levels falling sequentially to 17.6%, 10%, 3%, and 2.5%. A late-disclosed co-ingestion of chlorpyrifos and cypermethrin was managed with atropine and pralidoxime. He was discharged in stable condition.

Keywords: Adulterated biostimulant, Co-ingestion, Cyanosis, Methylene blue, Saturation gap
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INTRODUCTION

Methemoglobinemia is an uncommon but important cause of cyanosis in which the iron atom in haemoglobin is oxidised from its ferrous (Fe^{2+}) to its ferric (Fe^{3+}) form. Ferric haemoglobin cannot bind oxygen and shifts the oxyhaemoglobin dissociation curve to the left, further impairing oxygen release at the tissue level (1,2). It may be congenital, due to cytochrome b5 reductase deficiency or haemoglobin M disease, or acquired through exposure to oxidisers such as nitrates, dapsone, aniline dyes and nitrobenzenes (2,3).

Acquired methemoglobinemia from agricultural chemicals is well described, but the offending substance is usually a clearly labelled oxidiser such as a nitrite fertiliser or a nitrobenzene-based pesticide (4,5). Reports following the ingestion of plant "biostimulants" are rare, as their listed constituents humic acid, fulvic acid and seaweed-derived alginic acid are not known to cause clinically relevant haemoglobin oxidation (6). We report a young man who developed life-threatening methemoglobinemia (76.5%) within hours of ingesting around 100 mL of a commercially available biostimulant, in whom product adulteration was strongly suspected and an undisclosed organophosphate-pyrethroid co-ingestion was identified only on repeat history-taking.

CASE REPORT

A 26-year-old previously healthy male agriculturalist was brought to the emergency room two hours after the alleged ingestion of approximately 100 mL of a liquid biostimulant at his residence, labelled as containing alginic acid and humic acid. He had developed two episodes of non-bilious vomiting and progressive drowsiness, and was referred from a local government hospital. There was no history of seizure, head trauma, breathlessness, chest pain or focal neurological deficit. He was an occasional drinker, with his last binge on the evening before the ingestion taken together with the index substance, did not smoke, was on no medication, and had no relevant past or family history, in particular no family history of haemoglobinopathy or glucose-6-phosphate dehydrogenase (G6PD) deficiency.

On arrival he was drowsy and unresponsive to painful stimulus, with central and peripheral cyanosis (Figure 1).

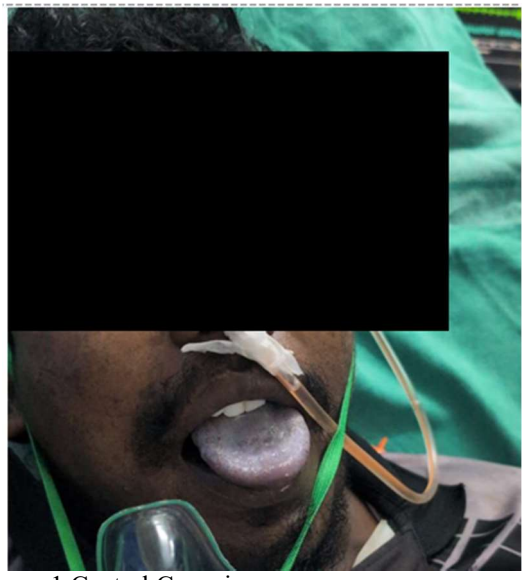

Figure:1 Central Cynosis

The blood pressure was 80/50 mmHg, pulse rate 120/min, peripheral oxygen saturation 80% on room air rising only to 90% on 10 L of supplemental oxygen, and the capillary blood glucose 52 mg/dL. The Glasgow Coma Scale score was E1V2M2 with bilateral pupils reactive to light. Cardiovascular and respiratory examinations were unremarkable, and the abdomen was soft and non-tender. ECG findings shows Sinus tachycardia, Short PR and downsloping ST depression with asymmetrical T inversion The chronological sequence of events is summarised in Table 1.

Table 1. Timeline of the index admission.

Time (from ingestion)	Event
0 h (10 February 2026, 10:00)	Ingestion of approx.100 mL of a liquid biostimulant at residence
0–2 h	Two episodes of vomiting, reduced responsiveness; taken to local government hospital, then referred
~2 h (ED arrival)	Drowsy, cyanosed; BP 80/50 mmHg, PR 120/min, SpO_2 80% on room air, CBG 52 mg/dL, GCS E1V2M2
ED + 15 min	IV thiamine 500 mg and 25% dextrose given; GCS improved to E3V3M6
ED + 30 min	Initial ABG: HAGMA with compensatory respiratory alkalosis; saturation gap and chocolate-brown blood noted on blotting paper
ED + 45 min	Repeat ABG with co-oximetry: methemoglobin 76.5%
ED + 60 min	IV methylene blue 2 mg/kg (120 mg) in 100 mL of 5% dextrose given
ED + 90 min	GCS improved to E4V4M6; noradrenaline started for persistent hypotension
ED + 2 h	Repeat history disclosed chlorpyrifos-cypermethrin co-ingestion; atropine 1.2 g IV stat and PAM 2 g IV stat with 4-hour infusion started
ED + 8 h	Methemoglobin 17.6%; serum pseudocholinesterase 10,559 U/L (normal); PAM stopped, pantoprazole infusion started
ED + 12 h	Methemoglobin 10%
ED + 24 h	Methemoglobin 3%
ED + 36 h	Methemoglobin 2.5%; noradrenaline tapered and stopped
Day 3	Shifted to ward; started on oral fluids and liquid diet
Day 5	Discharged in stable clinical condition

The first arterial blood gas on room air showed a high-anion-gap metabolic acidosis with a compensatory respiratory alkalosis.(Table 2) Despite oxygen, the saturation remained persistently between 75 and 80% with clear lung fields; this saturation gap, together with chocolate-brown discolouration of arterial blood on a blotting-paper test (Figure 2),

prompted suspicion of methemoglobinemia, and co-oximetry confirmed a methemoglobin level of 76.5%. The haemoglobin was 14.5 g/dL, total leukocyte count 19,100/mm³ and platelet count 315 × 10³/mm³; the coagulation profile, renal function and liver function were within normal limits. Serum pseudocholinesterase, sent after late disclosure of organophosphate co-ingestion, was 10,559 U/L (reference 5,900–12,220 U/L).

Figure 2: Blotting Paper Test

Pulmonary embolism, cyanotic congenital heart disease, and septic shock were considered but did not adequately account for the cyanosis unresponsive to oxygen with clear lungs; abnormal haemoglobin states, principally methemoglobinemia, were strongly favoured after the saturation gap and chocolate-brown blood were observed and were confirmed on co-oximetry. Intravenous methylene blue 2 mg/kg (total 120 mg) in 100 mL of 5% dextrose was given as a single stat dose. Supportive care included intravenous thiamine 500 mg, 25% dextrose for hypoglycaemia, and a noradrenaline infusion at 0.2 µg/kg/min for the hypotension. Following disclosure of organophosphate-pyrethroid co-ingestion, atropine 1.2 g intravenously and pralidoxime (PAM) 2 g were started, with N-acetylcysteine, ascorbic acid, and vitamin E as adjuvants; PAM was stopped once the pseudocholinesterase result returned within range.

After methylene blue the patient's consciousness improved progressively, with the Glasgow Coma Scale rising to E4V4M6. Serial arterial blood gas analysis every three hours documented a sequential fall in methemoglobin levels from 76.5% before treatment to 17.6%, 10%, 3% and 2.5% over the next 36 hours. He was transferred to the ward on day three, started on oral fluids and a liquid diet, and was discharged in stable condition on day five. No adverse events were attributable to methylene blue or to the other administered therapies.

Table 2: Arterial Blood Gas Analysis, Biochemical Parameters, and Associated Metabolic Abnormalities

Parameter	Value	Unit	Reference Range	Interpretation
pH	7.380	—	7.35–7.45	Normal pH
pCO_2	30.0	mmHg	32–45	Low; suggests respiratory compensation or respiratory alkalosis
pO_2	133	mmHg	83–108	Elevated; likely receiving supplemental oxygen
Na^+	133	mmol/L	135–145	Mild hyponatremia
K^+	3.4	mmol/L	3.5–5.0	Mild hypokalaemia
Ca^{2+}	0.84	mmol/L	1.15–1.33	Significant ionized hypocalcaemia
Cl^-	100	mmol/L	98–107	Normal
Hct	47	%	36–52	Normal
Glucose	351	mg/dL	65–95	Severe hyperglycaemia
Lactate	6.2	mmol/L	0.2–0.7	Markedly elevated; indicates lactic acidosis/tissue hypoperfusion
HCO_3^-	17.7	mmol/L	22–26	Low; metabolic acidosis
HCO_3^- (std)	20.2	mmol/L	22–26	Reduced buffer reserve
BE(B)	-6.1	mmol/L	-2 to +2	Base deficit; metabolic

				acidosis
BE(ecf)	-7.4	mmol/L	-2 to +2	Significant metabolic acidosis
tCO_2	18.6	mmol/L	23–29	Reduced total CO_2 content
pO_2(T)	133	mmHg	83–108	Elevated oxygen tension
pO_2(A-a)	-21	mmHg	<20	No significant oxygenation defect
tHb	14.6	g/dL	12–17	Normal haemoglobin
sO_2	99	%	95–100	Excellent oxygen saturation
Anion Gap	19	mmol/L	8–16	Elevated; high anion gap metabolic acidosis
Ca^{2+} (pH 7.4)	0.83	mmol/L	1.15–1.33	Significant ionized hypocalcemia

DISCUSSION

The present case describes a young, previously healthy man who developed severe acute methemoglobinemia (76.5%) within hours of ingesting around 100 mL of a liquid biostimulant labelled as containing only alginic acid and humic acid. Methylene blue 2 mg/kg produced a rapid and sustained reduction in methemoglobin levels with full clinical recovery, and a concurrent organophosphate-pyrethroid co-ingestion was identified only on repeat history-taking. Three points deserve emphasis: the value of the saturation gap as a diagnostic clue, the suspicion of product adulteration in apparently low-toxicity agricultural ingestions, and the importance of repeated history-taking in self-poisoning.

Severe methemoglobinemia in young adults is most often reported with nitrobenzene, aniline dyes, dapsone and topical anaesthetic exposures (3,4,7). Similar presentations after agricultural product ingestion have been reported by George *et al*, Yogesh *et al* and D'sa *et al*, where the offending agent was always a clearly identifiable nitrate or nitrobenzene-containing product (5,8,9). In contrast, the labelled constituents of the biostimulant ingested by our patient are not known oxidisers (6), and regulatory analyses of biostimulants marketed in South Asia have documented adulteration with nitrites, nitrates and aromatic amines used as preservatives or colourants (10,11). Adulteration is therefore the most plausible explanation for the severe methemoglobinemia in this case, given the rapid onset and the magnitude of the level.

The saturation gap, the difference between the pulse oximeter reading of 80% and the persistent clinical cyanosis, has been highlighted as the most useful bedside clue to methemoglobinemia (12,13). Similar observations were reported by Wright *et al*, do Nascimento *et al* and Cortazzo *et al*, who noted that pulse oximetry tends to plateau at 80–85% irrespective of the true arterial oxygen content (12,14,15). The chocolate-brown discolouration of arterial blood on a blotting-paper test has retained value as a rapid bedside screen where co-oximetry is unavailable (16). Methylene blue at 1–2 mg/kg is the antidote of choice for symptomatic disease or asymptomatic levels above 30%, with response expected within 30 to 60 minutes (17,18), and our patient's complete response to a single 2 mg/kg dose was consistent with Su *et al* and Iolascon *et al* (19,20). Where it is contraindicated, as in G6PD deficiency, ascorbic acid, N-acetylcysteine, hyperbaric oxygen or exchange transfusion remain alternatives (21,22).

The delayed disclosure of organophosphate-pyrethroid co-ingestion, emerging only on repeat history-taking after the methemoglobinemia had been corrected, similar observations by Eddleston *et al* and Paudyal (23,24). The principal limitations of this report are that the suspected adulteration could not be confirmed analytically, as the residual product was not retained for chromatographic analysis, and G6PD status was not tested before methylene blue administration because of the emergent presentation, although the favourable response and absence of haemolysis supported adequate activity.

CONCLUSION

Severe, life-threatening methemoglobinemia can follow the ingestion of an agricultural biostimulant whose labelled constituents are not themselves known oxidisers, and adulteration should be suspected. A wide saturation gap, central cyanosis unresponsive to oxygen and chocolate-brown arterial blood should prompt immediate co-oximetry and empirical methylene blue therapy. Repeated history-taking remains essential in self-poisoning, as clinically important co-ingestions may be disclosed only after the patient regains consciousness.

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