

“Acute Methemoglobinemia Due to Ingestion of Nitrobenzene: A Rare Case Report”

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Abstract: Nitrobenzene is a pale yellow oily liquid, with an odour of bitter almonds used in the synthesis of solvents like paint removers, manufacturing of lubricating oils and dyes and in shoe manufacturing units for production of synthetic rubber. The toxic effects after ingestion lead to methemoglobinemia. Methemoglobinemia, because of accidental ingestion of nitrobenzene is a life threatening emergency, difficult to diagnose clinically and not routinely suspected. Early aggressive management of severe poisoning, strongly suspected on clinical grounds may change the outcome of a patient. Our case had this rare presentation so we are presenting this case because of its rarity.

Keywords: Methemoglobinemia, Nitrobenzene, Methylene blue, Ascorbic Acid.

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I. Introduction

Nitrobenzene is a pale yellow oily liquid, with an odour of bitter almonds used in the synthesis of solvents like paint removers, manufacturing of lubricating oils and dyes and in shoe manufacturing units for production of synthetic rubber. It is slightly soluble in water, readily soluble in organic solvents such as alcohol, ether, and benzene, and highly soluble in lipids. Intoxication can be accidental or suicidal, or the side effect of some drugs, including metoclopramide.¹ The toxic effects after ingestion are due to the rapid development of methaemoglobin² resulting in a condition known as methemoglobinemia, because of oxidation of iron within the haemoglobin from the ferrous (Fe^{2+}) state to the ferric (Fe^{3+}) state, resulting in inability of oxygen transportation causing a brownish discoloration of the blood.³ Methemoglobinemia, because of accidental ingestion of nitrobenzene is a life threatening emergency but is difficult to diagnose clinically and not routinely suspected. Early aggressive management of severe poisoning, strongly suspected on clinical grounds may change the outcome of a patient. Our case had this rare presentation so we are presenting this case because of its rarity.

II. Case Report

A 18 years old female presented to casualty in altered sensorium with cyanosis and a greyish-brown hue, laboured respiration of 26/min, BP 90/60 mm of Hg, pulse rate 80/min, pupils with sluggish reaction, and SpO₂ of 45% at room air. Her chest was bilaterally clear. Blood samples drawn for ABG had a chocolate brown colour, which did not improve on exposure to 100% oxygen and showed compensated metabolic acidosis. Serum creatinine and electrolytes were within normal range. Her X-ray of the chest, ECG and complete blood counts were within normal limits following which a clinical diagnosis of severe acute methaemoglobinaemia of unknown origin was made.

Gastric lavage with charcoal was done immediately along with intravenous four millilitres (40 mg) of methylene blue, prepared as 1% (10 milligrams/millilitre solution prepared and sterilised in our laboratory) sterile solution given in dose of 1 milligram/Kg. This improved her SpO₂ to 92%, which dropped again after about six hours, when 40 mg IV methylene blue was repeated. An antibiotic was also added and urine output was maintained above 100 ml/hour with proper hydration. She became conscious after six hours with a stable BP of 120/80 mm of Hg and HR of 96/minute. Again after 12 hours her SpO₂ dropped to 84% with ABG showing a saturation of 92%. IV methylene blue (30 mg) improved SpO₂ to 97% over the next 15 minutes, only to return to 79% in the next six hours, with a similar response to another dose with ABG showing a saturation of 94% and a PaO₂ of 126, when she admitted to having consumed a liquid (around 200-250 millilitres, equivalent to 12.5 g of nitrobenzene) at her workplace (shoe factory) accidentally before falling ill. The SpO₂ remained between 93-96% for next 24 hours. With this waxing and waning picture of symptoms, purgation with lactulose, intravenous methylene blue every six to twelve hours (three days) and oral ascorbic acid per day up to seven days, was prescribed, till the smell of bitter almonds disappeared completely from the stools. She improved gradually and rapidly after the seventh day with SpO₂ of 94% on room air and was discharged after ten days of

hospital stay. She was advised to follow-up in physiotherapy for lung expansion/breathing exercises after discharge.

III. Discussion

MeHb is normally less than 1% of the total hemoglobin under physiologic conditions. When its levels increase, the condition is defined as methemoglobinemia resulting in a condition where the oxygen carrying capacity of haemoglobin is reduced because of oxidation of iron within the haemoglobin from the ferrous (Fe^{2+}) state to the ferric (Fe^{3+}) state, causing a brownish discolouration of the blood.³ In normal individuals, MeHb level must be greater than 10% to be clinically significant, and only mild symptoms like headache, fatigue, and nausea occur at a level of 20-30%.⁴ Exertional dyspnea, lethargy, and tachycardia occur at levels of 30-45%. Arrhythmias, coma, seizures, respiratory distress, and lactate acidosis occur at levels of 50-70%. Levels greater than 70% cause cardiovascular collapse and have a high degree of mortality if left untreated.⁵ Clinical suspicion should arise in a breathless patient with characteristic smell of bitter almonds, persisting cyanosis on continuous oxygen therapy without pre-existing cardiopulmonary disease, low arterial oxygen saturation, and abnormal arterial blood gas (ABG) analysis. Chocolate brown colour that fails to turn bright red on shaking is the main distinguishing feature suggesting methemoglobinemia. Presence of nitrobenzene compounds can be detected spectrophotometrically and estimated by the butanone test of Schrenk,³ methemoglobin levels in the blood, and urinary presence of p-nitrophenol and p-aminophenol.^{3, 4} Once formed, methemoglobin can be reduced enzymatically either via NADH-dependent reaction, catalysed by cytochrome b5 reductase, or an alternative pathway utilizing the nicotine adenine dinucleotide phosphate NADPH-dependent methemoglobin reductase system.¹ The treatment revolves around on the principles of decontamination and symptomatic and supportive management. The antidote of choice for the acquired (toxic) methaemoglobinaemia is methylene blue, which is an exogenous cofactor, which greatly accelerates the NADPH-dependant methemoglobin reductase system.^{3, 5} It is administered at a dose of 1 – 2 mg/kg (up to 50 mg dose in adults,) as a 1% solution over five minutes intravenously; with a repeat in one hour, if necessary. Toxic dose of methylene blue is more than 7mg/kg which can cause dyspnea, chest pain, and haemolysis. It is contraindicated in patients with G6PD deficiency, because it can lead to severe haemolysis.⁷ Ascorbic acid is an antioxidant that may also be administered in patients with methemoglobin levels of more than 30%.⁴ Other treatments include ascorbic acid which is an antioxidant (free radical scavenger which reduces the NAD^+); N-acetyl cysteine; RBC exchange transfusion; hyperbaric oxygen therapy and 10% Dextrose.^{1, 2, 6, 7}

In this case, without exceeding the maximum dose, repeated low dose methylene blue helped in tiding over the fluctuating symptoms due to the release of nitrobenzene from the body stores. Oral charcoal and regular purgation helped to eliminate the body stores of nitrobenzene and prevented secondary deterioration in the patient taking care of nutrition and adequate urine output.

IV. Conclusion

The treatment of poisoning caused by an uncommon compound is a challenge. The situation becomes graver when methaemoglobinaemia is of unknown origin. Acute Methemoglobinemia is usually associated with high mortality; hence an early aggressive management of severe poisoning, strongly suspected on clinical grounds may change the outcome of a patient. Methylene blue and ascorbic acid are the treatment of choice, while exchange transfusion and hyperbaric oxygen therapy are usually reserved for patients who are resistant to standard treatment. Our case had this rare presentation so we are presenting this case because of its rarity and we wish to point out the unavailability of intravenous methylene blue should not be a hindrance, as methylene blue powder is available readily and can be made into 1% solution and sterilized in laboratories.

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