Case Report

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Acute Acquired Methemoglobinemia Following Nitrobenzene Poisoning

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ABSTRACT

Nitrobenzene is an aromatic compound commonly used in agricultural fertilizers. It is capable of inducing methemoglobinemia when ingested in sufficient quantities. Methemoglobinemia impairs oxygen transport by dual mechanism of impaired oxygen binding and diminished oxygen unloading. We report a case of nitrobenzene poisoning accompanied by methemoglobinemia and later complicated by unconjugated hyperbilirubinemia secondary to hemolysis. Prompt treatment with intravenous methylene blue based on a clinical diagnosis in view of dropping SpO_2 unresponsive to oxygen with chocolate cyanosis and paradoxically elevated PaO_2 enabled favorable patient outcome. Other recommended modalities of treatment in acquired acute methemoglobinemia include vitamin C, hyperbaric oxygen and exchange transfusions.

Keywords: Methemoglobinemia; methylene blue; nitrobenzene; nitroboom

INTRODUCTION

Nitrobenzene is an aromatic pale yellow nitro compound with odor of bitter almonds that is used in industrial manufacturing of lubricating oils, synthetic rubber and drugs.[1] It oxidizes hemoglobin to methemoglobin causing methemoglobinemia.[2] Nitrobenzene is an infrequently encountered case of methemoglobinemia in our setup. We report a case of Acute acquired methemoglobinemia following nitrobenzene poisoning that presented to our hospital.

CASE REPORT

A thirty-two years male was brought to Star Hospital, Lalitpur, 5 hours after ingestion of one bottle of "Nitroboom" (50 ml of 20%nitrobenzene) with suicidal intent following family dispute. On examination the patient was unconscious with GCS 3/15; pulse 65/min regular, BP 110/70 mmHg, respiratory rate 27/min and patient was afebrile. Pulse oximetry showed a saturation of 74% which did not improve with supplemental oxygen. Patient was emergently intubated and with administrationof 100% FiO2 which still failed to normalize saturation. Patient was severely cyanosed with a muddy complexion. Rest of the examination was unremarkable.

ABG was performed in the emergency department which showed mixed metabolic and respiratory acidosis (Table 1). A muddy brown discoloration of blood sample was noted. Presumptive diagnosis of acute acquired methemoglobinemia secondary to nitrobenzene poisoning was made. Intravenous Methylene Blue 50mg in 100ml of 5% dextrose was given over 15 minutes which improved oxygen saturation over the next 15 minutes to 100%. Then the patient was admitted in ICU with mechanical ventilator support with FiO2 of 100%. Urine output of 0.5 to 1 ml/kg/hr was maintained by administration of Intravenous Furosemide and IV fluids. Intravenous Vitamin C was initiated. Six hours after admission, another episode of desaturation and worsening cyanosis was noted with SpO2 of 80% which resolved after administration of intravenous methylene blue. Patient subsequently improved and was extubated on 2nd day of admission. He was shifted to ward on 4th day of admission.

Table 1. Serial Arterial Blood Gas Values.

	pH	PO_2 (mm Hg)	PCO_2 (mm Hg)	HCO_3^- (mEq/L)	Lactate (mmol/L)
Admission	7.075	141	28.9	8.1	9.40
3 hrs	7.346	400	43.3	23.1	5.32
Day1	7.311	132	42.3	20.7	0.45
Day 2 (6 AM)	7.404	89	22.5	18.8	0.74
Day 2 (6PM) (post extubation)	7.364	97	35.3	19.6	0.56

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Table 2. Serial Blood Work Showing Unconjugated Hyperbilirubinemia and Neutrophillic Leucoytosis with Relative Lymphopeina.

	Bilirubin Total / Direct (mg/dl)	SGPT (units/L)	SGOT (units/L)	ALP (units/L)	Urea/ Creatinine (mg/dl)	Hemoglobin (g/dl)	Total counts (/ml)	Neutrophils (%)	Lymphocyte (%)
Admission	1.0/0.4	19.6	30.9	110.0	27.6/0.6	16.1	23600	90	08
Day 1	-	-	-	-	30.3/0.7	12.0	11700	86	14
Day 2	-	-	-	-	-/-	12.5	9300	76	23
Day 3	5.0/1.5	15.5	26.8	83.0	24.9/0.5	13.4	7400	74	23
Day 4	-/-	-	-	-	31.5/0.5	-	-	-	-
Day 5	6.8/1.9	20.5	22.2	97.0	32.8/0.9	12.5	6800	65	33
Day 6	4.8/1.0	21.0	21.6	87.0	30.6/0.9	-	-	-	-
Day 7	4.7/0.8	26.2	25.4	96.0	28/0.7	13.0	7000	68	29
Follow up (1 week)	1.7/1.2	23.4	19.9	102.0	-/-	-	-	-	-

A drop in hemoglobin was evident on day 1 whereas the deranged liver enzymes were detected on 3rd day of admission. The liver enzymes began normalizing after 6th day and the patient was discharged on 7th day of admission after successful psychiatric evaluation (Table 2). Follow up scheduled a week later was improving. Patient has not come for follow ups scheduled since then.

DISCUSSION

First reports of nitrobenzene poisoning came up in 1880's which were linked to exposure to writing ink[3] Since then multiple reports have shown their association with paint thinners, solvents, perfumes and agricultural fertilizers.[1] No prior documented case reports of nitrobenzene poisoning in Nepal were found on pub-med search.

Methemoglobin is formed via oxidation of hemoglobin by drugs or toxins(Figure 3).[2] The oxidative process involves conversion of ferrous (Fe2+) iron of the hemoglobin molecule to its ferric (Fe3+) form. The ferric form is incapable of binding oxygen whereas the affinity of remaining ferrous iron of the hemoglobin tetramer have increased affinity to oxygen. This has dual effects in blood oxygen transport. Firstly, there is decreased oxygen carrying capacity due to ferric iron and secondly the ability of the ferrous iron to release oxygen at the tissue end is diminished due to left shift in the oxygen-hemoglobin dissociation curve.[1-4]

Presentation following nitrobenzene poisoning is highly variable and correlates with the dose of exposure. Initial symptoms of nausea and vomiting are usually followed by rapid onset of methemoglobinemia.[1] Patients with 10-20% blood methemoglobin are commonly asymptomatic; dyspnea and tachycardia are seen at 20-30%; lethargy stupor and loss of consciousness occur at 55%. Levels above 55% result in Cardiac arrhythmias, cardiovascular collapse and CNS depression. Levels above 70% are uniformly fatal.[5] Small quantities of methaemoglobin are formed constantly and are continuously reduced, almost entirely by the reduced nicotine adenine dinucleotide (NADH Patients that survive initial phase of poisoning develop hemolytic anemia and unconjugated hyperbilirubinemia (Table 2).[1]

Diagnosis is largely clinical based on history and examination finding of falling saturation unresponsive to supplemental oxygen and characteristic chocolate colored cyanosis.[3,6] Another strong clue to diagnosis is paradoxically normal or elevated Partial pressure of Oxygen (PaO2) despite presence of clinical cyanosis and low oxygen saturation by pulse oximetry.[7] Confirmation requires Arterial blood gas(ABG) analysis and blood methemoglobin levels but is not essential for initiation of treatment.[6] Blood counts typically show neutrophillic leukocytosis with relative lymphocytopenia (Table 2).[1]

Treatment involves decontamination by gastric lavage, cardiorespiratory support, maintenance of steady urine output and management of methemoglobinemia.[2,3,5] Initial treatment of choice for methemoglobinemia is intravenous methylene blue(1-2mg/kg bodyweight).[2,3] It is co-administered with 5% dextrose as dextrose is needed to replenish NADPH which is essential for reduction of methylene blue to its active form of leucomethylene blue.[8] Furthermore, large doses (cumulative dose > 7mg/kg) of methylene blue can overwhelm the reductive capacity leading to accumulation of inactive oxidant form of methylene blue which causes hemolytic anemia and further aggravates methemoglobinemia. Hence, methylene blue must be used with caution in patients with known G6PD deficiency.[3,8]

Other effective treatments include vitamin C, which acts as an antioxidant and high flow oxygen via a non-rebreathing circuit, which enhances natural degradation of methemoglobin.[2,3,6] Ketoconazole and N-acetyl-cysteine have shown promising results in experimental studies but are not yet recommended for use in patients with methemoglobinemia.[9,10] Exchange transfusion and hyperbaric oxygen are second line treatments which are used if patient is unresponsive to methylene blue.[2,3]

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