A Rare Case of Fatal Cardiotoxicity and Methemoglobinemia Following Nitrobenzene Poisoning

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ABSTRACT

A 36 year old rural lady presented with cyanosis and restlessness after ingestion of plant nutrient containing Nitrobenzene 20%. She was diagnosed to be having methemoglobinemia , though treated with methylene blue and symptomatically, she succumbed to death the next day due to severe cardiotoxicity, acute pulmonary edema and cardiogenic shock.

Keywords: *Cardiotoxicity, Nitrobenzene, Methemoglobinemia, Methylene Blue*

INTRODUCTION

Nitrobenzene is an aromatic compound also known as nitrobenzol or oil of mirbane, used in industries, paint, printing and as lubricant oil. It is a pale yellow, oily liquid, odour resembles that of bitter almonds. In India, 20% nitrobenzene is widely used as pesticides and the lethal dose is reported to range from 1 to 10 gm by different studies[1-3]. Nitrobenzene ingestion primarily induces methemoglobinemia.

Methemoglobinamia is a condition in which the iron within hemoglobin is oxidized from the ferrous (Fe2+) state to the ferric (Fe3+) state, resulting in the inability to transport oxygen and carbon dioxide. Methemoglobinemia occurs when methemoglobin levels is more than 2% (normal-0-2% of hemoglobin). Presentation can vary from cyanosis to frank seizures, coma and death reflecting the level of methemoglobinemia. 100% oxygen when fails to correct cyanosis it suggests methemoglobinemia.

Acquired methemoglobinemia is much more common than congenital form. Although exposure to drugs is the most common cause of acquired methemoglobinemia but accidental intake of substances containing oxidizing agents should not be overlooked. Methylene blue is treatment of choice for acquired methemoglobinemia[4].

We report here a fatal case of acute nitrobenzene poisoning in a suicidal attempt by a 35 year old lady presenting as methemoglobinemia and cardiotoxicity.

CASE REPORT

A 35 year old lady presented to our emergency room with h/o vomiting and breathelessness. She was seen at a local hospital, and then referred to our hospital after gastric lavage.7 hours prior to presentation, she had consumed around 200 ml of plant nutrient containing nitrobenzene 20% (Ranger is the trade name), with suicidal purpose . There was no h/o convulsions, bleeding manifestations and loss of consciousness.

On examination: There was marked central and peripheral cyanosis present.

Pulse: 110/min, low volume , Blood Pressure: 80/60mmhg, SpO_2:74% with 10 litres of oxygen.

No pallor and icterus, extremities were cold.

Systemic examination

Cardiac system: S_1, S_2 heard, tachycardia present, no S_3 and murmurs.

Nervous system: conscious, restless, irritable, pupils dilated and sluggishly reactive to light

Respiratory and abdominal examination was clinically normal.

Investigations: Hemoglobin :11.5 g% , white cell count:15,600cells/mm^3, N:90%, L:10%, platelet count: 2.61 L/mm^3. ABG: pH:7.06, HCO_3:16, pO_2:80mmHg, pCO_2: 24mmHg, suggestive of severe metabolic acidosis

LFT: Normal

ECG : Showing sinus tachycardia, r $SR^{I}s^{I}$ pattern in lead 3, deep ST depression and T wave inversion in all the leads

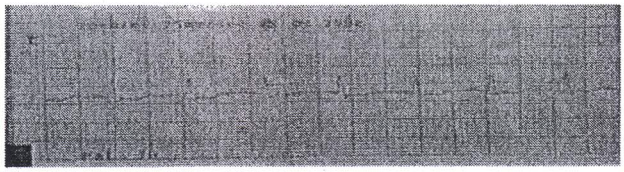

Fig. 1(a). Showing Lead-1:

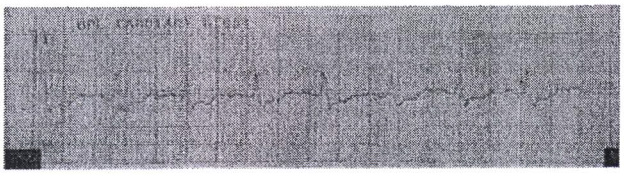

Fig. 1(b). Showing Lead-2:

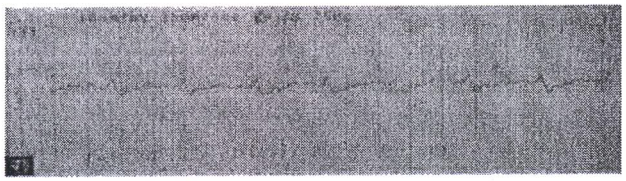

Fig. 1(c). Showing lead 3:

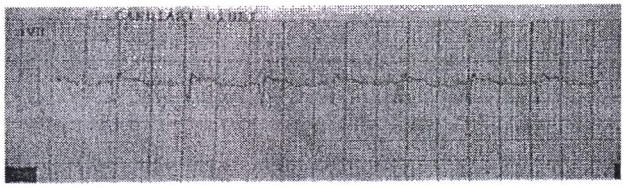

Fig. 1(d). Showing lead aVR:

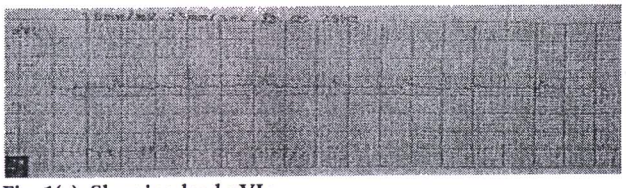

Fig. 1(e). Showing lead aVL:

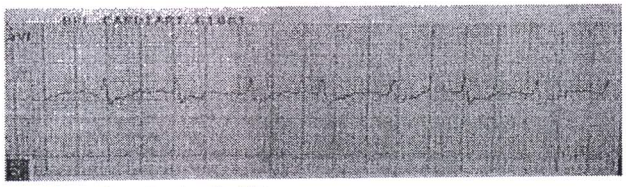

Fig. 1(f). Showing lead aVF:

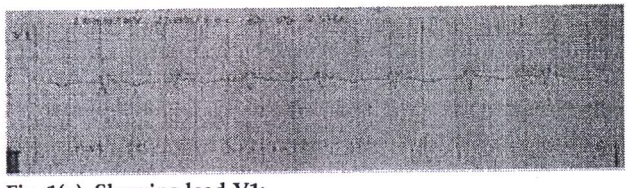

Fig. 1(g). Showing lead V1:

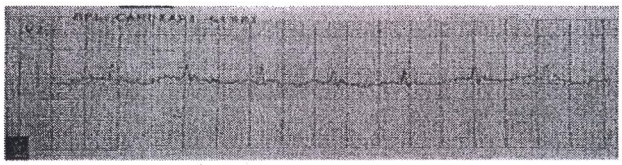

Fig. 1(h). Showing lead V2:

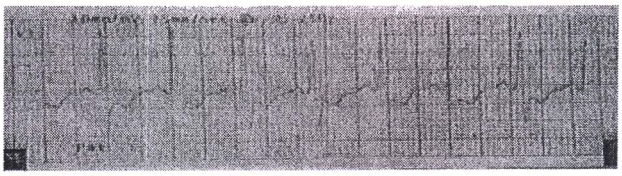

Fig. 1(i). Showing lead V3:

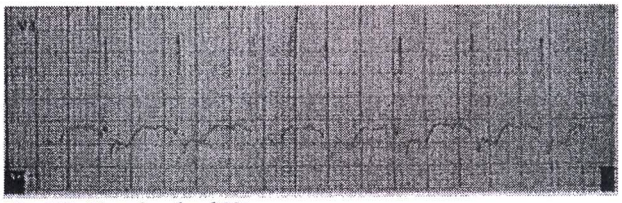

Fig. 1(j). Showing lead V4:

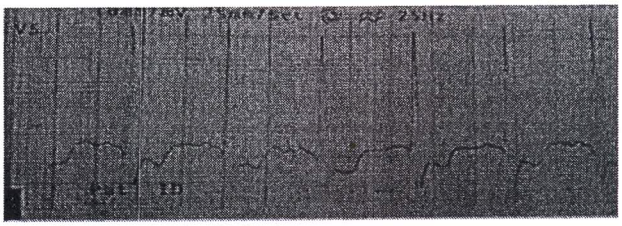

Fig. 1(k). Showing lead V5:

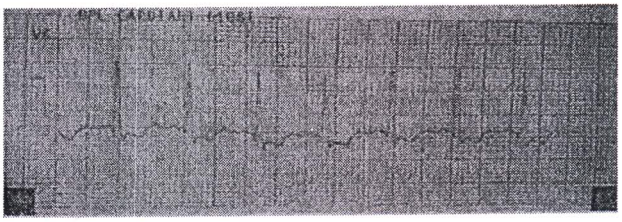

Fig. 1(l). Showing lead V6:

ECHO: Resting tachycardia, no regional wall motion abnormalities, LVEF-50%

Pseudocholinesterase: 4416 U/L.

CK-MB: 36 U/L.

Gross appearance of blood was chocolate brown. Filter paper test for methemoglobinemia was done and found to be positive.(that is dark colored blood of patient didn't get converted into bright red on exposure to air.

Methemoglobin levels-16%.

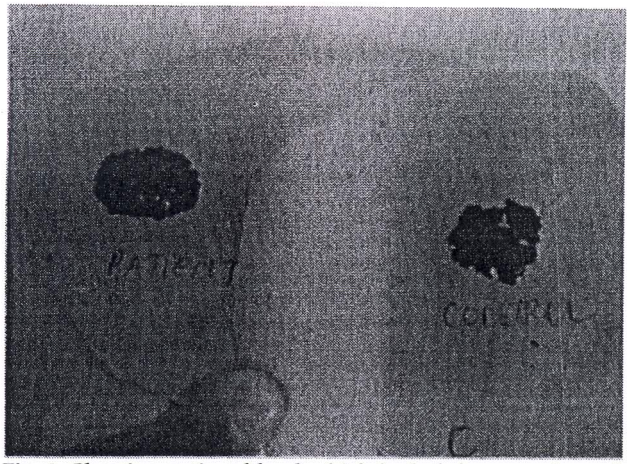

Fig. 2. Showing patient blood which is dark brown color and control blood which is bright red color.

There was no improvement in cyanosis even with high flow oxygen.

Gastric lavage was given with activated charcoal, Methylene blue at the dose of 1 mg/kg was given intravenously, there was no response. Dopamine infusion was started . Repeat ABG showed : pH:7.02, HCO_3:10, pO_2:80mmHg, pCO_2: 50mmHg, suggestive of persistent metabolic acidosis, without improvement.

6 hours later : A repeat dose of methylene blue was administered. Blood pressure and oxygen saturation didn't improve and tachycardia persisted.

12 hours later: Patient developed pulmonary edema, cardiac monitor showed unifocal ventricular premature beats, ventricular bigeminy, atrial premature beats, sinus tachycardia and ST-T changes p sted. Since she was desaturating she was put on ventilatory support,

24 hours later: patient had sinus bradycardia, cardiac arrest and succumbed to death inspite of resuscitative measures.

DISCUSSION

Normal methemoglobin is less than 1% of the total hemoglobin. Once formed, methemoglobin can be reduced enzymatically either via an Adenine dinucleotide (NADH)-dependent reaction, catalysed by cytochrome b5 reductase, or an alternative pathway utilizing the nicotine adenine dinucleotide phosphate (NADPH)-dependent methemoglobin reductase system[5].

Acute intoxication is usually asymptomatic up to the level of 10- 15% of methemoglobin, showing only cyanosis. Beyond 20%, headache, dyspnea, chest pain, tachypnea, and tachycardia develop. At 40 - 50%, confusion, lethargy, and metabolic acidosis occur leading to coma, seizures, bradycardia, ventricular dysrythmia, and hypertension. Fractions around 70% are fatal. Anemic or G6PD-deficient patients suffer more severe symptoms[5,6] . Leukocytosis has been reported, with relative lymphopenia[1]

Other effects include hepatosplenomegaly, altered liver functions, and Heinz body haemolytic anaemia[5,7] . Liver stomach, blood, and brain may act as stores and release it gradually[7] .

Recommended treatment is based on the principles of decontamination and supportive management. Methylene blue is the antidote of choice for the acquired (toxic) methemoglobinemia. It is an exogenous cofactor, which greatly accelerates the NADPH-dependant methemoglobin reductase system and is indicated if the methemoglobin levels, which are more than 30%[6]. Methylene blue is converted to leucomethylene blue which is the reducing agent. Leucomethylene blue increases the action of diaphorase-2 by more than five times though normally it has a very low activity. Dose being 1-2 mg/kg followed by bolus of 25-30 ml of normal saline, repeated an hour later upto maximum dose of 7 mg/kg over 24 hours[8].

Dose beyond 7 mg/kg/day will be harmful as the oxidizing action of methylene blue will become more than the reducing action of leucomethylene blue.

It is contraindicated in patients with G6PD deficiency, because it can lead to severe haemolysis. Ascorbic acid is an antioxidant that may also be administered in patients with methemoglobin levels of more than 30%[9]. Hyperbaric oxygen is reserved only for those patients who have a methemoglobin level > 50% or those who do not respond to standard treatment[5] .

CONCLUSION

We conclude that it is important to diagnose methemoglobinemia at an early stage as it is potentially treatable, if delayed can be life threatening. This patient had predominantly (rare and grave) cardiotoxic manifestations (i.e. tachycardia, persistent hypotension