Case Report

Nitrobenzene poisoning with methemoglobinemia

Mahesha Padyana[1], Anurag J Shetty[2], Pooja K Suresh[3]

From [1]FNB Trainee, Department of Critical Care Medicine, Manipal Hospitals Bengaluru, Bengaluru, Karnataka, India, [2]Consultant, Department of Gastroenterology, KMC Ambedkar Circle, Mangalore, Karnataka, India, [3]Associate Professor, Department of Pathology, Kasturba Medical College Mangalore, Mangalore, Karnataka, India

Correspondence to: Dr. Mahesha Padyana, FNB Trainee, Critical Care Medicine, Manipal Hospitals Bengaluru, Old Airport Road, #98, Bengaluru – 560 017, Karnataka, India. E-mail: padyana@gmail.com

Received - 21 December 2018 Initial Review - 07 January 2019 Accepted - 05 February 2019

ABSTRACT

Nitrobenzene is a rarely encountered poison in clinical practice. Methemoglobinemia associated with the poisoning can be fatal. Early identification of methemoglobinemia and treatment with methylene blue and supportive measures can prevent mortality. However, hemolysis can be an outcome of treatment with methylene blue. Here, we report the case of nitrobenzene poisoning in a 35-year-old male which was treated successfully.

Key words: *G6PD deficiency, Hemolysis, Methylene blue, Poisoning*

Nitrobenzene poisoning is rare in clinical practice. Nitrobenzene is a pale yellow-colored liquid with bitter almond odor. It is commonly used in the manufacture of aniline, benzidine, quinolone, drugs, dyes, solvent in shoe, metal polishes, and in screen printing [1]. Rarely, it is used as a flowering stimulant by gardeners as in our case. The most common manifestation of poisoning with nitrobenzene is methemoglobinemia and its early intervention can be life-saving. We report a case of nitrobenzene poisoning in a 35-year-old male which was later on successfully treated.

CASE REPORT

A 35-year-old male presented to the emergency department with an alleged history of ingestion of 22% nitrobenzene (Trade name - PROFIT) of around 100 ml. On examination, the Glasgow Coma Scale was E1V2M5 with cyanosis and a grayish-brown discoloration of palms and soles (Fig. 1). He had labored respiration with the rate of 36/min, blood pressure (BP) of 80/50 mm of Hg, and pulse rate of 140 beats/min. The patient had pupils with sluggish reaction and SpO_2 of 60% on room air. His chest was clear. Rapid sequence intubation done; however, SpO_2 remained at 81%.

Blood samples drawn for arterial blood gas (ABG) analysis had a chocolate brown color with a pH of 6.967, PaO_2 111 mm of mercury, $PaCO_2$ 24.8 mm of mercury, HCO_3 9.8 mEq/L, and SO_2 was undetectable. Based on the above-mentioned investigations, a provisional diagnosis of severe metabolic acidosis was made. An X-ray of the chest was normal and electrocardiogram showed tachycardia. Blood investigations revealed elevated total count and deranged renal parameters. Liver enzymes were elevated: Aspartate transaminase was 144 U/L and alanine transaminase was 139 U/L. A clinical and final diagnosis of methemoglobinemia was made keeping in mind the clinical, radiographic, and blood investigations.

He was started on vasopressors to improve the BP. Intravenous methylene blue (prepared as 1% sterile solution) 1 mg/kg was given to the patient. The ABG was repeated after 6 h with pH of 7.441, PaO_2 79.4 mm of mercury, $PaCO_2$ 28.1 mm of mercury, HCO_3 18mEq/L, and SO_2 91.4%. BP and sensorium improved over the next 24 h; however, the patient had dark green discoloration of urine (Fig. 2). Methemoglobin level was 14.9% (normal value up to 1% in adults).

The patient was weaned off the ventilator on day 3. His SpO_2 continued to be around 85–87% for the next 3 days even on 100% oxygen. On day 6, there was a drop in hemoglobin to 5.1 gm/dL. Lactate dehydrogenase was 750 units, total bilirubin was 2.5 units/L, and direct bilirubin was 1.3 units/L. Peripheral smear showed microcytic hypochromic anemia, anisopoikilocytosis with schistocytes, microcytes, and target cells suggestive of hemolysis (Fig. 3). Repeat methemoglobin was 6.25%. The patient required packed red cell transfusions. The patient also had ventilator-associated pneumonia which was managed successfully with antibiotics and he was discharged on day 14. A follow-up was planned after 1 month, but unfortunately, the patient was lost to follow-up.

DISCUSSION

Methemoglobinemia commonly caused by ingestion or skin exposure to an oxidizing agent. Aniline, benzocaine, dapsone, phenazopyridine (Pyridium), nitrites, nitrates, copper sulfate, and

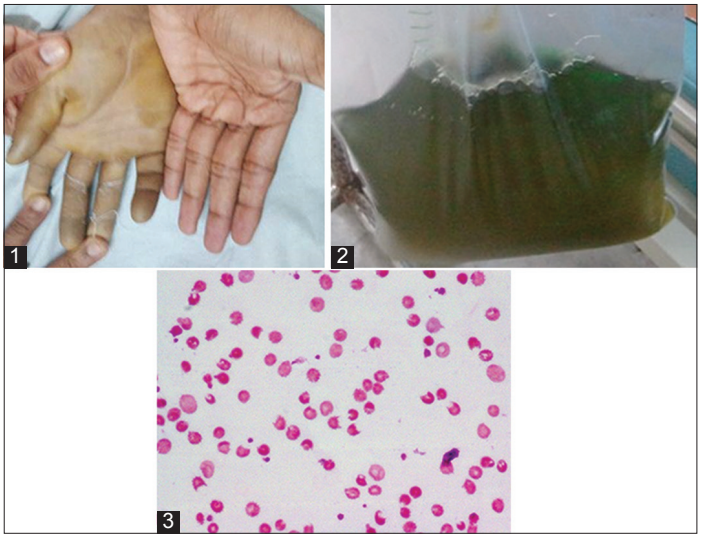

Figure 1: Cyanosis and a grayish-brown discoloration of palms, Figure 2: Dark green discoloration of urine, Figure 3: Peripheral smear showed microcytic hypochromic anemia, anisopoikilocytosis with schistocytes, microcytes, and target cells suggestive of hemolysis

naphthalene are the commonly encountered drugs and toxins with methemoglobinemia. Chlorates (sodium, potassium, or barium) are used in the manufacture of explosives, matches, dyes, weed killers and as a mouthwash, and weak antiseptic [2].

The rapid development of methemoglobinemia is responsible for the toxic effect of nitrobenzene [3]. The iron within the hemoglobin is oxidized from the ferrous (Fe^{2+}) state to the ferric (Fe^{3+}) state, resulting in the inability to transport oxygen and causes a brownish discoloration of the blood [4]. Methemoglobin once formed reduced enzymatically either through an Nicotinamide Adenine Dinucleotide (NADH)-dependent reaction, catalyzed by cytochrome b5 reductase, or an alternative pathway utilizing the Nicotinamide Adenine Dinucleotide Phosphate (NADPH)-dependent methemoglobin reductase system.

During acute intoxication, patients are asymptomatic showing the only cyanosis up to the level of 10–15% of methemoglobin. A headache, dyspnea, chest pain, tachypnea, and tachycardia develop when methemoglobin is >20%. At 40–50%, confusion, lethargy, and metabolic acidosis occur, leading to coma, seizures, bradycardia, ventricular dysrhythmia, and hypertension. Fractions around 70% are fatal. Anemic or G6PD-deficient patients suffer more severe symptoms [5].

Methylene blue is an exogenous cofactor, which accelerates the NADPH-dependent methemoglobin reductase system and is indicated if the methemoglobin levels, which are >30%, and hence, it is an effective antidote for methemoglobinemia [3]. It is administered intravenously at 1–2 mg/kg (up to 50 mg dose in adults) as a 1% solution over 5 min, with a repeat in 1 h, if necessary. Methylene blue is an oxidant at levels of >7 mg/kg and, therefore, may cause methemoglobinemia in susceptible patients [4]. Oral methylene blue (2 mg/kg) also can be used as an alternative to intravenous preparation [1]. It is contraindicated in patients with G6PD deficiency because it can lead to severe hemolysis. Ascorbic acid is an antioxidant also useful in some cases [4]. Exchange transfusion is indicated in severe cases [3]. Hyperbaric oxygen is reserved only for those patients who have a methemoglobin level >50% or those who do not respond to standard treatment [5]. N-acetyl cysteine has also been tried among some patients [4].

Hemolytic anemia has been described in a limited number of studies before, however, dropping hemoglobin and peripheral smear suggestive of hemolysis as in our patient suggestive of oxidative damage to the red blood cells [6].

CONCLUSION

Early diagnosis of methemoglobinemia with nitrobenzene poisoning and early initiation of treatment with methylene blue can result in the good outcome as in our patient. Nitrobenzene poisoning is uncommon also methylene blue intravenous preparations are not readily available. Methemoglobin estimation also takes time in semi-urban settings where clinical judgment has a more superior role in early detection and treatment.

REFERENCES

1. Guptha A, Jain N, Agrawal A, Khanna A, Gutch M. A fatal case of severe methaemoglobinemia due to nitrobenzene poisoning. Emerg Med J 2012;29:70-1.
2. Wright RO, Lewander WJ, Woolf AD. Methemoglobinemia: Etiology, pharmacology, and clinical management. Ann Emerg Med 1999;34:646-56.
3. Chongtham DS, Phurailatpam J, Singh MM, Singh TR. Methemglobinemia in nitrobenzene poisoning. J Postgrad Med 1997;43:73-4.
4. Saxena H, Saxena AP. Acute methaemoglobinaemia due to ingestion of nitrobenzene (paint solvent). Indian J Anaesth 2010;54:160-2.
5. Dutta R, Dube SK, Mishra LD, Singh AP. Acute methemglobinemia. Internet J Emerg Intensive Care Med 2008;11:1-5.
6. Perera M, Shihana F, Kularathne K, Dissanayake D, Dawson A. Acute methaemoglobinaemia after massive nitrobenzene ingestion. BMJ Case Rep 2009:35-9.

Funding: None; Conflict of Interest: None Stated.

How to cite this article: Padyana M, Shetty AJ, Suresh PK. Nitrobenzene poisoning with methemoglobinemia. Indian J Case Reports. 2019;5(1):59-60.

Doi: 10.32677/IJCR.2019.v05.i01.020