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Case Report

Late presentation of secondary cycling - nitrobenzene poisoning: A rare case report

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Abstract

We presented here a case of acute nitrobenzene poisoning in which effective clinical evaluation and timely management in form of repeated intravenous methylene blue and blood transfusions played a vital role to save a life. It is very important to take care of patient who presented late after heavy exposure form the secondary cycling of nitrobenzene from body stores. Clinicians should be aware of this uncommon, but treatable and potential serious poisoning of nitrobenzene. Methemogobinemia can leads to high mortality but effective treatment with methylene blue is preferential.

Key words

Acute methemoglobinemia, Methylene blue, Nitrobenzene poisoning, Blood transfusion.

Introduction

Nitrobenzene is also known as nitrobenzol, mirbane oil or essence of mirbane. When introduced into the body, it is metabolized by reduction to aniline. Nitrobenzene and aniline are typical aromatic nitro compounds and aromatic amino compounds that cause methemoglobinemia. Significant methemoglobinemia due to acute nitrobenzene poisoning is uncommon and rare but life threatening emergency condition. Once poisoning is suspected on clinical evaluation, early and effective management of it may change the outcome of a patient in positive manner.

Case report

A 30 years old, irritable, anxious male presented to emergency department who referred from other centre on mechanical ventilation with cyanosis and a greyish-brown hue. On examination, he had labored respiration of 26/min, blood pressure was 129/74 mm of Hg, pulse rate was 74/min, pupils with sluggish reaction, and SpO_2 of 89% only. There was a history of severe pain in the abdomen, nausea,

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vomiting, and dizziness, which was treated on admission at primary centre. At primary centre, oral methylene blue was given (5 ml, 12 hourly), as to non-availability of intravenous therapy. An urgent ultrasonography of abdomen was done which ruled out any abdominal catastrophe and showed a generalized mild to moderate hepatic inflammation. Blood samples were drawn for arterial blood gas (ABG) analysis which had a chocolate brown color, which did not improve on exposure to 100% oxygen and showed compensated metabolic acidosis. X-ray of the chest and ECG were within normal limits while WBC and liver enzymes were markedly raised. Serum creatinine and blood urea were within normal range. Hemoglobin at admission was 9.4 gm%, which dropped down to 6.3 gm% on 9th day. Similarly serum bilirubin at admission was 2.0 mg% which was raised to 13.0 mg%. A clinical diagnosis of severe acute methemoglobinemia due to nitrobenzene poisoning was made.

100 mg of methylene blue (prepared as 1% sterile solution) was given intravenously and repeated after 12 hours. This improved patient's SpO_2 to 92% and then after intravenous vitamin K; vitamin C, 10% dextrose, anxiolytics, oral iron, and intravenous antibiotic were also given. Urine output was maintained above 100 ml/hour with proper hydration, maintaining a normal central venous pressure (CVP).

Multiple blood and blood products like fresh frozen plasma (FFP) were transfused. Patient at admission had severe hypokalemia (2.5 mEq/L), which was corrected by intravenous slow potassium infusion. Methemoglobin estimation in blood was done and it was significantly high (11.1 units as compared to normal values of 0.00 to 2.0). He was extubated at 48 hours and maintained on a continuous positive airway pressure (CPAP) mask, with arterial blood gas (ABG) analysis which showed a saturation of 93% and a PaO_2 of 112. He improved rapidly after the 10th day with SpO_2 of 90% on room air. Patient had a single episode of generalized tonic clonic seizure (GTCS) on 11th day and was epsolinised, followed by oral dilantin tablets (100 mg TDS). CT head was absolutely normal but liver enzymes were raised. He was discharged on the 14th day on oral iron, folate, ascorbic acid, and liver enzyme supplements and breathing exercises.

Discussion

Nitrobenzene is a pale yellow, oily liquid, with bitter almond odor and it is widely used as an intermediate in the production of various solvents, like paint remover. Common occupational exposure of nitrobenzene is via inhalation or through absorption of skin [1, 2]. In 1886, first report of nitrobenzene poisoning was noted [3] and then after various fatality reports were come into noticed [3, 4]. Nitrobenzene poisoning can be accidental or suicidal in manner [5]. Accidental exposure may possible in patients who are consuming well water with extremely high levels of nitrites and nitrates in it [6]. Lethal dose of it is varied from 1-10 g, as per different scholar authors [7, 8, 9]. A systematic literature review of already published articles on it does not provide any significant conclusive matter regarding fatalities and dose of ingestion [8]. Nitrobenzene poisoning is usually presented as chronic poisoning or as occupational hazard with development of methemoglobinemia [10]. The clinical features of ingestion of such poison are due to the rapid development of methemoglobinemia [7, 11], which is a condition of altered hemoglobin formation in which the iron presented within the hemoglobin is oxidized into ferric (Fe^{3+}) state from the ferrous (Fe^{2+}) state, resulting in the inability to transport oxygen effectively [12, 13, 14] and causes brownish discoloration of the blood and functional anemia [6]. After formation of

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methemoglobin, it can be reduced enzymatically either via an adenine dinucleotide (NADH)-dependent reaction, which is catalysed by cytochrome b5 reductase, or an alternative pathway utilizing the nicotine adenine dinucleotide phosphate [15]. Certain drugs and chemicals can accelerate production of methemoglobin like antimalarial drugs such as chloroquine and primaquine; nitrites or nitrates, flutamide, inhaled nitric oxide, metoclopramide, local anesthetic agents like benzocaine; acetanilide, nitroprusside, sulfonamides, phenacetin, phenazopyridine hydrochloride, phenytoin, chlorates, probenecid etc. [16].

Normal physiological level of Methemoglobin is less than 1% of total hemoglobin [17]. At level of 10-15% of methemoglobin, person is usually asymptomatic with mild cyanotic changes. When methemoglobin level is 20-40%, headache, dyspnea, chest pain, tachypnea, and tachycardia develop [18]. At 40 – 50% level of methemoglobin, person feels confusion, lethargy, and metabolic acidosis which later on leading to coma, seizures, bradycardia, ventricular dysrythmia, and hypertension [19]. Methemoglobin level around 70% is considered as fatal [20]. More severe symptoms are noted in patients with anemia or G6PD deficiency [4, 7]. In certain cases, leukocytosis has been reported along with relative lymphopenia [8]. Altered liver function tests, hepato-splenomegaly, and Heinz body haemolytic anaemia are other significant features [4, 21, 22]. Nitrobenzene is metabolized in the body and converted into p-nitrophenol and aminophenol and later on excreted in urine (up to 65%), and in stools (up to 15%) after five days of ingestion. Liver, stomach, blood, and brain may act as storage house and release it gradually [21].

History of chemical ingestion, characteristic bitter almond smell, persisting cyanosis on oxygen therapy without severe cardiopulmonary disease, low arterial oxygen saturation, with normal ABG (calculated) oxygen saturation are very important for diagnosis. Methemoglobin detection can be done bedside by placing few drops of blood on white filter paper and observing for color change in which deoxyhemoglobin brighten and methemoglobin holds color [23]. Dark brown blood that fails to turn bright red on shaking, which suggests methaemoglobinaemia and this is supported by the chocolate red color of dried blood. Presence of nitrobenzene compounds may be confirmed spectrophotometrically and estimated by the butanone test of Schrenk [1], methemoglobin levels in the blood, and urinary presence of p-nitrophenol and p-aminophenol [3, 21, 24].

Plan of management is based upon the principles of decontamination along with symptomatic and supportive treatment. Methylene blue is the drug of choice (antidote) for the treatment of acquired (toxic) methaemoglobinaemia [25]. 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% [7]. It is administered intravenously at 1 – 2 mg/kg (up to 50 mg dose in adults,) as a 1% solution over five minutes; with a repeat in one hour, if necessary. Methylene blue is act as an oxidant at levels of more than 7 mg/kg, and therefore, may cause methaemoglobinaemia in susceptible patients [26]. 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% [27]. In recent studies, N-acetylcysteine has been shown to reduce methemoglobin, but it is not yet an approved treatment for methaemoglobinaemia [27]. Exchange transfusion is indicated in severe cases [7, 27]. Hyperbaric oxygen is reserved only

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for those patients who have a methemoglobin level > 50% or those who do not respond to standard treatment. Exchange transfusion is more widely and rapidly available compared to hyperbaric oxygen. Exchange transfusion involves replacement of the patient's red cells with donor cells and has been used in the treatment of various hemoglobinopathies [15].

In this case, we repeated low dose methylene blue and blood transfusions helped in tiding over the fluctuating symptoms due to the release of nitrobenzene from the body stores, without exceeding the maximum dose. Fresh blood transfusion improved the oxygen carrying capacity and haemoglobin content, improving the patient symptomatically. Oral charcoal and purgation up to five days helped to eliminate the body stores of nitrobenzene and prevented secondary deterioration in the patient .Taking care of nutrition, adequate urine output, and hepatoprotection prevented kidney and liver failure, which have been cited as late effects [3, 21]. Regular use of charcoal and purgation by peglag during hospital stay may be of some help according to some centers. Forced diuresis can lead to a rapid fall in methemoglobin levels and improved discoloration [8]. Ascorbic acid supplements are useful for follow-up management of methaemoglobinaemia [28].

Conclusion

Clinicians should be aware of this uncommon, but treatable and potential serious poisoning of nitrobenzene with secondary cycling from the body tissues. Methemogobinemia can leads to high mortality but effective treatment with methylene blue is preferential.

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