Case Report

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A Rare Case of Occupational Aniline Poisoning: Management in a Limited-Facility Setting

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Abstract

Cyanosis along with altered mental should bring all the possible ethiologies into her mind in a minimum of time, based on the trauma, medical, environmental, and occupational history of the patient. Poisoning with methemoglobinemia inducing agents is one of the most important differentials especially when a history of occupational exposure to these agents is present.The patient, a 41-year-old healthy woman and engineer, experienced symptoms after exposure to aniline leading to dizziness and weakness, prompting a visit to the emergency department with cyanosis and low oxygen saturation. Initial vital signs showed decreased oxygen levels and elevated respiratory rate with normal ABG values despite ongoing cyanosis. Patient required intubation, mechanical ventilation, and was diagnosed with ARDS based on chest X-ray findings. Management included IV diuretics, 100% oxygen, and antioxidant treatment in the ICU. Despite treatment, oxygen saturation remained at 88% on the first day.This case is a reminder of the importance of taking occupational history and management of aniline toxicity in a setting where methylene blue, the drug of choice for aniline toxicity, is not available in the drug stock.

Keywords: Aniline, aniline poisoning, emergency medicine, occupational medicine, toxicology

Introduction

Aniline, introduced to the chemical industry in the late 1800s (1), is primarily used for industrial manufacturing of dyes, drugs, rubber accelerators, and other chemicals (2). It can enter the body through inhalation, ingestion, or dermal absorption (3). Early toxic effects include methemoglobin (MetHb) formation and damage to red blood cells (RBCs) (4). Phenylhydroxylamine, an active metabolite of aniline, catalyzes MetHb formation in vivo (5). Additionally, rat models show splenic toxicity related to nitrated proteins found only in aniline-exposed rats (6).

Aniline exposure can lead to either acute or chronic poisoning. Acute poisoning is characterized by bluish lips, Heinz's bodies in the blood, and para-aminophenol in urine. Chronic poisoning symptoms include headache, unsteadiness, memory loss, sleeplessness, increased knee-jerk reflex, and finger tremors (7).

Standard therapies for acute aniline poisoning include intravenous infusion of methylene blue (MB), glucose, ascorbic acid, and exchange transfusions, but responses vary among patients. Lubash reported successful treatment with hemodialysis in one case(8). This case report describes a patient with unintentionalpoisoning of aniline, who admitted with the symptoms and signs of acute respiratory distress (ARDS).

Case Report

Our patient was a 41-year-old healthy woman, an engineer at a car liquid manufacturing company. She developed symptoms after six hours of unprotected cutaneous contact and respiratory aspiration of pure aniline in the laboratory. Her first symptom was dizziness while driving from her workplace to home. However, within two hours, her symptoms progressed to weakness and drowsiness, prompting her to seek help. She was subsequently brought to the emergency department (ED) by EMS, presenting with a cyanotic appearance despite receiving nasal oxygen, with a Glasgow Coma Scale (GCS) of 15/15.

On arrival, her vital signs demonstrated a significantly decreased oxygen saturation of 60% and an elevated respiratory rate of 22/min, while other vital signs were within normal ranges. Notably, she exhibited pronounced peripheral cyanosis, characterized by a bluish discoloration of the lips, fingertips, and toes. This cyanosis was indicative of severe hypoxemia and poor peripheral perfusion. Despite being on supplemental oxygen, the cyanosis persisted, suggesting that the hypoxemia was due to a failure of oxygen exchange at the alveolar level, rather than simply inadequate oxygen delivery.

The first arterial blood gas (ABG) sampling showed normal values, but the persistent cyanosis and low oxygen

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saturation despite oxygen supplementation through a reservoir mask were concerning. This raised suspicion for an underlying condition impairing gas exchange. The patient was then intubated and placed on mechanical ventilation (MV). Urinary catheterization revealed the excretion of brownish urine, suggesting a hemolytic event possibly due to aniline toxicity.

A chest X-ray revealed blunting of the left costophrenic angle, consistent with early signs of pulmonary edema. This, coupled with the patient's hypoxemia and the clinical context, led to the diagnosis of Acute Respiratory Distress Syndrome (ARDS). In this case, ARDS has been characterized by acute onset of respiratory failure due to non-cardiogenic pulmonary edema, marked by bilateral infiltrates on chest imaging, likely developed secondary to chemical pneumonitis and direct pulmonary toxicity from the inhalation of aniline.

The patient was transferred to the intensive care unit (ICU) for further management. Despite being on a ventilator with 100% FiO2, her oxygen saturation remained critically low at 88% on the first day of admission, indicative of severe ARDS. Management continued with intravenous (IV) infusion of loop diuretics, aiming to reduce pulmonary edema, and the ventilator settings were adjusted to optimize oxygenation and reduce ventilator-induced lung injury.

In addition, antioxidant treatment, including IV infusion of vitamin C (2 g daily) and N-acetylcysteine (NAC) (7 g every 8 hours), was initiated upon ICU transfer to mitigate oxidative stress and potential lung injury caused by the chemical exposure. The IV infusion of furosemide continued at a dosage of 2 mg/hr to manage fluid balance and minimize pulmonary edema.

Table 1: Laboratory test of first day of admission

Test	Result (reference values)
Complete blood count	
Red blood cells	3.51 cells/mcL (4.10-5.10)
Hemoglobin	9.4 g/dl (12.0-16.0)
Hematocrit	29.3% (39-50)
Platelets	245000 cells/mcL (150-450)
White blood cells	6400 cells/mcL , N: 70%, L:30% (4000-11000)
Arterial blood gas	
PH	7.44 (7.37-7.44)
pO_2	247.3 mmHg (80-100)
pCO_2	38.6 mmHg (35-45)
HCO_3	26.8 mmol/L (22-26)
Coagulation	
PT patient	13 sec
PT control	13 sec
PT activity	100% (70-100)
INR	1
PTT	30 sec(30-40)
Blood biochemistry	
Fasting blood glucose	82 mg/dl (70-115)
Blood urea Nitrogen	12 mmol/L (7-24)
Creatinine	0.9 mg/dl (0.6-1.3)
Aspartateaminotrans-	17 U/L (up to 31)
ferase Alanine amino-	11 U/L (up to 40)
transferase	110 U/L (80-306)
Alkaline phosphatase	142 mmol/L (135-145)
Sodium	3.8 mmol/L (3.5-5.1)
Potassium	7.9 mg/dl (8.5-10.5)
Calcium	4.3 mg/dl (2.6-4.5)
Phosphorus	

Discussion

Various conditions, including acute diarrhea, consumption of high-nitrate water and food, use of specific medications like topical anesthetics, silver nitrate, sulfonamides, phenacetine, and sodium valproate, or exposure to aniline, coloring compounds, or cleaning solutions, can potentially trigger acquired MET (9).

Aniline and its derivatives were among the earliest substances linked to MET. Safety measurements in industrial settings have reduced acute aniline poisoning cases compared to earlier decades (10).However, in our case, due to occupational exposure, aniline poisoningoccurred through inhalation and skin contact in a factory setting without proper protective measures.

MetHb is formed by a complex series of oxidation reactions. For aniline, it is through their metabolites in the body after biotransformation of aniline to phenylhydroxylamine by hepatic mixed-function oxidase enzymes. This metabolite then contributes to the formation of MetHbs (11).MET refers to the presence of greater than the average physiological concentration of 1 to 2% MetHb in RBCs (12).

In the setting of MET, the patient's condition is usually better than one would expect from the severity of cyanosis, but the cyanosis is unresponsive to oxygen therapy. For example, in our case, the patient's awareness was intact upon admission to ED. However, she was unresponsive to oxygen therapy via nasal cannula, and finally, the managing team decided to intubate her (13).

Pulse oximetry is not reliable, and ABG, as a complementary workup, often reveals normal partial pressures of oxygen (pO2) and carbon dioxide (pCO2), a normally calculated hemoglobin oxygen saturation, an increased MetHb concentration, and possibly metabolic acidosis(13). This pattern was also compatible with the ABG results drawn from the patient in the ED.

Intravenous MB is the preferred treatment for toxic MET. Although no controlled trials have been conducted, clinical experience suggests that MB can enhance the conversion of MetHb to hemoglobin by sixfold (14). However,there are reports of hemolytic anemia (HA) following IV administration of MB for treatment of aniline toxicity. This is attributed to the fact that both aniline and methylene blue can cause oxidative stress, which wrecks RBCs (15). Moreover, based on some case reports, MB sometimes cannot solve the problem alone, so more measurements, such as hemodialysis and exchange transfusion (ET), are

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required. For example, in a 4.5-year-old girl who accidentally was poisoned by aniline when she was given *cough syrup*, the treatment was done through two consecutive IV doses of MB. The therapy first reducedMetHbbut, after two hours, the MetHb levels rose again, which led to an alteration in cognitive level. Immediately, the ET was started, leading to a significant drop in MetHb level and clinical improvement (16). Another case report also described a patient who did not respond to MB infusion after a suicidal oral intake of 80 ml of aniline. She developed an episode of seizure during her transference to another medical facility for hemodialysis after 22.5 mg of IV MB and the exchange of 1000 ml of blood. After that, hemodialysis with re-administration of IV MB led to improvement of MET, skin discoloration, and level of consciousness. Another dose of MB was administered after hemodialysis, and the patient gradually regained consciousness 24 hours later (8).

However, in our case, due to the unavailability of MB, the treatment was established on symptomatic treatment, including intubation and intravenous furosemideto address ARDS, and systemic antioxidants (vitamin C and NAC). Fortunately, these actions and closemonitoring of the patient in the ICU resulted in the patient's full recovery. The patient was also in good health during follow-up visits.

In two cases of occupational exposure, similar to the presented case, inhalation of aniline fumes has been reported as the cause of fatal MET. In both of them, HA became apparent after treatment with MB, mirrored in a dropped number of RBCs (15). In our case, the RBC count was relatively stable, and there was no HA induced by aniline.

There is also one case of occupational poisoning of aniline with low levels of MetHb in which conservative management was performed only with supplementary O_2 and close monitoring of VS and laboratory tests (17). However, in another case of exposure to large amounts of aniline during unloading aniline from bulk trucks the management was done with supplementary O2 and IV administration of MB in 4 consecutive doses up to six hours. He presented to ED acutely ill and with cyanoderma on his entire body. He also developed skin lesions of primary burns and contact dermatitis,and cornea inflammation caused by aniline.The dermal and corneal lesions were treated by topical ointments and eye drops, respectively (17).

In conclusion, anilinepoisoning, aniline poisoning, by various routes, results in MetHb, which varies in severity. Management includes a range of measures, from simple supplementary O2 to endotracheal intubation, administration of MB to ET, and hemodialysis. To our best of knowledge, the presented case is the first case in which the IV furosemidewas part of the management and exclusively the MET was managed without MB, but with systemic administration of antioxidants. It is crucial to promptly identify the underlying cause of acquired MET to restore normal tissue oxygenation and metabolism, prevent long-term complications, and minimize the risk of recurrent episodes.

Conclusion

Aniline is an aromatic agent that has historically been used in chemical industries. Most of the reported incidences of aniline poisoning are between 1900-2000, which are related to industrial exposures. Our case was a young woman who suffered acute symptoms of aniline poisoning. Timely admission and therapeutical interventions avoided further damage that can be tissue ischemia due to prolonged MET. Aniline poisoning is a rare poisoning etiology, which often can be conferred from a thorough occupational history.

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