Case Report

Unusual complication of aluminum phosphide poisoning: Development of hemolysis and methemoglobinemia and its successful treatment

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Abstract

Methemoglobinemia and hemolysis are rare findings following phosphine poisoning. In this paper, a case of aluminum phosphide (AlP) poisoning complicated by methemoglobinemia and hemolysis with a successful treatment is reported. A 28-year-old male patient presented following intentional ingestion of an AlP tablet. In this case, hematuria, hemolysis and methemoglobinemia were significant events. A methemoglobin level of 46% was detected by CO-oximetry. The patient was treated with ascorbic acid and methylene blue and he also received supportive care. Two weeks after admission, the patient was discharged from the hospital. Hemolysis and methemoglobinemia may complicate the course of phosphine poisoning.

Keywords: Aluminum phosphide, hemolysis, methemoglobinemia, phosphine, poisoning

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Introduction

Aluminum phosphide (AlP) is an inexpensive and highly effective solid fumigant pesticide that is used in Iran.[1] Human poisoning is relatively common, and the mortality rate in Iran, as in many developing countries, is high. Mortality is often related to the absence of an effective antidote.[2]

AlP reacts with water, liberating phosphine (PH_3) gas. PH_3 inhibits mitochondrial oxidative phosphorylation, interferes with protein synthesis [3] and participates in free radical-induced toxicity.[4] These processes cause diffuse cellular dysfunction, leading to multiorgan failure.[5] The most consequential clinical manifestations of acute AlP poisoning are cardiovascular and respiratory.[3]

Uncommon complications following ingestion include gastroduodenitis, hepatitis, acute tubular necrosis, delayed esophageal stricture [6] and methemoglobinemia.[7]

In this article, we report a case in which the toxic effects were complicated with methemoglobinemia and hemolysis.

Case Report

A 28-year-old man with no significant past medical history was admitted to the Loghman Hakim Hospital Poison Center with a history of intentional ingestion of one tablet of AlP about 8 h prior to admission. He denied the ingestion of any other drug or intoxicant. The patient had nausea and vomiting on admission. Physical examination showed a lethargic man with the following vital signs: blood pressure (BP) 80/50 mmHg; heart rate (HR) 100 beats/min and respiratory rate (RR) 14 breaths/min. The conjunctivae were not pale and the scleras were not icteric. The general physical and neurologic examinations were not significant. As the ingestion had taken place about 8 h earlier, gastric decontamination was not performed.

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Table 1: Laboratory data of the patient during hospitalization

Parameter (normal range)	Days after admission							
	0	2	4	6	8	10	12	14
Blood glucose (70–110 mg/dL)	175	98	107	82	92	95	96	90
Creatinine (0.5–1.7 mg/dL)	0.8	0.6	0.7	0.8	0.8	0.9	1.1	0.9
Sodium (135–145 mEq/L)	142	133	135	142	146	138	140	141
Potassium (3.5–4.5 mEq/L)	3.1	4.3	4.1	3.1	4.2	4	4	4.2
Total bilirubin (0.2–1.3 mg/dL)	NM	8.6	14	8.9	NM	2.3	1	1
Direct bilirubin (< 0.2 mg/dL)	NM	0.5	1.4	2.1	NM	0.8	0.6	0.5
Aspartate aminotransferase (11–47 IU/L)	35	35	114	62	29	29	57	75
Alanine aminotransferase (7–53 IU/L)	24	24	41	52	31	36	29	47
Alkaline phosphatase (38–126 IU/L)	106	114	120	110	193	171	203	188
Prothrombin time (11–13 s)	13.6	18	14	12.5	12.3	14.4	12.9	11
Partial thromboplastin time (25–36 s)	25	30	33	25	23	25.9	25.7	29
International normalized ratio	1.3	1.4	NM	1.2	1.4	NM	NM	NM
Creatinine phosphokinase (20–200 U/L)	1050	1013	2351	2197	357	244	152	66
Lactate dehydrogenase (225–500 U/L)	1013	1113	3584	3332	1933	1307	1071	887
White blood cells (m^3)	8000	15000	14000	5600	5300	8100	8200	7700
Hemoglobin (g/dL)	16.4	7.6	6.8	8.2	8.5	8.2	8.2	8.8
Platelet count (m^3)	117,000	98,000	32,000	83,000	41,000	164,000	310,000	357,000

NM: Not measured

Laboratory results from the emergency department are reported in Table 1. Arterial blood gas analysis revealed mild metabolic acidosis (pH = 7.30, $PaCo_2$ = 35 mmHg, HCO_3 = 20 mEq/L).

The patient was admitted in the intensive care unit (ICU) for further monitoring and supportive care. He received two 50 mEq boluses of sodium bicarbonate intravenously and 1.5 L of normal saline over 2 h. Norepinephrine was administered as a vasopressor with improvement of his BP. Along with maintenance fluids, magnesium sulfate and calcium gluconate were also administered.

Thirty hours after admission, the patient began passing dark-colored urine and was noted to be icteric. His hemoglobin concentration decreased from 14.9 g/dL to 7 g/dL during the next 24 h. Further evaluation revealed both that there was no bleeding from any site and that the patient had intravascular hemolysis. Laboratory testing included negative Coomb's direct and indirect test, reticulocyte count 17.9%, peripheral blood smear anisocytosis, poikilocytosis and schistocytosis and a normal G-6-PD activity.

The patient was treated with hydrocortisone and cross-matched packed red blood cells. Six liters of saline along with 150 mEq of sodium bicarbonate was administered per day over the next 6 days in an effort to prevent precipitation of hemoglobin in the renal tubules. The norepinephrine and electrolyte infusions were gradually stopped over the next 72 h after admission.

On the third day of admission, bluish discoloration of the periphery and cyanosis of the mucous membranes were noted. His vital signs at that time were: BP 120/80 mmHg; HR 88 beats/min; RR 35 breaths/min; the cardiovascular, respiratory and abdominal examinations were all normal. A drop in oxygen saturation in spite of high FIO_2 and tachypnea prompted intubation and mechanical ventilation.

CO-oximetry revealed a methemoglobinemia concentration of 46%. Chest radiography and electrocardiography were normal. The patient received vitamin C (1 g/q6h/IV) for 24 h because methylene blue was not available initially. Twelve hours after treatment with vitamin C, the methemoglobinemia concentration decreased to 33%. Once obtained, methylene blue (1 mg/kg of 1% solution intravenously) was administered a total of six-times. By the use of high doses of methylene blue, the methemoglobinemia concentration decreased to 23%.

On the ninth day of admission, the patient was extubated. Two weeks after admission, the laboratory data showed normalization [Table 1] and patient was transferred to the general ward. After 24 h, he was discharged from the hospital.

Discussion

Hemolysis and methemoglobinemia are the rare

clinical presentations in acute AlP poisoning, and may complicate the course of this poisoning.

Jaundice due to hepatic damage may occur in a few patients with AlP poisoning.[8] This could be related to persistent hypoperfusion of the liver, although a direct toxic effect is also likely. However, in our patient, jaundice was due to intravascular hemolysis, as evidenced by a predominant indirect hyperbilirubinemia, normal liver enzymes, reticlucytosis and the presence of schistocyte in the peripheral blood smear. To date, intravascular hemolysis caused by AlP poisoning has been reported in only two patients, one of whom had G-6-PD deficiency.[9,10]

Morphological changes in erythrocytes are reported following *in vitro* incubation with PH_3 gas. However, although all cells displayed crenation, and no hemolysis or Heinz body formation was noted. Thus, it is unlikely that hemolysis can be related to the direct effects of PH_3 on the erythrocytes.[11] However, PH_3 may produce lipid peroxidation that can disturb the integrity of the cells and lead to massive cell damage and death.[12]

Generalized cyanosis in the presence of normal arterial oxygen tension and the failure of the cyanosis to resolve with oxygen therapy is an important diagnostic clue, and almost always represents methemoglobinemia.[13] Diagnosis is confirmed with multiple wavelengths CO-oximetry.

PH_3 and arsine are chemically very similar and thus occurrence of methemoglobinemia by both of them is not surprising.[13] The other mechanism of action of PH_3-induced methemoglobinemia is induction of free radicals.[14] In this case, oxidative stress may have a primary role due to the coexistence of methemoglobinemia and intravascular hemolysis.

In spite of our previous case report,[7] this patient was successfully treated by administration of vitamin C and methylene blue. One possible explanation is the physiological difference between patients or perhaps the severity of toxicity. Furthermore, ascorbic acid works slowly and generally is considered ineffective for the treatment of acute methemoglobinemia.[13] Methylene blue reduces methemoglobin to hemoglobin via the NADPH methemoglobin reductase pathway. The reason for unresponsiveness to treatment with methylene blue in our previous case[7] may be that conventional doses of methylene blue were ineffective in reducing phosphine-induced methemoglobin fractions, and it is same as other antioxidants like N-acetylcysteine.[13] In the present case, administration of vitamin C that follows by methylene blue may have a role in successful treatment. This hypothesis needs to be more evaluated in further experimental studies.

Conclusions

Jaundice in patients with AlP poisoning can be independent of hepatic damage. One should be aware of the possibility of the occurrence of intravascular hemolysis in such cases, particularly those involved in emergency care.

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