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A Rare Case of Aluminum Phosphide Induced Thrombotic Thrombocytopenic Purpura

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ABSTRACT

Aluminum phosphide (AlP) has remained a chemical cause of completed suicides in some developing countries. ALP toxicity can cause multi-system damage. As far as we know, this is the first case of ALP-induced Thrombotic Thrombocytopenic Purpura (TTP) and its successful management. A 34-year-old man, who had attempted suicide with ALP was admitted to our hospital. On the 3rd day of admission, the patient developed hematuria, hemolysis, and thrombocytopenia. Based upon available evidence, TTP was diagnosed. Following a complete patient evaluation, ALP was recognized as the probable cause of TTP. Following the treatment using prednisolone and therapeutic plasma exchange, the patient substantially improved. Finally, he was discharged on the 22nd day. Toxin-induced intravascular hemolysis should be considered for patients presenting with ALP toxicity. As reported in this patient, TTP is another manageable consequence of ALP poisoning.

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1- Introduction

Aluminum phosphide (ALP), also known as the rice tablet or the wheat pill, is a fumigant and a pesticide using for the protection of the grains. Although its distribution and consumption in many countries are currently prohibited, it remains a chemical cause of completed suicides in some Asiatic countries (1). This substance releases phosphine gas after exposure to moisture or water. Phosphine inhibits oxidative phosphorylation, impairs cytochrome oxidase, and disrupts protein synthesis, which all can lead to cell death. ALP toxicity can cause multi-system damage. ALP intoxication symptoms are non-specific and vary according to the route of intoxication, including respiratory, dermal, or oral exposure. The elapsed time of exposure to the toxin is also a determining factor in clinical features. Due to the cellular hypoxia mechanism of action, organs that consume the most oxygen in the body are more susceptible to the effects of ALP (1,2). The usual consequence after oral administration of this poison are as follows: mild toxicity can cause gastrointestinal discomfort, pain, and tachycardia, and on the other extreme in the case of severe toxicity, cardiovascular collapse, impaired nervous system, severe metabolic acidosis, respiratory and then renal and hepatic failure can occur. One of the most critical results is disseminated intravascular coagulation. Some clinical manifestations of ALP poisoning are less common but need to be taken into consideration while evaluating patients. These manifestations include polyserositis, hepatitis, acute tubular necrosis, delayed esophageal stricture, and methemoglobinemia (3,4). One of these complications is intravascular hemolysis or methemoglobinemia that can lead to hemolytic anemia (5-8). However, there was not any report regarding thrombotic thrombocytopenic purpura

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(TTP) following ALP poisoning; so this is the first case report of TTP and its successful management in an ALP intoxicated patient.

Case Description

A 34-year-old man who had taken an ALP tablet with a glass of water 20 minutes before the visit, was admitted to the emergency department. He had vomited 5 minutes after taking the pill. The used tablet was old and had been at the patient's home since at least a year ago. He had a 15 pack-year smoking history and also was opium addicted. His urine screening test was only positive for morphine. The patient's medical and drug history was negative for other conditions. At the time of admission, the patient was conscious and complained of nausea and epigastric pain. His vital signs upon arrival at the emergency room were as follows: Blood pressure=126/69 mmHg, Heart rate= 105 beats/min, Respiratory rate=16 breaths/min, T=37.3 ◦C, O2 saturation=95%, and his first venous blood gas analysis was: PH=7.29, PCO2=35 mmHg, HCO3-= 6.8 mmol/L that revealed metabolic acidosis. Supportive care, gastric lavage, and the cocktail for ALP toxicity were initiated for the patient, and he was admitted to the intensive care unit. A few hours later, the patient began to have low blood pressure; thus, norepinephrine was started at a dose of 5-10 mcg/min. On the same day, the patient was intubated, followed by loss of consciousness and decreased O2 saturation. Prescribed drugs until that time included: dextrose saline (1 liter q8h), sodium bicarbonate (50-150 ml 8.4% q8h base on the venous blood gas results), calcium gluconate (1 g q6h), magnesium sulfate (1 g q6h), vitamin C (500 mg/day), vitamin E (400 mg/day), N-acetylcysteine (1 g q8h), hydrocortisone (200 mg loading dose then 100 mg q8h), pantoprazole (40 mg/day), propofol and fentanyl. Cardiac examinations revealed a left ventricular ejection fraction (LVEF) of 20% and atrial fibrillation rhythm, which was managed by cardioversion. Heparin (5000 Unit IV, followed by 1000 Unit/hour) and amiodarone (150mg for 10 minutes, then1 mg/minutes for 6 hours, then 0.5 mg/minutes for 18 hours) were also started. On the second and third day of admission, gross hematuria and decreased hemoglobin levels were also observed. Additionally, the patient became icterus and the plasma bilirubin levels started to rise. Rifaximin and lactulose were prescribed for the patient. Viral markers were also negative. The liver ultrasound was normal. However, a liter of ascetic fluid was reported in the abdominal ultrasound results. The patient also had thrombocytopenia with a platelet count of 25000/mm3, So, heparin was discontinued. Peripheral blood smear (PBS) on the fourth and fifth day after admission was indicative of macrocytosis, hypochromia, anisocytosis, poikilocytosis, and schistocytes. A negative titer for direct and indirect Coombs test ruled out autoimmune hemolysis. There was no sign of blood discolorations, cyanosis, or unresponsive drop in O2 saturation, so methemoglobinemia was also excluded. In further examination, the team diagnosed TTP as a possible cause of clinical course; that characterized by thrombocytopenia and microangiopathic hemolytic anemia, so prednisolone 60 mg per day was prescribed and on the fourth day of admission therapeutic plasma exchange (2 liters) was performed for a total of seven sessions. On the 7th day, a G6PD (Glucose-6-phosphate dehydrogenase deficiency) activity test was requested. The test result was indicative of the moderate activity of the enzyme. The patient was also receiving two units of packed red blood cells every day from the 4th to 12th day. The patient's laboratory results are presented in Table 1. Fifteen days after ICU admission; he was transferred to the ward with a LVEF of 55%, and finally, on the 22nd day, the patient was discharged after the psychiatric consultation.

Table 1. Patient's Laboratory test results during intensive care unit admission.

Lab/day	UNIT	1	2	3	4	5	6	7	8	9	10	11	13
WBC× 10^3	/mm3	5.2	_	4.7	11.7	13.9	11	_	10.1	8.6	12.6	10.6	9.4
RBC	Mill/mm3	_	_	_	_	_	1.96	2.7	_	3.1	3.09	_	_
Hb	g/dl	14.8	_	12	5	6.4	6.1	7.7	_	9.1	8.9	8.4	7
PLT × 10^3	/mm3	239	_	158	_	101	100	56	_	45	25	42	56
MCV	femtoliters	_	_	_	_	_	98	92	_	96	96	_	_
Urea	mg/dl	41	51	_	_	_	1	_	_	70	65	53	40
Cr	mg/dl	1.1	1.2	_	_	_	94	_	_	1	0.7	1.1	1.1
INR	-	1.5	_	1.9	_	1.8	1.5	1	1	_	1	1	_
AST	IU/mL	135	_	149	_	123	79	_	_	37	19	21	23
ALT	IU/mL	74	_	55	_	50	46	_	_	28	17	21	22
ALP	IU/mL	170		134		146	172			151	167	161	141
BILI T/D	mg/dl	_	_	_	42/40	_	38/26	28/22	_	15/12	10/7	7/5	4/3
LDH	IU/mL	_	_	_	_	_	2298	_	_	1082	710	685	679
Retic count	1%	_	_	_	_	_	_	_	_	_	_	1%	_
G6PD	IU/gHb	_	_	_	_	_	_	5.9	_	_	_	_	_

P: Alkaline phosphatase, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, BILI T/D: Total bilirubin/Direct bilirubin, Cr: Creatinine, G6PD: Glucose-6-phosphate dehydrogenase, Hb: Hemoglobin, INR: International normalized ratio, LDH: Lactate dehydrogenase, MCV: Mean corpuscular volume, PLT: Platelets, RBC: Red blood cells, Retic: Reticulocyte, WBC: White blood cells.

Discussion

A 34-year-old patient who was a case of ALP poisoning developed hematuria, hemolysis, and thrombocytopenia during hospitalization. Before recognizing ALP as a hemolytic agent, other causes of hemolysis such as the activity of G6PD, drugs, foods, oxidative stress, and acute illness have to been ruled out. So all of the prescribed medications and other conditions with a potential to cause hemolysis were reviewed. In the medications list, vitamin C was the only drug that could cause hemolysis with a low probability. Albeit, at the prescribed dose, not only it cannot be considered as a hemolytic agent, but also due to its antioxidant effect, it can prevent hemolysis in patients with different levels of G6PD activity (9). Acute infection and acidosis (such as hemolysis caused by diabetic ketoacidosis) can also cause hemolysis in these patients (10). However, until the onset of hemolysis, there was no sign of infection in our patient. Additionally, due to early referral, mild toxicity, sufficient treatment with bicarbonate buffer, and fresh RBC, severe acidosis didn't occur (Table 1). As far as we know, no cases of TTP due to ALP poisoning have been reported. Despite unproven microvascular involvement, other evidence such as the Coombs-negative hemolysis, the formation of schistocytes on the PBS, increased bilirubin, and elevated values of serum lactate dehydrogenase (LDH) showed that the most likely diagnosis was microangiopathic hemolytic anemia. The patient also had thrombocytopenia with a platelet count of 25000/mm3 and bleeding in the form of hematuria. In our center, it was not possible to measure the ADAMTS13 protease activity. However, the PLASMIC score was calculated by using clinical conditions and laboratory results which was interpreted as moderate risk (11). Additionally, there was some evidence against the diagnosis of TTP, Including INR >1.5, mean corpuscular volume (MCV) >90 femtoliters, and the lack of petechia and purpura. Despite the life-threatening nature of TTP, treatment with TPE and corticosteroids was successful for our patient.

Toxin-induced intravascular hemolysis should be considered for patients presenting with ALP toxicity. As reported in this patient, TTP is another manageable consequence of ALP poisoning. Hemolysis due to this poison should be considered as a differential diagnosis when evaluating intoxicated patients.

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