Annals of Clinical Case Reports

Case Report
Published: 04 Jun, 2024

Surviving Aluminum Phosphide Poisoning Induced Cardiotoxicity - A Case Report

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Abstract

Introduction: Aluminum phosphide which is a cheap and commonly used rodenticide is also an effective solid fumigant that is frequently used for grain preservation. The pill contains around 44% inert elements to avoid disintegration of the tablet, ammonium carbonate, while the rest (about 56%) is aluminum phosphide. Because it is freely available in the market and accessibility is not controlled in developing countries, it is one of the commonly used agents for self-poisoning in different parts of the developing world.

Case Report: We presented a 48 years old black African female patient who was taken to private clinic after 6 h of intentional ingestion of two tablets of aluminum phosphide. She was presented with restlessness of 03 h duration with confusion. She had 06 episodes of vomiting of ingested matter. Upon examination, the patient was drowsy, pale, cold and clammy. She had non-recordable blood pressure and radial pulsation. Glasgow Coma Scale was 14/15. Routine lab investigations and initial Electrocardiogram were normal. Six hours after Intensive Care Unit admission, the Electrocardiogram showed atrial fibrillation with fast ventricular response, ST segment elevation and inverted T-waves. Cardiac troponin level was elevated. With the diagnosis of acute Aluminum Phosphide Poisoning with Cardiotoxicity (Acute Myocardial Infarction), hospital-based protocol for a hypotensive patient with aluminum phosphide poisoning was administered and medical treatment of myocardial infarction was given. These measures ultimately resulted in a complete resolution of clinical findings and laboratory derangements.

Conclusion: Exposure to phosphine gas released from ALP fumigants increases the risk of major morbidity and mortality. The mortality due to ALP poisoning is very high and variable. The use of magnesium sulphate to reduce cardiac arrhythmias and mortality is well documented but there is no uniformity in dose and frequency of its administration worldwide.

Keywords: Aluminum phosphide; Poisoning; Rat poison; Cardiotoxicity; Magnesium sulphate; Pesticides

OPEN ACCESS

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Received Date: *14 May 2024*
Accepted Date: *29 May 2024*
Published Date: *04 Jun 2024*

Citation:
Gebray HM, Chekol AL. Surviving Aluminum Phosphide Poisoning Induced Cardiotoxicity - A Case Report. Ann Clin Case Rep. 2024; 9: 2638.
ISSN: 2474-1655.

Introduction

The World Health Organization estimated that more than 7,000,000 people die every year because of suicide. Seventy-seven percent of all suicides occur in low- and middle-income countries. Pesticide ingestion is a common means of suicide. The commonly available pesticides are organophosphates, organochlorine, and Aluminum Phosphide (ALP) [1,2]. ALP, which is a cheap and commonly used rodenticide, is also an effective solid fumigant that is frequently used for grain preservation. ALP is marketed as dark grey 3-gram tablet and the common brand names are Celphos, Alphos, Synfume, Phostek, Phostoxin, Phosfume and Quickphos. The pill contains around 44% inert elements to avoid disintegration of the tablet, ammonium carbonate [3], while the rest (about 56%) is aluminum phosphide. The lethal dose of aluminum phosphide is between 0.15 and 0.5 grams (0.0053 and 0.0176 oz). Aluminum phosphide is available in the form of 3 gm pellets (releasing 1 gm phosphine gas) or 0.6 gm pellets (releasing 0.2 gm phosphine gas). Because it is freely available in the market and accessibility is not controlled in developing countries, it is one of the commonly used agents for self-poisoning in different parts of the developing world [4,5]. During contact with atmospheric air and hydrochloric acid in the stomach, ALP liberates lethal Phosphine (PH3) gas which is colorless, odorless gas. On exposure to air, it produces garlicky odor. Within minutes of ingestion, toxic features of poisoning may be seen like severe vomiting, resistant hypotension, metabolic acidosis, myocardial suppression, and Acute Respiratory Distress Syndrome (ARDS). Phosphine gas is rapidly absorbed by the lungs or gut, which causes systemic toxic effects, by free-radical injury and inhibiting cytochrome C oxidase enzyme. Early signs of

toxicity are manifested by shock and circulatory failure. No specific antidote is available until now, so aggressive supportive management is the key to survival in cases of ALP poisoning [1,6,7]. A retrospective study of 125 patients in Ethiopia showed high prevalence in females (57.6%). ALP poisoning is associated with a high mortality rate, ranging from 30% to 80%, mostly within the first 1 to 2 days after admission [8]. The mortality rate in hypotensive patients who were treated with Magnesium Sulphate ($MgSO_4$), IV Calcium gluconate, IV hydrocortisone and dopamine infusion was 55.6% [4]. A similar study in Iran suggested the mortality rate of ALP poisoning in Iranian population of 27% with good survival rate in younger age patients [9]. Here we presented a case who survived ALP induced cardiotoxicity.

Case Presentation

A 48-year-old black African female patient was taken to private clinic after 6 h of intentional ingestion of two tablets of ALP, locally known as rat poison. The reason for ingestion was marital disharmony. During her presentation, her husband stated that she had restlessness of 03 h duration with associated confusion. She was given half a liter of milk and following that she had 06 episodes of vomiting of ingested matter. During physical examination, she had non-recordable blood pressure and radial pulsation. Apical pulse rate was 112 beats per minute. Gastric lavage was not done. She was resuscitated by 1 liter of normal saline and referred to our hospital.

During her arrival at our emergency department, the family members gave additional history. She swallowed the tablets with water directly unpacking from the sealed container. She was found lied on the floor covered with her vomitus. She had fecal incontinence. She was agitated. Her family members denied any history of psychiatric illness or addiction or use of any recreational drugs. Upon physical examination, the patient was drowsy, pale, cold and clammy. Her blood pressure was 85/55 mmHg, radial pulse rate was 114 beats per minute which was feeble and low in volume, respiratory rate of 38 breaths per minute, Oxygen Saturation (SPO_2) was 97% at room air and a temperature of 35.2°C. There were clear and resonant lungs with good air entry bilaterally and had normal heart sounds with regular rhythm. On Central Nervous System examination, GCS (Glasgow Coma Scale) was 14/15 (4–4-6-best Eye response = 4/4, best verbal response = 4/5, best motor response = 6/6). She was not oriented to time, place and person. Her pupils were normal sized and reactive to light. Examinations on other systems were unremarkable.

Routine investigations (complete blood count, random blood glucose, troponin, liver functions and kidney functions) were sent which were in the normal limits (Table 1). Chest X-ray was normal. Electrocardiogram (ECG) was done which was normal sinus rhythm (Figure 1). After 03 h, she was admitted to Intensive Care Unit (ICU) for close monitoring and for administration of local protocol for hypotensive patients with aluminum phosphide poisoning.

In the ICU, her admission vital signs were as follows; non-recordable blood pressure, pulse rate was 118 beats per minute which was feeble and irregular in rhythm, respiratory rate was 28 breaths per minute and oxygen saturation was 96% at room air.

Six hours after ICU admission, the ECG was repeated and it showed atrial fibrillation with fast ventricular response (heart rate of 120 beats per minute), ST segment elevation on the antero-septal leads with inverted T-waves on inferior and lateral leads (Figure 2) cardiac troponin level was elevated (Table 1). Bed side echocardiography showed septal wall hypokinesis with ejection fraction of 50%.

Routine hospital based protocol for hypotensive patients with aluminum phosphide poisoning was administered which includes Dopamine 5 µg/kg/minute infusion; Hydrocortisone 200 mg IV QID for 48 h; Calcium gluconate 1 vial (10 mL of 10% solution) with 10 mL of NS to run over 10 min slowly, QID for 48 h; $MgSO_4$ 1 gm (2 mL of 50% solution) with 5 mL of NS IV push over 2 min, and $MgSO_4$ 0.5 mg (1 mL) with 1 mL of lidocaine IM on each buttock; Then $MgSO_4$ 1 gm in 100 mL of NS after 1 h, 2 h and 3 h for consecutive 3 h; Then $MgSO_4$ 1 gm in 100 mL of NS IV TID for 48 h.

With the diagnosis of acute Aluminum Phosphide Poisoning with Cardiotoxicity (Acute Myocardial Infarction), the following medications were added Aspirin 300 mg loading then 81 mg oral

Table 1: Laboratory values from admission time to discharge with reference ranges.

Lab results	At admission	After 24 h	After 2 days	At discharge	Reference
Hgb (g/dL)	13	--	--	--	12.3–15.3
WBC (10*3/ul)	7.9	--	--	--	4.00–11.00
FBS (mg/dL)	88	--	--	--	70–100
Sodium (mmol/L)	140	--	134	--	135–145
Potassium (mmol/L)	3.6	--	4	--	3.5–5.5
iCalcium (mmol/L)	1.2	--	1.09	--	1.05–1.35
Chloride (mmol/L)	100.4	--	98.9	--	96–108
ALT (mg/dL)	44.4	--	--	38.3	0–40
AST (mg/dL)	38.5	--	--	40.2	0–40
ALP (mg/dL)	189.6	--	--	166	0–270
BUN (mg/dL)	30	20	33.1	24.8	6–22
Creatinine (mg/dL)	0.9	1.35	1.2	0.8	0.3–1.3
Troponin I (ng/mL)	<0.01	1.98	1	<0.01	0.0–0.3
TSH (mIU/mL)	3.2	--	--	--	0.3–4.2
HIV test	Negative	--	--	--	--

Hgb: Hemoglobin; WBC: White Blood Cells; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; ALP: Alkaline Phosphatase; TSH: Thyroid Stimulating Hormone; HIV: Human Immunodeficiency Virus

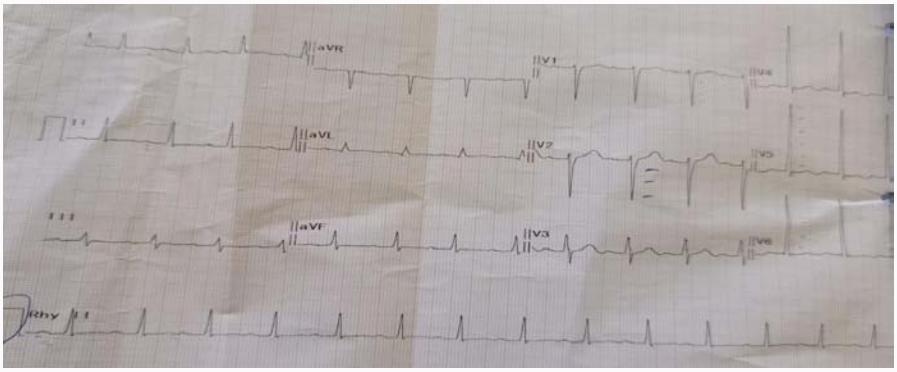

Figure 1: ECG of the patient at the emergency department showing sinus rhythm with heart rate of 94 beats per minute and left ventricular hypertrophy.

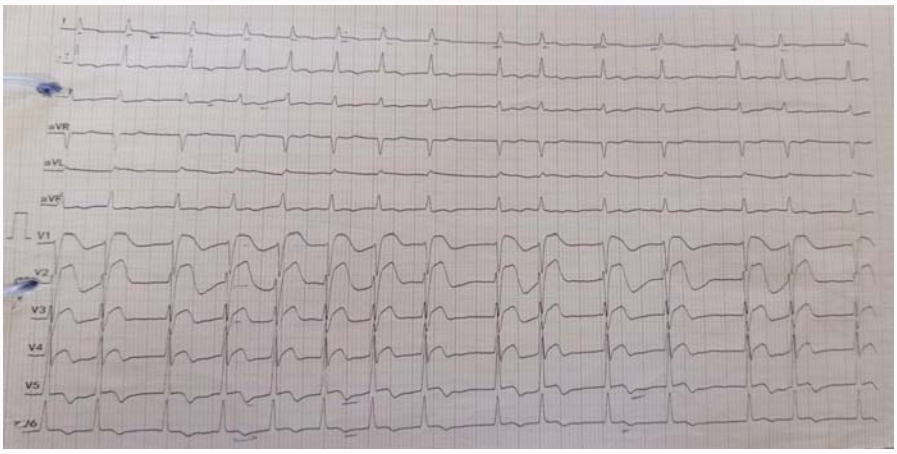

Figure 2: ECG of the patient in the ICU showing atrial fibrillation with fast ventricular response (heart rate of 120 beats per minute) and ST segment elevation on the antero-septal leads with inverted T-waves on inferior and lateral leads.

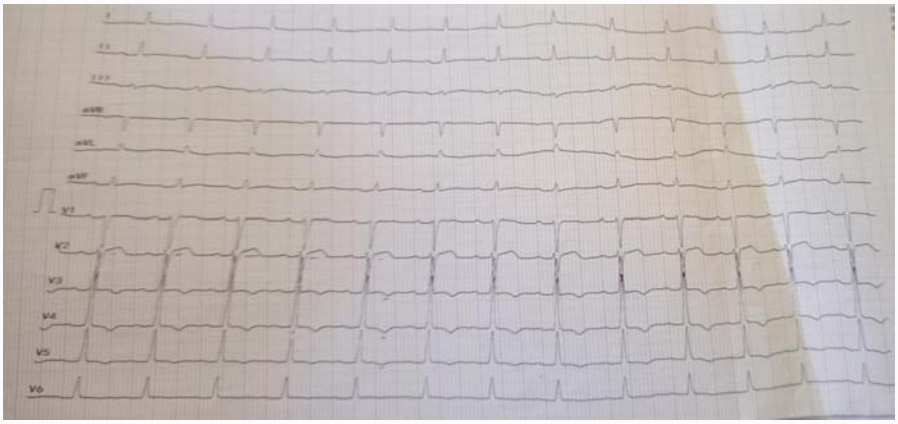

Figure 3: ECG of the patient on the second day in the ICU showing sinus rhythm with heart rate of 100 beats per minute and significant improvement of the ST segment elevation and T-wave inversions.

daily, clopidogrel 300 mg loading then 75 mg oral daily, atorvastatin 80 mg oral daily, unfractionated heparin 60 International Unit (IU)/kg Intravenous (IV) loading followed by 12 IU/kg/h *via* infuser and cimetidine 200 mg IV twice per day for stress ulcer prophylaxis.

On the second day of admission in the ICU, her blood pressure returned to normal, 100/60 mmHg, pulse rate was 86 beats per minute and hence the dopamine was tapered off. Her CNS examination improved with GCS returning to normal 15/15, and she became oriented to time, place and person. The repeated ECG in the ICU showed complete resolution of the atrial fibrillation and significant improvement of the ST segment elevation (Figure 3). She stayed another 24 h in the ICU for close monitoring of her vital signs. After staying for 03 days in the ICU she was transferred to medical ward and discharged to home on the next day after proper psychiatric evaluation and counseling. She came to follow up clinic after 02 weeks and she had normal investigations including troponin and ECG.

Discussion

ALP poisoning is the second most common cause of death due to pesticide poisoning after organophosphate. ALP is a solid fumigant and ideal pesticide since 1940 as it is cheap, most efficacious and easy to use and freely available over the counter in India, Morocco [3], Nepal [6], Iran [10] and Ethiopia [4]. ALP has a relatively high vapor pressure, which allows it to penetrate porous material effectively. Phosphine, like cyanide, inhibits mitochondrial cytochrome oxidase and cellular oxygen utilization. The direct toxic effects of phosphine on cardiac myocytes, fluid loss and adrenal gland can induce profound circulatory collapse [3].

In most patients, like ours, vomiting, abdominal pain and restlessness are frequent presenting complaints. Cardiovascular involvement results in weak pulse, tachycardia, tachypnea, acidosis, marked hypotension, palpitation and ultimately unresponsive shock. Patients remain mentally lucid until cerebral anoxia because of shock. Several ECG changes including ST segment elevation/depression, PR and QRS interval prolongation, complete heart block to ectopic pace making and also fibrillation have been reported. Patients can present with antero-inferior wall ischemia, right bundle branch block and T-wave flattening/inversion simulating myocardial ischemia. One study showed that 10% developed cardiac arrhythmia and the most frequent arrhythmia was atrial fibrillation (31% of patients) followed by ventricular fibrillation (20%), ventricular tachycardia (17%) and AV block (12%). These changes are because of toxic injury to myocardium [10,11]. Our patient's ECG showed atrial fibrillation with fast ventricular response, ST elevation on the antero-septal leads, and T wave inversions on infero-lateral leads.

Laboratory investigation may show Leucopenia, increased ALT (Alanine Aminotransferase) or AST (Aspartate Aminotransferase) and metabolic acidosis which indicates severe toxicity. Electrolyte analysis may show decreased magnesium, whereas potassium may be increased or decreased [3,10]. Our patient had normal complete blood count, AST, ALT, creatinine and urea level. We didn't do arterial blood gas analysis and serum magnesium level because they were not available in the town.

Our patient presented with repeated vomiting, restlessness and hypotension which are also common presenting symptoms in patients with ALP poisoning [8,12]. Since there are no effective antidotes till now, there has been different treatment practices worldwide associated with different ranges of mortality rate. For instance, Trimetazidine for reversal of cardiovascular manifestations of phosphine poisoning, coconut oil for prevention of absorption of ALP, Digoxin for the management of cardiogenic shock, hydroxyethyl starch, venoarterial extracorporeal membrane oxygenation, magnesium sulphate, infusion of GIK (Glucose-Insulin-Potassium) and different inotropes have been used in different centers [8,13,14]. Our patient was managed in the ICU with dopamine infusion, magnesium sulphate, hydrocortisone IV injection, and calcium gluconate infusion. This approach was practiced for more than 10 years in Felege Hiwot Referral Hospital, in Northwest Ethiopia. In retrospective study of two and half years, done in Felege Hiwot Referral Hospital, the overall mortality of ALP poisoning patients was 31.2% while mortality in hypotensive patients who were treated with the above regimen was 55.6% which was used to be nearly 100% prior to the practice of this approach [4]. The use of intravenous magnesium sulfate has been shown to reduce the mortality up to 50% in many studies [6]. In a study of 50 patients, individuals receiving repeated doses of intravenous magnesium showed significant improvement in indicators of oxidative stress and a lower incidence of mortality in comparison with control participants [3]. Magnesium sulfate acts by stabilizing the cell membrane and hence reducing the incidence of fatal arrhythmias. Another role of magnesium sulfate is to decrease the free radical injury due to its anti-peroxidant effect. Different studies have concluded different doses of intravenous magnesium sulfate.

Our patient had serious myocardial toxicity as demonstrated by ECG and raised cardiac biomarker, which are predictors of poor survival and high mortality [15]. A study from Iran showed that the combination of low blood pressure (systolic blood pressure below 90 mmHg), lower blood pH, and time elapsed from consumption to treatment (greater than one hour) predicted almost 77.3% of mortality in cases of ALP poisoning. Additionally, patients with low blood pressure are highly likely to die, having a mortality rate of 91.7% [16]. Similarly, another study showed that the survival of patients had a significant relationship with the number of tablets consumed, the time elapsed to reach the first treatment center, hypotension, blood pH, and Bicarbonate (HCO_3) levels. They showed that the mortality rate of ALP poisoning was higher in patients with a systolic blood pressure below 90 mmHg, a blood pH <7.2, or an HCO_3 level <15.0, who took over half of a rice tablet, or for whom more than half an hour elapsed from consumption to treatment [16]. Our patient had most of the predictors of high mortality rate; she presented to her first treatment center after 6 h of ingestion, she had low blood pressure and she took 2 tablets. Fortunately, with our effective management, she survived and discharged with complete improvement.

Conclusion

Exposure to phosphine gas released from ALP fumigants increases the risk of major morbidity and mortality. The mortality due to ALP poisoning is very high and variable, and depending on a number of factors including the lack of specific antidote or standardized treatment guideline and presenting with the poor prognostic signs. The use of magnesium sulphate to reduce cardiac arrhythmias and mortality is well documented but there is no uniformity in dose and frequency of its administration worldwide. We presented a patient who survived ALP poisoning with cardiotoxicity after aggressive management by local treatment protocol which incorporates $MgSo_4$, dopamine and hydrocortisone.

Challenges and Limitation

Aluminum phosphide poisoning is a life-threatening condition yet without an effective antidote. Affecting every system in the body, it is a very challenging condition to treat patients effectively without a uniform management guideline worldwide.

One of the limitations of this report is the nature of the case report being retrospective design giving no chance to establish a cause-effect relationship. As it is a retrospective study, certain clinical parameters and laboratory values were not complete due to documentation problems and limitations of the setup. The recommended gastric lavage with Potassium Permanganate ($KMnO_4$) solution was not used in this case, because $KMnO_4$ is not available in Ethiopia. The other is since it is a case report from a single center; it may not be representative of the general population. These limitations might have a negative impact on the generalizability of the findings.

Acknowledgment

We would like to thank all the clinicians involved in the

management of this patient especially the ICU team.

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