CASE REPORT

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A Rare Case of Aluminum Phosphide Poisoning Survival: Role of Early and Aggressive Supportive Therapy

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Abstract

Aluminium phosphide is a cheap, effective and commonly used pesticide but a major cause of suicidal deaths in rural areas. Released phosphine gas causes rapid cell hypoxia due to inhibition of oxidative phosphorylation leading to circulatory failure along with formation of highly reactive hydroxyl radicals. The diagnosis of aluminium phosphide poisoning is based on history, and foul garlicky or decaying fish odor. However, in gastric aspirate or breath, silver nitrate impregnated paper test is done, for confirming the diagnosis. There is no antidote available, so treatment is totally supportive. In our case the patient was treated immediately with all essential measures with close monitoring. The patient survived and was discharged in a stable condition.

Key words: Aluminium phosphide, phosphine gas, KMnO4 gastric lavage, dextrose insulin infusion, glutathione, survival.

Introduction

Aluminium phosphide is a solid fumigant pesticide. In India, it is marketed as tablets of Celphos or Quickphos and used to preserve grains. As a pesticide, it is available as 3 gm tablets or powder and is a leading cause of suicidal poisoning in North India[1].

Aluminium phosphide is highly water soluble and decomposes in the presence of moisture. The reaction between water and aluminium phosphide liberates phosphine gas[2].

$AlP + 3H_2O \rightarrow Al(OH)_3 + \mathbf{PH_3}$

$AlP + 3HCl \rightarrow AlCl_3 + \mathbf{PH_3}$

The deleterious effects of the poison are due to phosphine and the management is directed to sustain life till phosphine is excreted.

Case report

A 16-year-old healthy male was admitted with alleged history of intentional ingestion of 1 tablet of Celphos (3 gms). For that, he was admitted in a local hospital, initially for 12 - 14 hours, and received initial treatment in the form of injection sodium bicarbonate, gastric lavage with potassium permanganate (1: 10,000). On admission to our hospital the patient was restless, his skin was cold and clammy. His vitals were as follows: BP: 80/50 mmHg, pulse: 80/per minute and regular, respiratory rate: 20 per minute, RBS: 154 mg/dl and SpO2 94% on room air. His GCS was: E4V4M6, with APACHE II score of 23 points with predicted mortality of 46%. We admitted the patient to ICU, and all relevant investigations, including ABG and echocardiogram, were done and immediate resuscitative treatment started. As per ABG, patient had severe metabolic acidosis (pH 7.03, pCo2: 30 mmHg, pO2: 185 mmHg, HCO3: 7.9 mmol/ltr, BE: 22.9 mmol/ltr, SpO2: 99%), Also, patient was in shock, so inotropes were started in the form of Noradrenaline (8 mg in 46 ml normal saline at a rate of 10 ml/hr infusion) and Vasopressin (4 mg in 46 ml normal saline at a rate of 2.4 ml/hr infusion) along with normal saline infusion @ 120 ml/hour with hourly monitoring of BP, urine output and other vitals. IV sodium bicarbonate was started as 100 ml bolus followed by 100 ml per hour IV infusion with 3 hourly ABG monitoring. After 12 - 14 hours of admission in ICU, significant correction of metabolic acidosis and shock was achieved. Over the next 24 hours, Vasopressin infusion was gradually weaned off, Noradrenaline and bicarbonate infusion were slowly tapered off according to BP and ABG, and subsequently stopped. Inj Magnesium sulphate, IV 2 gm stat and 2 gm hourly for 3 consecutive hours were given followed by 1 gm, 4 hourly for 5 days with monitoring of serum magnesium levels, (given as a membrane stabilizer to prevent arrhythmias). We also started Inj Human insulin as per GIK regimen: 10 IU regular insulin in 25% dextrose with 10 ml KCL over 3 - 4 hour infusion, three times a day for 5 days as insulin is known to increase cardiac contractility. Tab Trimetazidine 200 mg (sustained release) twice a day was started once patient started accepting orally, as it increases myocardial oxygenation, decreases intracellular acidosis and reduces oxygen consumption. ECG on admission revealed ST elevation in chest leads suggestive of myocarditis. 2D echo was normal with

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ejection fraction of 55% and showed no RWMA. Cardiac enzyme, CPK was also increased which favoured myocardial ischaemia. Cardiologist opinion was obtained. The cardiac condition was monitored with regular ECGs for any worsening of ST-T changes or arrhythmias. Patient had leucocytosis (TLC: 15,000/mm^3) for which Inj Ceftriaxone 1 gm BID was given. On day 3, ECG showed spikes of ill-sustained VT which gradually resolved. A repeat 2D echo on day 3 was normal. Thereafter, patient had severe hypocalcaemia, managed with IV calcium gluconate (10 ml, 10% calcium gluconate in 100 ml saline, IV, TDS). Patient's LFT were also deranged due to oxidative injury caused by phosphine gas, which was managed with hepatoprotectors (Tab Ursodeoxycholic acid, 300 mg, BD) and antioxidant therapy to prevent oxidative injury due to free radicals with IV glutathione (600 mg, IV, BD) given. Due to oxidative injury, kidney function was also affected, which was managed conservatively with IV acetylcysteine (600 mg, IV, BD as antioxidant, replenishing cellular glutathione) and IV fluids to increase renal washout of phosphine. Patient also required NIV support on day 5 for pulmonary oedema and hypoxia. On day 7, patient was haemodynamically stable with no acidosis or oxygen requirement. He was discharged in haemodynamically stable condition on day 12. An informed consent for publishing this case was obtained from his father.

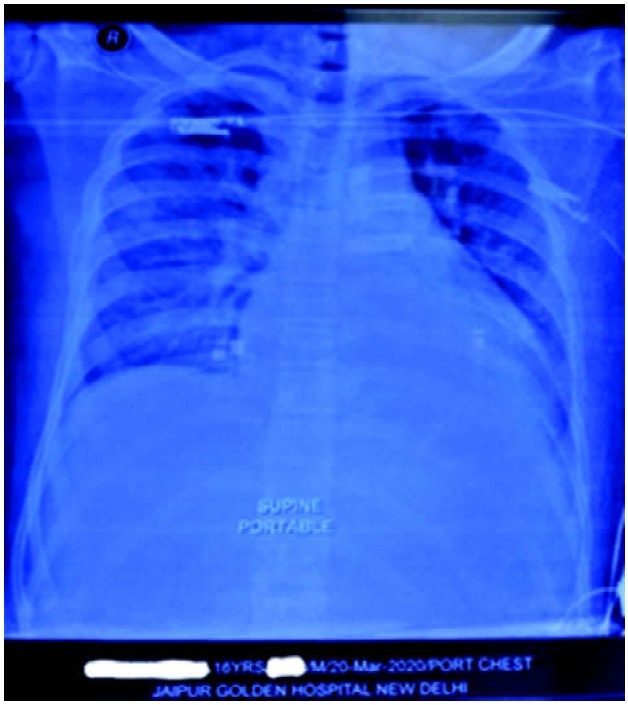

Fig. 1a: *Chest X-ray: (a) Day1: clear X-ray, (b) Day 3: Suggestive of pulmonary oedema (cephalisation of vessels and patchy shadowing of air bronchogram with increased cardiac size).*

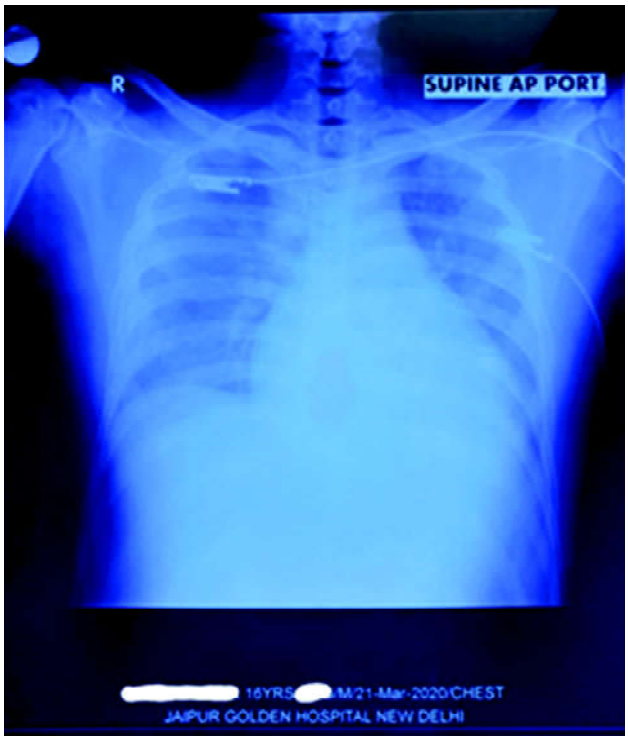

Fig. 1b:

Table I: Serial ABGs of the patients.

	19/4/2020 Day 1	20/4/2020 Day 2	21/4/2020 Day 3	22/4/2020 Day 4	23/4/2020 Day 5
pH	7.03	7.38	7.45	7.40	7.37
pO2 (mmHg)	185	26	52	99	110
PCO2 (mmHg)	30	61	45	49	28
HCO3 (mmol/l)	7.9	36.6	31.3	26.4	16.2
S. Lactate (mmol/l)	3.2	7.2	2.2	1.8	0.6
SpO2 (%)	99	69	88	94	99
BE(B) (mmol/l)	-22.9	-12.9	-7.3	-5.0	1.0

Discussion

In India, aluminium phosphide (AlP)is marketed as tablets of celphos, alphos, quick phos, phostoxin, etc.[3]. In India, this poisoning was not known before 1980. The first case in India was reported in 1981 from MGM Medical College, Indore[4]. The incidence of this poisoning has been increasing steadily and is now the commonest mode of suicide in the agricultural community in Northern India[5]. Overall, mortality in cases of aluminium phosphide poisoning varies between 70 - 100%. It is higher in those who consume more than two tablets and none of the patients who had ingested more than 3 tablets survived[6-8]. Suicide was the most common cause of death with 94%, followed by accident

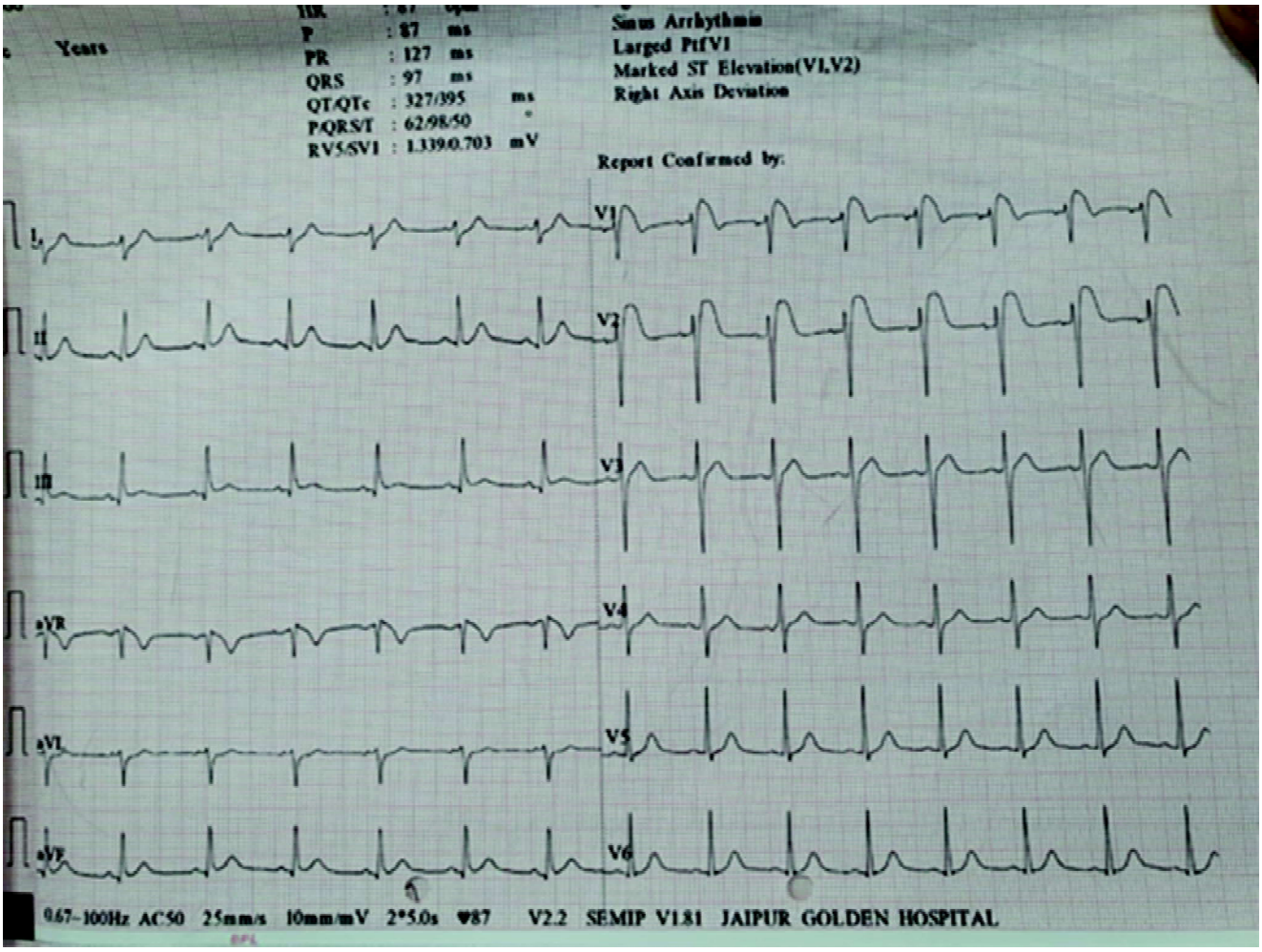

Fig. 3a: *ECG: (a) on day of admission: Showing marked ST elevation in lead V1.*

with 5% of cases, and homicide accounted for 1% of deaths[9].

According to Karamjit *et al* (2003) the pattern of poisoning varied in urban and rural areas, with a higher incidence of poisoning deaths in rural (64%) than in urban areas (36%)[10]. Aluminium phosphide was the most common poison consumed, being responsible for 50% of deaths, followed by insecticides 24%[9]. Poisoning deaths increased from 19% in 1996 to 24% in 2005. The age group most commonly affected was 16 - 25 years (49%). The male to female ratio was 1.9: 1.0 and the rural to urban ratio was 1.5: 1.0[9].

Human toxicity occurs either due to the ingestion of AlP (commonest mode) after exposure and injury from phosphine inhalation (uncommon) or even after absorption through the skin (rare). After ingestion, AlP releases phosphine gas in the presence of HCl in the stomach, which is rapidly absorbed throughout the gastrointestinal tract, leading to systemic toxic effects involving the heart, lung, kidney, and liver – with manifestations of serious cardiac arrhythmias, intractable shock, acidosis, and pulmonary oedema. After absorption, phosphine is oxidised to oxyacids. Phosphine is excreted in the urine as hypophosphite and also through the lung in the unchanged form.

In addition to the corrosive action of phosphine, the mechanism of toxicity includes failure of cellular respiration due to the effect on mitochondria, inhibition of cytochrome-oxidase and formation of highly reactive hydroxyl radicals. Cellular injury due to lipid peroxidation is also suggested. There is a decrease in the level of catalase and increase in the activity of superoxide dismutase in patients of AlP poisoning. The reduction of glutathione concentration in different tissues in AlP poisoning also explains the cellular injury as glutathione is a protection factor against oxidation, by catalysing the reduction of the oxygen peroxide in O_2 and H_2O. Indicators of oxidative stress (reduced glutathione, malonyldialdehyde) reach peak levels within 48 hours of exposure to poison, approaching normalisation by day 5[11].

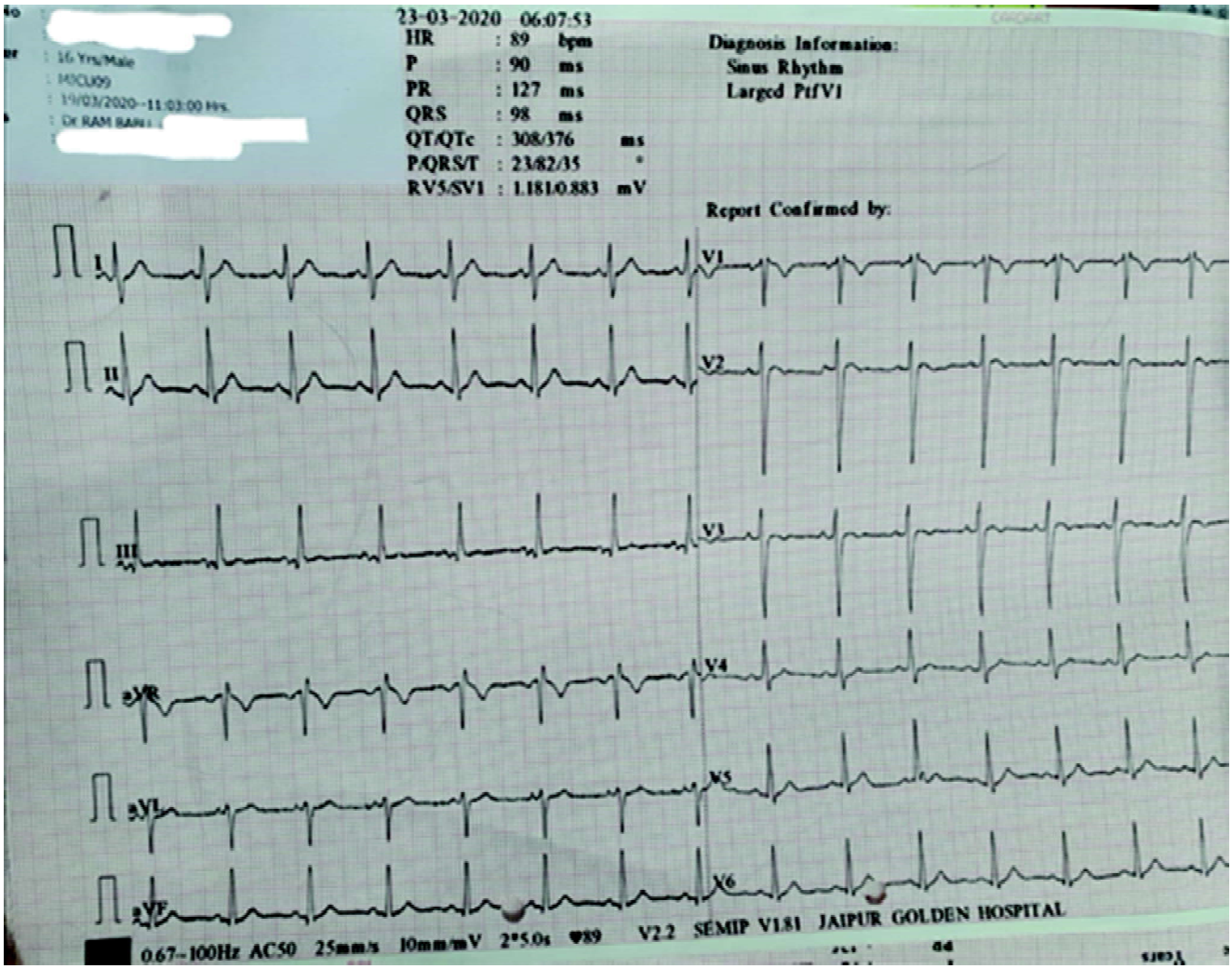

Fig. 3b: *Normalised ECG on day 3.*

Gastric lavage is important in the initial stages. The management principles aim to sustain life with appropriate resuscitation measures until phosphine is excreted from the body. If phosphides have been ingested, ***do not induce emesis***. Gastric lavage with sodium bicarbonate and potassium permanganate (1: 1,000) has also been recommended by earlier studies as KMnO4 solution oxidizes phosphine to non toxic phosphate[12,13]. But recent advances and studies have shown better results of gastric lavage with sodabicarb and vegetable oils.

All patients of severe AlP poisoning require continuous invasive haemodynamic monitoring and early resuscitation with fluid and vasoactive agents. Fluid therapy could be guided by central venous pressure (CVP) or pulmonary artery wedge pressure (PAWP) monitoring. For refractory hypotension, norepinephrine or phenylephrine could be used. Readiness of anti-arrhythmic agents, DC cardioversion and temporary pacemaker should be available at the bedside. Vasoactive agents with more β-receptor agonist action like dopamine and dobutamine should be used cautiously as they are prone to inducing arrhythmias. The reversibility of myocardial injury over few days was objectively assessed by repeated echocardiography[14] Gupta *et al* showed normalisation of the echocardiographic findings in patients who survived AlP poisoning on day 5[14].

Magnesium sulphate acts as a membrane-stabilising agent and also corrects hypomagnesaemia. It also helps in preventing arrhythmias. It may be given in a dose of 2 - 3 gms as a loading dose and then 1 gm every eight hourly. N-acetyl cysteine has been found to be useful by Bogle *et al* in 2006[15].

Intravenous sodium bicarbonate could be considered for mild-to-moderate metabolic acidosis or as a rescue therapy in severe acidosis before dialysis is commenced. In a recent study, using intravenous sodium bicarbonate for the

"aggressive correction of acidosis" protocol resulted in significant improvement in patient outcome (30% vs 55%)[16].

As insulin is known to increase cardiac contractility, GIK regimen was started (100 ml 25% Dextrose + 10 ml KCl + 8 U rapid Insulin)[17]. Numerous reasons exist for the continued interest in GIK despite its variable track record in clinical trials: (1) Substantial laboratory evidence supports a cardioprotective effect in various models of ischaemia/ reperfusion; (2) some clinical trials have demonstrated positive results in specific patient subgroups; (3) the treatment is relatively "nontoxic" and free of major clinical side-effects; and (4) recent evidence suggests that insulin itself, a component of GIK, administered as a strategy to restore normoglycaemia, may be cardioprotective because it has antiinflammatory, antiapoptotic, and provasodilatory properties[18,19].

Trimetazidine is a piperazine derivative. It has been experimentally shown that in ischaemic tissues it improves production of ATP, decreases intracellular acidosis and decreases overproduction of free radicals, this it rectifies most of the metabolic adverse effects of ischaemia[21].

This poisoning has a high mortality (30 - 100%) and survival is unlikely if more than 1.5 g is ingested[22]. Although the lethal dose is 150 - 500 mg for an adult, case reports of survival have been reported even after the ingestion of 9.0 g or more.

In a retrospective analysis of one of the largest series (471 patients) of AlP poisoning, arterial pH, serum bicarbonate level and ECG abnormalities were significantly poor prognostic factors[23]. Other poor prognostic factors were shock, altered mental status, high APACHE II score, acute kidney injury, low prothrombin rate, hyperleucocytosis, requirement of mechanical ventilation, lack of vomiting after ingestion, hyperglycaemia and time lapsed after exposure[24]. As in our case, patients had a low GCS, high APACHE II, with signs suggestive of acute kidney injury with low urine output and deranged kft with maintained renal size and echogenicity on USG, hyperleucocytosis(TLC: 15,000/mm^3).

Conclusion

The case fatality ratio due to A/P poisoning has declined significantly in the last decade due to improved intensive care. Strict implementation of nationwide pesticide regulations, including restricting the availability of this poison, being aware of its toxicity and providing improved medical management in consultation with regional or national poison control centres could further reduce the mortality due to AlP toxicity, as there is no antidote available presently.

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