Case Report

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Induction of Brugada electrocardiogram pattern with aluminum phosphide poisoning: a case report

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Introduction and importance: Aluminum phosphide (ALP) is a commonly used suicidal agent in an agrarian country like Nepal. The unmasking of the Brugada pattern in the electrocardiogram (ECG) associated with ALP poisoning is a rare phenomenon, and studies pertaining to it are scarce in the medical literature.

Case presentation: An 18-year-old female presented to the emergency department with multiple episodes of vomiting, headache, blurring of vision, and abdominal pain after 4 h of consumption of ALP with suicidal intent. A 12-lead ECG revealed a coved ST-segment elevation and T-wave inversion in leads V1–V3 with right bundle branch block suggestive of a type 1 Brugada pattern. Her past medical and family history was not significant. The patient made an uneventful recovery with the required supportive treatments.

Clinical discussion: Cardiac arrhythmias are the major cause of death in ALP poisoning. Unmasking of the Brugada ECG pattern is a rare but potentially fatal complication implicated in various pharmacological toxicities, including tricyclic antidepressants, cocaine, procainamide, disopyramide, flecainide, and rarely with ALP.

Conclusions: ALP poisoning can unmask the Brugada ECG pattern, which can lead to ventricular fibrillation and/or sudden cardiac death.

Keywords: aluminum phosphide, Brugada electrocardiogram pattern, case report, poisoning

Introduction

Aluminum phosphide (ALP) is a common fumigant used in stored grains to control rodents and insect pests. It is a common suicidal agent in an agrarian nation like Nepal due to its widespread availability[1]. Rodenticides containing metallic phosphide compounds of zinc, aluminum, calcium, and magnesium release phosphine by the action of the stomach's hydrochloric acid, which noncompetitively inhibits cytochrome oxidase in the mitochondria and results in cell hypoxia[2]. ALP has direct toxic cardiac and metabolic effects. Patients usually present with nonspecific complaints like nausea, vomiting, vertigo, and abdominal pain. It is within 8–10 h after ALP ingestion that the patient develops refractory heart failure, hypotension, multiple organ failure, malignant ventricular arrhythmias, and subsequently death[3].

HIGHLIGHTS

- Cardiac arrhythmias are the major cause of death in aluminum phosphide (ALP) poisoning.
- The Brugada electrocardiogram (ECG) pattern associated with ALP poisoning is rare but increases the risk of fatal ventricular fibrillation and sudden cardiac death.
- The Brugada ECG pattern resolves with successful treatment of ALP poisoning.

Patients are usually treated conservatively by gastric lavage with potassium permanganate, coconut oil, sodium bicarbonate solution, and vasopressors and the mortality rate is very high, ranging from 37 to 100%[4]. Although multiple organs can be affected, the heart remains to be the most commonly affected organ. Hypotension, myocarditis, congestive heart failure, and various electrocardiogram (ECG) manifestations might develop with ALP poisoning. The common ECG changes are like that of myocardial infarction, conduction abnormalities, different arrhythmias, and very rarely, the unmasking of the Brugada ECG pattern can be seen[4].

We hereby report the first case from Nepal in which the patient developed unmasking of the Brugada pattern in the ECG after ingestion of ALP with suicidal intent, which fortunately was transient and eventually improved gradually with conservative

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treatment. This case has been reported in line with the SCARE (Surgical CAse REport) criteria[5].

Case presentation

An 18-year-old female presented, after 4 h of ingestion of two tablets named 'celphos' (ALP), with suicidal intent at our emergency department. The patient complained of multiple episodes of vomiting, headache, blurring of vision, and abdominal pain shortly after ingestion. She was taken to a nearby hospital where she was given intravenous (i.v.) fluids, pantoprazole, and gastric lavage was done with potassium permanganate. Her prior medical history was unremarkable for syncopal events, palpitation, or arrhythmias. Neither did she had any psychiatric illnesses (including eating disorders), nor was she under any medications for anxiety, depression, or psychosis. She also denied being a cigarette smoker and alcohol or any other recreational drug consumer. In addition, there was no preceding viral illness or family history of sudden cardiac death (SCD).

On presentation, her respiratory rate was 22 breaths per minute and her oxygen saturation (SpO_2) was 96% in room air. The pulse rate was 98 beats per minute, regular and low volume, and blood pressure (BP) was 90/60 mmHg – her Glasgow Coma Scale of 15/15. The pupils were bilaterally 2 mm, round, regular, and reactive. Her tongue and mucous membranes were dry. Abdominal examination revealed mild epigastric tenderness without guarding or rigidity. Examination of other organ systems was unremarkable. Her BMI was 22.76 kg/m^2.

An arterial blood gas analysis done immediately revealed a high anion gap metabolic acidosis (pH: 7.2, anion gap: 27.4). Routine blood investigations revealed normal blood hemogram, normal kidney and liver functions, and normal electrolytes. A 12-lead ECG revealed a coved ST-segment elevation and T-wave inversion in leads V1–V3 with right bundle branch block morphology suggestive of a type 1 Brugada pattern (Fig. 1). The serum troponin and CK–MB (creatine kinase–myocardial band) were negative. Bedside transthoracic echocardiography was normal. Ultrasonography of the abdomen and pelvis showed an ectopic right kidney with mild ascites. She was admitted to the intensive care unit (ICU) and was managed conservatively with i.v. fluids, parenteral drotaverine, ondansetron, and pantoprazole. Close monitoring was done for vitals and ECG changes.

After 2 days of ICU stay, she made an uneventful progressive recovery. She was shifted to the general ward and was subsequently discharged after 4 days of hospital stay. Her subsequent ECG findings reverted back to normal with the isoelectric ST segment (Figs 2 and 3). Provocative and genetic tests were not done as the patient refused any further testing.

Discussion

Upon ingestion, the ALP decomposes into a highly toxic gas named phosphine under the action of hydrochloric acid in the stomach. Phosphine blocks the electron transport chain and oxidative phosphorylation by noncompetitively blocking the cytochrome oxidase of mitochondria leading to cellular hypoxia, necrosis, and eventually cell death[6]. To elaborate, phosphine is a highly reactive radical that penetrates the intracellular space and disrupts mitochondrial function by reacting with the mitochondrial respiratory chain as the primary source of reactive oxygen species (ROS) production and creating extensive oxidative stress[7]. It is evident from the literature that the main sites of

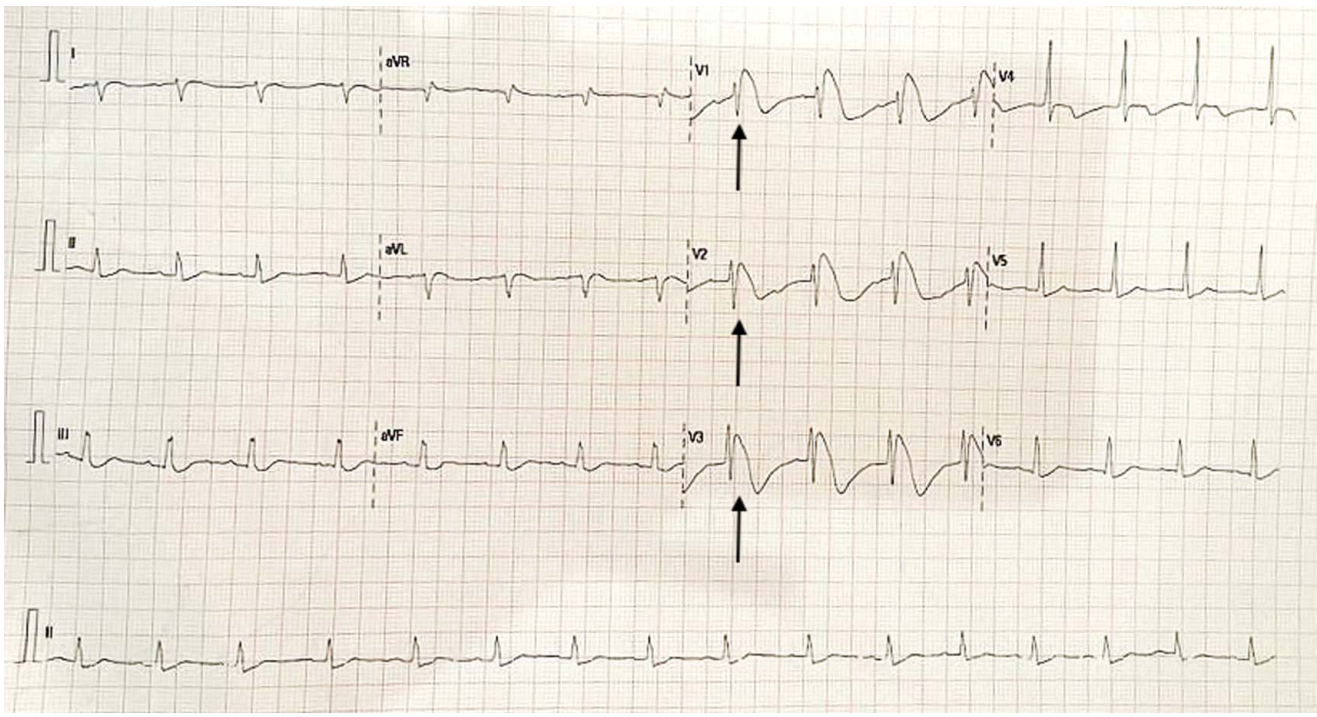

Figure 1. Electrocardiogram on the first day of admission revealing coved ST-segment elevation and T-wave inversion in lead V1–V3 (black arrows) with right bundle branch block, suggestive of type 1 Brugada pattern.

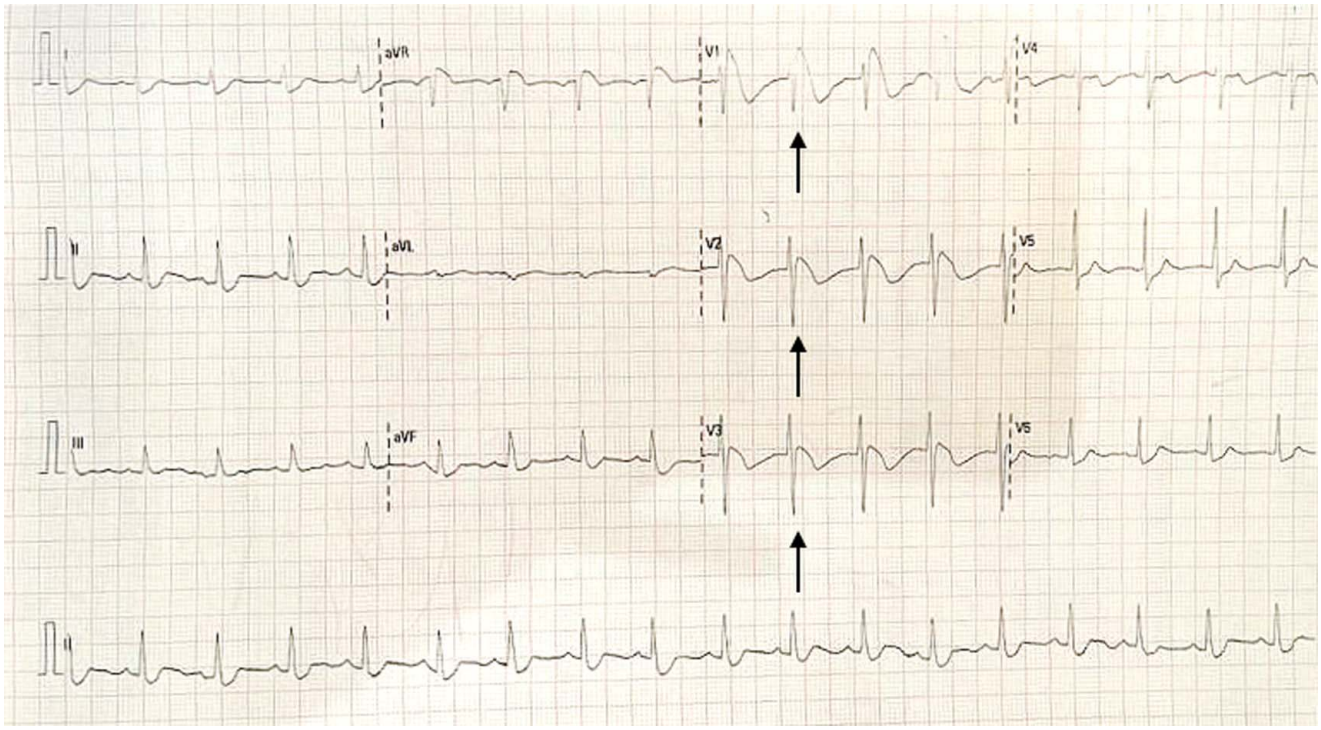

Figure 2. Electrocardiogram on the 3rd day of discharge showing gradual normalization of coved ST segment in mid-precordial leads (black arrows).

interaction between phosphine and the electron transport chain are in the complex i.v. and cytochrome *c* oxidase, which leads to the inhibition of mitochondrial membrane potential[8]. In addition to it, phosphine reduces the activity of complexes I and II, which reduces the activity of mitochondrial complexes and inhibits its aerobic respiration, leading to mass production of ROS, impaired adenosine triphosphate synthesis, and eventually energy failure[9].

The most common cause of morbidity and mortality in patients with ALP poisoning is cardiovascular toxicity. The usual cardiac symptoms are chest pain, dyspnea, palpitation, and syncope. Cardiac manifestations include congestive heart failure, arrhythmias, myocarditis, pericarditis, pericardial effusion, subendocardial infarction, and cardiogenic shock[10]. Sinus tachycardia is the most common rhythm abnormality on ECG in the first 3–6 h, and later ST-T changes and arrhythmias predominate[11]. ALP intoxication can also produce various other ECG changes like PR prolongation, widening of QRS complexes, atrial fibrillation, premature supraventricular and ventricular beats, bundle branch blocks, and sinoatrial block[12]. A number of cardiac arrhythmias are frequently encountered and are regarded as the major cause of death in ALP poisoning. In a study conducted by Siwach *et al.*[13], patients with ALP poisoning experienced ventricular tachycardia (VT) in 40% of cases, ventricular fibrillation (VF) in 23.3%, supraventricular tachycardia (SVT) in 46.7%, and atrial fibrillation (AF) in 20% of cases. It takes 3 weeks for the ECG changes to normalize if the patient survives[13]. Echocardiographic features include dilated cardiomyopathy, poor ejection fraction, regional wall motion abnormalities, pericardial effusion, and increased pulmonary capillary wedge pressure[14]. Postmortem examination reveals myocardial fiber destruction, myocyte vacuolation, neutrophilic infiltration, and cell necrosis[15].

The Brugada syndrome (BrS), first described in 1992, is an autosomal dominant disease caused by dysfunctional ion channels (sodium, potassium, and calcium) that manifests as a classical ECG pattern and eventually predisposes an individual to malignant ventricular arrhythmia[16]. It is caused by loss-of-function mutations in the gene, named SCN5A, which encodes for cardiac sodium channel Nav1.5. Upon genetic testing, this mutation is found only in about 11–28% of patients[17]. The mechanism of arrhythmia in BrS is complex. It has been shown that the transmural dispersion of repolarization is the underlying cause of ST-segment elevation in the right precordial leads of the ECG[16]. The transmural dispersion of repolarization is mainly because of the significant difference in the transient outward current (I_{to}), which is intrinsically larger in the epicardium in comparison to the subendocardium. In addition, there is a loss of depolarizing current owing to the SCN5A loss-of-function mutations. This results in a loss of action potential (AP) dome in the epicardium and eventually leads to phase-2 reentry upon arrival of the subendocardium action potential wavefront[18]. The concealed BrS can be unmasked by fever, class IA and IC antiarrhythmic drugs such as procainamide, disopyramide, flecainide, calcium channel blockers such as nifedipine and diltiazem, tricyclic antidepressants such as amitriptyline and desipramine, and other drugs such as cocaine, lithium, etc[19]. Metallic phosphide poisoning is a much rarer entity that can trigger the Brugada ECG pattern and the studies regarding it are few and far between.

Brugada phenocopy is an electrocardiographic phenomenon characterized by the type 1 or 2 Brugada pattern, which can be triggered by a variety of underlying clinical conditions in an individual who does not have a genetic mutation. The ST-

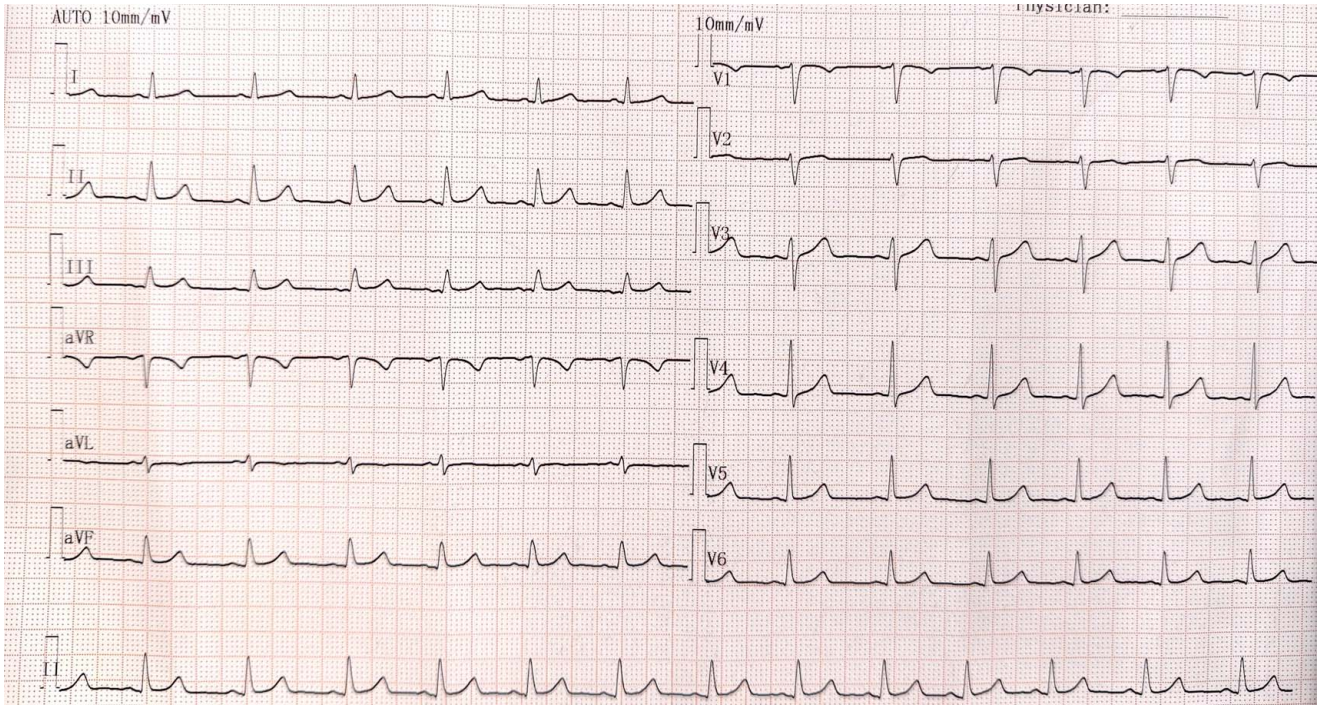

Figure 3. Electrocardiogram at the time of discharge shows isoelectric ST segment in the mid-precordial leads.

segment elevation in Brugada phenocopy is explained by a transmural gradient that arises from an accentuated I_{to}-mediated AP notch and a loss of AP dome in the epicardium but not the endocardium. The loss of the AP dome is the result of disruption in the homeostasis of active inward and outward currents at the end of phase 1 of AP[20]. Type 1 BrS is characterized by a coved ST-segment elevation $\geq$2 mm (0.2 mV) followed by a negative T wave. Type 2 BrS has a saddleback appearance with a high take-off ST-segment elevation of $\geq$2 mm with a trough displaying $\geq$1 mm ST elevation followed by either a positive or biphasic T wave. Type 3 BrS has either a saddleback or coved appearance of ST segment with an ST-segment elevation of <1 mm[21]. The following are the established diagnostic standards for Brugada phenocopy (the first four standards must be met). (1) Brugada morphologic type 1 or type 2 ECG pattern. (2) Existence of a diagnosable and treatable underlying illness. (3) The ECG pattern returns to normal after the underlying problem has been treated. (4) The lack of symptoms, clinical history, and family history indicate a low pretest chance for BrS. (5) A provocative negative test using a sodium channel blocker (such as procainamide, flecainide, or ajmaline). (6) A negative genetic test result[22]. In our case, the first four standards were met. However, due to unavailable diagnostic resources in our country, our patient did not undergo a provocative drug challenge and genetic testing. Therefore, unmasking an underlying genetic BrS could not be excluded.

Brugada phenocopies can result from a variety of disorders. They are (1) metabolic (hyperkalemia, hypokalemia, acidosis, hyponatremia), (2) ischemic (inferior wall myocardial ischemia, right ventricular infarction, vasospastic angina), (3) mechanical compressive factors (pectus excavatum, mediastinal mass, hemopericardium), (4) myocardial/pericardial diseases (myocarditis/pericarditis), and (5) other (electrocution, Ebstein's anomaly) miscellaneous causes[22,23]. Atypical causes of myocardial infarction, such as right coronary artery dissection, have also been reported to cause Brugada phenocopy[23]. Heavy metals like zinc and copper can serve as endogenous regulators of sodium, potassium, and calcium channels, including NaV1.5 sodium channel, which might possibly produce a Brugada ECG pattern[24]. However, the pathophysiological basis for the Brugada ECG pattern in metallic phosphide poisoning is not fully understood[3].

Whether it is BrS or a Brugada phenotype, both can enter into the same life-threatening arrhythmogenesis pathway, and the patient is at increased risk of ventricular fibrillation and SCD[4]. This mandates intensive monitoring of patients with Brugada pattern ECG.

Conclusion

There is a dearth of medical literature regarding the induction of the Brugada ECG pattern with ALP poisoning. Such an ECG pattern can lead to fatal ventricular fibrillation and/or SCD. Hence, the treating physicians need to be very watchful while treating a case of ALP poisoning. Since no specific antidote is available for ALP poisoning, symptomatic treatment and electrolyte correction are the key to the successful management of the ailment.

Ethical approval

Ethical approval is not required for writing the case report from the institutional review board in our institute, that is Institutional Review Committee, Institute of Medicine, Kathmandu, Nepal.

Consent

Written informed consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent from the patient for publication is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

P.A.: writing – original draft, data curation, and conceptualization; S. S.: writing – original draft, review, and editing, and supervision; V.Y., H.S., S.S., and E.P.: writing – original draft, review, and editing; S.KC.: writing – review and editing; N.KC.: data curation and writing – review and editing; A.K.M.: data curation, writing – review and editing, and conceptualization.

Conflicts of interest disclosure

The authors declare that they have no conflicts of interest.

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