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Aluminium phosphide fatal poisoning associated with a Brugada-like ECG pattern. Case presentation

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Abstract: Aluminium phosphide has direct toxic cardiac and metabolic effects, leading to multiple organ toxicity. We hereby present the case of a young woman who was admitted at the hospital in severe shock with a sudden onset and a rapidly severe evolution, unresponsive to treatment; the final diagnosis, based on imaging and biological samples, was acute fulminant myocarditis due to aluminium phosphide poisoning. The patient's symptoms started about 10 hours before the admission and the family rejected the possibility of any potential poisoning.

Key Words: poisoning, aluminium phosphide, Brugada-like ECG pattern.

Aluminium phosphide has direct toxic cardiac and metabolic effects, leading to multiple organ toxicity. The onset symptoms of aluminium phosphide poisoning are unspecific (nausea, vomiting, vertigo), but within 8-10 hours the patients' general condition may rapidly alter with signs of heart failure and arterial hypotension unresponsive to supportive treatment. In the absence of a helpful collaboration with the patient (or his/her family) that could suggest the possibility of contact with aluminium phosphide, a positive diagnosis is hard to pinpoint.

In the first hours there are few altered biological constants. Subsequently, the haemodynamic instability is complicated by the occurrence of malignant ventricular arrhythmias and ultimately by multiple organ failure, usually leading to the patient's death.

Case presentation

The patient, a 16-year old women, apparently regurgitated a greenish liquid after having eaten an apple. Her sister remembered that the family had stored "some pelleted rat poison in a safe place". After the events, she supposedly checked and didn't find the poison. The patient had previously declared her wish to "poison herself".

The initial admission was in a county hospital but, because of her extremely severe condition, she was later transferred to an emergency hospital in Bucharest. Here, the patient was admitted in a severely altered status, confused, with signs of clinical shock (anuria, systolic BP of 60 mmHg, cold extremities, hepatomegaly, turgid jugular veins). The ECG identified evolutionary changes compared to the initial one (done in the county hospital), showing sinus tachycardia, minor right bundle branch block, 2-3 mm ST elevation in V1-V3 with a „hockey

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stick" appearance (a Brugada-like pattern).

In this context, it was suspected the diagnosis of acute fulminant myocarditis with predominant right ventricular involvement complicated by cardiogenic shock. The patient is immediately moved to the ICU, where was monitored and provided with mechanical, inotropic and vasopressor support, in maximum doses.

The result of blood pseudocholinesterase was 2713 UI/L. Biological samples were obtained in order to determine the blood aluminium level, that yielded positive with a value 1.2 mg/L compared to the maximum normal value of 0.4 mg/L which supports the diagnosis of rodenticide poisoning (aluminium phosphide).

In the next few hours the patient's condition was extremely severe, with signs suggestive for MSOF, a marked haemodynamic instability, unresponsive to fluid replacement therapy, and inotropic and vasopressor support in maximum doses; after several cardiac arrests that were responsive to CPR measures she died in cardiac arrest secondary to ventricular fibrillation.

Gross pathology at the autopsy identified meningocerebral stasis and edema, pleural and peritoneal effusion, pulmonary consolidation, myocardial ischemia areas, liver dystrophy, renal stasis.

The histopathological examination identified the following: in lungs - diffuse alveolar lesions in the early exudative stage, minimum alveolar and bronchial haemorrhage and vascular lumens with a tendency towards thrombosis with bright birefringence granules in alveolar spaces and alveolar septa in polarized light; in the heart nonspecific chronic lesions with rare areas of subendocardial myocytolysis, myocardial hypoxic lesions and focal pleomorphic inflammatory infiltrate; in the liver - areas of haemorrhagic liver necrosis, granular and vacuolar dystrophic changes; in the kidneys – areas of acute cortical tubular epithelial necrosis, marked tubular epithelial granular and vacuolar dystrophic changes, extra capillary glomerulitis, stasis, and frequent numerous birefringent granules, located mostly in the renal convoluted tubules, identifiable under polarized light (Figures 2-4).

The thanatochemistry from the pericardial fluid revealed a CK-MB of 22473 U/L, a positive test for troponin I, and a negative test for myoglobin.

The toxicologic examination identified substances used in the patient's treatment, in therapeutic doses. The gastric contents negative for phosphine and a positive test for aluminium in serum (0.11 μg/ml), liver (2.65 mg/kg), kidneys (2.61 mg/kg), gastric contents (9.03 mg/kg).

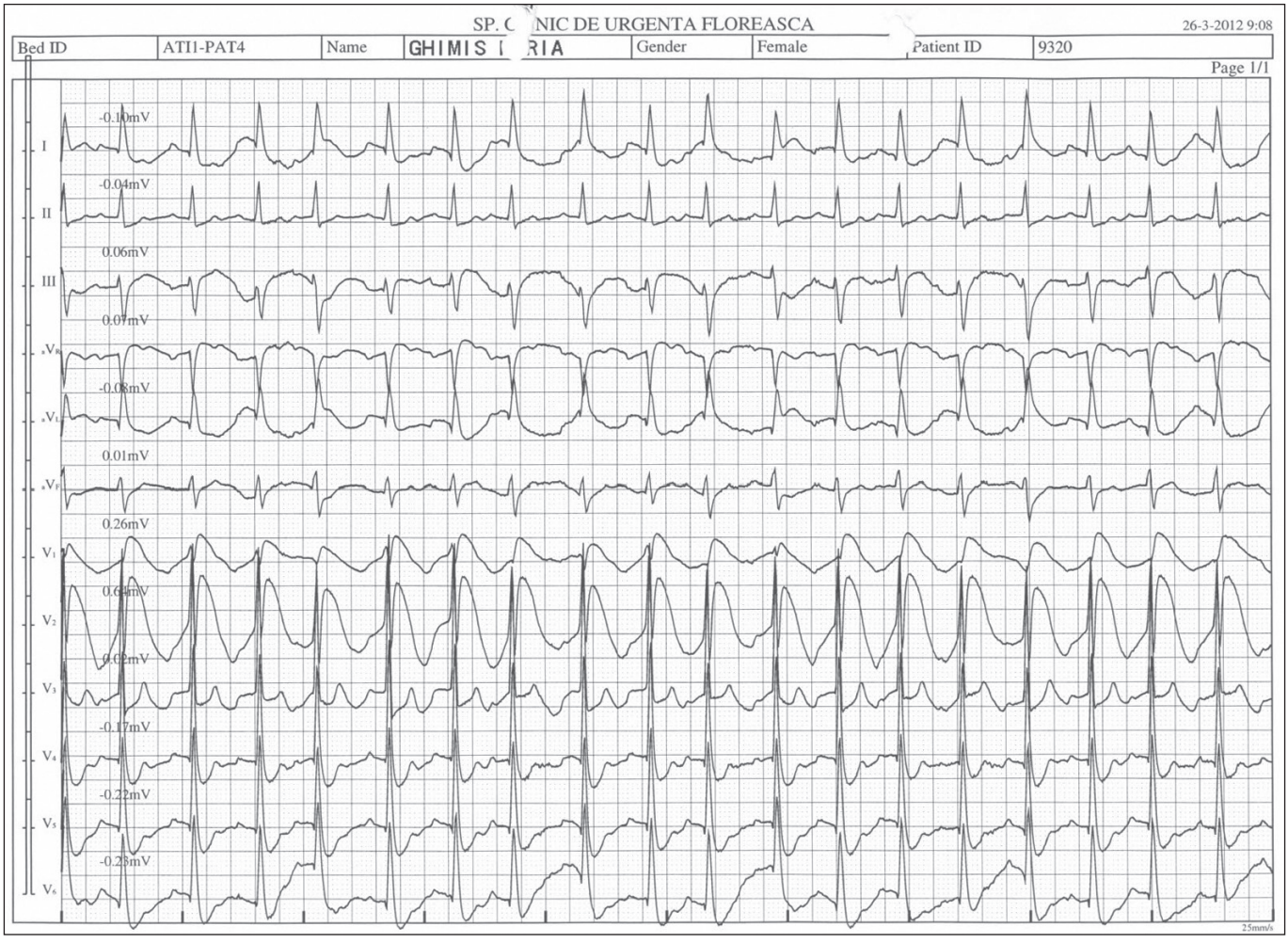

Figure 1. Brugada-like pattern (10 hours after the onset).

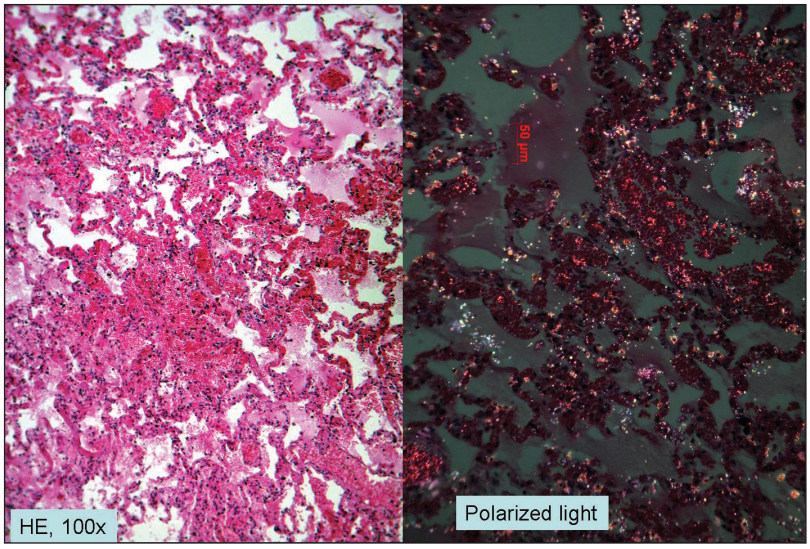

Figure 2. Congestion, edema and focal intra-alveolar micro hemorrhages, HE, 100x (left); bright birefringence granules in alveolar spaces and alveolar septa under polarized light (right), 200x.

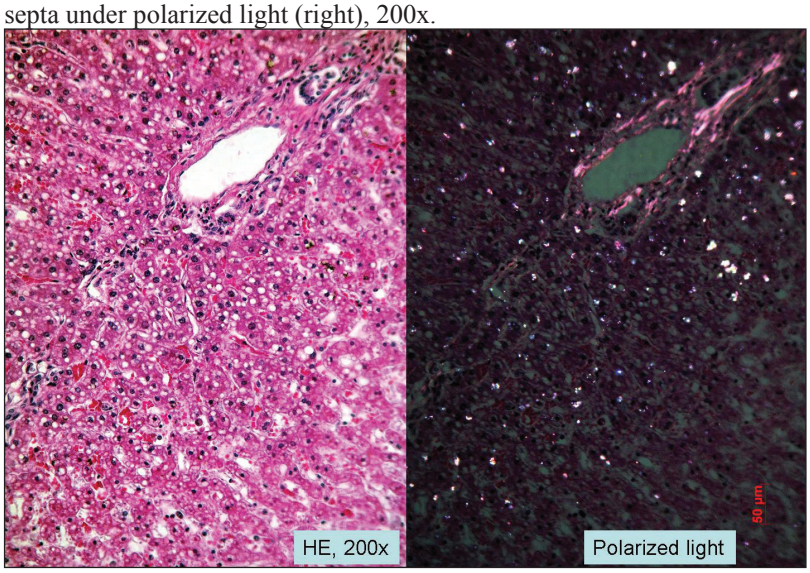

Figure 3. Periportal micro vesicular steatosis and mild congestion, HE, 200x (left); scattered bright birefrigent granules in periportal hepatocytes under polarized light (right).

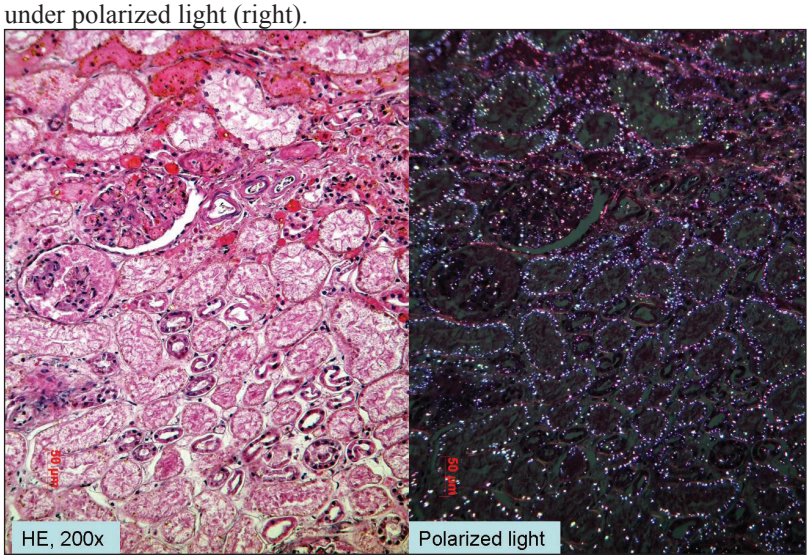

Figure 4. Marked granular and vacuolar degenerescence of the epithelia of the convoluted tubules, HE, 200x (left); large amounts of bright birefringence granules in the cytoplasm of the epithelia from convoluted tubules under polarized light (right), 200x.

DISCUSSIONS

The aluminium phosphide, under the action of the hydrochloric acid in the stomach, decomposes into phosphine, a highly toxic gas, which is lethal in concentrations of 20:100000, by blocking the cytorchrome-C oxidase and, subsequently, the mitochondrial oxidative phosphorylation [1]. Phosphine has effects on other metabolic pathways as well, including ones involved in protein synthesis, and on oxyhaemoglobin, by turning it into methaemoglobin and hemichrome species [2]. Aluminium phosphide boosts superoxide dismutase activity and decreases the catalase activity, that generates an extremely high volume of free radicals that accelerate lipid peroxidation; this in turn leads to structural changes of the cellular and nuclear membrane with consequent apoptosis.

Aluminium phosphide poisoning is known to be associated with various ECG abnormalities, ranging from signs suggesting an acute myocardial infarction, to atrial fibrillation, premature supraventricular or ventricular contractions, ST changes, bundle branch blocks, increased PR interval [3], sinoatrial block [4], etc.

A Brugada-like pattern, as identified in our case, has been previously described in literature [4] without an exact depiction of the pathophysiological mechanism.

Toxicologically, the phosphine can be detected with various methods, such as CG [5, 6], GC-MS [5], HS-CG [7] or SEM-EDX and XRD [8]. If a longer period of time passes from ingestion to death, blood and urine samples have no useful value. Thus, in a case presentation, Anger *et al.* could identify the aluminum phosphide in the brain 10 days after ingestion (where the concentration of the phosphine was of 94 ml/g), liver (24 ml/g) and kidneys (41 ml/g) using ICP-MS (Inductive Coupled Plasma - Mass Spetroscopy)[9].

Gross pathology of phosphide intoxication includes a slightly blue colouring of the lividities, although they may also be pink (caused by the inhibition of the respiratory chain). The gastric mucosa is atrophied, sometimes with parietal inflammatory infiltrations. The congestion of the internal organs is very frequent. The lungs may associate interlobular and marginal haemorrhages [10]. Histopathologically, phosphide poisoning is associated with signs

of organ ischemia, hypoxia, inflammatory infiltrates, congestion and edema, particularly in the lungs, kidneys and the adrenal[11]. In the brain was described the disorganization of the cerebral cortex, the presence of rounded neurons with convex edges, eccentric nuclei with signs of degeneration, and degenerated Nissl bodies in the cytoplasm. In subcortical areas were described a decreased density of the glial cells, nerve fiber degeneration and necrotic areas. The cerebellar cortex may display neuronal degeneration, with the disappearance of the Purkinje cells processes [12]. Pathologic changes in the kidney include tubular edema, obliteration of Bowman's capsule, increased glomerular cellularity, or inflammatory infiltrate with glomerular sclerosis [13]. Ultrastructurally, aluminium generates in the kidneys an increased number of lysosomes in the proximal convoluted tubules, vacuolation of the organelles and mitochondrial lesions of varying degrees [14]. The main causes of death in poisoning with metal salts of the phosphine are cardiogenic shock [15], multiple organ failure [16], acute respiratory failure [17], or refractory shock [4].

In our case, the aluminium phosphide could not be identified per se due to technical limitations. However, corroborating clinical and history data with the toxicological ones (above normal aluminium levels) the diagnosis of fatal poisoning with aluminium phosphide could be inferred beyond reasonable doubt.

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