Cardiac and Respiratory Arrest in a 12-Year-Old Girl with Acute Permethrin Toxicity: A Case Report

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Case report

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Abstract

Background

Permethrin (PER) is widely employed as the most frequently used type I synthetic pyrethroid insecticide. Despite its worldwide application, reports of pediatric toxicity following permethrin administration are scarce.

Case presentation

The present case report involves a 12-year-old Afghan girl, with no previous medical problems, who drank an unknown insecticide covertly at home. Two hours after ingestion, she was taken to the emergency room with neither breathing signs nor a heartbeat. She was immediately transferred to the cardiopulmonary resuscitation (CPR) room, and her spontaneous circulation was returned after a few minutes of CPR. She was then intubated, volume resuscitated with intravenous normal saline, and connected to the mechanical ventilator after being transferred to the ICU ward. The patient remained comatose without spontaneous breathing, her pupils became bilateral mydriasis, and central diabetes insipidus became evident after three days due to apnea and hypoxic brain damage following insecticide ingestion. The chemical analysis of the insecticide bottle showed 10% permethrin without organophosphates, as initially expected. Unfortunately, after seven days, the patient passed away due to resistant hypotension and severe brain damage.

Conclusion

Permethrin is widely used globally as an insecticide. However, there are many unmet needs in permethrin toxicity treatment, and the treatment is mainly supportive. Depending on the amount and dose of permethrin, the most common symptoms can vary from headache, dyspnea, and vomiting to metabolic acidosis and cardiac and respiratory arrest, which can lead to hypoxic brain damage and death, as was the outcome in our case.

Background

Permethrin ($C_{21}H_{20}Cl_2O_3$) is the most frequently used type I synthetic pyrethroid insecticide, which is extensively used worldwide [1]. However, the expanded use of permethrin might cause various toxic effects on humans, including neurotoxicity, immunotoxicity, cardiotoxicity, hepatotoxicity, digestive system toxicity, and cytotoxicity, and also reproductive, genotoxic, and hematotoxic effects [2]. According to the European Chemicals Agency (ECHA), the hazard classification of permethrin is aquatic chronic 1 with code H410 [3]. The main molecular targets of synthetic pyrethroids are voltage-dependent sodium channels (VDSC); they bind to these channels and delay the inactivation of sodium channels, resulting in neurotoxic effects, and ultimately, death [4]. The main type of exposure is dermal absorption, while its major neurotoxic mechanisms include oxidative stress, inflammation, neuronal cell loss, and mitochondrial dysfunction [5].

Despite its global application, there have been scarce reports of pediatric toxicity following permethrin administration. The present report describes the case of a 12-year-old girl with cardiac and respiratory arrest resulting from self-induced oral toxicity by permethrin.

Case Presentation

A 12-year-old Afghan girl, with no previous medical problem, drank an unknown insecticide covertly at home. Two hours after ingestion, symptoms of headache, vertigo, vomiting, dyspnea, and confusion presented at home, and after 20 minutes, she was taken to the emergency room with neither breathing signs nor a heartbeat. She was immediately transferred to the cardiopulmonary resuscitation (CPR) room. A few minutes following CPR, spontaneous circulation was returned achieved with chest compression, bag valve mask, artificial ventilation, and two doses of 1 mg intravenous epinephrine. Moreover, gastric lavage and activated charcoal administration were performed after intubation. Then, she was volume resuscitated with intravenous normal saline and connected to the mechanical ventilator after being transferred to the ICU ward. Following admission to ICU, she presented excessive lacrimation, salivation, and myoclonic muscle twitches. Physical examinations indicated pinpoint pupils with no reflex to light, downward plantar reflex, normal lung sounds, tachycardia in heart sounds, normal blood pressure, and the normal respiratory rate. She was in a deep coma in the interim with a Glasgow coma score of 3, while electrocardiography showed sinus tachycardia (Fig. 1). Computed tomography (CT) scans of her head and chest, along with abdominal X-rays, were normal (Fig. 2). Even though her laboratory test results showed metabolic acidosis in arterial blood gas and increased blood levels of CK-MB (creatine kinase myocardial band), other indicators were normal (Table 1).

In the ICU, her muscle twitches and metabolic acidosis were controlled with intravenous atracurium 5 mg and levetiracetam 5 mg and bicarbonate sodium vials, respectively. In the days following hospitalization, the patient had normal blood pH in her arterial blood gas analysis samples. Moreover, in the ICU, she was administered two doses of 1 mg intravenous atropine to treat muscarinic symptoms; however, there was no therapeutic response. The patient continued to be comatose without spontaneous breathing, her pupils became bilateral mydriasis, and her central diabetes insipidus became evident after three days due to apnea and hypoxic brain damage following the insecticide ingestion. We suspected central diabetes insipidus after observing hypernatremia in her blood test, which was higher than 4.5 liters in the 24-hour urine volume. It was diagnosed based on decreased urine specific gravity and abnormal plasma copeptin level.

The chemical analysis of the insecticide bottle showed 10% permethrin, without organophosphates, as initially expected (Table 1). Unfortunately, she passed away after seven days due to resistant hypotension and severe brain damage.

Discussion And Conclusions

Permethrin, a synthetic pyrethroid insecticide with widespread usage, is administered as the first-line therapy for scabies in pediatric patients older than two months [6]. Pyrethroids impact voltage-dependent sodium chloride and chloride channels [7]. However, toxicities are scarce in gastrointestinal, neurologic, and respiratory systems due to this compound [8]. Pyrethroids are categorized into types I and II, and permethrins are considered type I (i.e., the cyclopropane group) [9]. Exposure to type I pyrethroids results in reflex hyperexcitability, paresthesias, and fine tremors known as the T syndrome. Type II pyrethroids (e.g., cypermethrin and deltamethrin) have an alpha-cyano group, which results in salivation, choreoathetosis, coarse tremors, and seizures, as well as effects on the skeletal and cardiac muscles, also known as the choreoathetosis–salivation (CS) syndrome. However, toxicity is more life-threatening with type II pyrethroids than with type I pyrethroids due to coma and convulsions [10]. Based on the reported acute toxicity of permethrin, i.e., an LD50 of 430 to 4000 mg/kg for industrial permethrin in rats, it is slightly toxic through the dermal route. The 4-hour inhalation LC50 for the rats was more significant than 23.5 mg/L, indicating practically no inhalation toxicity. The toxicity of permethrin depends on the isomers' ratio, with the cis-isomer being comparatively more toxic. Concerning chronic toxicity, rats fed 150 mg/kg/day for six months showed a slight increase in liver weight. Pyrethroids exposure induced weight loss in the rats, although the acute oral toxicity of permethrin was low. Moreover, regarding chronic toxicity, permethrin induced anxiety-like behaviors, excitatory behaviors, and Gln-Glu-GABA circulatory dysfunction in blood. Mainly, permethrin had also reproductive toxicity [11].

Following 4 to 48 hours of the intentional ingestion of pyrethroid, gastrointestinal, neurologic, or pulmonary signs and symptoms will appear [7], including headache and fatigue as the most common symptoms. However, several fewer common signs and symptoms, such as hepatic and renal dysfunction, are inevitable [7]. Nausea, vomiting, sore throat, and epigastric pain are symptoms of the oral consumption of pyrethroids [8].

The deliberate use of a large volume of permethrin by a 12-year-old girl with suicidal intent is rare. As confirmed by similar studies, mortality is rare among these patients [2, 9, 12]. In particular, most permethrin toxicity cases have occurred through dermal contact, as opposed to our case of pediatric oral permethrin toxicity. Drago et al. reported cases in which children inadvertently took low doses of permethrin [2], and in the study by Yang et al., 38 out of 48 patients with a mean age of 49 ± 3 years took permethrin to commit suicide; however, there was only one case of mortality among them [9].

Bhaskar et al. studied a 28-year-old female who committed suicide by ingesting prallethrin as another synthetic pyrethroid insecticide. After consumption, her laboratory test results were normal during the first 24 hours. Following the first day, she developed metabolic acidosis and sinus arrest, which were corrected after 3 days, and she was discharged from the hospital after one week. They concluded that cardiac arrhythmia was likely to occur because of pyrethroid consumption [12].

Some molecular pathways might be involved in cardiotoxicity with pyrethroids. In particular, pyrethroids, such as permethrin, can damage neuronal sodium channels by inducing a persistent steady-state sodium current within depolarized membranes, leading to cardiac hypotrophy, an increase in calcium release, and

the enhancement of the Nrf2 gene expression levels in older animals. The levels of cytosolic calcium are essential to the cardiac muscle's contractile state. Moreover, permethrin induces oxidative damage to purine bases in cardiac cells [13].

Yang et al. evaluated 48 patients with symptoms of poisoning due to permethrin consumption. Among them, 73% demonstrated gastrointestinal symptoms, while 33% had central nervous system involvement. Other symptoms included pulmonary involvement and renal and hepatic dysfunctions, respectively. Moreover, only 4% had arrhythmias and only one patient died. Thus, it was concluded that poisoning was more common with type II pyrethroids than with type I pyrethroids [9]. Permethrin ingestion can lead to apnea and hypoxia, resulting in critical and irreversible organ damage. Brain injury can be progressive, as it occurred in our case, and it can cause many complications [5, 14]. In this report, the patient developed central diabetes insipidus, which deteriorated her condition. Central diabetes insipidus has been found in a variety of disorders that mainly arise from hypothalamus damage. Polyuria and polydipsia occur when more than 80-90% of the Arginine Vasopressin -secreting neurons in the supraoptic and paraventricular nuclei are damaged. Patients with hypothalamic neuronal damage from oxidative stress pathways can develop hypoxia and are likely to develop central diabetes insipidus. Extensive destruction can be caused by several acquired pathological processes, including idiopathic conditions [15]. Atracurium, employed in this study, controlled the muscle twitches and prevented rhabdomyolysis. However, atropine had no positive effect on the patient.

Our primary limitations in this case study were the lack of proper treatment guidelines and an antidote for pediatric permethrin toxicity. Despite the initial uncertainty about the ingested insecticide, the rarity of the case, and poor cooperation from the patient's family, we successfully diagnosed the case in the early stages based on the patient's signs and symptoms and provided the best possible management. We believe that our proposed method can be applied to patients in future cases. However, despite the timely control of the disease, due to the high dosage and volume of the ingested insecticide and the delay in hospitalization, the patient inevitably suffered from irreversible brain hypoxia and went into a coma. The flowchart of the treatment strategy and the process administered for this patient is presented in Fig. 3. This flowchart can be used in similar cases to obtain the best treatment results.

Permethrin is a widely used insecticide. However, there are many unmet needs in permethrin toxicity treatment, including the lack of evidence-based guidelines for most complications, the absence of a specific antidote for poisoning caused by this insecticide, and the ineffectiveness of atropine for muscarinic signs. Moreover, this treatment is mainly supportive. Depending on the amount and dose of permethrin, most common symptoms can vary from headache, dyspnea, and vomiting to metabolic acidosis and cardiac and respiratory arrest, which can lead to hypoxic brain damage and death, as occurred in our case.

Abbreviations

PER: Permethrin; CPR: cardiopulmonary resuscitation; ECHA: European Chemicals Agency; VDSC: voltage-dependent sodium channels; CT: Computed tomography; CK-MB: creatine kinase myocardial band; CS: choreoathetosis–salivation

Declarations

Ethics approval and consent to participate

The research obtained approval by the School of Medicine of Tehran Islamic Azad University of Medical Sciences. The participant of the study was volunteer who had given informed consent to the study.

Consent for publication

The participant had given informed written consent to report the individual patient data.

Availability of data and materials

The clinical documentation of the presented case cannot be made public due to the detailed identifiable information of the patient.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

HAA and HZA examined the patient, reviewed the CT-scan, ECG and drafted the manuscript. SMG extracted the history and patient reports on ECGs and CT-scans. MST reported the patient findings and lab data. MM re-read the CT-scans and ECGs. MM organized the surveillance of the patient and designed the health program. All authors read and approved the final manuscript.

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Tables

Table 1. Results of the laboratory tests for the patient.

Toxicology Urine Laboratory	Result	Reference
Amphetamine	Negative	-
Methamphetamine	Negative	-
Cocaine	Negative	-
Morphine	Negative	-
Methadone	Negative	-
Barbiturates	Negative	-
pH	5	-
Tetrahydrocannabinol	Negative	-
Tricyclic antidepressants	Negative	-
Permethrin	Positive	-
Buprenorphine	Negative	-
Tramadol	Negative	-
Benzodiazepines	Negative	-
Lab Data	**Result**	**Reference**
Blood Culture X2	(1&2) No Growth After 48 Hours	-
Urine Culture X2	No Significant Uropathogenes Isolated	-
White Blood Cells	11800 count	4000-11000
Red Blood Cells	4.84 mill/cumm	3.9 - 5.6
Hemoglobin	13 g/dl	11 - 16.5
Platelets	243000 count	150000-450000
Creatine Kinase	157 IU/L	24-170
Troponin	0.012 ng\ml	<0.04
CK-MB	99 IU/L	<24
Blood Urea	21 mg/dl	15 - 40
Creatinine	0.8 mg/dl	0.6 – 1.4
Arterial Blood Gas pH	6.99	7.35 - 7.45
PCO2	37.9	40
HCO3	9.3 mmol/l	24

3 Days After Admission		
Plasma Copeptin	2.3 pmol/L	≥3.6
Urine Specific Gravity	1.003	1.005 - 1.030
Serum Sodium Level	159 meq/l	135 - 145
Blood Glucose Level	126 mg/dl	< 140
AST	41 IU/L	< 31
ALT	22 IU/L	< 31
Alkaline Phosphatase	309 IU/L	64 - 306

PH: Potential of Hydrogen; CK-MB: Creatine Kinase- Myocardial Band; PCO2: Pressure of Carbon Dioxide; HCO3: Hydrogen Carbonate; AST: Aspartate Transaminase; ALT: Alanine Transaminase

Figures

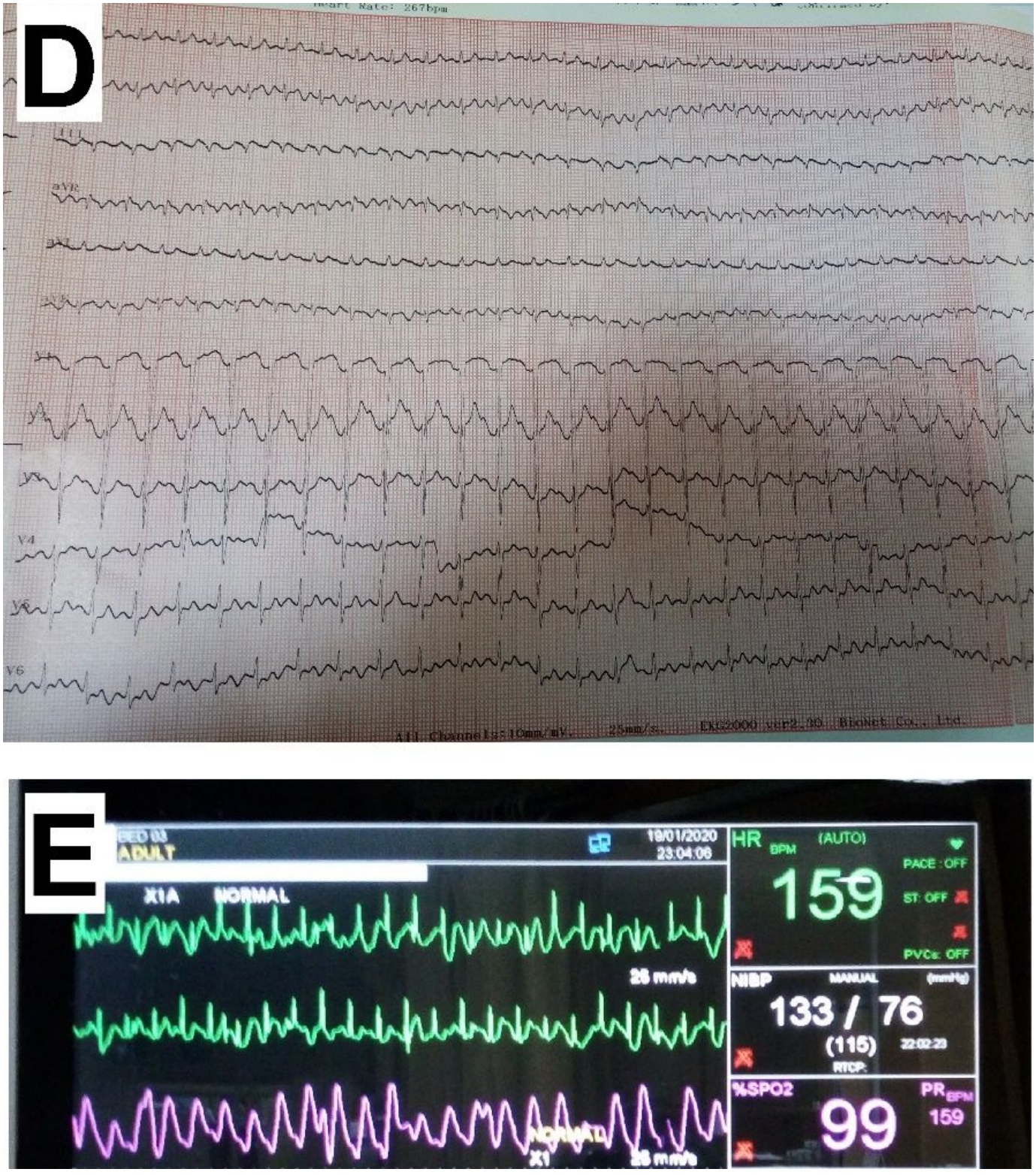

Figure 1

ECG (D) and vital signs monitoring (E), demonstrating sinus tachycardia after ICU admission. HR: Heart Rate; BPM: Beats per Minute; NIBP: Non-Invasive Blood Pressure; SPO2: Oxygen Saturation.

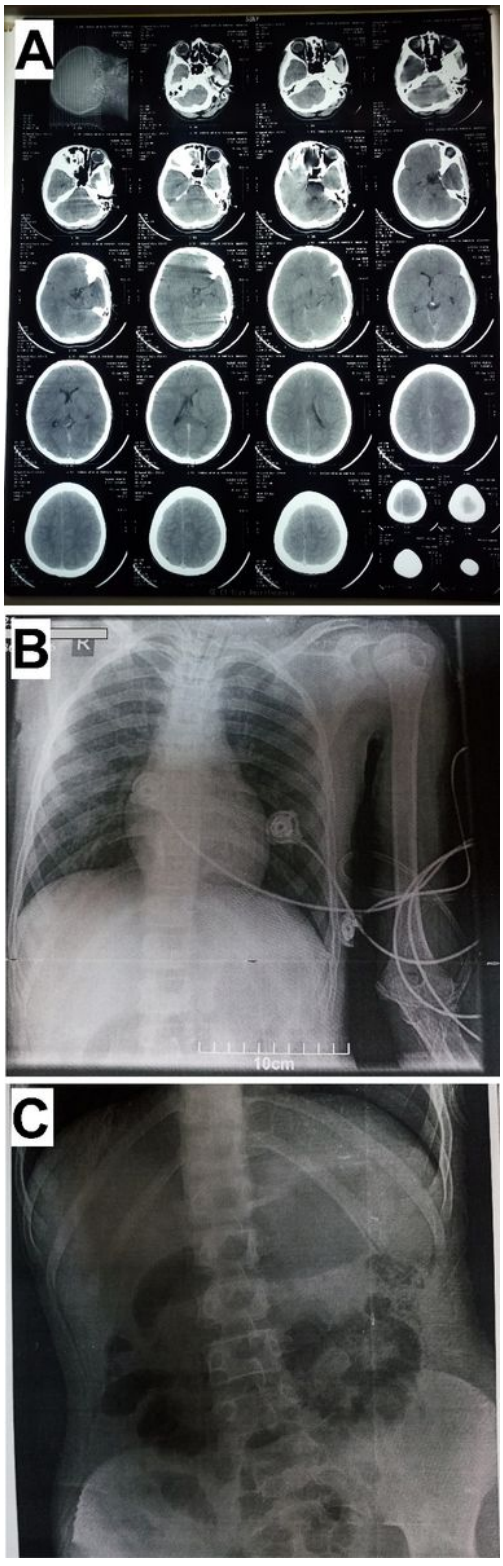

Figure 2

Head CT scan (A), chest (B), and abdominal X-rays of the patient (C). The imaging was performed after CPR, and the results were normal.

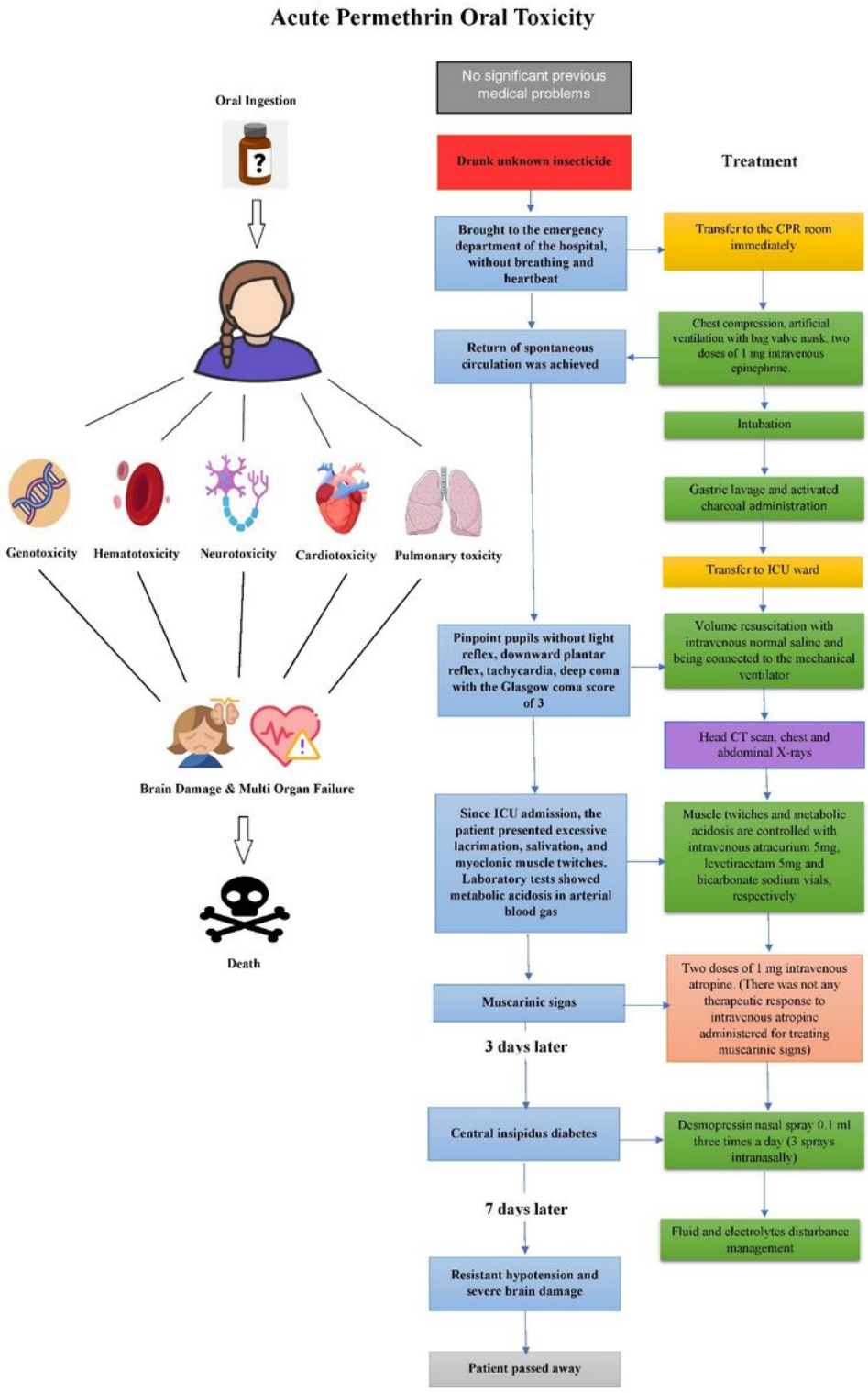

Figure 3

The treatment strategy flowchart for the case.