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A case of tetramine poisoning: a lethal rodenticide

致命滅鼠劑「毒鼠強」中毒個案

We report a fatal case of suicide presenting with convulsions and subsequently multi-organ failure. Rodenticide poisoning was not suspected until the next day when tetramine was detected in the patient's blood, urine, and food residues. Tetramine is a potent rodenticide with a rapid action and high mortality. The poison has been banned worldwide but is still readily available in Mainland China. Outbreaks of poisoning are reported frequently and doctors should be alert for this lethal toxin.

本文報告一宗自殺死亡個案。病人出現抽搐，繼而多個器官功能衰竭。直至次日在死者血液、尿液和和食物殘餘中驗出「毒鼠強」，才意識到是中滅鼠劑毒。「毒鼠強」是烈性滅鼠劑，發作迅速且致命率高，已被全球禁用，但仍在中國大陸使用。由於中毒病例經常出現，醫生處理時應留意致命滅鼠劑的中毒可能。

Introduction

Tetramine (tetramethylene disulphotetramine) is an odourless and tasteless rodenticide. It is extremely hazardous, being 100 times more toxic than cyanide. Human poisoning frequently occurs and victims develop convulsions and die within hours of ingestion. Management includes anticonvulsant treatment and early haemofiltration. Tetramine has been banned worldwide because of its lethal toxicity but repeated outbreaks of poisoning continue to occur in Mainland China. Sporadic cases have been recently reported in the United States and Hong Kong,[1-3] thus doctors must remain vigilant for this potent toxin. We report a case of tetramine poisoning and discuss the problems of diagnosis and management.

Case report

A 53-year-old man with good past health was found collapsed in the toilet of a public library. A suicide note and a bag of leftover food were also found. The ambulance crew noted tonic-clonic convulsions en route to the emergency department. The patient was subsequently resuscitated and intubated following cardiac arrest. Upon admission to the intensive care unit, the Glasgow Coma Scale score was 2/15. He developed status epilepticus that was controlled with intravenous lorazepam. Physical examination revealed no focal neurological signs. No rigidity was noted and chest, abdominal, and cardiovascular examination was unremarkable. Electrocardiogram showed sinus tachycardia. Chest X-ray and echocardiogram were normal. He was put on 100% oxygen. Blood gas analysis revealed severe metabolic acidosis: pH 6.338; partial pressure of carbon dioxide, 56.54 mm Hg; partial pressure of oxygen, 22.93 mm Hg; bicarbonate, 3.0 mmol/L; and base

Key words:
Bridged compounds;
Poisoning;
Rodenticides;
Status epilepticus

關鍵詞：
架橋連接化合物；
中毒；
滅鼠劑；
癲癇持續

Hong Kong Med J 2005;11:507-9

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excess, -41 mmol/L. Renal and liver biochemistry was normal and haematology revealed a haemoglobin level of 126 g/L, white blood cell count of 9.4 x 10^9 /L, platelet count of 279 x 10^9 /L, serum sodium level of 157 mmol/L, and serum potassium level of 4.5 mmol/L. A few hours after admission, the patient developed a high fever of 40ºC, followed by rapid deterioration in renal and liver function, disseminated intravascular coagulopathy, rhabdomyolysis, gastro-intestinal bleeding, and profound shock.

Urine toxicology screening was negative. The day following admission, rodenticide poisoning was suspected and samples sent for confirmation. Tetramine was detected: urine, blood, and food sample concentrations were 133.5 ng/mL, 81.6 ng/mL, and 56.4 μg/g, respectively. The blood level indicated moderate toxicity.[4] Continuous venovenous haemofiltration was commenced but the patient continued to deteriorate with persistent metabolic acidosis and multi-organ failure. The blood tests just prior to death showed pH 6.947, platelet count of 103 x 10^9 /L, creatinine level of 434 μmol/L, alanine transaminase level of 3004 IU/L, creatine kinase level of higher than 20 000 IU/L, international normalised ratio of 3.71, and D-dimer level of 1.0 μg/mL. The patient succumbed 2 days after admission. The mode of death appeared to be prolonged seizure activity with rhabdomyolysis and hypoxia leading to multi-organ failure. The final diagnosis was intentional suicide by tetramine.

Discussion

Rodenticides are among the most toxic substances known and are readily available; poisoning may occur accidentally or deliberately. It is important to be familiar with their uses and to identify the actual agent used so that appropriate management in the case of poisoning can be rapidly instituted. A wide variety of rodenticides is available in Mainland China. It includes tetramine that is extremely dangerous and has been banned by the government since 1991. Nonetheless illegal trading is common and banned rodenticides account for over two thirds of rodenticides sold in China.[5]

The chemical name of tetramine is tetramethylene disulphotetramine (molecular formula $C_4H_8N_4O_4S_2$). Commonly referred to as dushuqiang or Four-Two-Four, it is a neural toxin, first synthesised in 1949. It acts by binding noncompetitively and irreversibly to the gamma-aminobutyric acid (GABA) receptor on neuronal cell membranes and blocking chloride channels.[6] This leads to excitation of the central nervous system and induces convulsions. Tetramine is a highly effective rodenticide with a LD50 in rats of 0.1 mg/kg. It is also very toxic to humans: a dose of 5 to 12 mg is considered lethal.[7] It is not easily degraded and can remain in the environment and the food chain for prolonged periods.

Reports of tetramine poisoning are frequent in Mainland China. Symptoms of nausea, vomiting, abdominal pain, and reduced level of consciousness with convulsions soon after ingestion are consistent with tetramine poisoning. The time interval between ingestion and symptom onset ranges from 10 to 30 minutes. Severe poisoning results in coma and death from respiratory and multi-organ failure.[8] The unique features of tetramine poisoning are the rapid onset of convulsions that are difficult to control, multi-organ failure, and high mortality.

Despite its unique features, tetramine poisoning can be difficult to diagnose. First, it is an illicit rodenticide and may not be listed on the product label. The victim, often comatose, cannot provide any useful history. Second, although common in Mainland China, it is little known to health care professionals in Hong Kong. The literature is very confusing as tetramine is also present in a variety of compounds, including the toxin from salivary glands of gastropods. Finally, presentation mimics many medical conditions and poisoning due to other substances. Diagnosis of tetramine poisoning can thus be delayed or missed.

Laboratory confirmation requires detection of tetramine in the blood, vomitus, or urine of suspected victims; severity of poisoning is related to the blood tetramine level.[4] Routine toxicology does not currently screen for tetramine that will go undetected unless specific assays are employed. The Hospital Authority Toxicology Reference Laboratory has now developed a special tetramine confirmation assay to provide prompt laboratory diagnosis.[9]

Treatment includes elimination of tetramine by gastric lavage and activated charcoal, seizure control with anticonvulsants, and various supportive measures. Supportive treatment in a poisoned infant has resulted in survival with brain damage.[3] Haemoperfusion and haemofiltration can reduce mortality and morbidity especially when commenced within 12 hours of ingestion.[10]

There is currently no established antidote for tetramine poisoning. Sodium dimercaptopropane-

sulphonate (Na-DMPS) is a synthetic compound that has been used in the treatment of heavy metal poisoning and has been shown to effectively control convulsions and reduce mortality in animal studies.[11] It acts by increasing GABA binding to its receptor in the brain.[12] Isolated reports of successful treatment with DMPS in cases of human tetramine poisoning are largely from Mainland China and more clinical studies are required to confirm its efficacy.[13-15] Dimercaptopropanesulphonate is not registered in Hong Kong and is therefore not available for use. Tetramine poisoning due to dermal exposure has also been reported.[16] Health care workers should take precautions to prevent secondary exposure.

Conclusion

The patient in this report committed suicide by ingesting tetramine rodenticide and died from multi-organ failure. Diagnosis was confirmed by the detection of tetramine in blood, urine, and food remains. Tetramine is a lethal toxin that acts rapidly to produce prolonged convulsions leading to multi-organ failure. A few cases of tetramine poisoning have been reported in Hong Kong. Early recognition and treatment is essential and health care workers should be alert for this toxin.

Acknowledgement

We would like to thank the Government Laboratory for providing tetramine standard material.

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