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Case report

Tetramine poisoning: A case report and review of the literature

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ABSTRACT

Background: Tetramethylene disulfotetramine (TETS), a banned neurotoxic rodenticide, has accounted for numerous intentional and unintentional poisonings in mainland China. Since the first known case of human illness caused by tetramine occurred in NewYork, in May 2002, TETS has caused more than 50 human poisonings in Western countries.
Aim: To analyze pathological changes of TETS poisoning and to provide evidence for forensic identification.
Methods: We report the case of a 28-year-old female who suffered from tetramine poisoning and died of multi-organ failure. We also performed a retrospective study of 40 cases of poisoning, from pathological autopsy reports, by analyzing and summarizing the related the literature from 1996 to 2010. Based on pathologic autopsies and the literature, we summarize the pathological changes related to tetramine poisoning.
Results: Signs of asphyxia were obvious upon pathological examination. Edema and congestion of organs, particularly in the brain, were seen in all cases. Subarachnoid and cerebral hemorrhaging were also common signs of tetramine poisoning.
Conclusion: In forensic practice, tetramine poisoning should be considered when the patient has signs of abnormal excitation of the central nervous system, convulsions, hyperspasmia, and cerebral hemorrhage.

1. Introduction

Tetramethylene disulphotetramine (TETS), commonly called tetramine (molecular formula $C_4H_8N_4O_4S_2$), is a nerve toxic compound of rodenticide that was first synthesized by a German company in 1949. TETS acts by binding noncompetitively and irreversibly to gamma-aminobutyric acid (GABA) receptors on neuronal cell membranes and by blocking the chloride channel. This prevents GABA-mediated inhibition in the central nervous system, leading to excitation of the central nervous system and convulsions [1,2].

TETS is an odorless, tasteless, white crystalline powder that easily dissolves in water. The chemical properties of tetramine are stable and its metabolism is slow [3]. The LD50 (50% lethal dose or the single dose of an agent that kills 50% of exposed laboratory animals) of TETS in mammals is 0.1–0.3 mg/kg, and a total dose of 5–12 mg is considered to be lethal for humans. In addition, TETS also can cause harmful secondary poisoning in the human body [4]. The most common route of exposure to TETS is ingestion. Occupational exposures through inhalation occur but TETS is not absorbed through intact skin [5]. The latent period for the effects of TETS to be observed ranges from 10 to 30 min, and the time interval between the onset of symptoms and fatal outcome ranges from 1 to 2 h [6]. Latency time and severity of symptoms are closely related to the amount of poison, personal physical status, and time of rescue.

TETS poisoning leads to broad excitation of the central nervous system and induces convulsions in the absence of apparent effects on peripheral nerves, neuromuscular junctions and skeletal muscle [7]. Refractory status epilepticus and coma appear to be the hallmarks of typical tetramine poisoning, accompanied by symptoms of convulsions, trismus, frothing at the mouth, and urinary incontinence characteristic of the symptoms of epileptic seizures.

TETS has been banned worldwide because of its lethal toxicity; however, it remains easily purchased in many areas and is popular as an inexpensive rodenticide in mainland China [8]. TETS is also commonly used for suicide and public poisoning incidents such that poisoning cases continue to occur sporadically in China as well as the United States [9]. Thus, clinical studies and fundamental research on the use and actions of TETS continue to be of significant importance for the diagnosis and treatment of TETS poisoning.

2. Literature search and review

We searched the Medline, Entrez PubMed and China Science Citation Index electronic databases for all years and all languages using the key words ‘tetramine’ and ‘poison’; and performed a

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Table 1
Report cases of TETS poison (1998–2010).

Authors and publication year	Age/sex	Cause	Exposure route	Primary symptoms	Autopsy and pathology findings[a]
Zhou et al. (1998) [4]	25/M	Homicide	Digestive system	Convulsions, lips cyanosis	Edema and congestion of organs; fatty changes in liver
	40/F	Suicide	Digestive system	Coma, nausea and vomiting	Cerebral vascular congestion; protein casts and calcium deposition in kidney
	25/F	Homicide	Digestive system	Convulsions	Subarachnoid hemorrhage; fatty changes in liver
	5/F	Homicide	Digestive system	Convulsions	Subarachnoid and focal brainstem hemorrhages
	27/F	Homicide	Digestive system	Convulsions, coma	Dark red fluids in heart
Chen (2004) [14]	8/M	Accident	Digestive system	Convulsions	Cerebral vascular congestion; bleeding points in gastric mucosa and on heart surface
	7/M	Accident	Digestive system	Nausea	Dark red fluids in heart; bleeding points in gastric mucosa
	5/F	Accident	Digestive system	Convulsions	Bleeding points in gastric mucosa
Wu et al. (2005) [12]	25/F	Homicide	Intramuscular injection	Coma	Edema and congestion of brain
Xu et al. (2006) [13]	33/M	Accident	Digestive system	Headache, dizziness	Fatty changes in liver; protein casts and calcium deposition in kidney
	10/M	Accident	Digestive system	Cough, nausea	Interstitial pulmonary edema and congestion
Jiang et al. (2000) [11]	6–62 M:F=10:7	Suicide 5/17; homicide 10/17; accident 2/17	Digestive system	Convulsions 17/17; coma 15/17; dizziness 9/17; lips cyanosis 11/17; nausea 6/17; etc.	Dark red fluids in heart 17/17; bleeding points in gastric mucosa 14/17, on heart surface 8/17 and on lung surface 8/17; cerebral vascular congestion 2/17
Wu et al. (1999) [10]	NA[b]/M:F=5:6	Suicide 2/11; homicide 6/11; accident 3/11	Digestive system	Convulsions 11/11; coma 11/11; nausea 10/11; dysphoria 11/11; etc.	Subarachnoid hemorrhage 8/11; bleeding points in gastric mucosa 10/11, on heart surface 6/11; fatty changes in liver 2/11
Current case	28/F	Suicide	Digestive system	Convulsions, coma	Subarachnoid and focal brainstem hemorrhages; fatty changes in liver

[a] We listed only the main autopsy and pathology findings from the literature; common signs found in autopsy, such as edema and congestion of organs, were not provided in all cases.
[b] NA, no data available.

retrospective analysis and summary of 40 pathological autopsy reports of cases of TETS poisoning from 1998 to 2010 [4,10–14] (Table 1). Most cases were reported in Chinese. Selection criteria for inclusion of literature reports were as follows: publication in an established peer-reviewed journal; accurate and detailed case history; autopsy description; toxicological findings and pathology diagnoses. Patients were not recorded by name when their medical records were accessed. The data were based on case reports at autopsy. In all cases, the stomach, stomach contents, part of the liver and heart, blood, or other samples had been submitted for toxicological analysis and TETS poisoning was confirmed.

Since 1996, 40 cases of TETS poisoning have been reported in Mainland China. These affected 20 females and 20 males aged 5–62 years (median 35 years). According to these studies, 10/40 of the poisoning cases occurred by accident, 21/40 by homicide and 9/40 by suicide.

Postmortem studies of TETS-poisoned patients revealed common signs of circulatory hypoxia, such as cyanosis of lips and nails. Some patients had signs of tongue bites, bloody noses, mouths with secretory fluids, and asymmetric pupil sizes. Lesions as a result of TETS poisoning involved multiple organs.

Brain: In 21/40 cases, cerebral vascular congestion was observed; subarachnoid hemorrhaging was observed in 11/40 cases. Bleeding sites were found in the cerebrum and, in some cases, in the cerebellum; focal brainstem hemorrhages were reported in 2 cases. Microscopically, cerebral edema was seen and some neurons may have shrunk in volume; red stained cytoplasm, nuclear deviation, nuclear pyknosis, and absence of nuclei were observed in some cases.

Heart: Bleeding points were visible on the surface of the heart in 19/40 cases, with multi-distribution in the apex of the heart but also in the ventricular septal endocardium of ventricles. Dark red fluid in the heart was found in 19/40 cases. Microscopically, myocardial interstitial edema, leukocyte infiltration, and occasional myocardial necrosis were seen.

Stomach: Food was found in most patients stomachs. In 37/40 cases, gastric mucosa changed in color to dark brown, dark green or gray. Bleeding points were found in the stomach at the lesser curvature and fundus. Microscopically, gastric submucosal congestion, edema and gastric smooth muscle spasms were observed.

Lung: Interstitial pulmonary edema and congestion were visible in almost all cases. In 8/40 cases interstitial and lung surface bleeding points were seen. Some cases also were combined with pneumonia and lung abscess formation. Microscopically, alveoli were filled with fluid and loose interstitial edema was evident with leukocyte infiltration in some cases.

Liver: Edema, congestion and fatty changes were observed in 6/40 cases. Microscopically, the structure of the surviving hepatic lobule was complete and liver cells were swollen from fatty degeneration, with general micro-vesicular fatty changes.

Kidney: Edema and congestion were observed by light microscopy, especially in the kidney tubules. Protein casts and calcium deposition were seen in kidney tubules in 3/40 cases.

Other organs: The surface of the spleen, pancreas, adrenal gland, bladder and other organs were covered with various sizes of hemorrhagic foci.

In summary, edema, congestion and bleeding were common signs in most organs. Bleeding had different forms: in brain, subarachnoid hemorrhaging formed while in stomach, lung and other organs, bleeding points were seen.

Frequency of various signs observed in autopsy is summarized in Table 2:

3. Poisoning case report

3.1. Case history

A 28-year-old woman was admitted to the hospital after an episode of severe coma and tonic-clonic convulsions. Critical treatment included cardiopulmonary resuscitation and tracheal