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Fatal arsenic poisoning — A case report

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GERHARDSSON L, DAHLGREN E, ERIKSSON A, LAGERKVIST BEA, LUNDSTRÖM J, NORDBERG GF. Fatal arsenic poisoning — A case report. *Scand J Work Environ Health* 14 (1988) 130–133. A worker was buried under arsenic trioxide in an industrial accident. He was almost immediately released but had inhaled and swallowed substantial amounts of arsenic dust. In spite of intensive treatment, circulatory collapse could not be prevented, and he died 6 h after the exposure. The treatment, autopsy findings, and arsenic concentrations in tissues and body fluids are described and discussed.

Key words: arsenic, fatality, tissue concentrations, toxicity, treatment.

At the Swedish copper smelter where this accident occurred, large quantities of crude arsenic, containing more than 90 % arsenic trioxide, are stored in silos. Because the product is partly handled manually, the workers are instructed and trained in proper preventive measures, including the use of protective clothing and breathing masks during dust exposure. Very few accidents have occurred, and the one reported is the only one with a fatal outcome since the start of the smelter in 1930.

This fatality was caused by an unexpected fall of arsenic trioxide, which completely buried a worker. His filter mask was clogged. In order to get air, he removed the mask in panic and inhaled arsenic dust in large quantities for 5–10 min before he was released.

Case history

In a 25-m high arsenic silo, crusted arsenic trioxide was unloaded from below by the use of explosives. During the operation a fragile vault was formed part way up in the silo. At about 1320 on 17 March 1987, a worker was standing just outside the open door when the vault suddenly collapsed and completely buried him. A nearby worker saw the accident and managed to find him and to free his head within 1–2 min. However, the protective mask was clogged, and the half-suffocated worker tore it off, the result being a

massive inhalation of arsenic dust. He also swallowed substantial amounts of the dust in the early phase of the rescue operation. Five to ten minutes later the worker was fully released and immediately taken to the occupational health service center. He was conscious and managed to walk from the car into the facility. After a quick examination he was immediately taken by ambulance to the local hospital. Upon arrival at about 1400 he was vomiting, coughing heavily, and suffering from dyspnea. The physical examination revealed tachycardia and dullness to percussion over the lower two-thirds of the left lung and the basal part of the right lung.

The Swedish Poison Information Centre in Stockholm was contacted. In accordance with their instructions, gastric lavage was immediately undertaken, followed by the administration of a suspension of activated charcoal. An intravenous injection of 8 mg of betamethasone was given to prevent airway obstruction.

At 1640 he received an intramuscular injection of 50 mg of promethazine, and an intravenous infusion of 200 mg of doxycycline was started. Thirty minutes later he was given an intramuscular injection of 300 mg of British Anti-Lewisite[®] (BAL), ie, 2,3-dimercapto-1-propanol, a heavy-metal chelator.

At 1800 arterial blood showed metabolic acidosis (pH 7.20, base deficit 15.5 mmol/l, standard bicarbonate 11.5 mmol/l, carbon dioxide pressure 4.09 kPa, and oxygen gas pressure 10.75 kPa). The acidosis was treated with sodium bicarbonate (total buffer capacity 200 mmol). The patient was restless and irritated and his condition gradually deteriorated. As the systolic blood pressure fell from 70 to 45 mmHg (9.3 to 6.0 kPa) an intravenous infusion of dopamine was started and oxygen therapy (4 l/min) was initiated.

At 1900 arterial blood showed no signs of improvement (pH 7.19, base deficit 16.4 mmol/l, standard bicarbonate 10.8 mmol/l, carbon dioxide pressure 3.91 kPa, and oxygen gas pressure 8.99 kPa). Shortly after

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1900 ventricular fibrillation occurred. Endotracheal intubation and ventilation combined with external cardiac massage was immediately started followed by two direct current shocks of 400 J. A few minutes later, the electrocardiogram showed widened QRS complexes and bradycardia. The patient was then given intravenous injections of atropine (0.5 mg twice), epinephrine (1 mg), calcium chloride (1 g), and an intravenous infusion of isoprenaline (isoproterenol) was started. No improvement was recorded; instead the cyanosis became more pronounced. Intracardial injections of calcium chloride (1 g, twice) and epinephrine (1 mg, three times) were administered, but no response was seen, and the patient died at 1920.

Autopsy findings

The worker suffered from severe adipositas (thickness of abdominal wall fat 6.5 cm), and his total body weight was 100 kg. External examination revealed no injuries. In the internal examination, moderate edema was seen in the mucosa of the piriform recess on both sides, while the epiglottis was normal. The trachea and the main bronchi showed widespread mucosal and submucosal hemorrhages. Microscopically, the mucosa was sloughed over large areas, exposing recent, intense hemorrhages of deeper layers. The lungs were very heavy (total weight 1 437 g) with decreased elasticity and showed widespread intraalveolar hemorrhages with massive edema. Generally there was intense visceral congestion, including microscopically identified interstitial hemorrhages also in the thyroid gland. The mucosa of the esophagus had a velvety appearance macroscopically, and the stomach contained 400 ml of black charcoal slurry. There was a small subserosal hemorrhage of the stomach, which extended into the muscular and submucosal layers. No etching of the mucosa in the esophagus, the stomach, or the intestine was seen. The liver showed moderate, patchy steatosis. Massive subendocardial hemorrhages were seen in the left ventricle of the heart, and these hemorrhages were microscopically seen to extend into the subendocardial myocardium. Furthermore, the myocardium showed widespread foci of necrosis, but leucocyte diapedesis was not present. Insignificant findings were small cavernous angiomas of the pons and of the right parietal lobe cortex. Other parts of the central and peripheral nerves were histologically normal.

Tissue concentrations

The body fluid levels of total arsenic upon the worker's arrival at the hospital are shown in table 1, and the tissue concentrations in autopsy specimens in table 2. The analyses were made by flame and flameless atomic absorption spectrophotometry at the research laboratory at the smelter. Since the middle of the 1970s the smelter laboratory has participated in a national quality control program, with particular reference

to water samples originating from and administered by the Swedish National Environmental Protection Board. Furthermore, since the 1970s an exchange of urine arsenic samples has taken place with other Swedish laboratories. The research laboratory has consistently produced reliable analyses.

Discussion

The acute toxicity of an inorganic arsenic compound depends largely on its solubility, and on whether the compound is ingested in a dissolved or undissolved form (15). Animal data indicate that trivalent arsenic is more toxic than the pentavalent form (5). The fatal dose of ingested arsenic trioxide for humans varies from 70 to 180 mg (13).

In this case, the worker inhaled dust with a very high concentration of arsenic trioxide. In addition, he swallowed a considerable amount of arsenic trioxide during the rescue operation.

Very few data are available on the acute deposition and absorption of inhaled arsenic in man. However, both human and animal data indicate that more than 90 % of an ingested dose of dissolved arsenic trioxide is absorbed in the gastrointestinal tract (10, 12). Due to the short time interval (about 6 h) between exposure and death, only a fraction of the inhaled and ingested amount of arsenic trioxide may have been metabolized and excreted in the urine. For most arsenic compounds the kidneys are the main route of excretion.

The values of total arsenic in the body fluids of the worker (table 1) were 100–1 000 times higher than those in the urine and blood of people without occupational exposure to arsenic (3, 4, 7, 11). The concentration of 3.4 mg/l in blood was, however, of the same magnitude as blood values found in fatal human arsenic poisonings from suicide and homicide cases and

Table 1. Concentrations of total arsenic in body fluids shortly after admittance to the hospital.

Fluid	Concentration (mg/l)
Urine	1.9 ^a
Blood	3.4
Gastric fluid	550.0

^a Inorganic arsenic + methylated metabolites (monomethylarsonic acid and dimethylarsinic acid) = 1.55 mg/l.

Table 2. Tissue concentrations of total arsenic at autopsy.

Tissue	Concentration (µg/g wet weight)
Brain (frontal cortex)	0.3
Myocardium (left ventricle)	1.2
Kidney (cortex)	1.4
Lung (peripheral)	2.9
Liver	3.8
Blood	2.3 ^a

^a Neutron activation analysis performed at the Swedish Environmental Research Institute (IVL), Stockholm.

from children who accidentally ingest arsenic compounds (1). Consumption of seafood rich in organic arsenic may temporarily increase the urinary concentration of total arsenic to more than 1 mg/l (9).

As shown in table 2, the autopsy tissue concentrations of total arsenic were highest in the liver, followed by the lung and kidney. These values were 10–100 times higher than arsenic concentrations reported for autopsy samples of healthy people from Scotland (8) who had no known occupational exposure to arsenic and who died as a result of trauma. Moreover, the values were about 100 times higher than the concentrations found in autopsy samples of lung, liver, and kidney from active and retired workers who came from the same smeltery and who died from malignancies or cardiovascular and cerebrovascular diseases (6, 14). However, the brain, kidney, and liver values in table 2 are 10–100 times lower than concentrations reported from a compilation of 19 cases of fatal arsenic poisonings of persons who probably did not receive hospital treatment (1).

Arsenic reacts with SH groups in tissue proteins and thus interferes with a number of enzyme systems essential to cellular metabolism. The inhalation of arsenic trioxide may cause symptoms such as cough, dyspnea, and chest pain, often accompanied by irritation of exposed skin or mucous membranes, eg, nasal mucosal irritation, bronchitis, and conjunctivitis. Symptoms from the gastrointestinal tract are usually not manifest in these cases.

The classic symptoms after acute arsenic poisoning from oral intake are oral and epigastric burning, followed by nausea, vomiting, tenesmus, tympanites, and profuse "rice water" diarrhea. Death, often preceded by tachycardia, hypotension, muscular twitchings, convulsions, and circulatory collapse, may ensue within 1–2 d (1, 15). Occasionally, ingestion of a large, rapidly absorbed dose of an arsenic compound may cause a prompt, profound circulatory collapse, stupor, and convulsions. Vomiting and diarrhea may be inconspicuous or absent, and death can supervene within a few hours (1). In the present case, the worker showed a mixture of symptoms from both respiratory and gastrointestinal intake. The initial symptoms (cough, dyspnea, bronchitis, and conjunctivitis) were due to the inhalation of and airborne exposure to arsenic trioxide. Gradually, however, gastrointestinal symptoms such as epigastric burning, nausea, and vomiting increased, and 1 to 2 h after the exposure they dominated the clinical picture. These symptoms were followed by tachycardia, hypotension, and circulatory collapse, and death ensued about 6 h after the accident because of the very high exposure dose.

Anatomic changes from fatal inorganic arsenic poisoning by oral intake are hemorrhages and ulcers of the gastrointestinal tract, hepatocellular necrosis, renal tubular necrosis, pulmonary edema and emphysema, and subendocardial hemorrhages with interstitial myocarditis (1). The shorter the survival interval, the

less prominent the anatomic changes. In hyperacute poisonings anatomic changes will be essentially negative or restricted to gastric mucosal hyperemia (1). In the present case, the pathoanatomic findings agreed well with the survival interval.

Treatment

The treatment recommended by the Swedish Poison Information Centre for the acute ingestion and inhalation of arsenic is gastric lavage followed by the administration of milk and/or a suspension of activated charcoal. Antacids may also be provided. Replacement of fluid losses, correction of metabolic acidosis, and elevation of blood pressure by vasopressor agents is often necessary.

Immediate treatment with intramuscular injections of BAL (2.5–5 mg/kg of body weight) every 4 h during the first 24 h is recommended. Dithiols, like BAL, compete with enzyme sulfhydryl groups in the reactions with arsenic-containing compounds. Experimentally, other antidotes such as meso-dimercaptosuccinic acid (DMSA), 2,3-dimercapto-1-propanesulfonic acid, Na salt (DMPS), and N-(2,3-dimercaptopropyl)-phthalamidic acid (DMPA) have had effects similar to those of BAL (2). However, their use has not yet reached clinical practice.

In the present case, it was not possible to prevent the circulatory collapse due to the massive exposure. To prevent accidents of this type in the future, the arsenic handling routines have been reconsidered, and the preventive measures have been reinforced at the smeltery. Remote control is now used for the unloading operations. When explosives must be used, the application should be made from the top level of the silos. In addition the inspection areas have been further restricted. It might also be an advantage if BAL could be administered already at the occupational health service center.

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