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CASE REPORT

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Acute Selenium Poisoning: Suicide by Ingestion*

ABSTRACT: Selenium is a ubiquitous element in the environment essential to the human diet and widely utilized in industrial processes. Fatal human selenium intoxication is rare. The authors report a case in which investigators recovered a bottle of gun-bluing agent beside a 24-year-old man. He exhibited signs and symptoms typical of acute selenium intoxication presenting with nausea and vomiting, followed by pulmonary edema and rapid cardiovascular collapse approximately 3 to 4 h after ingestion. Classic electrocardiographic (EKG) changes, which have been reported to occur in acute selenium intoxication, included sinus tachycardia with ST wave alteration. Toxicological results confirmed elevated blood and tissue concentrations. The cause of death was ascribed to acute selenium intoxication, which ensued rapidly after oral consumption. The manner of death was suicide. This case report, which presents an overview of acute and chronic selenium poisoning, underscores the value of thorough toxicologic analyses of tissue and body fluids in humans.

KEYWORDS: forensic sciences, selenium, intoxication, poisoning, toxicology

Selenium (Se) is a gray metalloid of the sulfur group (including oxygen, sulfur, selenium, tellurium, and polonium) that is widely used in commercial applications, thus constituting a common source of human exposure (1–6). Industrial usage includes solar energy, semi-conductor processing, and the manufacturing of electronics and ceramics (1,2). It is present in steel and copper alloying, metal pigmentation in photographic cells, glass and paint manufacturing, rubber vulcanization, nutritional supplements and Selsun™ shampoo. Additionally, it is among various compounds utilized for polishing and bluing the exterior metallic surface of handguns (1,2).

Selenium salt is widely distributed in soil, grains and forages (2). It is an essential dietary trace element. The adult recommended daily allowance (RDA) by the Federal Drug Administration (FDA) for human consumption is 50–200 μg. Normal serum concentrations fall in the reference range of 46–143 μg/L (3). A nutritional supplement, selenium is commercially available as a nonprescription medication in tablet form or as a multivitamin with mineral supplementation (2). Inadequate intake causes selenium deficiency syndrome marked by muscle weakness and pain (2,3,5). At normal levels, selenium functions as an antioxidant by contributing to free radical sequestration at the cellular level and enhances the effect of Vitamin E (3). Selenium is preferentially taken in by erythrocytes and is an essential cofactor for the enzymes erythrocyte glutathione and type 1 iodothyronine deiodinase (2,3).

Ingested selenium is well absorbed from the gastrointestinal tract and widely distributed in the body. Relatively higher organ and tissue concentrations are stored in the gastric mucosa, heart, liver, kidney, lungs, pancreas, spleen and testes (3,4). Selenium clearance in humans appears to follow a two-compartment model characterized by an initial distribution phase of 6 hours and a final elimination half-life phase of 17.5 h (7). This two-compartment model is supported by the clinical presentation of selenium overdose: an initial gastrointestinal phase during absorption, followed by approximately 3-to-4 hours post-ingestion, multi-organ failure after the selenium had distributed from the central blood compartment to the tissues.

Distinctive physical forms of selenium produce graded levels of intoxication. Less severe degrees of toxicity result from exposure to hydrogen selenide, organic selenium compounds in grain, inorganic selenium in the form of sodium selenites, sodium selenates, selenomethionine and metallic selenium (2–4,8). Intake of selenium in the selenide form of selenious acid (monohydrated selenium dioxide, H_2O_3 Se) has a nearly universally fatal outcome. Ingestion of other forms of selenium, i.e., selenium dioxide (O_2Se), may cause various levels of multiorgan dysfunction. Cardiovascular morbidity, such as cardiac arrhythmias, toxic cardiomyopathy, and hypotension associated with decreased peripheral vascular resistance, occurs with both fatal and non-fatal selenious acid ingestion (4). The biochemical mechanism of toxicity for selenium and related compounds is not fully understood. However, there exists experimental support for several potential mechanisms of toxicity (4), including:

1. Substitution for sulfur in sulfhydryl-containing enzymes necessary for oxidative reactions in cellular respiration via effects on the mitochondrial and microsomal electron transport.
2. Substitution for sulfur in other essential enzymes and proteins.
3. Mediation of oxidative stress mechanisms.
4. Interfering with the normal redox-regulating activities of glutathione peroxidase.
5. Mediation of apoptotic and free radical formation.
6. Disruption of normal thyroid hormone functions via the deiodinase enzymes.

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The following case is presented to highlight the typical symptoms and signs of acute selenious acid intoxication, report pertinent autopsy and toxicological findings, and distinguish features of acute from chronic selenium intoxication.

Case History

A 24-year-old man, with a history of depression and alcohol abuse, was observed by his mother to be actively vomiting. She reported a strong garlic-like odor in the room. A 2-ounce bottle of *G-96 Instant Gun Blue* was next to him on a table. The subject had been despondent for several weeks and, on the morning of his death, stated that he was going to kill himself. His mother reported a paternal family history of clinical depression.

Called to the home, the emergency medical response team observed the victim hallucinating. Upon arrival in the emergency department (ED), he was alert, combative, and hallucinatory. Pertinent vital signs were as follows: heart rate (HR) 114/min, blood pressure (BP in mm Hg) 113/67, respiratory rate 26/min, and an oxygen saturation (O_2 sat.) of 96%. Over the next three hours, the decedent's condition remained unchanged with persistent tachycardia and hypotension. Abnormal laboratory values included an elevated peripheral white blood count $21.2 \times 10^3/\mu L$, hemoglobin 19.3 g/dL, hematocrit 57.7%, prothrombin time 34.7 sec, international normalized ratio (INR) 7.6, and serum potassium 3.1 mmol/L. All other laboratory studies including a routine toxicology screen were noncontributory. EKG performed approximately one hour after the ingestion showed sinus tachycardia with non-specific ST wave changes and a QTc of 498 msec. Three hours thereafter, the patient's condition rapidly deteriorated. He suddenly became cyanotic, lost consciousness, and experienced cardiopulmonary arrest. EKG monitor showed ventricular fibrillation that degenerated into asystole. Advanced cardiopulmonary resuscitation, which included application of a transcutaneous pacemaker followed by an intravenously inserted pacemaker, was unsuccessful. In consultation with the Regional Poison Control Center, the clinicians attributed the death to complete electromechanical cardiac failure presumptively associated with acute selenium toxicity due to ingestion of the gun-bluing agent.

Autopsy Findings

At autopsy, the decedent's oral mucosa and lips appeared mildly cyanotic. A strong metallic garlic odor emanated from the opened body cavity. Internal examination was notable for diffuse mucosal hyperemia and focal hemorrhage of the gastric cardia and fundus (Fig. 1). Faint slate blue tinting of the gastric mucosa was evident. Thin variegated dark brown and light blue tinged liquid gastric contents were collected. The lungs were edematous. Investigators submitted a bottle of *G96 Instant Liquid Gun Blue* (59.1cc)

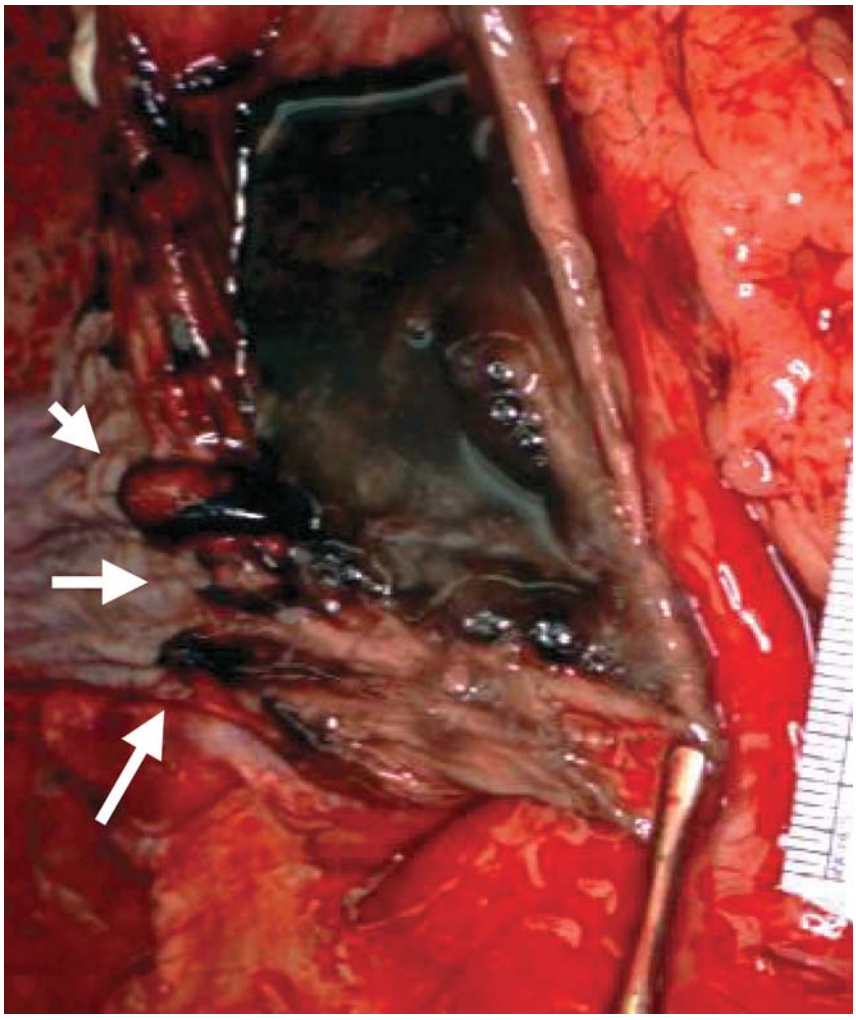

FIG. 1—*Autopsy photograph of the esophageal gastric junction. Arrows show focal mucosal hemorrhage.*

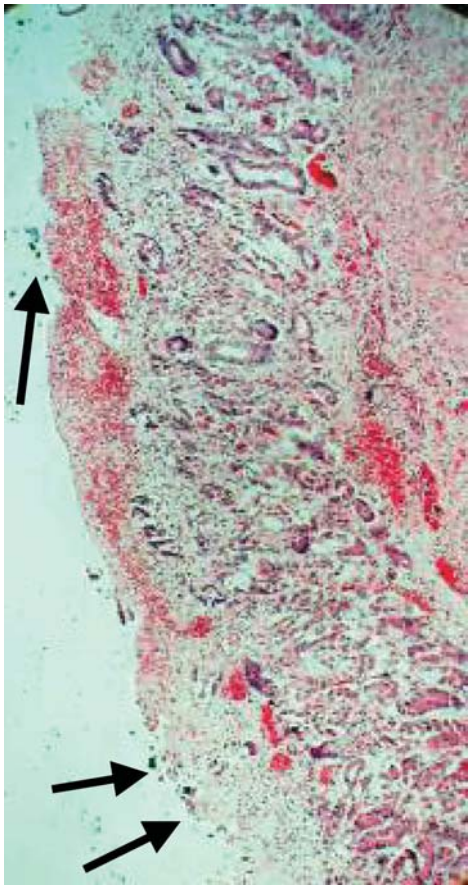

FIG. 2—*Microscopic examination of the stomach with mucosal hemorrhage. Arrows depict black particulate matter.*

containing a residual 5 ml of transparent light blue liquid. Microscopical sections of the stomach revealed diffuse hemorrhage with adherent blue-black acellular material intermixed with acute inflammation (Fig. 2).

Toxicological Analysis

The serum selenium concentration, measured from blood drawn in the ED approximately one hour after ingestion, was reported several days later at 30,000 μg/L. The postmortem peripheral whole blood selenium concentration was 13,000 μg/L. In addition, selenium tissue concentrations from brain, kidney and liver were markedly elevated at 1.74 μg/g, 7.83 μg/g, and 10.02 μg/g, respectively. Vitreous humor and bile selenium concentrations were 31 μg/L and 15,000 μg/L, respectively. Selenium concentrations in the antemortem blood and the postmortem fluid and tissue specimens were determined by graphite furnace atomic absorption spectrophotometry. Toxicological examination for alcohols and drugs of abuse was negative. The cause of death was attributed to acute selenium intoxication from intentional gun-blue ingestion. The manner of death was suicide

Discussion

The present case exemplifies the characteristic cardiotoxicity of acute selenium poisoning. To our knowledge, three features from the case have not been previously reported: 1) antemortem and postmortem determination and comparison of selenium concentrations in various intravascular and tissue matrices 2) vitreous fluid selenium concentrations, and 3) bile selenium concentrations. Blood and tissue concentrations of selenium in this case are compared to previous studies.

The significant decrease in the blood selenium concentration, ranging from antemortem levels of 30,000 μg/L (serum) to postmortem concentrations of 13,000 μg/L (whole blood), probably represents the early distribution phase from the central compartment into the tissues and not true clearance from the body. In therapeutic conditions, serum selenium concentrations are approximately 70% of whole blood concentrations due to the uptake of selenium into erythrocytes (9). However, this difference decreases significantly as the serum concentration increases (10). In an acute, massive overdose represented by the present case, the disparity in serum and whole blood concentration is likely to be small. The 57% decrease between the antemortem serum concentration and postmortem whole blood concentration is not attributable solely to the different matrices, but rather to the early distribution phase.

Toxic doses of selenium occur at the highest tissue concentrations in the liver, kidneys and heart, as demonstrated by the present case and the pharmacokinetic studies by Pentel et al., Quandrani et al., Matoba et al. and Schellman et al. cited in Table 1 (4,8,11,12,13). Postmortem tissue selenium concentrations in the present case correspond to those reported in these previous studies. Vitreous fluid concentrations of selenium have not been documented to date. Normal selenium values for this matrix are unavailable for comparison. The vitreous concentration in this case does not appear elevated in comparison to that of blood or bile. Therefore, we postulate that vitreous fluid may be a poor specimen for investigating potential acute selenium-related deaths. In contrast to the vitreous fluid, bile concentrations were markedly elevated in this case and close to the postmortem whole blood concentrations (Table 1). There are no reported normal values for comparison. Thus, this case demonstrates that the bile selenium concentrations may be a potentially useful body fluid marker of recent acute selenium overdose by ingestion when liquid blood specimens are not readily available or are contaminated.

Clinical suspicion of selenium intoxication rests initially on recognition of a constellation of signs and symptoms. Acute, typically fatal selenious acid intoxication by either intentional or accidental ingestion in humans is infrequent and requires appropriate toxicological analysis (2,8,11). Most reported cases of acute selenium poisoning involve industrial accidents via inhalation of selenium dust or fumes causing respiratory irritation (2,8). Civil et al. described characteristic signs of acute poisoning 15 min after ingestion of toxic levels of selenium: garlic breath malodor, gastrointestinal disturbance, agitation, muscular spasms often leading to convulsions, and ultimate cardiorespiratory failure (1). The malodor of the breath, attributed to methylated selenium, i.e., dimethyl selenide, reflects high blood concentrations of selenium (14).

Autopsy findings of acute intoxication commonly consist of gastric mucosal congestion, pulmonary and cerebral edema, and hepatic congestion with hepatocyte cytoplasmic glycogenosis (1,4,7,11,14). In this report, the mother of the victim immediately noted a foul garlic odor permeating from the room where she found her nauseated son. She also found the bottle of gun-bluing agent beside him. The autopsy with toxicological analyses confirmed the clinical diagnosis of acute selenium intoxication.

Because poisoning in this case resulted from ingestion of a commercially available gun-bluing agent, brief discussion of its unique toxicological significance is necessary. Gun-bluing lubricating agents generally contain selenious acid, which is a potent

TABLE 1—*Postmortem selenium fluid and tissue concentrations in fatal cases compared with reported normal concentrations.*

Sample	Present Case	Quadrani (4)	Matoba (11)	Schellmann (12)	Pentel (8)	Normal Values‡ (13)
Blood*	30,000 (Antemortem serum)	12,000	2600	18,400	2435	66 to 104 serum 80 to 130 whole blood
	13,000 (Postmortem whole blood)					
Gastric contents*	52,000	270,000	18,000			
Bile*	15,000					
Vitreous fluid*	31					
Kidney†	7.8			1.53		0.89
Liver†	10		5.4	1.61	0.79	0.35 to 0.65
Brain†	1.7		1.2	0.47		0.11 to 0.17
Heart†	11				3.36	0.33
Spleen†	Not done		3.5			0.37
Lung†	Not done		12.7	5.78		0.30
Skeletal muscle†	1.7					0.4
Hair†	Not done					0.64

* μg/L.
† μg/g wet weight.
‡ Concentrations without a range are means and not absolute values.

cardiotoxic substance (1,15). As demonstrated by this case, cardiac toxicity occurs rapidly after ingestion of small quantities of selenium. T-wave EKG abnormalities are ascribed to diffuse myocardial damage. EKG changes, such as prolonged QT interval, premature ventricular contractions with ST wave alterations associated with hypotensive shock, and rapidly ensuing pulseless ventricular fibrillation, constitute the hallmark clinical cardiovascular pathophysiologic features of acute selenium intoxication. One co-author previously reported a lethal case of accidental selenium intoxication from ingestion of a gun-bluing agent by a toddler (4). The child initially became hypotensive and subsequently developed ventricular fibrillation in the ED. Pentel et al. reported a similar case of acute selenium intoxication in a woman who ingested selenious acid from a gun-bluing agent and survived for 8 days (8). She exhibited severe hypotension ascribable to the direct cardiotoxicity of the ingested selenium. The decedent had also ingested typewriter cleaner (perchloroethylene) and three household oil-based preparations with petroleum distillates. Cardiac tissue selenium concentration was 40 times above normal eight days after consumption of the selenium. This case supports the conclusion that elevated myocardial selenium concentrations correspond to clinically recognized cardiac arrhythmias. Cardiac tissue concentrations of selenium in the present case were extremely high and well above concentrations in other tissues.

In comparison to acute poisoning, selenosis resulting from chronic selenium intoxication usually results either from consumption of organic selenium compounds in edible seleniferous plants and/or livestock, nutritional supplements, or by occupational exposure to industrial inorganic selenium (2,3). Classic signs and symptoms of selenosis consist of nonspecific gastrointestinal disturbances such as a metallic taste and a garlic-like breath odor, alopecia, nail changes, dermatitis and tooth decay. More severe complications include musculoskeletal dysfunction, neuropathy, liver failure, coma and death (2,3,15,16).

The Centers for Disease Control reported a case of chronic selenium intoxication from oral consumption of a higher than recommended daily dosage of an over-the-counter vitamin containing organic selenium (2,14,16). The drug company recalled these particular vitamins due to their super-potency. The victim had consumed 77 of 90 tablets when she learned of the recall. Her serum concentration was 528 ng/mL (4 times greater than normal). Although she did not die, she suffered from increasing fatigue, alopecia, fingernail changes, and gastrointestinal symptoms. The blood level of selenium may have been higher if she had not simultaneously consumed a Vitamin C supplement, which reduced the selenite to the poorly absorbed elemental selenium (1,16). Analysis of the multivitamin tablets yielded selenium concentrations 182 times higher than indicated by the label.

Evaluation of chronic toxicity in humans is fraught with confounders in seleniferous geographic areas, such as in parts of Utah, Arizona, Wisconsin and northern Italy (17,18). The "normal" reference range in human blood and urine is probably dependent on differential selenium levels in various geographic environments. Those living in areas with relatively selenium-deficient ground water may exhibit blood levels near zero. Others inhabiting seleniferous areas with high concentrations of the mineral have correspondingly higher selenium blood concentrations. In the early 1960's an endemic of fatal chronic selenosis occurred in the Hubei Province, China where high concentrations of selenium were detected in the soil and coal beds (3). Widespread selenium poisoning, in which victims exhibited the classic symptoms of chronic intoxication, caused nearly 50% mortality. The US Environmental Protection Agency (EPA) determined that 0.05 parts per million selenium concentration is the maximum contaminant level (MCL) in safe drinking water as the standard to protect animals and humans in higher seleniferous geographic regions (18). Likewise, urine concentrations may range from undetectable in persons in low selenium environments, to 22–203 μg/L in persons living in high selenium ground water environments (2,12,19). Asymptomatic industrial workers exposed to aerosolized selenium may have urine selenium concentrations between 120 and 350 μg/L. The current occupational exposure limit for selenium is 0.2 mg/m^3. Long-term physiological accommodation to mild chronically elevated blood selenium concentrations may occur in these geographically or occupationally selected groups without overt side effects (19,20).

Finally, appropriate specimen collection and analysis rests on whether acute or chronic selenium intoxication is the postulated diagnosis. Routine heavy metal screens of whole blood or urine generally do not detect selenium (2,3). Serum or plasma specimens are recommended for detection of acute selenium intoxication (3). Graphite furnace atomic absorption with Zeeman background

correction and neutron activation are methods of choice for quantitation of serum or plasma selenium. Inductively coupled plasma-mass spectroscopy (ICP/MS) is another current analytical technique. In chronic selenium intoxication, whole blood is the preferred matrix because selenium is primarily stored in the α and β globulins of erythrocytes and remains elevated longer in whole blood than in the serum (2,3,6,9). In cases of chronic or past exposure to selenium, nail and hair collection may be potentially useful. (2). Hair analysis may be limited as a testing medium, however, because of possible exposure to selenium sulfide in antidandruff shampoos.

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