CASE REPORT

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Acute Arsenic Intoxication: Forensic and Toxicologic Aspects (An Observation)

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ABSTRACT: The authors report on an acute suicidal arsenic intoxication (di-arsenic-trioxide). Death can occur one week after ingestion, despite intensive care. The forensic, anatomo-pathological and toxicologic aspects are reported. Forty titrations are realized at the level of the biologic fluid in viscera, by absorption spectrophotometry. These data are compared with those in standing literature, especially with the rates determined in normal subjects, following simple environmental impregnation.

KEYWORDS: toxicology, arsenic, intoxication, suicide, autopsy

Clinical manifestations of arsenic overdose are polymorphous, in particular, digestive [*3,11*], cardiovascular [*16*], neurologic [*12*], cutaneous [*21*], and renal [*12*]. Here, we are reporting on the forensic and toxicologic aspects seen in the course of clinical observation.

Clinical Observation

A 25-year-old man weighing 65 kg ingested 8 g of di-arsenic-trioxide with suicidal intentions. Three hours later, the onset of digestive distress with abdominal pain and vomiting occurred. Gastric lavage was performed and BAL therapy. Gastric lavage was repeated a few hours later. The following day, a gastrotomy was performed. The arsenic dose recovered via the lavages and gastrotomy is unknown. The man died eight days later, with a clinical picture of hepatonephritis and encephalopathy.

Forensic Aspects

The external examination of the cadaver revealed a mild jaundice, an edema of the penis and testicles, multiple petechiae. Cadaveric lividities were abundant—bright red, constellated with purple stains, with the onset of desquamations.

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A significant dermoepidermic separation was evident on the right and the left flanks. Evisceration showed moderately abundant, slightly pink bilateral pleural effusion. The heart weighed 420 g and the wall of the left ventricle was slightly hypertrophic; the lungs were the site of a significant hemorrhagic edema, clearly predominant in the base sections. The right lung weighs 1100 g and the left lung 1000 g. Hepatomegaly was also seen (liver) ascitis, a major ulcero-necrotico-hemorrhagic gastritis, in contrast to a fairly normal esophagus. The kidneys were congestive; the spleen weighed 300 g; the brain is simply congestive and the other viscera do not reveal any notable lesions.

Anatomo-Pathological Aspects

The esophagus was simply congestive, especially at subnucleus level. The stomach revealed pan-parietal necrosis. Diffused hepatic steatosis was determined; the centrolobular veins were moderately dilated, the pericentral lobular hepatocytal ridges are atrophic and the sinusoids were dilated. There is no portal lesion. The lung is in the site of a diffused edematous alveolitis. The spenic parenchyma is congested.

The kidneys revealed a simple glomerular form of congestion. The myocardium only carried discrete congestive lesions, which predominate in the subepicardial region. The skin revealed either a simple congestive condition, with hematic raptus of the superficial skin vessels, or a dermoepidermic separation with respect to the outstanding parts of the dermal papilla. The other viscera do not reveal any notable lesion.

Toxicological Aspects

The titrations are realized by atomic absorption. The method of atomization in pyrolytic coated graphite tube furnace (Spectro AA 30 with furnace GTA 96 from Varian) was used for measurements under following conditions: 1% nitric acid matrix, palladium as chemical modifier with ascorbic acid as antioxydant. Furnace operating parameters were 18 μL fixed volume injected, dry stage of 60 s from 90°C to 120°C under 3 L/mn argon gas flow followed by an ash stage of 90 s to 800°C, a gas stop step of 2 s then a ramp test to 2400°C in 1.2 s and an atomized hold step at 2400°C for 1.2 s again. Read command and no gas flow during these two last steps. All of this was concluded with a cleaning step at 2500°C and maximum gas flow. Instrument parameters: 193.7 nm wavelength, 0.5 nm spectral bandwidth and 10 mA lamp current.

Correction for background absorption is accomplished by measuring the total absorption and substracting from it the background absorption in using simultaneously a deuterium lamp. Then, calculation was available with the standard additions calibration method, peak area mode, two replicates, reslope rate at five.

In the course of intensive care, the concentrations determined are the following (Table 1), (fatal outcome at J8). Table 2 indicates the results at the level of nails and hair, broken down into three parts (proximal third, medium third, distal third). The other concentrations are summarized in Tables 3 (biological fluids), 4 (viscera) and 5 (brain).

Discussion

Arsenic is the twentieth most abundant element in the earth's crust [*2*] and is present in all living organisms. It exists in natural source (fires) but mainly in artificial sources. Arsenic is used extensively in agriculture in the form of a diplombic and tricalcic arseniates, destroying parasites and pests. In industry, arsenic is seen in the course of the extraction, manipulations, and processing of minerals, also the industry of coloring agents for glass. Finally, in the therapeutic field, several chronic intoxication observations have been reported [*10,20*]. Inorganic arsenics have a toxicity rating reported to be 100 times

TABLE 1—*Toxicological results during the course of the eight day intensive care phase.*

Day	Serum Concentration (mg/L)	Concentration in Urine (mg/24 h)
DO[a]	0,15	
D1	N/A[b]	N/A
D2	N/A	50
D3	0,10	45
D4	0,10	36
D5	0,15	40
D6	0,20	40
D7	0,15	42
D8	0,20	30

[a]N/A = Not available.
[b]DO = Time of admission.

TABLE 2—*Arsenic concentrations in the hair and nails following suicidal ingestion.*

Specimen	Arsenic Concentration (mg/100 g)
Nails	⅓ Proximal = 2.75 ⅓ Median = 2.2 ⅓ Distal = 1.6
Hair	⅓ Proximal = 2.4 ⅓ Median = 1.1 ⅓ Distal = 1.1

TABLE 3—*Arsenic concentrations in biological fluids in a fatal case.*

Specimen	Arsenic Concentration
Colon	1.4 mg/100 g
Vitreous humour	0.050 mg/L
Ascite fluid	1.8 mg/L
Duodenal fluid	250 mg/L
Gastric fluid	1000 mg/L
Pericardial fluid	0.050 mg/L
Pleural fluid	0.050 mg/L
Vesicular fluid	7.5 mg/L
Total blood	1.03 mg/L
Urine	0.5 mg/L

higher than in the organic forms [*19*]; these are trivalent or pentavalent. Organic arsenic compounds are aliphatical or aromatic derivates, either tri- or pentavalent. Digestive absorption varies between 30 and 50% in relation to a certain number of factors including granulometry [*13*]. Soluble derivates of mineral arsenic are particularly well absorbed. The inorganic pentavalent forms lead to a higher absorption rate than bivalent forms [*13*].

TABLE 4—*Arsenic concentrations in a fatal case.*

Specimen	Arsenic Concentration (mg/kg)
Aorta	5
Liver	35
Fat	1.85
Tongue	5.3
Muscle	6.3
Myocardium	3
Bone	1
Pancreas	5
Skin	6.7
Lung	2.75
Prostate gland	7.4
Spleen	40
Kidneys	10
Adrenal gland	17

TABLE 5—*The distribution of arsenic in the brain following suicidal ingestion.*

Specimen	Arsenic Concentration mg/kg
Medulla oblongata	2
Cerebellum	2.5
Corpus collosum	1.4
Frontal lobe	2.5
Occipital lobe	2.5
Parietal lobe	1.8
Temporal lobe	2
Marrow	1.2
Pons varolii	3
Thalamus	3

Cutaneous absorption is low except in cases of damaged skin [*22*]. Thirty percent of the arsenic is related to plasmatic proteins (over 95% of the arsenic is fixed at the level of the globine and hemoglobine) [*11*]. Arsenic accumulates mainly in nails, hair, and teeth. Also, transmission is possible through the placenta [*13*], as well as through breast feeding.

Catabolism enables the reduction of pentavalent inorganic arsenic into trivalent arsenic [*15*]. It is then methylated into an organic derivate (monomethyl-arsenic and dimethyl-arsenic or cacodylic arsenic).

Elimination is both digestive and urinary (60% at least in the urinary form) [*3*]. Organic arsenic is easier to eliminate than pentavalent inorganic arsenic, which eliminates more rapidly than trivalent inorganic arsenic.

Toxicity

The trivalent derivates are more toxic than pentavalent forms [*19*]. Soluble forms (arsenites and arsenates) are more toxic than nonsoluble forms [*19*]. At cell level, arsenic toxicity is mainly due to an inhibition of enzymatic cell reactions, through an effect on

the sulfhydryl groups in enzymes. Gradual increasing tolerance to arsenic appears to be significant.

The customary rates seen outside intoxication are shown in Table 6. The toxic doses are difficult to determine in view of toxicokinetic and individual factors (susceptibility, immunization). Usually, toxic effects are observed for values greater than 100 μg/L in the serum. At cell level, sodium arsenite can induce mutant colonies in vitro, presenting mitochondrial respiratory insufficiencies. At low doses, arsenic increases the proliferative response to mutagenes, whereas at high doses the opposite is observed [*24*]. In vivo, arsenic has the capacity to produce genetic damage in mice in the course of cultures, but cannot produce genetic lesions that can be transmitted to offspring [*7*]. Arsenic inhibits the activity of numerous enzymes, by combining with thiols, in particular those of DNA polymerase, inhibiting the in vitro incorporation of nucleides.

Pentavalent arsenic is an oxidative phosphorylation decoupler. Arsenic acts at the level of the Krebs cycle, by attaching to the lipoic acid, and inhibiting the ATPase. There also is a perturbation field of cell breathing, in terms of a microchondrial hepatic swelling, and a drop in the pyruvate/malate relation.

Finally, the arsenic reduces the activity of the delta-ALA-synthetase, and of the hemi-synthetase, and increases the rate of urinar uroporphyrin.

Discussion of Results

In our observation, we can highlight the fact that during the intensive care phase, seric concentrations are very high, ranging between 0.1 and 0.2 mg/L; the same is true for urinary concentrations, which vary between 12 and 35 mg/L. Forensic concentrations enable the investigation of the dissemination of the poison through the various fluids and viscera. Accumulation in nails and hair is highly significant, which is not surprising in view of arsenic's affinity for thiol groups. It is noticed that accumulation occurs the proximal part of nails and hair more than the distal part. Amongst biological fluids, blood, urine and vesicular fluids evidence a high rate of concentration; the same is true for the content in the digestive system (1g/L for gastric fluid) despite intensive-care therapy. On the other hand, the pleural and pericardial fluids are only lightly impregnated, as is the case for the vitreous ocular fluids. In the viscera, concentrates vary between 0.1 mg/100 g(bone), and 0.74 mg/100 g (prostate); most of the viscera are within these limits. But four sites offer a much higher concentration than the previously mentioned: the liver (3.5 mg/100 g), the kidney (1 mg/100 g), the adrenal gland (1.7 mg/100 g) and above all the spleen (4 mg/100 g). Usually hemato-encephalic transfer is at a low rate, brain concentrations are, however, not to be neglected.

It is interesting to compare arsenic levels found in our observation with selected literature. Selected cases of arsenic levels in different tissues are summarized in Table 6. Remember that these values are considered to be normal and concern cases apart from any intoxication.

Normal arsenic values in hair, axillary, and pubic hair are reported by Fazekas [*9*], (Table 7). Plaques [*18*] reported on five chronic intoxications [*18*]. The arsenic values are in Table 8. Blood toxic levels are quoted by Eckert [*8*] as ≥ 1 mg/L and lethal blood levels ≥ 10 mg/L.

We call attention to illustrative cases of acute intoxications [*19*], with arsenic levels presented in Table 9. Note that in this case, the body was exhumed 47 days after death (Table 10). Finally, cases of homicidal arsenic poisoning reported by Adelson showed following visceral concentrations (Table 11) [*1*].

Conclusion

Acute arsenic intoxication is not uncommon. Thanatology and toxicology data in our observation confirm those in standing literature. It is interesting to note that apart from

TABLE 6—*Values found in selected cases apart from any intoxication. Comparison with our observation.*

Topography	Dardenne [4]	Doris [5]	Baron, Schweinsberg [2]	Yamato [23]	Our Observation
Hair	< 0.22 mg/Kg	< 5 mg/Kg	< 0.060 mg/Kg	0.075 mg/Kg	24 mg/Kg
Liver					35 mg/Kg
Nails	< 0.30 mg/Kg	< 10 mg/Kg	0.420 mg/Kg		21 mg/Kg
Skin		< 0.5 mg/Kg			6.7 mg/Kg
Total blood	< 0.225 mg/L				1.3 mg/L
Serum	< 0.016 mg/L	< 0.010 mg/L	< 0.002 mg/L		0.200 mg/L (maximum)
Urine	< 0.100 mg/L	< 0.010 mg/L	0.074 mg/L	0.121 mg/L	0.500 mg/L (autopsy)

TABLE 7—*Normal arsenic values.*[a]

Average of Concentration (μg/100 g)	Hair	Axillary hair	Pubic hair
Men	33,08	4,77	4,55
Women	28,12	4,67	4,92

[a]Established from Fazekas and Rengei [*9*].

TABLE 8—*Arsenic concentrations in five chronic intoxications* [*18*].

Specimen	Arsenic Concentration (mg %)
Hair	1 to 3,5
Nails	0,4 to 0,5
Hand skin	0,6
Pubic hair	2,1 to 3,05

TABLE 9—*Case of arsenic poisoning* [*19*].

Wet Tissue	Arsenic (ng/g)
Brain	0.7
Stomach	19.0
Stomach contents	654.0
Intestine	41.0
Intestine contents	369.0
Liver	61.0
Spleen	4.4
Kidney	21.0
Pancreas	0.9
Heart	1.5
Adrenals	7.3
Lungs	2.4
Urine	11.0
Bile	4.3

TABLE 10—*Arsenic in other tissues.*

Material	Arsenic (ng/g)
Hair (Scalp end to 25 mm)	7.6
Hair (Remaining 65 mm)	2.9
Femur (marrow)	0.6
Femur (bone)	0.9
Thigh (muscle)	2.5
Thigh (skin)	2.1
Foot (epidermis)	4.1
Foot (dermis)	4.1
Finger nail (root end)	43.0
Finger nail (tip end)	35.0
Toe nail (root end)	48.0
Toe nail (tip end)	35.0

TABLE 11—*Visceral concentrations of arsenic in two cases of homicidal arsenic poisoning [1].*

Site	Case 1	Case 2
	mg of arsenic trioxide per 100 mg of tissue	
Liver	0,5	2,0
Kidney	0,75	1,0
Brain	0,04	0,2
Spleen	0,27	0,4
Blood	0,03	0,09
Hair		9,4
Nails		0,7
Stomach content		8,0

the hair and nails, the relationship for which arsenic is well known, the conventional biological fluids and the sera offer concentrations that are sometimes significant, facilitating forensic toxicology assays.

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