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Abstract

A case of Acute Arsine Poisoning with Hemolytic Anemia and Acute Renal Failure

Kyoungsook Jeong, Ji Ho Lee, Chang Sun Sim, Jong Soo Lee¹⁾, Hiroshi Yamauchi²⁾, Yangho Kim

*Department of Occupational and Environmental Medicine, Department of Internal medicine¹⁾,
Ulsan University Hospital, University of Ulsan College of Medicine, Ulsan, Korea
Department of Preventive Medicine, St. Marianna University School of Medicine, Kawasaki, Japan²⁾*

Background: There has been no reported case of arsine poisoning in Korea so far. This article presents the first reported case of arsine poisoning with hemolytic anemia accompanied by acute renal failure. Initially we suspected an infectious agent to be the cause of this case but later discovered that it was arsine poisoning suffered while working at a zinc-smelting industry in the process of recovering the cadmium by-product. We report this case and discuss the arsine poisoning.

Case report: A 27-year-old man employed at a zinc-smelting industry was exposed to arsine while working in the process to recover the cadmium by-product. On the 4th day at work, he had to redissolve defected by-product into a pot and began to experience febrile sensation, diarrhea, upper quadrant abdominal pain, jaundice, and anorexia. After he was admitted to a hospital, the laboratory results showed hemolytic anemia, acute renal failure and elevated concentration of arsenic. He was thus diagnosed as suffering from arsine-poisoning and underwent hemodialysis and supportive therapy. He recovered from the poisoning after 51 days and was discharged from the hospital.

Discussion: When workers dealing with arsenic-containing material present with hematuria, nausea, vomiting, abdominal pain, and dyspnea followed by hemolysis with acute renal failure, arsine poisoning must be suspected and diagnosis followed by treatment must commence immediately. If any future cases occur, blood and urine samples should be kept in storage so any necessary analysis can be processed later.

Key Words: Arsine poisoning, Hemolysis, Acute renal failure

1775 (arsine, AsH₃)
가 가 ,
가 가 , ,
(Romeo et al., 1997; WHO, 2002).

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: (Tel: 052-250-7281) E-mail: yanghokm@nuri.net

가 가
 (Hatlelid et al., 1996; Romeo et al., 1997;
 WHO, 2002).

Yoshida et al., 2004)(Fig. 1).

- 3가 (As³⁺) 가
 1- (monomethylarsonic acid: MMA) 가
 2- (dimethylarsinic acid: DMA) 2 ~ 24 가
 4 ~ 6 가
 (WHO, 2002; Loffredo et al., 2003; 24 ~ 48 가

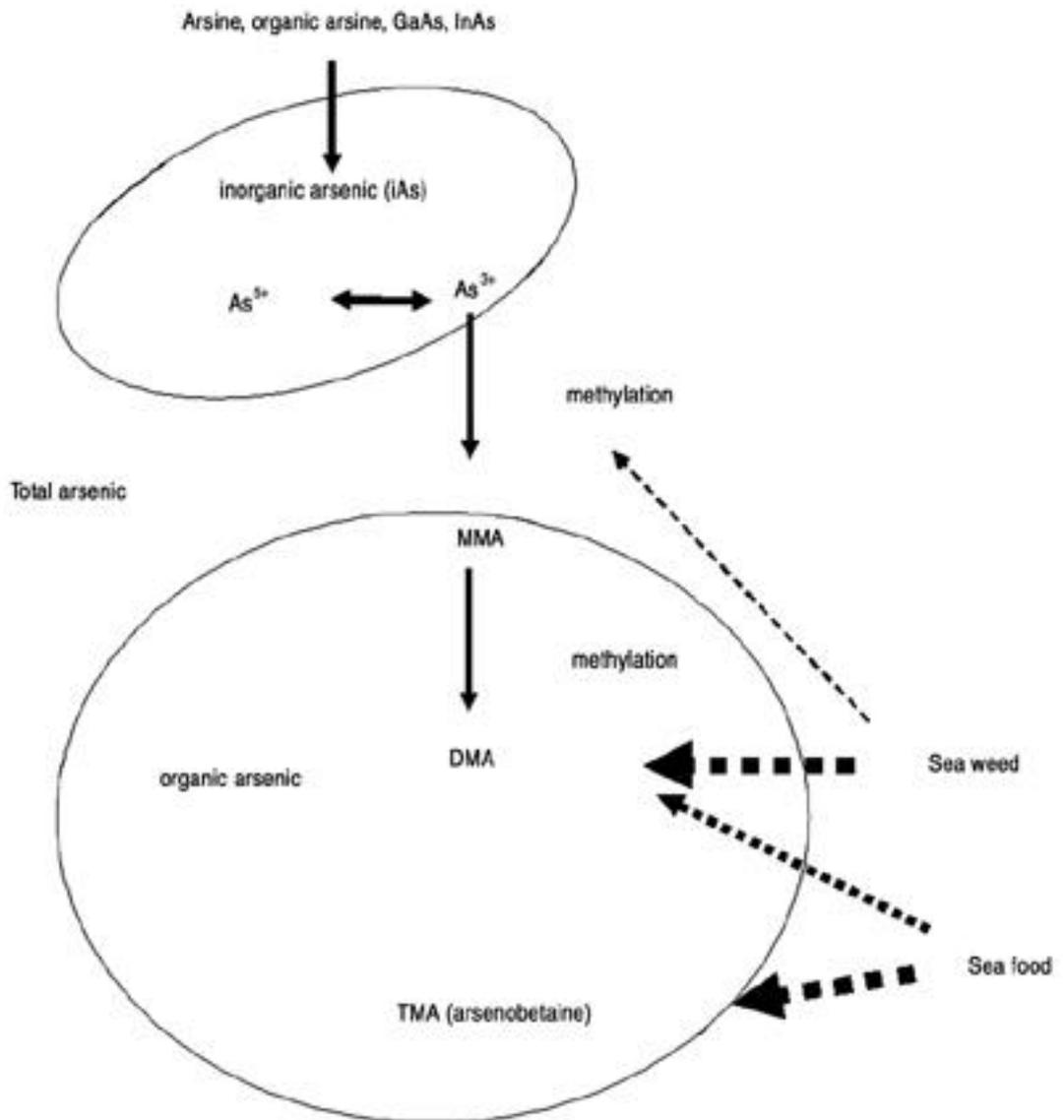


Fig. 1. Metabolic pathway of arsenic compounds (Kim et al., 2004)

Inhaled arsine, organic arsine compound, gallium arsenide, and indium arsenide are dissolved in the body fluids and oxidized to As³⁺. Part of As³⁺ is further oxidized to As⁵⁺. As⁵⁺ may undergo reduction in the body to As³⁺. As³⁺ is methylated in the body to form monomethyl arsonic acid (MMA) and dimethylarsinic acid (DMA) which are excreted in the urine. DMA in urine is also from dietary origin such as seaweed (arsenosugar) or some kind of seafood such as mussels (dimethylarsinate). Trimethyl arsonic acid (TMA) in urine is mainly from dietary origin such as seafood (arsenobetaine). Inorganic arsenic (iAs) is also from dietary origin such as seaweed named hijiki.

(Landrigan et al., 1982; Romeo et al., 1997; WHO, 2002).

1815 가
1 , ,
9
(Buchanan, 1962) 1815 1928 247
, 1928 1974 207
51 25%
(Fowler & Weissberg, 1974).

(Lee et al., 2004), (Lee et al., 2000),
(Lee et al., 1998),
(Kim et al., 1998),
(Koh, 1974; Kang et al., 1980; Ahn et al., 1984)

140/80 mmHg, 94 / ,
20 / , 36.7°C
: (hematocrit) 13.1%, (hemoglobin) 5.7 g/dl,
13.80 K/ μ , 4.1 mg/dl,
3.4 mg/dl, AST 268 IU/L, ALT 55 IU/L, BUN 173.2 mg/dl, creatinine 12.13 mg/dl

50 mg/dl(
, 5.0 mg/dl), LDH 8660 IU/L (218~472 IU/L) 가 , erythropoietin 14.02 mU/mL (9.00~26.00 mU/mL)
, 4.5 g/dl,
10.4%, (reticulocyte production index: RPI) 0.31 L (1 L)
(haptoglobin) 15 mg/dl (50~230 mg/dl)

가 , ,
(Coombs test)
, (total iron binding protein: TIBC) 가
(anisocytosis), 가 (poikilocytosis) (normocytic anemia)

, 2
ml , 2
19 ml .

가
3~5/HPF
1.79 μ g/dl (0~1 μ g/dl),
35.2 μ g/L (0~10 μ g/L)
6 0.49 μ g/dl, 2.88 μ g/L

가
가 NIOSH method 7300
ICP-MS (Elan DRC , Perkin Elmer, USA)
80 ppm,

60~70 ppm (0.002~0.0073%)
 10 µg/L (0.003~0.113 µg/dl), MMA 1.82 µg/dl (non-detection), DMA 12.5 µg/dl (0.031~0.138 µg/dl) (Table 1).
 11 5 7
 (iAs: inorganic arsenic), MMA, DMA, TMA 5 0.9
 St. Mariana mg/dl, 0.6 mg/dl AST, ALT
 Hiroshi Yamauchi 2 10
 2 ml 2
 4N-NaOH 2~4 ml 26 12 30
 , 100 °C 3 가 , 10 가
 ml (Yamauchi & 600 ml/ 가
 Yamaura, 1984). 49 51
 16.24 µg/dl (0.076~0.674 µg/dl), iAs 1.92 µg/dl (Table 2).

Table 1. Blood arsenic species analysis (unit: µg/dl)

HD	iAs	MMA	DMA	TMA	Total As
11	1.92	1.82	12.5	ND	16.24
16	1.24	0.83	4.69	ND	6.76
18	0.97	0.52	3.09	ND	4.58
22	0.88	0.52	3.06	ND	4.46
25	0.87	0.31	1.88	ND	3.06
29	0.83	0.31	1.66	ND	2.80
32	0.67	0.21	1.25	ND	2.13
43	0.38	0.14	0.58	ND	1.10
reference*	0.03 (0.02)	ND	0.071 (0.017)	0.121 (0.147)	0.221 (0.147)

HD: hospital days, iAs: inorganic arsenic, MMA: monomethylarsonic acid, DMA: dimethyl arsenic acid, TMA: trimethylarsonic acid, ND: non-detection, reference* : each value is mean (standard deviation) of 49 non-exposure workers

Table 2. Clinical course and laboratory changes

HD	Clinical course	Hb (mg/dl)	Cr (mg/dl)	AST (IU/L)	Blood total As (µg/dl)	Urine output (ml/day)
1	Febrile sense, nausea, poor oral intake	5.7	12.13	268		6
2	Hemodialysis #1, Pack RBC 1 unit transfusion	5.3	13.74	324		8
3	Hemodialysis #2, Pack RBC 2 units transfusion	7.3	13.20	242		24
5	Hemodialysis #3	6.0	13.96	54		20
7	Hemodialysis #4, Pack RBC 2 units transfusion	5.6	14.20	30		14
11	Hemodialysis #5	7.1	10.98	19	16.24	10
16	Hemodialysis #7	7.2	14.36	15	6.76	25
18	Hemodialysis #8	7.3	9.26	13	4.58	45
22	Hemodialysis #10	7.9	12.77	15	4.46	54
25	Hemodialysis #11	8.0	7.77	15	3.06	100
29	Hemodialysis stop	8.4	6.04	21	2.80	500
32		8.0	4.76	14	2.13	1800
43		8.2	2.25	19	1.10	2750
51	Discharge	8.6	1.43	18		2800

HD: hospital days, Hb: hemoglobin, Cr: serum creatinine, AST: aspartate transferase, As: arsenic

(CH3AsO3HNa)

가 31

44 가 , ,
1 14~20
(hyperkalemia) (oliguria)

. Johnson (1953) 54

가 3 . Hocken Bradshaw(1970)

(filter press)
(pressing briquettes)

(Table 3). , 가

. 3 26

12 가 ,

가 .

(Johnson, 1953).

(hematocrit) 13.1%, (hemoglobin) 5.7 g/dl,
13.80 K/ μ , 4.1 mg/dl,
3.4 mg/dl, AST 268 IU/L, ALT 55 IU/L,
BUN 173.2 mg/dl, creatinine 12.13 mg/dl ,
50 mg/dl,

. Buchanan(1962)

LDH 8660 IU/L (218~472 IU/L) 가
, erythropoietin 14.02 mU/mL (
9.00~26.00 mU/mL) , 4.5
g/dl, 10.4%, (retic
ulocyte production index: RPI) 0.31 L(1
L), (haptoglobin) 15 mg/dl
. RPI

, 9 3
, 1 10
30 2

1 0.309%
5 3 , 0.1%

RPI가 가

1 , 10

2% 가 50% , 가 (Rosenstock ,
2005).

Jenkins (1965) 8

가 가 , , 가
가 가 . 가
. Coles (1969) 가

가 4
1

6 ,

. DePalma(1969)

(LaDou, 2004)

Table 3. Review of arsine poisoning cases (continue)

Reference	Work description	Clinical course & others
Pinto et al. (1950); Spolyar & Harger (1950)	Hot dross coated with water (contained metallic aluminium and arsenic)	5 Fatality out of 13 affected males
Steel & Feltham (1950)	An arsenic trioxide-containing product and zinc dust in a basic solution.	37-year-old male had mild colicky upper abdominal pain and bloody urine and recovered after supportive treatment.
Johnson (1953)	Recovery of cadmium as a secondary output of a zinc smelter and the addition of concentrated acid to tank.	2 Male with hematuria after 12 days of hospitalization
Buchanan (1962)	Experiment with arsine	Inhalation caused symptoms of vomiting, shivering an hour later, and weakness, then died after 9 days
	Desilvering lead and zinc ores	
	Hydrochloric acid added to argenticous zinc ores	3 Fatality out of 9 affected males
	10 Carboys of commercial HCl with one ton of spelter	1 Fatality
	Process of dissolving zinc in HCl	5 Cases, including 3 fatalities 0.309% of arsenic detected in the zinc.
	Manufacturing of aniline dyes, certain salts of iron and zinc; the extraction of various ores and the smelting of zinc; the manufacture of bleaching powder and sodium sulphate using arseniferous sulphuric acid; and the operations of plumbing, brazing and galvanizing.	
	Manufacturing zinc chloride from galvanizers' refuse and HCl. HCl contained arsenical impurity less than 0.1%	1 Fatality out of 10 affected males Common symptoms include jaundice, hematuria, intense thirst, burning chest pain, diarrhea, depression, prostration and collapse.
	Entering tanks which had contained sulphuric acid for the purpose of removal of sludge and other deposit	1 Fatality out of 3 affected males
	Preparation of cadmium by the action of 50% sulphuric acid on cadmium sponge	3 Men affected. Cadmium sponge contain 2% of arsenic. An arsenical content of the refuse amounts to only 0.01 to 0.02%.
Kipling & Fothergill (1964)	Slag-washing plant; process of washing arsenic-containing slag during copper-aluminium alloy production. From this slag, arsine can be generated by hydrolysis of aluminium arsenide, the production of nascent hydrogen by finely separated aluminium in an alkaline medium, or an electrolytic action between the revolving iron drum and the aluminium.	5 Men affected and were self-limited.
Jenkins et al. (1965)	Sulfuric acid and powdered zinc were added (in the presence of steam) to flue dust from a blast furnace	GI troubles and giddiness after 3hr and hematuria after 5 hr of exposure Hb fell to 7.9 g/dl at 3 day after exposure, Hospitalized for 18 days after admission.
Konzen & Dodson (1966)	Loading sodium arsenate into an aluminum tank and checking inside the tank	50-year-old man developed an acute episode of headache, nausea, vomiting,

Table 3. Review of arsine poisoning cases

Reference	Work description	Clinical course & others
Elkins & Fahy (1967)	Trucking company; An aluminium tank that previously stored sodium arsenite solution trailer was cleaned with a phosphoric acid solution. Most probably, arsine was formed	dyspnea and chest pain after inhalation of a gas. He had anemia, and dark urine and jaundice at 2 to 4 days after exposure. Recovered 6 weeks later. 2 Self-limited males
Muehrcke & Pirani (1968)	Handling and transporting cylinders containing arsenic compounds; A solution containing sodium hydroxide and arsenic trioxide was removed from an aluminium tank for 30 min.	32-year-old male with jaundice and vomiting 4h after exposure; CVA tenderness 8h later; semicomatous on 2nd day. Peritoneal dialysis and exchange transfusion then peritoneal dialysis for 26 days; On 42nd day after exposure, hemodialysis was done. He was discharged on 74th day.
Coles et al. (1969)	Refinery of zinc and lead by producing a mixture of molten lead and zinc then molten zinc is transferred to a final liquation (holding) chamber before casting into slabs. A closed chamber containing (arsenic-contaminated) metal was doused with water.	2 Males developed acute intravascular hemolysis after exposure to arsine gas. one developed acute renal failure and required peritoneal dialysis. His renal function returned to near normal within 3 months.
DePalma (1969)	An aluminum ladder placed in a tank containing sodium arsenite and witnessed bubbling at the foot of the ladder	3 Men affected. All men had nausea, vomiting, abdominal pain and hematuria. One with disorientation and impaired mentality All were treated with 2 exchange transfusion and peritoneal dialysis discharged on the 54th day after exposure.
Hocken & Bradshaw (1970)	At an industrial drain, carrying a zinc-galvanized bucket cleaned out an (arsenic-containing) clog	47-year-old man hospitalized due to jaundice, vomiting, and blood-stained urine after carrying a galvanized bucket and spade. oligouric renal failure with acute hemolytic anemia was self-limiting minor hepatocellular damage and transient initial pulmonary edema developed.
Pinto (1976)	Copper smelter and refinery processes containing significant amount of arsenic and produces arsenic trioxide as a by-product. The plant produces nickel sulfate. The operation to dip a sulfuric acid solution out of a tank containing precipitated nickel sulfate and pour it into another tank. regularly used a plastic bucket to remove the sulfuric acid solution from the tank. On the day of the poisoning, the plastic bucket was used accidentally it to bale out the sulfuric acid.	A 27-year-old man had mild burning chest pain, abdominal pains and nausea and hematuria. At exposure day he received 12 unit of exchange transfusion. discharged 8th day after exposure and returned to work on 26th day.
Clay, Dale, & Cross (1977)	In bronzing process, an alloy consisting mainly zinc with only a small amount of copper, instead of the customary brass, was dipped in the bronzing solution.	2 Males died on 8th day after exposure.
Levy et al. (1979)	A chemist occupied a room that contained sodium arsenate into an aluminum/platinum group metal alloys. The crushed alloys were later found to be	After a death from arsine poisoning, exposure assessment was done at the refinery and laboratory.

Table 3. Review of arsine poisoning cases (continue)

Reference	Work description	Clinical course & others
	spontaneously evolving arsine.	The patient with arsine nephrotoxicity was asymptomatic.
Parish et al. (1979)	Chemical company-cleaning a clogged drain; Arsine was formed by the reaction among drain cleaner containing sodium hydroxide, sodium nitrate, and aluminium chips on an arsenic residue.	2 Men affected and were hospitalized with acute fulminant hemolytic anemia and renal failure. One received two 10-unit exchange transfusions and hemodialysis, but progressed to chronic renal failure and is receiving dialysis therapy. The other discharged 18 days after exposure with moderately impaired renal function.
Williams et al. (1981)	Cleaning a cyclorama with a dilute base solution. The painting contained zinc and arsenic	
Gosselin et al. (1982)	In the repair of a zinc furnace	4 Workers affected. 2 patients recovery just after exchange transfusion, 2 patients gradually returning to normal between the 10th and 30th days.
Braszczyńska et al. (1983)	Zinc refining furnace and furnace repair	Urine As < 100 µg/L in workers
Rogge et al. (1983)	A 46-year-old chemist inadvertently inhaled arsine at work.	Abdominal cramps, hemolytic jaundice and massive hemoglobinuria after several hours.
Phoon et al. (1984)	Mixing a particularly large quantity of dross with tin ore which was wet because of rain at a tin smelting plant	5 Men affected and survived with proper management, exchange blood transfusions and peritoneal dialysis.
Marchiori et al. (1989)	In a small family workshop during blackening operations on zinc/aluminium alloy manufactured parts with acid solutions	
Risk & Fourtes (1991)	Aluminum transmission cases cleaned with caustic detergent bath. Arsenic-containing pesticides coated the cases	35-year-old man with nausea, headache, dizziness, and progressive lower extremity weakness and paresthesia.
Romeo et al. (1997)	Working in a small galvanizing plant for ten years. Employed in the burnishing, copper- and nickel-plating of small metal articles at the shoe industry. Engaged in burnishing metal (Fe-Zn) shoelace eyelet holes, using a dilute solution of CuSO ₄ (3%), HCl (32%), and As ₂ O ₃ (2%).	He had hematuria the next day of exposure and was hospitalized with complaint of fever and jaundice. recovered after receiving hemodialysis and exchange transfusion.
Kinoshita et al. (2004)	A 54-year-old man ingested 20 g of arsenic trioxide in a suicide attempt and underwent gastric lavage and total gastrectomy to avoid intestinal perforation and arsenic poisoning.	During his treatment, eye pain, sore throat, headache, and general fatigue experienced by 22 medical staff members are attributable to arsine produced as a result of the reaction of arsenic trioxide with gastric acid.

가

7

가

가

가

1~2 (LaDou, 2004; Rosenstock et al., 2005) 가

가 (oliguria) 3 가

가

가

90%

As³⁺ (SH-

) DNA 가

SH-

5가 3가

3가 MMA DMA (Fig. 1).

(seaweed) arsenosugar DMA (iAs) (seafood) arsenobetaine TMA (arsenosugar DMA arsenosugar DMA (GaAs), InAs 3가

5~6 24~28 가

가 (Hakala & Pyy, 1995; Ma & Le, 1998; Kim et al., 2004; Yamauchi et al., 2004).

sis) 가 (ACGIH) iAs + MMA + DMA (IMD) . Figure 1 IMD + TMA TMA (ACGIH, 2004). ACGIH (biological exposure index: BEI) 35 μg As/g creatinine 가 background , 50 μg As/g creatinine 가 iAs MMA 1,000~10,000 μg As/g creatinine 가 (Kim et al., 2004). 가 49 MMA 0.076~0.674 μg As/dl 11 , 5 iAs 1.92 μg As/dl, MMA 1.82 μg As/dl, TMA non-detection, 16.24 μg As/dl , MMA, DMA 가 TMA가 가 15 가 가 (species analy-

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