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A Report of 2 Cases of Acute Hydrogen Arsenide Poisoning

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Abstract: Arsenic and its compounds are widely found in nature. They are often absorbed into the human body through the respiratory tract, skin and digestive tract, and distributed throughout the body through the blood. It is more common in coal burning arsenic poisoning and drinking water arsenic poisoning. In recent years, arsenic poisoning related to industrial production has also been reported. Two cases of hydrogen arsenide poisoning related to industrial production were reported and analyzed in order to improve the treatment level.

Keywords: hydrogen arsenide poisoning, blood purification, special effect antidote, cluster therapy

Introduction

Arsenic is a kind of metal element, there are three allotropes of gray arsenic, yellow arsenic and black arsenic, arsenic often exists in nature in trivalent and pentavalent. Arsenic is easily oxidized or sublimated into highly toxic substances in humid air, such as arsenic trioxide, commonly known as "Pishuang" (Chinese); And hydrogen arsenide and so on. Arsenic can bind to important enzymes in cell metabolism and affect cell metabolism, leading to multi-system function damage. Arsenic poisoning and its compounds are harmful to human health. Arsenic poisoning caused by coal burning and drinking water is more common in clinical practice. In recent years, arsenic poisoning related to industrial production has also been reported. Two patients with acute hydrogen arsenide poisoning via respiratory route were admitted to our department in June 2021.

Case Presented

At about 13:00 on June 15, 2021, a suspected heavy metal poisoning incident occurred in a metal smelter in Ningxia, which smelted iron containing silicon, tin, antimony and other ores to produce a special steel. Two workers developed symptoms of dizziness, headache, fatigue, nausea, vomiting, abdominal pain and diarrhea after dismantling the smelting furnace. They were found to have liver and kidney function impairment after visiting the local municipal hospital, and were transferred to the Emergency ICU of our hospital at 5:00 a.m. on June 16. Details of the two cases are reported as follows:

Case one, a 45-year-old male, who was previously healthy, presented with nausea, vomiting, abdominal pain, diarrhea, and liver and renal failure, anuria, hemolysis, hemolytic anemia, and cyanosis when he came to the hospital. He then developed delirium, irritability, and severe jaundice. Case two, a 36-year-old male, who was previously healthy too, came to the hospital with similar symptoms to Case one, but relatively mild neurological symptoms. Case two had clear consciousness and mild skin cyanosis. Both of them had transient platelet elevation and then decreased rapidly. Critical platelet values were reported in case one for two consecutive weeks, and in case two for one consecutive week. Case one was hospitalized for 56 days, during which respiratory failure, tracheal intubation, mechanical ventilation, post-tracheotomy, and successfully weaned from the ventilator; Circulatory failure, intermittent pulse indicating continuous cardiac output monitoring (PICCO), improve cardiac function (See Figure 1). Case two was hospitalized for 50 days.

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Figure 1 Clinical characteristics and treatment of patients: Anuria; Hemolysis; Continuous renal replacement therapy (CRRT); Plasma exchange; Pulse indicating continuous cardiac output monitoring (PICCO).

Following up for one month and two months after discharge, the liver and kidney function and blood routine were normal, and no obvious sequelae were left.

The blood samples of case one and case two were sent to Beijing Gaoxin Borui Quality Inspection Technology Service Co., LTD. (now the company is transferred to Beijing Gaoxin Hospital) and the South Hospital of the Fifth Medical Center of PLA General Hospital. Blood arsenic concentration was rechecked after treatment. The drug test report is attached (Table 1). Related laboratory results of cases 1 and 2 during treatment (Table 2 and Table 3).

Treatment

Cases one and two were treated with symptomatic treatment such as fluid replacement, vitamin C, maintenance of water, electrolyte and acid-base balance, hormone methylpredone 500mg shock treatment for 3 days of anti-inflammatory, prevention and treatment of infection, omeprazole inhibits gastric acid secretion and stomach protection to prevent gastrointestinal bleeding, organ function protection and nutritional support treatment. On admission, acute hemolysis, hemolytic anemia and thrombocytopenia, liver function impairment, renal failure, anuria occurred in both patients. Intermittent transfusion of suspended red blood cells corrected anemia, platelet elevated platelet level. Continuous renal replacement therapy (CRRT) combined with plasma exchange and drug liver protection treatment. Case two received 17 times of CRRT and 3 times of plasma exchange, and case one received 24 times of CRRT and 6 times of plasma exchange. Case one developed respiratory and circulatory failure during hospitalization, and was given mechanical

Table 1 Blood Arsenic Concentration in Cases 1 and Cases 2

Element (ng/mL)	Case 1			Case 2			Reference Range
Arsenic	485.6[a]	337[b]	17[c]	239.3[a]	134[b]	16.5[c]	<31.6
Mercury	0.7[a]	0.8[b]		0.8[a]	0.6[b]		<2.5
Lead	7.8[a]	17[b]		12.5[a]	13.5[b]		<29
Cadmium	0.03[a]	0.3[b]		0.02[a]	0.2[b]		<0.4
Thallium	0.02[a]	0.03[b]		0.01[a]	0.02[b]		<0.1
Chromium	35.6[a]	17.6[b]		39.2[a]	16[b]		14–87
Antimony	0.5[a]			0.3[a]			<4.8

Notes: [a]Beijing Gaoxin Borui Quality Inspection Technology Service Co., Ltd. reported that the blood samples were retained on June 16 and received on June 17. The reporting time was June 17. [b]The test report of the Fifth Medical Center South District of PLA General Hospital retained samples on June 16 and was delivered to the Fifth Medical Center South District of PLA General Hospital by express on June 20. The report time was June 23. Considering the reason of time retention, there may be errors, but they can prove arsenic poisoning. [c]Retest of blood arsenic concentration after treatment was reported by the Fifth Medical Center South of PLA General Hospital.

ventilation by endotracheal intubation. Later, tracheotomy was performed to strengthen the management of shortness of breath, and the patient was removed from the ventilator. Vasoactive drugs were used to maintain blood pressure. Eight times of PICCO was given to guide the treatment. All patients were given the special detoxification drug sodium dimercaptopropanesulfonic acid (5mg/Kg) by intramuscular injection or intravenous injection according to the instructions, indicating that the disease was gradually reduced, and the treatment lasted for 5 courses until the blood arsenic concentration was normal in the retest (Table 1).

Results

After treatment with the appeal scheme, the symptoms of case one and case two were improved, and the organ function indexes as shown in Table 2 and Table 3 were gradually improved, the urine volume was gradually increased, and the blood arsenic was reduced to normal after re-examination. After that, the patients were transferred to the emergency ward for consolidation treatment and discharged without conscious symptoms. In case one, the tracheal tube was blocked and removed before discharge. All patients were followed up for two months without conscious symptoms. The liver and kidney function, blood routine and urine volume were normal.

Table 2 Test Results for Case 1

Time (d)	1	3	5	7	14	21	28	Followed Up for 1 Month	Followed Up for 2 Months
Alanine aminotransferase (U/L)	60	46	82	51	34	86	125	35	19
Aspartate aminotransferase (U/L)	721	91	229	80	46	76	125	22	30
Bilirubin (umol/L)	452	96	86	97	105	31	20	9	5
Creatinine (umol/L)	406	237	197	272	230	285	500	105	79
Potassium (mmol/L)	6.09	3.04	3.61	4.1	3.8	4.9	4.9	5	3.8
Albumin (g/L)	>60	35	31	25	24	28	30	43	43
Creatine kinase (U/L)	406	620	1097	902	59			27	35
Lactate dehydrogenase (U/L)	>10,750	6918	8274	2901	2489	1314	552	445	121
Hemoglobin (g/L)	40	79	97	86	95	118	109	114	128
Platelet*10~9/L	873	104	29	9	45	165	444	87	210
Urine output (mL)	0	0	0	0	0	500	1650	Normal	Normal
Myoglobin (ng/mL)	303	343	>500	333					
Plasma free hemoglobin (mg/L)	685			50					

Table 3 Test Results for Case

Time (d)	1	3	5	7	14	21	28	Followed Up for 1 Month	Followed Up for 2 Months
Alanine aminotransferase (U/L)	60	97	47	41	21	14	8	14	31
Aspartate aminotransferase (U/L)	324	351	71	17	11	10	23	12	22
Bilirubin (umol/L)	299	110	28	17	13	9	10	6	6
Creatinine (umol/L)	373	293	315	326	417	596	472	115	96
Potassium (mmol/L)	5.45	4.2	4.1	4.6	4.3	4.8	5	4.4	
Albumin (g/L)	>60	34	21	23	25	28	50	50	45
Creatine kinase (U/L)	134	571	116	50	39			74	
Lactate dehydrogenase (U/L)	>10,750	10,425	4460	1091	737	545		218	
Hemoglobin (g/L)	95	78	101	97	93	93	121	137	139
Platelet (*10~9/L)	408	55	53	83	277	207	339	350	281
Urine output (mL)	0	0	0	0	50	850	3400	Normal	Normal
Myoglobin (ng/mL)	116	>500	>500						
Plasma free hemoglobin (mg/L)	555			26					

Discussion

Arsenic and its compounds can bind to important enzymes in cell metabolism after entering the body, affecting cell metabolism and leading to multi-system function damage. The main pathogenesis is as follows: 1. Inhibition of enzyme activity: trivalent arsenic combines with dithiol or carboxyl groups on enzyme protein molecules to form stable complex or circular compounds, thus inhibiting enzyme activity. 2, leading to apoptosis. 3. Oncogenic mechanism: (1) DNA damage; (2) Abnormal gene expression; (3) DNA methylation reaction; (4) Oxidative stress and generation of reactive oxygen species.

The two patients in this paper started with gastrointestinal symptoms: frequent vomiting and diarrhea, followed by neurological symptoms, liver and kidney function impairment, cyanosis of the skin, acute hemolysis, hemolysis anemia, low platelet count, and significantly elevated blood arsenic. Therefore, the diagnosis of acute arsenic poisoning was established. After encountering acid and water, the slag containing zinc and arsenic is easy to form extremely toxic gas: hydrogen arsenide. Combined with the working environment of the two patients, the disease occurred after dismantling the smelting furnace containing slag, so the final diagnosis of acute hydrogen arsenide poisoning was made. The results show that arsenic can induce the hypermethylation of 6 sites in the Foxp3 promoter by upregulating the expression of recombinant DNA Methyltransferase 1 (Dnmt1) mRNA, leading to the down-regulation of Foxp3 mRNA, Tregs, and interleukin 10 (IL-10, anti-inflammatory cytokine) levels, and increased the levels of interleukin 17 (IL-17, pro-inflammatory cytokine) in the peripheral blood of patients with arsenic poisoning, manifested as the disruption of pro- and anti-inflammatory T cell balance and multiple organ damage.[1] There is a transient platelet increase at the beginning of the onset of both diseases, and then a rapid decrease, and even continuous detection reports the critical value, which may be related to the extensive damage of vascular endothelium caused by the high concentration of hydrogen arsenide in the blood, leading to the massive activation and consumption of platelets, and the formation of extensive platelet thrombosis.[2] In this case, the platelet levels of the two patients gradually returned to normal after the blood arsenic concentration decreased after treatment with platelet infusion and arsenic removal. Arsenic is known to cause neurological dysfunctions such as impaired memory, encephalopathy, and peripheral neuropathy as it easily crosses the blood-brain barrier. According to news reporting originating in Odense, Denmark, by Vertical News journalists, research stated, “During the summer of 1955, mass arsenic poisoning of bottle-fed infants occurred in the western part of Japan due to contaminated milk powder, and more than 100 died; some childhood victims were later found to suffer from neurological sequelae in adolescence.[3] The symptoms of dizziness, headache and fatigue were present in all cases at the onset of arsenic poisoning. Case 1 had delirium and irritability. Some authors have reported that there was no obvious positive result of EMG after acute arsenic poisoning, and there

was no evidence of neurological damage during follow-up after dimercaptopropanol treatment.[4] Liver is the most important detoxification organ in human body. It is also damaged by poison, namely arsenide. On admission, the liver transaminase was elevated and liver function was impaired in the two patients. It was considered that arsenic induced hepatocyte apoptosis, and a variety of signal transduction pathways led to hepatocyte injury, and then liver failure.[5–8] After active liver protection and plasma exchange, the liver enzyme index of the patient quickly returned to normal. In this paper, both cases presented with anuria, elevated serum creatinine and acute renal failure, which may be related to oxidative stress, altered vascular response to neurotransmitters, impaired vascular muscular calcium (Ca2+) signal, and interference of renin-angiotensin system (RAS), leading to renal impairment.[9] In addition to conventional drug treatment after acute arsenic poisoning, studies have shown that venous hemofiltration combined with hemoperfusion in the treatment of severe arsenic poisoning can reduce renal injury, promote patient recovery and enhance prognosis.[10,11] The findings of Irshad Kanwal et al indicate that Resveratrol remarkably ameliorated the hepatic and renal toxicity in arsenic-exposed rat model due to its strong antioxidant potential.[12] This study may be helpful in future for improvement in the prognostic and novel therapeutic interventions.Chelation therapy is considered as a safe and effective strategy to combat metal poisoning. Jflora et al prepared Solid Lipid carrier loaded with Monoisoamyl 2, 3-Dimercaptosuccinic acid (Nano-MiADMSA), and compared their efficacy with bulk MiADMSA for treating arsenic-induced neurological and other biochemical effects.They conclude that treatment with Nano-MiADMSA is a better therapeutic strategy than bulk MiADMSA in reducing the effects of arsenic-induced oxidative stress and associated neurobehavioral changes.[13] In China, the use of sodium dimercaptopropanesulfate remains the mainstay of treatment, and early treatment is necessary to prevent irreversible complications.[14] Because two cases were included in this paper, the number of cases was relatively small, but the clinical symptoms were consistent with the manifestations of acute arsenic poisoning. More cases can be accumulated in the later stage to analyze the clinical common characteristics, strengthen the understanding of arsenic poisoning and improve the treatment ability.

Both patients achieved good efficacy and no sequelae occurred during follow-up. The experience is as follows: (1) early removal of toxicants is the key. In the case of unclear toxicants, early detection of toxicants can be carried out for qualitative purposes, and the determination of toxicants can also be carried out for quantitative purposes. Specific drugs should be given as soon as possible after arsenic poisoning is confirmed. (2) Timely life support treatment, protect vital organ function, maintain water, electrolyte and acid-base balance, prevent and treat complications; (3) Blood purification therapy should be carried out as early as possible, or even combined application of multiple blood purification methods, to restore organ function early and improve prognosis; (4) If circulatory failure occurs, it is feasible to monitor cardiac output and lung water with PiCCO under the application of vasoactive drugs to guide treatment and improve cardiac function. In general, as with sepsis, a series of cluster treatments for arsenic poisoning and its compounds can improve cure rates.

Conclusion

Once arsenic poisoning occurs, early diagnosis is particularly important. If the diagnosis is confirmed, a series of treatment measures should be started to improve the organ function early and save lives.

Data Sharing Statement

All data are provided in this manuscript.

Ethics Clearance

Ethical clearance was obtained from the Ethics Committee of the General Hospital of Ningxia Medical University. Agreement No.:KYLL-2021-227. General Hospital of Ningxia Medical University, Yinchuan, China.

Consent

Written consent was obtained from the patients for the publication of this case report and accompanying images.

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Disclosure

The authors declare that they have no competing interests.

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