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Case Report

Arsenic Poisoning from Repeated Exposure to Burning Herbal Products Containing Realgar: A Case Report

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ABSTRACT

Background: Arsenic poisoning from repeated exposure to burning herbal products containing realgar has not been reported in the literature. We report a case of arsenic poisoning from repeated exposure to burning traditional Chinese herbal products containing realgar for more than one year.

Case details: A 39-year-old male developed intermittent fever, loss of appetite, hair loss and bluish discoloration of the trunk and limbs one year before admission, followed by diffuse thickening of soles and palms and gradually worsened tingling and numbness of distal parts of limbs and weakness of extremities over the course of the year prior to hospital admission. Characteristic clinical presentation of arsenic poisoning included hyperpigmentation, spotty raindrop pigmentation, Mees' lines and high arsenic levels in the blood, urine and hair confirmed the diagnosis. Patient's signs and symptoms significantly improved following termination of arsenic exposure and treatment.

Conclusion: Inhalation of pyrolyzed herbal products containing realgar resulted in arsenic poisoning. Our patient showed significant clinical improvement following termination of arsenic exposure and treatment. The adverse health effects of burning herbal products containing realgar are a serious public health issue.

Keywords: Arsenic poisoning; Inhalation; Burning; Realgar; Herbal products; Chelation therapy

INTRODUCTION

Arsenic poisoning is associated with the inhalation of airborne arsenic from the combustion of coals containing high arsenic concentration and from mining operations.[1, 2] As far as we know, arsenic poisoning associated with inhalation of burning herbal products containing realgar (arsenic sulfide) has not been reported. Burning herbal products in the house is a common ritual practice in Asian countries to attract luck and prosperity. We report a case of arsenic poisoning from repeated exposure to burning herbal products containing realgar.

CASE REPORT

A 39-year-old male presented to an emergency department with nausea and vomiting. The patient was admitted to our rheumatology department because his history, physical examination and laboratory findings (e.g., fever, weight loss, skin lesions, cytopenia, gastrointestinal and neurological involvement) were thought to be consistent with an autoimmune disease. He denied occupational exposure as a real estate agent, denied excessive alcohol use and was on tenofovir treatment for hepatitis B for the past year. Other family members denied symptoms and remarkable past medical history. They had a regular diet with one or two portions of fish or seafood a week, neither of contaminated water intake and direct use of realgar. As the patient believed burning herbal products containing realgar would bring good fortune, he intermittently burned the herbal products for almost 10 years and the frequency increased to four time per month since 1 year ago and he stopped the behavior four months before admission.

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The patient's symptoms onset was about one year ago when he first developed intermittent fever and loss of appetite, followed by hair loss and bluish discoloration of the skin of the trunk and limbs. Nine months before the admission, he developed diffuse thickening of soles and palms as well as a gradual worsening of tingling and numbness of distal parts of limbs.

Five months before the admission, he was unable to climb stairs and rise from a chair due to muscle weakness, which worsened to the point that he was bedridden for several days before presenting to an emergency department. He had recurrent nausea and vomiting throughout the 2 months prior to presentation. During the course of this past year, the patient presented to three different healthcare facilities, but was misdiagnosed as dermatomyositis, Guillain-Barre syndrome and discharged each time.

Physical examination showed normal vital signs, hyperkeratosis on the skin of the upper back, spotty raindrop pigmentation on the palms and soles, Mees' lines over the nails of fingers and toes (Figure 1). Other clinical findings included distal muscle weakness, muscle atrophy, distal paraesthesia with stocking-glove distribution and weight loss of 20 kg over the past year.

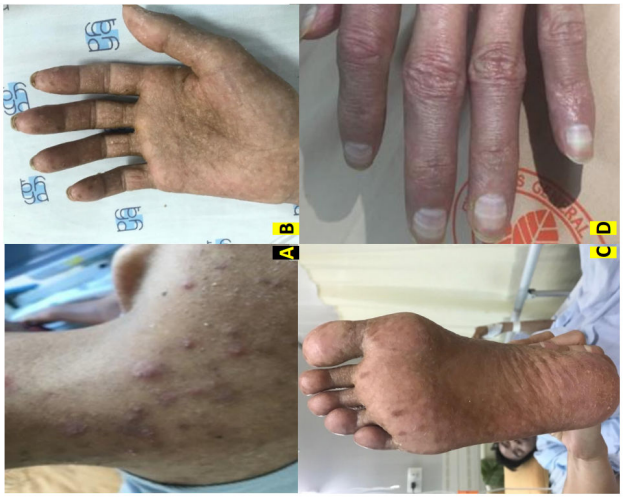

Figure 1: Clinical presentation of a 39-year-old man with arsenic poisoning due to repeated exposure to burning realgar-containing herbal products for over one year. (A) Hyperkeratosis on the skin of the upper back, (B) Spotty raindrop pigmentation on the palm, (C) Spotty raindrop pigmentation on the sole, (D) Mees' lines over fingernails.

Important laboratory results were shown in Table 1. In particular, high arsenic concentrations in blood, hair and urine confirmed the diagnosis of arsenic poisoning. Elevated liver enzymes were found with HBV marker profile including positive HBsAg and undetectable HBV DNA.

Imaging tests included abdominal ultrasonography and CT scan both showing coarse echogenicity of the liver, cirrhotic change and ascites. Transient elastography showed liver stiffness of 9.0 kPa (Normal: < 6 kPa). Nerve conduction studies in both forearms and legs showed chronic sensorimotor axonal neuropathy, predominantly in the lower limbs.

Table 1: Important laboratory results.

Laboratory results	Values
Arsenic concentrations (4 months after last exposure)	
Whole blood	27.08 µg/L (range <18) ñ
Hair arsenic	188.18 µg/g (range <1.0) ñ
Urine	399.4 µg/L (range <100) ñ
Complete blood count	
Haemoglobin	100 G/L (range 120-175) ò
Mean corpuscular volume (MCV)	102.1 fL (range 78-100) ñ
Mean corpuscular haemoglobin (MCH)	33.3 pG (range 26.7-30.7) ñ
White blood count	3.33 G/L (range 4-10) ò
Neutrophils count	0.7 G/L (range 1.8-7.5) ò
Platelet count	255 G/L (range 150-450) ó
Liver enzymes	
Aspartate transaminase (AST)	110 U/L (range <45) ñ
Alanine transaminase (ALT)	52 U/L (range <40) ñ
Alkaline phosphatase (ALP)	158 U/L (range <100) ñ

Thanks to Mees' lines, which is strongly associated with arsenic poisoning, and other characteristic skin lesions including spotty raindrop pigmentation and hyperpigmentation;[3] and laboratory findings of high arsenic concentrations in the blood, urine and hair suggesting repeated arsenic exposures resulting in a large arsenic body burden, the diagnosis was established. Family members were far less exposed to the source than he was, inferred from absence of any clinical symptoms and results of laboratory tests shown in Table 2. From such clues, we inquired about his herbal products use and the analysis of a sample of

herbal products containing dried herbs and realgar powder revealed arsenic concentration was 312 mg/kg.

Table 2: Family members were far less exposed to the source than he was, inferred from absence of any clinical symptoms and results of laboratory tests.

Arsenic concentrations	Wife	1st child	2nd child	3rd child	Normal range
Urine	230	360	590	420	<100 µg/L
Hair	2.12	0.49	0.54	1.62	<1 µg/g

He was treated with chelation therapy while his wife and children were not due to absence of symptoms and signs. The therapy was initiated with intravenous 2,3-dimercapto-1-propane sulfonic acid (DMPS) for the first week, followed by oral 2,3-dimercaptosuccinic acid (DMSA) and oral DMPS in the second week and third week, respectively. He was then discharged with the prescription of oral DMPS for the following 6 weeks.

On follow-up 10 weeks after discharge, he gained 10 kg in weight, improved muscle strength and was able to walk slowly without assistance while tingling and numbness slightly decreased. Skin lesions almost disappeared and no more gastrointestinal complaints were noted. Macrocytic anemia and leukopenia subsided.

He was evaluated before and after the treatment by System of Clinical Scoring of the Symptom and Signs.[4] There was a significant decrease score from 11 (including 1 point for weakness, anorexia, pallor, ascites and loss of ankle jerk each and 2 points for pigmentation, keratosis and paraesthesia each) to 3 (loss of ankle jerk and paraesthesia).

Since hair arsenic concentration can be a useful marker for follow-up investigation,[5] we noted its significant decrease to 4.93 ppm, complete blood count and serum liver enzymes returned to normal. Imaging tests showed no evidence of liver cirrhotic changes and no ascites. The transient elastography showed a decrease of liver stiffness to 6.1 kPa. Nerve conduction studies showed great improvement in Table 3.

DISCUSSION

The diagnosis of arsenic poisoning in our patient was delayed in of a high body arsenic burden.

Table 3: Serial Finding of Nerve Conduction Studies.

Motor Nerve Conduction	Latency ms	Amplitude Distal Proximal mV	Velocity m s	F latency ms
Median R				
A	6.0 (N: <4.4)	0.6/0.4 (N: >4.5/4.3)	34.9 (N: >49.4)	NR (N: <29)
B	4.1	2.0/1.8	50	30.6
Ulnar R				

the past year. He was misdiagnosed as dermatomyositis and Guillain-Barre syndrome in other healthcare facilities. At this admission, he was also misdiagnosed as autoimmune disease and was admitted to rheumatology service, where the correct diagnosis was made based on characteristic physical findings associated with arsenic poisoning and laboratory confirmation

Though inorganic arsenic is a well-known poison, realgar is thought to be safe with few reports on toxicities or adverse effects and has been used in Traditional Chinese Medicine for many centuries. [6] However, heating realgar may result in the release of its pyrolysis product - arsenic trioxide, which is highly toxic.[7] This may explain why inhalation of realgar-containing herbal products is the source of arsenic poisoning in our case.

Our patient had multi-organ abnormalities, including skin lesions, cytopenia, neuropathy and liver disease. However, there was significant clinical improvement at 10 weeks follow-up. Arsenic associated liver damage is uncommon and includes liver dysfunction, hepatoportal sclerosis, hepatomegaly, liver fibrosis, and cirrhosis [8]. The liver disease of our case was suggested by cirrhotic changes and ascites evident on imaging studies. Such changes were not necessarily irreversible cirrhosis but indicated morphological changes of the liver. As liver biopsy was not performed, we do not know what actual damage of the liver is. Elevation in levels of ALP, AST and ALT is reported as markers of liver damage in arsenic poisoning [9]. Whether these are the abnormalities is due to arsenic poisoning or hepatitis B was difficult to differentiate. The improvement after treatment suggests his liver disease was reversible and may be partly related to arsenic toxicity.

Termination of a continuous exposure and nutritious supplement are very critical in managing arsenic poisoning. Chelation therapy can reduce arsenic stores in the body,[10] but clinical benefits attributable to chelation therapy is controversial. While most case reports indicate irreversibility of established adverse organ effects from arsenic toxicity, the improvement in bone marrow recovery, neuropathy and liver condition observed in our case has been very encouraging.

A	4.1 (N: <3.6)	3.8/3.3 (N: >5.5/5.0)	46.9 (N: >54)	37.9 (N: <29)
B	2.8	5.9/5.8	54.8	28.6
Peroneal R				
A	7.7 (N: <3.2)	0.5/0.3 (N: >1.0/1.8)	29.6 (N: >39.8)	NR (N: <53)
B	5.3	1.3/1.2	45.2	50.7
Tibial R				
A	8.6 (N: <3.6)	0.7/0.3 (N: >3.1/3.3)	22.2 (N: >39.9)	NR (N: <53)
B	4.5	1.0/0.9	32.3	49.2
Sensory Nerve Conduction				
	Latency (ms)	Amplitude (μV)	Velocity (m/s)	
Radial R				
A	NR (N: <2.9)	NR (N: >13.8)	NR (N: >46.1)	
B	1.9	2.1	52.6	
Ulnar R				
A	4.2 (N: <2.9)	2.9 (N: >7.04)	33.3 (N: >47.5)	
B	3	1	46.7	
Sural R				
A	NR (N: <3.6)	NR (N: >5.6)	NR (N: >36.2)	
B	3.5	2.1	40	
A = performed before treatment; B = performed at 10 weeks follow-up				
R = Right; N = Normal Range; NR = not recordable				

CONCLUSION

This is the first case of arsenic poisoning due to inhaling the products from pyrolysis of herbal preparations containing realgar. Although multi-organs were affected, the short-term outcome was impressive as the patient clinically improved a lot, correlated with the results of laboratory and imaging tests. We feel that the weight of chelating therapy has contributed in patient's recovery is worthwhile for further investigation.

DECLARATION OF INTEREST

The authors report no declaration of interests. The authors alone are responsible for the contents and writing of this article.

REFERENCES

1. Li D, An D, Zhou Y, Liu J, Waalkes MP. Current status and prevention strategy for coal-arsenic poisoning in Guizhou, China. J Health Popul Nutr. 2006;24(3):273.
2. Martin R, Dowling K, Pearce D, Sillitoe J, Florentine S. Health effects associated with inhalation of airborne arsenic arising from mining operations. Geosciences. 2014;4(3):128-175.
3. Ratnaike RN. Acute and chronic arsenic toxicity. Postgraduate Med J.2003;79(933):391-396.
4. Guha Mazumder DN, De BK, Santra A, Ghosh N, Das S, Lahiri S, Das T. Randomized placebo-controlled trial of 2, 3-dimercapto-1-propanesulfonate (DMPS) in therapy of chronic arsenicosis due to drinking arsenic-contaminated water. J Toxicol: Clin Toxicol.2001;39(7):665-674.

5. Wu B, Chen T. Changes in hair arsenic concentration in a population exposed to heavy pollution: Follow-up investigation in Chenzhou City, Hunan Province, Southern China. J Environ Sci. 2010;22(2):283-289.

6. Liu J, Lu Y, Wu Q, Goyer RA, Waalkes MP. Mineral arsenicals in traditional medicines: orpiment, realgar, and arsenolite. Journal of pharmacology and experimental therapeutics. 2008;326(2): 363-368.

7. Chen SJ, Zhou GB, Zhang XW, Mao JH, de Thé H, Chen Z. From an old remedy to a magic bullet: molecular mechanisms underlying the therapeutic effects of arsenic in fighting leukemia. Blood. 2011;117(24):6425-6437.

8. Lu T, Liu J, LeCluyse EL, Zhou YS, Cheng ML, Waalkes MP. Application of cDNA microarray to the study of arsenic-induced liver diseases in the population of Guizhou, China. Toxicol Sci. 2001 Jan 1;59(1):185-192.

9. Islam K, Haque A, Karim R, Fajol A, Hossain E, Salam KA, Ali N, Saud ZA, Rahman M, Rahman M, Sultana P. Dose-response relationship between arsenic exposure and the serum enzymes for liver function tests in the individuals exposed to arsenic: a cross sectional study in Bangladesh. Environmental health. 2011;10(1): 64.

10. Flora SJ, Pachauri V. Chelation in metal intoxication. International journal of environmental research and public health. 2010;7(7):2745-2788.