RARE CASE REPORT OF CHRONIC ARSENIC POISONING

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INTRODUCTION: Today, arsenic is primarily used in the production of glass and semiconductors., Arsenic may be found as a water or food contaminant, particularly in shellfish and other seafood, and often contaminates fruits and vegetables, particularly rice.

Today, arsenic poisoning occurs through industrial exposure, from contaminated wine or moonshine, or because of malicious intent. The possibility of heavy metal contamination of herbal preparations and so-called nutritional supplements must also be considered.

CASE REPORT: A 64 yr old male patient presented with chief complaints of tingling and numbness in both hands and feet since last 6 months, difficulty in picking up of small objects, difficulty in breaking of chapatti, difficulty in buttoning and unbuttoning of button of shirt, there was also history of sleeping of chappals from the toes.

Physical examination showed diffuse hyperpigmentation over the trunk, it was typically like rain drop pigmentation type, and there were absent deep tendon reflexes in all joints of the body and there was hyperaesthesia to pinprick and touch sensation in both the lower limbs and upper limbs, distribution of hyperaesthesia was in form of gloving and stock pattern,patient also had MEEs lines over the nail bed. Patients investigations were carried which revealed high arsenic levels.

DIAGNOSIS: Diagnosis of peripheral neuropathy due to arsenic poisoning was kept.

TREATMENT: Patient was treated with chelating agents like DIMERCAPROL

BACKGROUND:

Description:

- Arsenic is a naturally occurring part of the earth's crust and is found as a contaminant in various metal ores.
- It is used in metallurgy for copper and lead alloy hardening, as a dopant in the semiconductor industry, and in the manufacturing of a variety of products, including pigments and glass. Arsenic has also been used in pesticides such as rodenticides and fungicides.
- Historically, arsenic trioxide was used in various types of medications; for example, in the U.S., for the treatment of a rare form of myeloid leukemia.
- Arsenic compounds may be either inorganic or organic. Both compounds can be found in either the trivalent (3+) or pentavalent (5+) valence states, but they differ significantly in toxicity.
- In general, inorganic arsenic compounds are more potent toxicants.

- Organic arsenic, found in fish, shellfish, and seaweed, is considered to be essentially nontoxic to humans; this includes mostly trimethylated compounds such as arsenobetaine and arsenocholine.
- Arsenic is excreted in the urine; most or all is cleared in approximately 2 days.
- When urine is assayed for total arsenic content, the presence of essentially nontoxic 'fish arsenic' can result in a false-positive result; patients should be advised to refrain from eating all fish, shellfish, and other marine foods for a minimum of 3 days, and preferably 5 to 7 days, before testing.
- Arsine is a highly toxic gas that can be generated from arsenic compounds under certain conditions, for example, when an arsenic oxide compound comes into contact with an acid; it causes intravascular hemolysis with resultant renal failure

Chronic arsenic poisoning has been reported from 9 prefectures and involves 32 villages and 9,000 families. Of 40,000 directly exposed persons, 3,000 have been diagnosed with arsenic poisoning

Chronic arsenic poisoning

Environmental exposure in groundwater:

- Naturally occurring high levels of arsenic that exceed the World Health Organization (WHO) standard (10 μg/L) in groundwater used for drinking and cooking have been reported from Bangladesh, China, India (West Bengal), Taiwan, Thailand, Argentina, Mexico, Chile, Hungary, the UK, the U.S. (mainly in the Southwest), Russia, Ghana, and New Zealand.
- In many of these areas, epidemics of chronic arsenicosis have occurred with arsenical skin conditions such as melanosis; leukomelanosis ('raindrops on a dusty road') pigmentation changes; and hyperkeratosis, particularly on the palms of the hands and soles of the feet. Chronic arsenicosis has also been associated with an excess of skin cancers and with an excess of cancers of the lung, liver, colon, bladder, and kidney
- In a systematic literature review of chronic arsenic exposure from naturally occurring contamination in ground water, the authors noted that 59 out of 64 districts in Bangladesh had patients with chronic arsenicosis and that the source was groundwater from tube wells. The tube wells were originally installed to prevent water-borne infectious diseases transmitted in contaminated surface water

Environmental exposure from arsenic in coal:

- In Southwest Guizhou Province in China, coal from the region has extraordinarily high concentrations of arsenic (>100 ppm) and also has high concentrations of other toxic metals and fluoride
- This coal has become the main source of energy for domestic heating and for drying foodstuffs. It is burned on unvented indoor stoves, which has resulted in indoor airborne arsenic concentrations as high as 93 to 261 $\mu g/m^3$; this is many times higher than the Chinese Air Quality Permission Standard of 3 $\mu g/m^3$. Also, arsenic released from the burning coal contaminates drying foodstuffs, which have been found to contain arsenic concentrations of 4.13 to 695.0 mg/kg; 6 to 990 times higher than the Chinese food standard for arsenic

Burning of arsenic compound-treated wood:

- Burning aged and weathered wood treated with an arsenic compound in an open burn facility has demonstrated that 11% to 14% of the arsenic in the wood was released with the air emissions; the remainder was found in the residual ash
- Reported seasonal chronic arsenic poisoning from burning arsenic-treated wood indoors in a wood stove has been limited to a single report of 8 members of a rural family

Risk factors:

Host factors:

- Nutritional factors, such as lower-than-normal intake of B vitamins and folic acid, have been associated with arsenic-related cardiovascular diseases

Genetic factors:

- Methylation of inorganic arsenic, primarily hepatic, generates monomethylarsonic acid, pentavalent (MMA^{V}), which is then reduced to monomethylarsonic acid, trivalent (MMA^{III}); a second methylation generates dimethylarsinic acid, pentavalent (DMA^{V}). MMA^{III} seems to be more toxic than either inorganic arsenic or the pentavalent intermediates. Genetic polymorphism may influence the methylation pathways and allow accumulation of more toxic MMA^{III}
- The role of arsenic in development of cardiovascular diseases is likely related to an increase in the production of reactive oxygen species. Induction of oxidative stress by arsenic may influence gene expression, inflammatory response, and endothelial nitric oxide homeostasis. Thus, genes involved in endogenous reactive oxygen species defenses could modify the effect of arsenic on the vascular endothelium. In epidemiologic studies from Taiwan, certain gene expressions have been correlated with hypertension risk. Glutathione S-transferases are also involved in the detoxification step of phase II metabolism and catalyze the formation of arsenic-glutathione conjugates required for biliary excretion of arsenic. A genetic polymorphism of glutathione S-transferase P1 has been associated with an increased prevalence of carotid atherosclerosis in a population in Taiwan chronically exposed to arsenic in drinking water

Populations with potentially increased risk of arsenic exposure:

- Persons living in proximity to sites where arsenic was produced, used (particularly as an agricultural pesticide), or disposed; those living near a hazardous waste site where disposed arsenic has leached and contaminated environmental media; those living near certain anthropogenic point sources such as smelters, coal-fired power plants, or incinerators; those whose drinking water contains levels of arsenic exceeding established guidelines/regulations
- Workers in certain industries that produce or utilize arsenic, especially if recommended/regulated safety procedures are not followed, such as in the smelting industry, the manufacture or application of arsenical pesticides, coal boiler maintenance, and the semiconductor industry
- Workers who grind, sand, drill, or otherwise manipulate wood treated with an arsenic compound or who work in the treatment process itself
- It should be noted that an increased risk of exposure to arsenic does not necessarily correlate with an increased risk of arsenic poisoning

Chronic arsenic poisoning:

- Persons who live in areas where naturally occurring arsenic exists in aquifers from which ground water is used for drinking water
- In certain areas of China, those burning easily obtainable coal with a high concentration of arsenic in unvented, indoor spaces
- Industrial exposures can impact workers involved in smelting of contaminated metal ores, manufacturing of certain types of glass, manufacturing of certain metal alloys, manufacturing and application of arsenical pesticides, and those in the semiconductor industry where arsenic is used as a dopant

Diagnosis:

Summary approach:

- Clinically, typical signs and symptoms of acute arsenic poisoning include moderate-to-severe gastrointestinal symptoms such as nausea, vomiting, hematemesis, abdominal cramping, or diarrhea; hypotension or cardiovascular shock from fluid and electrolyte losses and 'third spacing'; and electrocardiogram abnormalities. Encephalopathy may occur
- Typical signs and symptoms of chronic arsenic poisoning include skin changes of palmar-plantar hyperkeratoses, leukomelanosis skin pigmentation changes; skin cancer (a single patient may have more than one cell type); 'stocking-and-glove' sensory or mixed sensory-motor peripheral neuropathy; pancytopenia, with decreased values for all formed blood elements from bone marrow suppression; abnormal liver and renal function tests; and cancers of the bladder, kidney, liver (angiosarcomas), colon, and lung
- The diagnostic test of choice is a 24-hour urine arsenic test. Spot urine tests may help guide the diagnosis, especially in acute exposure, but are less reliable than 24-hour urinary excretion
- In occupational exposure settings, urine arsenic levels of less than 100 µg/L are generally considered acceptable. For the general population, urine arsenic levels of less than 50 µg/L or less than 25 µg per 24 hours are generally considered acceptable
- There should be at least a 3-day (preferably 5-7 d) period between testing and the patient's most recent fish or seafood consumption, as relatively nontoxic 'fish arsenic' (organoarsenical compounds) will cause elevated total arsenic levels
- If the urine arsenic can be speciated (MMA^{III} and DMA^{V}), this helps to identify whether patients have increased excretion of relatively nontoxic organic arsenic or increased excretion of toxic inorganic arsenic compounds; elevated speciated arsenic levels indicate toxic inorganic arsenic excretion and are more concerning. Many laboratories can only assay for total arsenic excretion, and thus clinical correlation is required
- Blood arsenic testing is generally unreliable and is not recommended. The short half-life of arsenic in blood, typically 3 to 4 hours, means that blood arsenic levels can become undetectable while significant urinary arsenic excretion is still occurring
- Hair and nail evaluations for arsenic poisoning are only useful for population studies, to define 'exposed' versus 'unexposed' populations; they are neither reliable nor appropriate in the evaluation of individual patients

Clinical presentation:

Symptoms:

- In acute ingestion, moderate-to-severe gastrointestinal symptoms such as nausea, vomiting, hematemesis, diarrhea, and abdominal cramping/pain
- Distal paresthesias
- Motor weakness
- Fatigue

Other historical information:

Acute arsenic poisoning (ingestion):

- Type of arsenic compound ingested; the amount, or dose, ingested; the time of ingestion
- Occurrence of typical gastrointestinal symptoms such as nausea, vomiting, abdominal cramping, diarrhea

Chronic arsenic poisoning:

- Occupational exposure to arsenic
- Source of drinking water and results of any arsenic assays, if available
- Type of home heating sources used
- Use of arsenic trioxide as chemotherapy for a rare type of leukemia
- Use of traditional Asian medicines
- Availability of arsenic for potential suicidal or homicidal ingestion, for example, availability of arsenic compounds in the workplace that may be taken home, old retained arsenic pesticides, access to arsenic trioxide

Signs:

- Skin pigmentation changes with hypo- and/or hyperpigmentation; leukomelanosis ('raindrops on a dusty road')
- Palmar-plantar hyperkeratosis
- Skin cancer, such as basal cell carcinoma or squamous cell carcinoma
- Non-cirrhotic portal hypertension with bleeding esophageal varices and splenomegaly
- Blackfoot disease with extremity gangrene, which is a unique peripheral vascular disease where the extremities, particularly the lower extremities, develop dry gangrene (black foot) and may auto-amputate
- Raynaud phenomenon
- Hypertension (chronic poisoning)
- Hypotension (acute poisoning)
- Cardiac dysrhythmias/electrocardiogram abnormalities/QT interval prolongation
- Peripheral neuropathy: sensory or mixed sensory-motor peripheral neuropathy, usually in a 'stocking-and-glove' distribution
- Toxic delirium and encephalopathy
- Mees lines (transverse white bands of the nails); uncommon

Diagnostic testing:

- Most recommendations in this section are based on clinical expert opinion, given the relative lack of evidence-based medicine on this topic

- For patients suspected of having acute or chronic arsenic poisoning, the preferred diagnostic test is analysis of 24-hour urinary arsenic excretion . Speciated arsenic testing is performed to look for MMA^{III} and DMA^{V}, methylated metabolites of inorganic arsenical compounds
- Complete blood count , liver function tests , and renal function tests are performed to test for effects caused by acute or chronic arsenic exposure
- Electrocardiogram is performed to test for rhythm or conduction disturbances caused by acute and chronic arsenic exposure; QT prolongation has been reported in some cases

Treatment:

Summary approach:

- Removal from further exposure is important
- Supportive care, based on the presenting symptoms, such as adequate replacement of fluid and electrolytes in acute arsenic poisoning
- The role of chelation therapy in the treatment of arsenic poisoning has not been clearly established. Recommendations are generally based on clinical expert opinion, given a relative lack of evidence-based medicine on this topic. Chelation therapy is sometimes used for patients who are acutely symptomatic, depending on their clinical presentation; decisions regarding chelation therapy should be made in consultation with a medical toxicologist or regional poison control center. If chelation therapy is determined to be appropriate for an acutely symptomatic patient, DMSA (2,3-dimercaptosuccinic acid) and DMPS (dimercaptopropane sulfonic acid) may be considered.
- There have been anecdotal case reports of clinical benefit in acute and chronic arsenic poisoning victims treated with DMSA and DMPS, but some large studies have cast doubt on actual clinical benefit; increased urinary arsenic excretion after treatment has often been documented without relevance to clinical outcome
- D-penicillamine was formerly used to treat acute arsenic poisoning, but has generally been abandoned by clinicians because it has only a single sulfhydryl binding group and can therefore only bind one mole of arsenic per mole of drug. Also, there is potential cross-allergenicity in patients with penicillin allergies
- Dimercaprol has also largely been abandoned in clinical practice because of difficulty in administration and adverse effects profile. However, in rare cases of acute toxicity associated with severe gastrointestinal effects, such as vomiting and diarrhea, it is the agent of choice until the patient can take oral DMSA

Prognosis:

Acute arsenic poisoning:

- Patients who survive the initial gastrointestinal and hypotensive syndromes are at risk for later development of bone marrow depression with pancytopenia and peripheral neuropathy
- Pancytopenia most often fully resolves after arsenic exposure ceases
- Peripheral neuropathy may completely or partially resolve over a period of weeks to months, or may be permanent

Chronic arsenic poisoning:

- Patients are at increased risk for a variety of cancers, skin pigmentation disorders, gastrointestinal disturbances, liver disease, anemia, peripheral neuropathy, and acrocyanosis with potential development of Raynaud phenomenon or gangrene (black foot disease); recovery depends on the particular effect
- If chronic exposure continues, patients are unlikely to fully recover
- In those who develop arsenic-related cancer, recovery depends on the site of the cancer, whether metastases have occurred, and the medical treatment provided
- Those who develop black foot disease generally either suffer auto-amputation or require surgical amputation of the affected extremities
- Pancytopenia may fully resolve if exposure ceases
- Peripheral neuropathy may completely or partially resolve if exposure ceases, but may be permanent

EVIDENCE REFERENCES:

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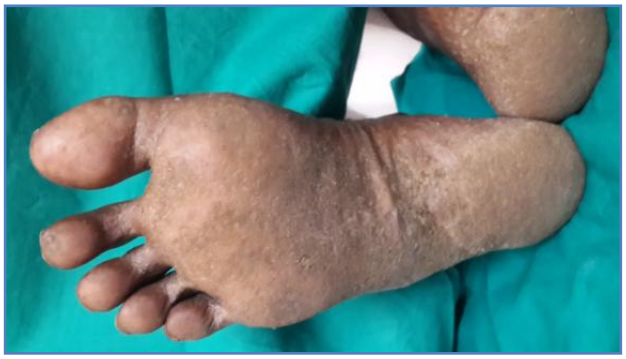
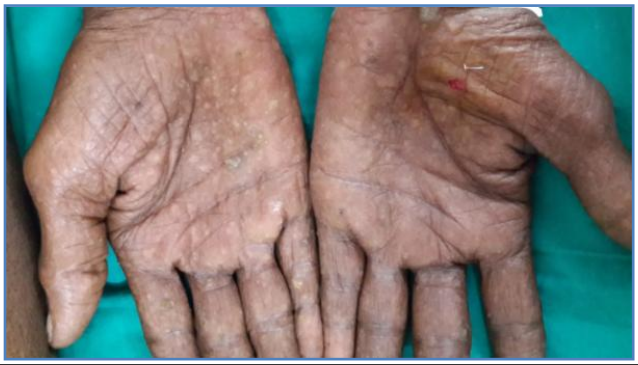
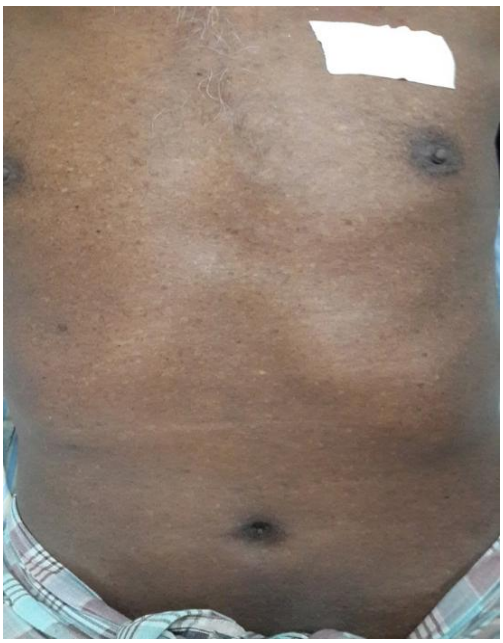


Shows punctate keratosis over the soles



Shows raindrop hyperpigmentation and punctate keratosis over the palms



Shows raindrop hyperpigmentation and punctate keratosis over the palms

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