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Case Report
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SIGNIFICANT ENDOWMENT OF CLINICAL PHARMACIST IN HEMOLYTIC UREMIC SYNDROME (HUS) INDUCED BY ARSENIC: CASE REPORT

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ABSTRACT

Arsenic is a heavy metal which is a natural component of the earth's crust. It exists in compounds that may be organic or inorganic. It is highly toxic in its inorganic form. Poisoning can occur by ingestion, inhalation and dermal absorption. Elimental arsenic is the least toxic. Trivalent arsenic is well absorbed through the skin and is 60 times more toxic than pentavalent arsenic, which is well absorbed by the gut. Arsenic has been used in many medicines and was widely used to treat syphilis until the mid 20th century. It is currently used to treat acute promyelocytic leukemia and other myeloprolifiration disorders. Arsenic exposure is usually occupational or environmental but can result from deliberate poisoning. Symtoms usually start within 30 minuts to 2 hours. Acute arsenic ingestion is typically followed by a severe gastroenteritis, garlic odour and hypersalivation. The organs of the body that are usually affected by Arsenic poisoning are the lungs, skin, kidneys, and liver. The final result of Arsenic poisoning is coma to death. Purpura or small areas of bleeding in the skin may be seen because of low platelet counts (thrombocytopenia)

Keywords: *Trivalent Arsenic, Dermal absorption, Promyelocytic leukarmia, Purpura, Thrombocytopenia.*

INTRODUCTION

Arsenic poisoning is a medical condition caused by elevated levels of Arsenic in the body. The dominant basis of Arsenic poisoning is from ground water that naturally contains high concentrations of arsenic. Groundwater most often becomes contaminated naturally; however, contamination may also occur from mining or agriculture. Through drinking water, more than 200 million people globally are exposed to higher than safe levels of arsenic. The areas most affected are Bangladesh and West Bengal. Acute poisoning is uncommon [1, 2].

Fig. 1: The skin may become dry and hard

According to Medilexicon's medical dictionary:
Arsenic: Atomic no. 33, atomic wt. 74.92159; forms a number of poisonous compounds, some of which are used in medicine. Denoting one of its compounds, especially arsenic acid."

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Table No. 1: Three Allotropic forms of Arsenic.

Arsenic	Yellow	Alpha arsenic
Arsenic	Black	Beta arsenic
Arsenic	Grey	Gamma arsenic

Alone yellow Arsenic is not toxic but upon conversion to black, it becomes toxic. Arsenic is a metalloid that resembles a metal. It is silver grey, shiny, brittle and crystalline in nature. Penta Arsenics are less toxic than Tri Arsenics [3].

Signs and symptoms:

Symptoms of Arsenic poisoning begin with headaches, confusion, severe diarrhoea, and drowsiness. As the poisoning develops, convulsions and changes in fingernail pigmentation may occur. When the poisoning becomes acute, symptoms may include diarrhoea, vomiting, blood in the urine, cramping muscles, hair loss, stomach pain, and more convulsions.

The organs of the body that are usually affected by Arsenic poisoning are the lungs, skin, kidneys, and liver. The final result of Arsenic poisoning is coma to death. Long term exposure to Arsenic is related to vitamin A deficiency which is related to heart disease and night blindness. Most reported Arsenic poisonings are caused by one of arsenic's compounds, also found in drinking water, Arsenic trioxide which is 500 times more toxic than pure Arsenic. Arsenic is related to heart disease (hypertension related cardiovascular), cancer, stroke (cerebrovascular diseases), chronic lower respiratory diseases, and diabetes. In typical HUS, gastroenteritis occurs with abdominal cramping, vomiting and profuse bloody, watery diarrhea, as a symptom up to a week before the onset of HUS. This may cause significant dehydration, weakness and lethargy, as well as electrolyte imbalances because of the loss of sodium, potassium, and chloride in the vomit and diarrhea. These symptoms may resolve before the onset of anemia and the kidney failure symptoms of HUS. The anemia and uremia usually present with weakness, lethargy, and sleepiness. Seizures may occur. Purpura or small areas of bleeding in the skin may be seen because of low platelet counts (thrombocytopenia) [4].

Diagnosis: Arsenic may be measured in blood or urine. There are tests available to diagnose poisoning by measuring Arsenic in blood, urine, hair, and fingernails. Urine testing needs to be done within 24–48 hours for an accurate analysis of an acute exposure. Hair is a potential bioindicator for Arsenic exposure due to its ability to store

trace elements from blood. Incorporated elements maintain their position during growth of hair.

Hemolytic anemia: The red blood cell count is low and a peripheral blood smear, in which blood is examined under a microscope, will show that the red cells have been damaged and destroyed. This differentiates hemolysis (hemo=blood + lysis=destruction) from anemia caused by decreased production of blood cells in the bone marrow.

Thrombocytopenia: a low platelet count

Uremia: Kidney function can be measured by testing the level of waste products in the blood normally filtered by the kidney. BUN (blood urea nitrogen) and creatinine are measures of this kidney function. When levels rise, it is an indication of kidney failure or uremia in which the kidneys cannot clear the waste products of metabolism from the body [5].

Pathophysiology:

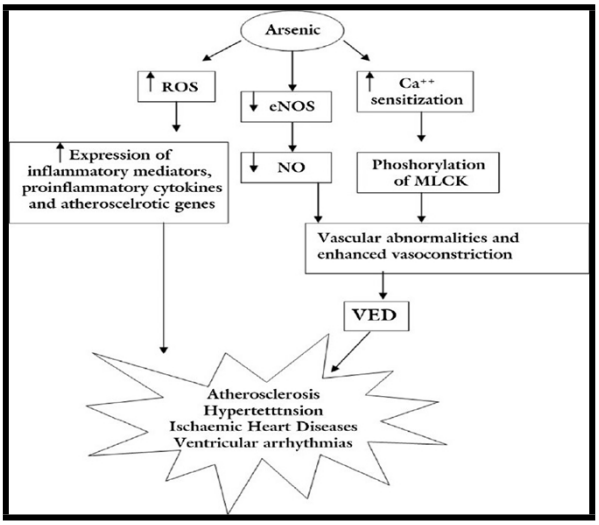

Fig. 2: Pathophysiology

Treatment:

Chelation therapy: Chemical and synthetic methods are now used to treat Arsenic poisoning. Dimercaprol and dimercaptosuccinic acid are chelating agents which removes the arsenic away from blood proteins.

Dimercaprol: Dose: 3.5mg/kg for 7-10 days

Pencillamine: Dose: 30mg/kg body wt. for every 6 hour and duration is for 5 days.
The most important side effect is hypertension [6].

Mineral supplements:

Supplemental potassium decreases the risk of experiencing a life-threatening heart rhythm problem from Arsenic trioxide [7].

Nutritional intervention:

People stay in specific areas that are at risk of Arsenic contamination due to water supply should eat one to three cloves of garlic per day as a preventative.

CASE REPORT OF HEMOLYTIC UREMIC SYNDROME (HUS)

A 56 year old man was referred to ED for evaluation of dark red urine.

Complaints: General feeling of sickness, diffuse muscle pain, transient episodes of diaphoresis and chills, with no fever, bilious vomiting for the past 24 hours. Appearance of dark red coloured urine resembling blood.

Past Medical History: positive for chronic gastritis, no H/o haematological disorders, taking Proton Pump inhibitors.

Social History: occasional smoker and No H/o alcohol abuse.

Table No. 2: Investigations Reports

BLOOD PRESSURE	132/78 mm Hg
HEART RATE	78 beats/min.
TEMPARATURE	36.8ºC
RESPIRATORY RATE	18 breaths/min.
HAEMOGLOBIN	13.8gm/Dl
MCV	101.4 FL
CRP	8.5mg/L
SERUM CREATININE	1.55mg/dL
PLATELETS	$209X10^9$/L
WHITE BLOOD CELLS	$18.01X\ 10^9$/L
BLOOD UREA	80mg/dL

Urinary tract ultra sound:

- Slight perennial edema at right kidney
- Prostate was normal

The patient was admitted to urology department for suspected UTI. A few hours later, condition was deteriorated developed Jaundice, fever (38.6ºc), diarrhoea and mental confusion.

Table No. 3: Urology Reports of developed Jaundice

Haemiglobin	8gm/L
Total bilirubin	5.82mg/dL
Elevatⁿ of inflammatory markers	108mg/L
Serum creatinine	3.5mg/dL

The patient was transferred to intermediate care unit of internal medicine department. Due to worsening of renal dysfunction, acute renal failure was recently developed; haemoglobin level is also low resulting in anaemia.
i.e., haemolytic anaemia + renal failure lead to haemolytic-uremic syndrome.

Treatment: plasmapheresis and RBC is transfused if needed.

Significance of Clinical Pharmacist:

Patients History: Patient worked in a factory of *zippers* where chemical compounds were frequently used in platting techniques. At this time, patient recalled accidental inhalation of toxic gas nearly 32 hours before (while performing plating process with no protection). Gas is a mixture of Tin's oxidant that contains metal alloy. Exposure was not more than 5 min, after 4 hours felt sick. Detail information about chemical was requested immediately by health care professionals.

At day 3, nearly after 90 hours, composition of Tin's oxidant was known that contains

HCL (40-45%); $CUSO_4$ (1.2-1.4%); AS_2O_3 (5-6%)

Now blood and 24hr urine samples sent to lab for the measurement of Arsenic and Copper levels.

Treatment: chelation therapy was initiated, i.e., pencillamine (1800mg/day) and is done before lab results for Arsenic and Copper intoxication.

Patient completed 3 days of Pencillamine, and then Dimercaprol is administered.

Dimercaprol: Dose 200mg (4 hourly for 6 days)
(6hourly for 7^{th} and 8^{th} day);
(12hourly for 9^{th} and 10^{th} day)

On day 7, confirmed high levels of Arsenic and Copper.

Table No. 4: Reports of high levels of Arsenic and Copper on day 7

Arsenic	24 hour urine sample	445	Normal value <100ug/L
Arsenic	Blood	297	Normal value <70 ug/L
Copper	24 hour urine sample	137	Normal value <15 ug/L
Copper	Blood	74.5	Normal value <1.5 ug/L

During the hospital stay, patients symptoms were gradually reduced and recovery of haematological, renal and liver disturbances was observed but inflammatory signs at intramuscular site developed as a consequence of Dimercaprol treatment. After 13 days of chelation therapy, patient was discharged and referred for follow up appointments at internal medicine and nephrology clinic.

DISCUSSION

Arsenic is one the four most hazardous toxicants, along with cadmium, lead, and mercury. Metal poisoning can result from exposure to inhaled dusts, fumes or vapours. Another possible route comes from ingestion of contaminated food, drinks or by hand-to-mouth exposure. This patient presented with many of the classical clinical findings attributed to Arsenic acute intoxication. Acute toxicity with Arsenic manifests within hours as nausea, vomiting, diarrhoea, abdominal pain. Severe poisoning may result in multi-organic failure, delirium, seizures, coma, and ultimately death. If the patient survives, bone marrow suppression, peripheral neuropathy and skin lesions may develop. Primary treatment in acute Arsenic poisoning involves rapid decontamination and early initiation of chelation therapy with agents such as Dimercaprol (British Anti-Lewsite, BAL), edentate (EDTA), succimer (DMSA, dimercaptosuccinic cid) and Penicillamine. No specific antidote is available. plasmapheresis was performed regarding the hypothesis of a haemolytic-uremic syndrome, before any toxicodrome was suspected [8-10].

CONCLUSION

We reported a rare case of haemolytic anaemia following Arsenic and Copper acute intoxication. Common consequences of Arsenic poisoning are haemolysis and renal failure. Because of the severity of the clinical course, including multi-organic failure and a high risk of death, therapeutic strategies should be initiated without formal laboratory confirmation. Evidence-based treatment options are limited. Use of chelating agents such as dimercarprol is recommended. No clinical parameters predict the required duration for plasma exchange. The feasibility of continued plasma exchange is often determined by practical, logistical issues such as the safe and efficient function of the central venous catheter or a patient's ability to return for outpatient treatment. Discontinuing plasma exchange treatment is the only way to know whether a durable remission has been achieved, and many cycles of stopping and resuming plasma exchange may be required.

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