Letter to the Editor

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Arsenic intoxication with renal failure managed with hemodialysis alone: A case report

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SUMMARY Arsenic has widespread use in agriculture, in alternative medicine and in treatment of certain malignancies, therefore it is vital to timely recognize and treat arsenic toxicity in a suspected patient. Hemodialysis conventionally is thought to play only a supportive role in managing arsenic toxicity but it can be life-saving when chelation is not possible or available. A middle-aged female with a history of non-dialysis-dependent chronic kidney disease (CKD) was brought to the emergency with altered sensorium. On presentation, she was hemodynamically stable with pallor and exfoliating lesions on palms, hyperkeratotic lesions on soles and hyperpigmented macules on the trunk. Investigations revealed pancytopenia and deranged kidney function tests. In view of skin lesions, the toxicological analysis was sent which revealed high levels of Arsenic (594 and 2,553 mcg/L in blood and urine respectively). Thus, a diagnosis of metabolic encephalopathy with the underlying cause being uremic or/and arsenic intoxication was made. Considering renal failure, she was managed with thrice-weekly hemodialysis. Chelation was not possible due to unavailability of agents during lockdown in Coronavirus disease (COVID-19) pandemic. Following dialysis, there was a significant improvement in sensorium, skin lesions, and pancytopenia depicting the utility of hemodialysis in such cases. Thus, hemodialysis is an effective and perhaps underutilized modality in the treatment of arsenic intoxication with impaired renal function.

Keywords Arsenic, arsenic poisoning, treatment, hemodialysis, chronic kidney disease (CKD)

To the Editor,

Arsenic is an important component of medicinal, agricultural, and industrial usage. At least 140 million people in 50 countries are exposed to high arsenic levels in drinking water including India, Bangladesh, Argentina, Chile, Mexico, and the United States of America (*1*). With increasing use of arsenic in alternative medicine and in treatment of myelodysplastic syndrome, acute promyelocytic leukemia, multiple myeloma, and other malignancies, it is important to recognize and treat arsenic toxicity in suspected patients (*2*). The use of chelating agents in intoxicated patients with renal failure can be deleterious due to lack of their urinary elimination. The role and efficacy of hemodialysis as standalone therapy in management of arsenic intoxication in renal failure patients is not much known.

A 31-year-old lady from central India with a history of non-dialysis-dependent chronic kidney disease (CKD) for the past four months was brought to emergency with complaints of drowsiness and irrelevant talking for the past six hours. On presentation, she had a pulse rate of 136/min, blood pressure 150/100 mm Hg, respiratory rate 24/minute, and GCS E4V2M1. There was pallor along with exfoliating skin lesions over both palms, diffuse warty hyperkeratotic lesions on soles, blotchy diffuse hyperpigmentation on the forehead and perioral area, and multiple discrete hyperpigmented macules over the chest and abdomen (Figures 1A and 1B).

The patient was intubated in the emergency for airway protection. Initial investigations revealed pancytopenia (hemoglobin 4.7 g/dl, total leukocyte count 2,000/mm^3, platelet count, 60,000/mm^3), normal electrolytes, and deranged renal function (blood urea, 314 mg/dL and serum creatinine, 11.3 mg/dL). Point-of-care ultrasonography revealed bilateral atrophic kidneys with raised echotexture and loss of corticomedullary differentiation which was consistent with chronic renal dysfunction. Other investigations like non-contrast computed tomography (NCCT) head and cerebrospinal fluid examination (CSF) were within normal limits. Urgent hemodialysis was done in view of uremic encephalopathy. Considering skin lesions, toxicological

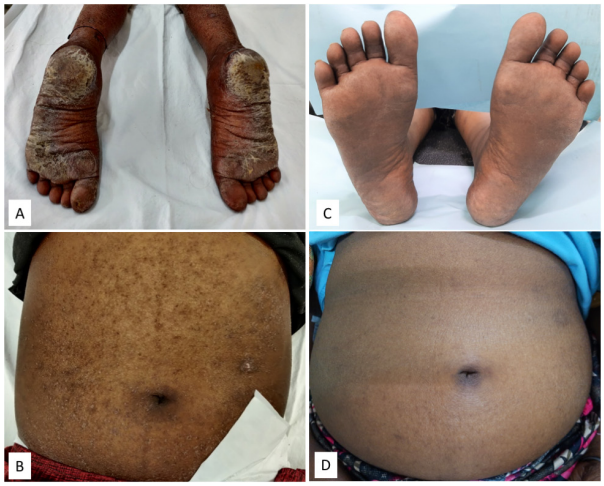

Figure 1. Cutaneous lesions at presentation (A and B) and at follow up after 3 months (C and D). A: Diffuse hyperkeratotic maculopapular lesions over soles; **B**: Multiple discrete hyperpigmented macules and papules in raindrop pattern and papulonodular lesions with atrophic center over the abdomen. **C**: Skin lesions over soles showing resolution at 3 months; **D**: Skin lesions over abdomen showing resolution at 3 months.

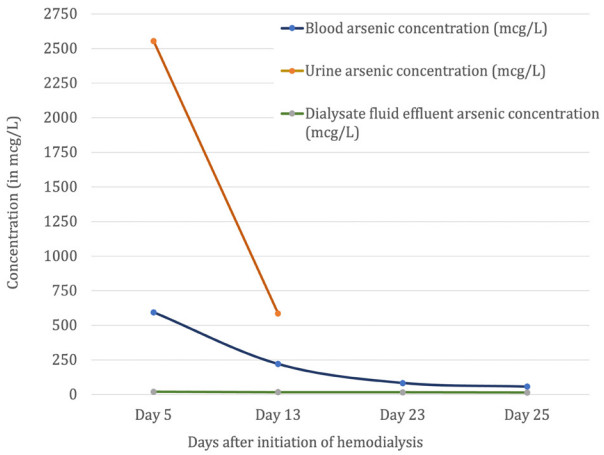

Figure 2. Arsenic concentration in blood, urine and dialysate fluid effluent exhibiting a decreasing trend with regular sessions of hemodialysis.

Table 1. Concentration of arsenic in blood, urine and dialysate fluid effluent

Days after initiation of first hemodialysis	Blood arsenic concentration [in mcg/L]	Urine arsenic concentration [in mcg/L]	Dialysate fluid effluent arsenic concentration [in mcg/L]
Day 5	594 µg/L	2,553 µg/L	20 µg/L
Day 13	220.63 µg/L	585 µg/L	17.125 µg/L
Day 23	83.3 µg/L	-	16.26 µg/L
Day 25	56.7 µg/L	-	14.3 µg/L

Reference range for arsenic is < 62 mcg/L in blood and < 35 mcg/L in urine.

analysis of blood and urine samples for heavy metals was sent which revealed blood arsenic concentration of 594 mcg/L [normal < 62 mcg/L] and urine arsenic concentration of 2,553 mcg/L [normal < 35 mcg/L].

A detailed evaluation was done to find the source of arsenic intoxication: blood, urine, and hair samples of the family members were tested, groundwater sample from home was analyzed, and a detailed history was sought but no environmental/ occupational source of arsenic exposure could be identified. For managing arsenic intoxication, chelating agents were considered. Dimercaptosuccinic acid (DMSA) was relatively contraindicated owing to its unfavorable extracorporeal removal by hemodialysis while British Anti-Lewisite (BAL) had a risk of redistribution to the central nervous system thus exacerbating neurological dysfunction. Lockdown due to Coronavirus disease (COVID-19) pandemic created logistical issues in procuring dimercaptopropanesulfonic acid (DMPS). Consequently, regular hemodialysis was initiated thrice weekly with 4-hour sessions of middle flux hemodialysis (using ELISIO® dialyzer membrane on Fresenius 4008S Dialysis Machine). The patient's arsenic levels decreased progressively (Table 1 and Figure 2) while her sensorium, pancytopenia, and cutaneous lesions improved. She was extubated and discharged on thrice-weekly hemodialysis. At follow-up after 3 months, her skin lesions and overall condition had improved considerably (Figures 1C and 1D).

Arsenic is a metalloid that binds to sulfhydryl groups and interferes with numerous enzyme systems involving cellular respiration, DNA synthesis, and repair. In acute poisoning, gastrointestinal complaints (like vomiting, abdominal pain, and diarrhea), renal injury, acute encephalopathy, and garlic odor in breath are observed. In chronic intoxication, peripheral neurologic and dermatological manifestations are prominent. Chronic arsenic exposure is also associated with the development and progression of chronic kidney disease and various malignancies including skin, lung, kidney, bladder, and prostate (*3-6*).

The characteristic dermatological manifestations like melanosis and hyperkeratosis can provide significant diagnostic clues towards arsenic intoxication. Arsenical hyperkeratosis appears predominantly on palms and soles and is the most sensitive marker for the detection of arsenicosis at an early stage (*7*). In this case, high arsenic levels, altered sensorium, and acute renal failure favored acute intoxication while the presence of dermatological manifestations suggested chronic exposure. An

environmental or occupational source of arsenic exposure couldn't be identified after detailed history and analysis of various samples (including groundwater and those of family members) for arsenic intoxication, probably suggesting that it was homicidal in nature.

In acute intoxication, decontamination and supportive care form the mainstay of therapy along with chelation and hemodialysis when indicated. The available chelating agents include BAL (dimercaprol) and DMPS (both given parenterally), and DMSA (given orally). BAL remains initial agent of choice in patients with reduced consciousness or decreased gastrointestinal motility as it can be given intramuscularly. In the setting of impaired renal excretion in CKD patients, the use of chelators can be deleterious since the arsenic mobilization induced by chelation can lead to aberrant organ deposition, particularly in the central nervous system. In renal failure, DMPS appears to be the treatment of choice because of its favorable properties allowing arsenic clearance during extracorporeal blood purification (*8*). Hemodialysis is also an effective tool in the treatment of arsenic intoxication as it leads to a considerable reduction in blood arsenic levels (*9,10*). One of the studies has also demonstrated the effective role of plasma exchange in the treatment of arsenic poisoning (*11*).

In most published studies, arsenic intoxication has been managed with chelation along with hemodialysis in patients with renal failure (*8*). This is the first case report demonstrating meaningful clinical benefit with hemodialysis alone in patients with renal injury and arsenic intoxication. The improvement in sensorium, the reversal of skin lesions, and pancytopenia show that hemodialysis may be used more than just rescue therapy especially in patients with renal failure. The trend in values of arsenic concentration in dialysate fluid effluent, blood and urine suggest that hemodialysis can be effective as a standalone modality in treating arsenic intoxication when the use of chelators is not possible. It also supports that hemodialysis may be considered upfront in emergency management of patients with arsenic intoxication till the chelating agents are arranged.

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