A Rare Report of Heavy-Metal-Associated Hemodialysis-Dependent Chronic Kidney Disease Secondary to Ayurvedic Medication

Himansu Sekhar Mahapatra¹, Sutanay Bhattacharyya¹ and Vineeta V. Batra²

Abstract

Introduction: Heavy metals are a component of many traditional medications. However, they continue to be used for trivial causes. Chronic heavy metal exposure is an important but under-recognized cause of renal damage. We report to our knowledge the first case of a heavy-metal-associated chronic kidney disease secondary to Ayurvedic medication.

Case Report: A 24-year-old with history of chronic Ayurvedic medication for altered bowel habits presented with neuromuscular symptoms and bilateral lower limb swelling and was found to have hypocalcemia and renal dysfunction. He was initiated on dialysis and underwent an uncomplicated renal biopsy which was suggestive of chronic glomerulosclerosis. In view of significant exposure to Ayurvedic medication, he underwent heavy metal screening in blood, urine, and renal biopsy tissue along with the Ayurvedic medication he had. His blood tested positive for cadmium, copper, and mercury along with same positive results in Ayurvedic medication. He underwent chelation with dimercaprol 250 mg iv for 7 days with blood samples testing negative repeatedly for the same heavy metal that tested positive earlier. However, in view of significant chronicity, he became dialysis dependent and was initiated on twice weekly hemodialysis. His persistent gastrointestinal symptoms were attributed to nonspecific colitis following a computed tomography of the abdomen and colonoscopy with biopsy. He responded to rifaximin and probiotics.

Conclusion: Heavy metal exposure, secondary to chronic Ayurvedic medication intake, is an unrecognized cause of renal dysfunction. The use of such medications for trivial purposes is rampant, especially in developing countries like India. Delaying diagnosis can lead to permanent renal damage with patients eventually becoming dialysis dependent.

Keywords
Ayurvedic medication, heavy metal, chronic kidney disease

Introduction

The use of Ayurvedic medicines is increasing in many areas, particularly developing world. Heavy metals are a major component of many traditional medications including lead, mercury, and arsenic.¹ The ill effects of chronic ingestion of heavy metals are protean. Chronic heavy metal exposure is an important but under-recognized cause of renal damage. The diagnosis is usually made by the finding of unexplained renal dysfunction and the history of exposure to a drug containing the heavy metal. Usually, heavy-metal-induced renal dysfunction is in the form of acute interstitial nephritis. Here, we report to our knowledge the first case of a heavy-metal-associated dialysis-dependent chronic kidney disease, secondary to Ayurvedic medication.

Case Report

A 24-year-old male without any comorbidity had intermittent loose stools for 4 months. He was taken to a local practitioner where he was prescribed Ayurvedic medications, which he took for 3 months. He was evaluated every month by the same practitioner who changed his medications. Although all the medications prescribed were Ayurvedic, his symptoms did not improve. Around 1 month prior to admission he complained of muscle cramps, twitching, and easy fatigability. On evaluation, he was found to have hypocalcemia with corrected calcium of 6.9 mg/dL. He was referred to our hospital in view of the above complaints. His examination showed visible carpopedal spasm, but other signs of hypocalcemia were absent. Reports of other examinations were normal. Post admission he had progressive bilateral lower limb swelling without any shortness of breath,
palpitation, and syncope. Urine examination was bland with subnephrotic proteinuria of 1.8 g/day. Ultrasonography of kidneys showed the size of right kidney as 8.8 cm and that of left kidney size as 9 cm. He was treated with iv calcium with correction of the neuromuscular symptoms. In view of advanced azotemia with volume overload, he was initiated on hemodialysis via double lumen jugular catheter on right side of neck. After 2 sessions of hemodialysis, he underwent an uncomplicated renal biopsy. Because he had a long duration of intake of indigenous medication intake, blood, urine, and renal tissue samples were sent for heavy metal screening. The Ayurvedic medications that the patient was taking were also sent for screening of heavy metals. Trace metals were assessed using the technique of inductivity coupled plasma mass spectroscopy (ICP-MS) based on the method of Association of Official Analytical Chemist 2015 (AOAC 015). Blood samples and the Ayurvedic medications tested positive for cadmium, copper, and mercury, with the highest concentration of heavy metal being mercury, both in blood and the medications (Tables 1 to 4). Urine and tissue samples were negative for heavy metal. He was treated with a chelating agent dimercaprol 250 mg iv od for 7 days and repeat samples were sent for heavy metal screening. Blood samples were negative for heavy metals which were previously positive. However, his renal dysfunction was persistent and renal biopsy report showed chronic glomerulosclerosis on light microscopy with no immunofluorescence deposits and normal electron microscopy findings (Figures 1 and 2). He became dialysis dependent and arteriovenous fistula was created for further dialysis vascular access. Regarding his symptoms of diarrhea, he underwent computed tomography of the abdomen, which showed lead pipe colon. Subsequently, he underwent colonoscopy with biopsy. Colonoscopy showed mild erythema in the ascending colon, and biopsy showed features of mild infiltration of mononuclear cells in lamina propria. In view of nonspecific colitis, he started taking probiotics and rifaximin 550 mg BD. His symptoms improved. He is now on maintenance hemodialysis, thrice weekly, and is planning for renal transplant.

Discussion

Ayurvedic medicines consist of herbs that are often intentionally combined with metals, such as lead, mercury, iron, and zinc, because of the belief that these metals contribute to their therapeutic effect. Approximately 20% of the Ayurvedic supplements contain potentially toxic concentrations of several heavy metals. Results of a World Health Organization survey indicated that about 70% to 80% of the world populations rely on nonallopathic or traditional medicines, mainly of herbal sources, in their health care. This widespread use of herbal medications, combined with the fact that many cases of heavy metal toxicity may not be recognized clinically, makes the contamination of such herbal medication with metals and other toxicants a serious global public health concern. The kidney is an organ susceptible to heavy metal poisoning that can occur acutely or because of chronic exposure.

The exact cellular processes underlying the metal-induced nephrotoxicity are not yet fully understood. Growing attention is directed toward the effect of metals on the oxidative status of cells and the production of reactive oxygen species as well as their effect on cellular antioxidant defenses such as superoxide dismutase and glutathione peroxidase. Oxidative stress can cause disruption of cellular macromolecules such as DNA, proteins, and lipids.

The most common renal lesions include acute tubular necrosis, cortical necrosis, and interstitial nephritis. Both acute and chronic exposure to heavy metals can cause tubulointerstitial injuries without any obvious morphological changes, and they can occur within days of exposure to the offending drug.

In the literature, heavy-metal-induced acute interstitial nephritis has been reported with a resolution of symptoms after the removal of exposure. However, to the best of our knowledge there has been no reports showing dimercaprol as a chelating agent to copper, cadmium, and mercury.

![Figure 1. Light Microscopy of Renal Biopsy—Showing Sclerosis of Glomerulus (Arrows) (PAS; X40).](image1.png)

![Figure 2. Light Microscopy of Renal Biopsy—Showing Interstitial Fibrosis in Striped Pattern (Arrows) (JMS; X10).](image2.png)

Abbreviations: PAS, periodic acid schiff stain; JMS, Jones methenamine silver stain.
Table 1. Table Showing Heavy Metals in Blood.

| S. No. | Name of Heavy Metals | Method of Test Used | Technique | Results |
|--------|----------------------|---------------------|-----------|---------|
| 1      | Copper (ppm)         | AOAC 2015.01        | ICP-MS    | 1398.32 (LOQ: 6.0 ppm) |
| 2      | Arsenic (ppm)        | AOAC 2015.01        | ICP-MS    | BQL (LOQ: 0.22 ppm) |
| 3      | Cadmium (ppm)        | AOAC 2015.01        | ICP-MS    | 5.49 (LOQ: 0.3 ppm) |
| 4      | Mercury (ppm)        | AOAC 2015.01        | ICP-MS    | 15531.31 (LOQ: 0.2 ppm) |
| 5      | Lead (ppm)           | AOAC 2015.01        | ICP-MS    | BQL (LOQ: 0.5 ppm) |

Available Literature

- Increased level of copper in the erythrocytes showed a correlation with increasing severity of renal failure\(^7\)
- Not available
- Oxidative stress induced renal damage\(^8\)
- Most common presentation: Nephrotic syndrome\(^9\)
- Chronic lead nephrotoxicity consists of interstitial fibrosis and progressive nephron loss\(^10\)

Abbreviations: ICP-MS, inductivity coupled plasma mass spectroscopy; AOAC, association of official analytical chemist; PPM, parts per million; LOQ, limit of quantification; BQL, below quantification limit.

Table 2. Heavy Metals in Agnitundivati (Ayurvedic Medication).

| S. No. | Name of Heavy Metals | Method of Test Used | Technique | Result |
|--------|----------------------|---------------------|-----------|--------|
| 1      | Copper (ppm)         | AOAC 2015.01        | ICP-MS    | 140.15 (LOQ: 6.0 ppm) |
| 2      | Arsenic (ppm)        | AOAC 2015.01        | ICP-MS    | 372.73 (LOQ: 0.22 ppm) |
| 3      | Cadmium (ppm)        | AOAC 2015.01        | ICP-MS    | BQL (LOQ: 0.3 ppm) |
| 4      | Mercury (ppm)        | AOAC 2015.01        | ICP-MS    | 36059.3 (LOQ: 0.2 ppm) |
| 5      | Lead (ppm)           | AOAC 2015.01        | ICP-MS    | 1.45 (LOQ: 0.5 ppm) |

Abbreviations: ICP-MS, inductivity coupled plasma mass spectroscopy; AOAC, association of official analytical chemist; PPM, parts per million; LOQ, limit of quantification; BQL, below quantification limit.

Table 3. Heavy Metals in Navayaslauha (Ayurvedic Medication).

| S. No. | Name of Heavy Metals | Method of Test Used | Technique | Result |
|--------|----------------------|---------------------|-----------|--------|
| 1      | Copper (ppm)         | AOAC 2015.01        | ICP-MS    | 91.77 (LOQ: 6.0 ppm) |
| 2      | Arsenic (ppm)        | AOAC 2015.01        | ICP-MS    | 6.44 (LOQ: 0.22 ppm) |
| 3      | Cadmium (ppm)        | AOAC 2015.01        | ICP-MS    | BQL (LOQ: 0.3 ppm) |
| 4      | Mercury (ppm)        | AOAC 2015.01        | ICP-MS    | 34.66 (LOQ: 0.2 ppm) |
| 5      | Lead (ppm)           | AOAC 2015.01        | ICP-MS    | 9.18 (LOQ: 0.5 ppm) |

Abbreviations: ICP-MS, inductivity coupled plasma mass spectroscopy; AOAC, association of official analytical chemist; PPM, parts per million; LOQ, limit of quantification; BQL, below quantification limit.

Table 4. Heavy Metals in Krimimudgar Rasa (Ayurvedic Medication).

| S. No. | Name of Heavy Metals | Method of Test Used | Technique | Result |
|--------|----------------------|---------------------|-----------|--------|
| 1      | Copper (ppm)         | AOAC 2015.01        | ICP-MS    | 19.10 (LOQ: 6.0 ppm) |
| 2      | Arsenic (ppm)        | AOAC 2015.01        | ICP-MS    | 3.18 (LOQ: 0.22 ppm) |
| 3      | Cadmium (ppm)        | AOAC 2015.01        | ICP-MS    | BQL (LOQ: 0.3 ppm) |
| 4      | Mercury (ppm)        | AOAC 2015.01        | ICP-MS    | 53123.91 (LOQ: 0.2 ppm) |
| 5      | Lead (ppm)           | AOAC 2015.01        | ICP-MS    | 3.41 (LOQ: 0.5 ppm) |

Abbreviations: ICP-MS, inductivity coupled plasma mass spectroscopy; AOAC, association of official analytical chemist; PPM, parts per million; LOQ, limit of quantification; BQL, below quantification limit.
Although the repeat blood reports showed absent heavy metals reported prior to chelation, his renal dysfunction remained persistent, and he became dialysis dependent. One of the limitation is the fact that there was an absence of heavy metal deposits in renal biopsy tissue, which fails to establish a clear cause effect. However, in the absence of other risk factors for renal dysfunction, and the temporal association of medication intake and development of renal dysfunction, it is fair to say that the etiology of chronic kidney disease in this patient is secondary to heavy metal components in Ayurvedic medication.

**Conclusion**

Practitioners providing services to populations using nonconventional medicines, especially in developing countries like India, should have a high index of suspicion of metal toxicity when confronted with one or more known adverse effects of metal ingestion. These heavy metals have significant nephrotoxicity, and delaying diagnosis with increasing cumulative exposure to such medications might lead to permanent renal damage, requiring long-term dialysis.

**Declaration of Conflicting Interests**

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

**Funding**

The authors received no financial support for the research, authorship, and/or publication of this article.

**ORCID iD**

Sutanay Bhattacharyya [https://orcid.org/0000-0001-9062-1035](https://orcid.org/0000-0001-9062-1035)

**References**

1. Dargan P, Gawarammana IB, Archer J, House IM, Shaw D, Wood D. Heavy metal poisoning from ayurvedic traditional medicines: an emerging problem? *Int J Environ Health*. 2008;2:463-474.
2. Saper RB, Phillips RS, Sehgal A, et al. Lead, mercury, and arsenic in US- and Indian-manufactured ayurvedic medicines sold via the internet. *JAMA*. 2008;300:915-923.
3. Saper RB, Kales SN, Paquin J, et al. Heavy metal content of ayurvedic herbal medicine products. *JAMA*. 2004;292:2868-2873.
4. Raviraja A, Vishal Babu GN, Sehgal A, et al. Three cases of lead toxicity associated with consumption of ayurvedic medicines. *Indian J Clin Biochem*. 2010;25:326-329.
5. Johri N, Jacquillet G, Unwin R. Heavy metal poisoning: the effects of cadmium on the kidney. *Biometals*. 2010;23:783-792.
6. Moorby S, Samuel AE, Moideen F, Peringat J. Interstitial nephritis presenting as acute kidney injury following ingestion of alternative medicine containing lead: a case report. *Adv J Emerg Med*. 2018;3:e8. doi: 10.22114/AJEM.v0i0.100.
7. Avasthi G, Singh HP, Katyal JC, Avasthi R, Aggarwal SP. Copper, zinc, calcium and magnesium in chronic renal failure. *J Assoc Physicians India*. 1991;39:531-534.
8. Eom SY, Yim DH, Huang M, et al. Copper–zinc imbalance induces kidney tubule damage and oxidative stress in a population exposed to chronic environmental cadmium. *Int Arch Occup Environ Health*. 2020;93:337-344.
9. Gao Zhennan, Wu Na, Du Xuqin, Li Huiling, Mei Xue, Song. Yuguo Toxic nephropathy secondary to chronic mercury poisoning: clinical characteristics and outcomes. *Kidney Int Rep*. 2022; doi: https://doi.org/10.1016/j.ekir.2022.03.009.
10. Goyer RA. Mechanisms of lead and cadmium nephrotoxicity. *Toxicol Lett*. 1989;46:153-162.