The Journal of the International Federation of Clinical Chemistry and Laboratory Medicine

eJIFCC

Broadening the list of differential diagnosis for acute abdomen – a case report from Nepal

Vivek Pant[1], Keyoor Gautam[2], Devish Pyakurel[2], Aabha Shrestha[2], Santosh Pradhan[1], Neeraj Joshi[3]

[1] *Biochemistry, Department of Clinical Biochemistry, Samyak Diagnostic, Jawalakhel, Lalitpur, Nepal*

[2] *Pathology, Department of Pathology, Samyak Diagnostic, Jawalakhel, Lalitpur, Nepal*

[3] *Department of Internal Medicine, Nidan Hospital, Pulchowk, Lalitpur, Nepal*

ARTICLE INFO

Corresponding author:
Vivek Pant, MD
Department of Clinical Biochemistry
Samyak Diagnostic, Jawalakhel
P.O.Box: 11708, Lalitpur
Nepal
E-mail: drvpant@gmail.com

Key words:
ayurvedic medicine, lead toxicity, acute abdomen, blood lead level

ABSTRACT

When a patient has an acute abdominal pain, it is important to identify if the underlying cause is life threatening. To that end, a thorough medical history and relevant investigation will be pivotal. Here we report a case of lead toxicity where the patient presented with an acute abdomen following intake of Ayurvedic medicines. The baseline blood lead level was 82.3 µg/dl. The Ayurvedic medicines when analyzed for its lead content, revealed high lead concentration. We observed that the cessation of Ayurvedic medication along with D-penicillamine therapy was beneficial in reducing the blood lead level and in alleviating abdominal pain. Our findings implicate the need of awareness program regarding the potential health hazards associated with the use Ayurvedic medicines.

INTRODUCTION

Lead poisoning has been recognized as a major public health problem, particularly in developing nations like Nepal. (1) Air, dust, soil, paints, cosmetics, dietary and herbal supplements, and soiled parental work clothing are potential sources of exposure to lead. Lead can have a wide range of biological effects depending on the level and duration of exposure, including effects on heme synthesis, the central nervous system, kidneys, alimentary tract, and other organs. (2) The effect is mediated through increased oxidative stress, ionic mechanisms, and apoptosis. (3)

Lead colic is a rare cause of abdominal pain. (4) The diagnosis is most often reached in a context of professional exposure or in populations at risk of contact with lead. Due to previously reported cases of lead colic in Ayurvedic medicine user, this cause is important to be considered in abdominal pain of unknown origin. (5, 6)

Products used in Ayurvedic medicine contain herbs, metals, minerals, or other materials that may be harmful if used improperly or without the direction of a trained practitioner. Doses of metals in Ayurvedic medicine in practice are based on recommendations given in ancient Ayurvedic texts. Nearly half of the medicines used in the Ayurvedic formulary intentionally contain at least one metal to enhance potency of the drug. (7) The addition of lead is believed to have fungicidal properties and improve shelf-life of the medicine. These medicines can have drug interaction with the allopathic medicine.

Nepalese people have a growing fascination with natural remedies and traditional medicines. (8) Practitioners of Ayurveda in Nepal undergo recognized institutional education and training and are licensed by the government body. Though traditional medicines have been used in Nepal, there is little quality control or trials. Some unscrupulous drug manufacturers mix allopathic medicines in Ayurvedic drugs, usually steroids and since the patient feels temporary relief; he ascribes it to the Ayurvedic medicine. (9) Uncontrolled use of herbs, use of heavy metals, lack of quality control and adding steroids damages the quality of Ayurvedic medicine. (9) In Nepal, patient with chronic diseases like arthritis, asthma, hemorrhoids, insomnia, autoimmune diseases and skin diseases have more tendency to use ayurvedic medicines. Acute clinical presentation in patients using Ayurvedic medicine adulterated with heavy metal like gold and alkaloids has been reported from Nepal previously. (10) To the best of our knowledge, acute clinical manifestation due to lead toxicity after consumption of Ayurvedic medicine has not been reported from Nepal earlier.

CLINICAL DIAGNOSTIC CASE

A 38-year-old man presented to a gastroenterologist with a one month history of progressive epigastric pain without radiation. The pain had increased in intensity in the last two days. He reported dark and hard stool, decreased appetite, tiredness, and nausea. He did not have any significant medical or surgical history. However, he had been taking Ayurvedic medication for three months to increase his sperm count, which was prescribed to him by a licensed Ayurvedic practitioner in Kathmandu. He is in the army by profession. He consumed alcohol occasionally and was a non-smoker.

His vital signs were stable. On physical examination, no signs of peritonitis were observed. Physical examination was remarkable for abdominal tenderness in the epigastric area. Testicular examination and per rectal examination were normal.

Laboratory evaluation revealed a hemoglobin level of 9.7 g/dL (Reference range - 13.5 – 16.9 gm %) with a mean corpuscular volume (MCV)

of 87.1 fL (Reference range - 81.8 – 95.5 fL) and a reticulocyte count of 3.8% (Reference range - 0.5 – 2%). Hemoglobin and MCV were measured using the Sysmex automated hematology analyzer XN 330 (Sysmex, Milton Keynes, UK). Reticulocyte count was measured by microscopy. The liver, pancreas and kidney function tests were normal except for a mild increase in transaminase level. Imaging included a CT scan and an abdominal ultrasound, neither of which revealed any abnormalities. In addition, an upper gastrointestinal endoscopy and colonoscopy revealed no abnormalities either.

The serum iron chemistry, antinuclear antibody screening, vitamin B12, folate and thyroid-stimulating hormone were in normal range. His peripheral blood smear showed anisocytosis with normochromia. There was no evidence of hemolysis. The hemoglobin electrophoresis was normal too. Subsequently, blood lead level (BLL) was measured and the result showed an elevated level of lead at 82.3 µg/dL (normal <10 µg/dL). Measurement of BLL was performed using the Lead Care II instrument (Magellan Diagnostics Inc., N. Billerica, Massachusetts, USA) based on the principle of anodic stripping voltametry. The zinc protoporphyrin level was 310 mg/dL (normal <40 mg/dL) and was measured using hematofluorometer (Helena Laboratories, Beaumont, Texas, USA).

The patient's history showed no other potential sources of lead exposure than the intake of Ayurvedic medicine. He lived in a modern house. None of his family members had similar symptoms. He is an army by profession and he reported that he performs most of his work using gloves and protective clothing in order to minimize exposure if any.

Extracts from the seven Ayurvedic medicines that the patient was using, were evaluated

Table 1 Lead level in the Ayurvedic drugs the index patient was using

Name of Ayurvedic drug	Lead concentration (In parts per million)
Prawal Pishti	11.18
Siddha Makara Dhvaja Guti	102.53
Chankrashekhar ras	12.89
Shatawari Granules	4.53
Musli pak (Laghu)	11.54
Vanari	13.74
Vanga Bhasma	209.70

Note: *Prescribed limit of lead in Ayurvedic medicine is less than 10 ppm (22).*

using an atomic absorption spectrophotometer. The test showed a high concentration of lead in six out of the seven medicines. (Table 1)

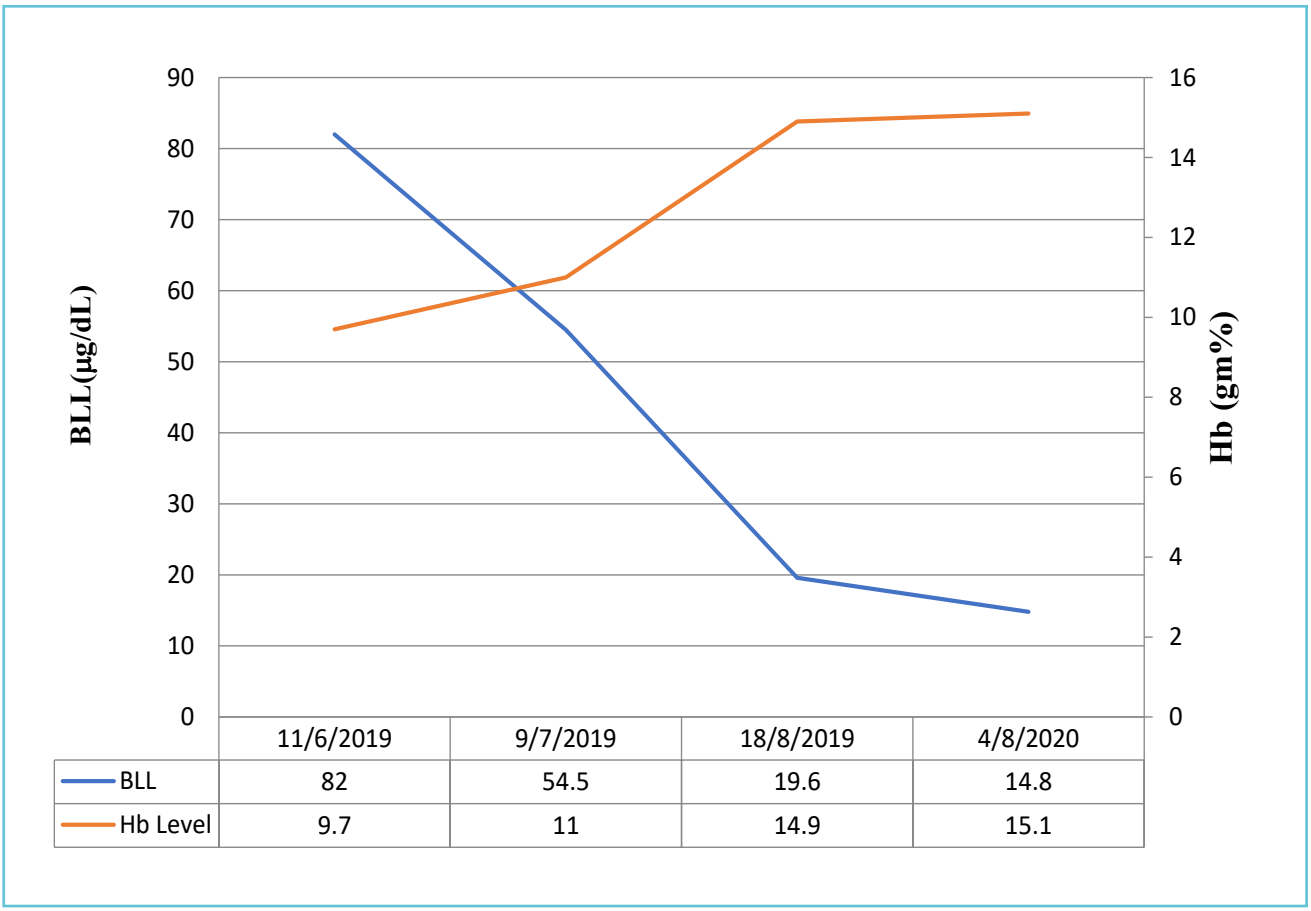
Patient was managed on outpatient basis. He was prescribed with D-Penicillamine 250 mg one hour before meal, initially once a day for one month then twice a day for another two months and thrice a day for the fourth month. Patient's BLL alleviated over time (Figure 1). His symptoms were resolved after 2 weeks of treatment.

DISCUSSION

Acute lead toxicity that results from short-term, high dose lead absorption causes normocytic or microcytic anemia, abdominal pain and constipation, arthralgias and myalgias, and central nervous system impairment including headache, mood disorder and encephalopathy. (11) Our patient manifested many of the known signs and symptoms of acute lead toxicity, including abdominal pain, constipation, anemia and abnormal liver enzymes.

The exact pathogenesis of lead induced abdominal colic is unknown. However, proposed mechanisms include alterations in the visceral smooth muscle tone due to action of lead on visceral autonomic nervous system, changes in the sodium transport in small intestinal mucosa, porphyrinopathy and lead induced interstitial pancreatitis. (12, 13) Abnormal liver enzyme is possible due to the depletion of the antioxidants savings of the cells in acute lead toxicity. (14) Lead interferes with a variety of heme

Figure 1 Patient blood lead level (BLL) versus hemoglobin (Hb) trended over time



	11/6/2019	9/7/2019	18/8/2019	4/8/2020
BLL	82	54.5	19.6	14.8
Hb Level	9.7	11	14.9	15.1

biosynthetic enzymes, including delta-aminolevulinic acid that conjugates levulinic acid to form porphobilinogen and ferrochelatase which incorporates ferrous iron into protoporphyrin IX ring. This results in anemia, hypersideraemia, reticulocytosis and basophilic stippling, due to the persistence of cytoplasmic proteins. (15, 16) Basophilic stippling of erythrocytes is typical but not specific for lead poisoning. (15, 17) In our patient, the basophilic stippling was not seen.

Several cases of lead intoxication associated with Ayurvedic medicines have been reported worldwide. (18 -21) Patients taking these medicines are often overlooked and are usually not evaluated for lead exposure until serious manifestations have occurred. Clinical practitioner in geographical area with Ayurvedic medication users should have a high index of suspicion of lead toxicity among persons with characteristic signs and symptoms in the absence of occupational exposure.

The World Health Organization has prescribed a limit for lead contents in herbal medicine at 10 ppm. (22) Six Ayurvedic medicine out of seven, that patient was using had higher lead concentration. (Table 1) The Vanga Bhasma named Ayurvedic medicine which the index case was using contained the highest amount of lead (209.70 ppm) out of these six Ayurvedic medicines, when analyzed through atomic absorption spectrophotometer. The lead concentration in all seven Ayurvedic medicines is shown in Table 1. Heavy metals are commonly incorporated into Ayurvedic preparations as ashes or bhasmas. Experts in this field claim that role of bhasmas is to enhance the herbal products potency via facilitating the entry into the relevant cells and if adequately prepared are safe for administration. Use of bhasmas in Ayurvedic medicine leading to lead toxicity has been reported previously. (23, 24)

In adults, the decision to use chelation therapy is ultimately clinical but may be guided by the BLL. The two chelating agents most commonly used to treat adults are oral succimer [meso-2, 3-dimercaptosuccinic acid (DMSA)] and edetate calcium disodium (CaEDTA). (25) D-penicillamine was used in our patient since this is the only available treatment option in Nepal.

The pace of improvement may be highly variable, ranging from weeks to years, depending on the magnitude of intoxication. (26) It has been found that chelation therapy reduces blood lead concentrations acutely, but the levels rebound within weeks to months after treatment due to redistribution from bone, requiring repeated courses of treatment. Our patient recovered quickly and the BLL decreased linearly. The acute high dose intake of Ayurvedic medicine in our patient might be the cause for diminished lead distribution to the bone and linear decrease in BLL. However, our patient is advised for an annual blood lead and zinc protoporphyrin level examination and, avoidance of exposure to lead by preventing use of improperly prepared contaminated Ayurvedic drugs.

LEARNING POINTS

- The adulterated Ayurvedic medicine due to its easy availability and lack of focused scientific research has potential to cause more cases of lead toxicity.
- Clinicians should consider lead toxicity secondary to Ayurvedic medicine intake in their differential diagnoses of anemia, with abdominal pain.
- Health risks posed by the Ayurvedic medicine should be discussed among healthcare providers and awareness should be increased among general public.

❖❖❖❖❖

Consent

Written informed consent was obtained from the patient for publication of this case report.

Acknowledgement

We appreciate the kindness and technical help from Mr. Ram Charitra Shah and Mr. Sunil Babu Khatri.

Author contributions

VP conceptualized and designed the study. This manuscript is written by VP. Data collection and laboratory analysis was performed by SP and AS. NJ was the physician involved in patient management. KG, DP and NJ revised and approved the final version of this manuscript.

❖❖❖❖❖

REFERENCES

1. Gautam K, Pant V, Pradhan S, Pyakurel D, Bhandari B, Shrestha A. Blood lead levels in rag-pickers of Kathmandu and its association with hematological and biochemical parameters. EJIFCC. 2020 Jun; 31(2):125.

2. Papanikolaou NC, Hatzidaki EG, Belivanis S, Tzanakakis GN, Tsatsakis AM. Lead toxicity update. A brief review. Medical science monitor. 2005 Oct 1; 11(10):RA329-36.

3. Sakai T. Biomarkers of lead exposure. Industrial health. 2000; 38(2):127-42.

4. Van Vonderen MG, Klinkenberg-Knol EC, Craanen ME, Touw DJ, Meuwissen SG, De Smet PA. Severe gastrointestinal symptoms due to lead poisoning from Indian traditional medicine. The American journal of gastroenterology. 2000 Jun 1; 95(6):1591.

5. Raviraja A, Babu GV, Sehgal A, Saper RB, Jayawardene I, Amarasiriwardena CJ, Venkatesh T. Three cases of lead toxicity associated with consumption of ayurvedic medicines. Indian Journal of Clinical Biochemistry. 2010 Jul 1; 25(3):326-9.

6. Sood A, Midha V, Sood N. Pain in abdomen--do not forget lead poisoning. Indian journal of gastroenterology: official journal of the Indian Society of Gastroenterology. 2002; 21(6):225-6.

7. Gogtay NJ, Bhatt HA, Dalvi SS, Kshirsagar NA. The use and safety of non-allopathic Indian medicines. Drug safety. 2002 Dec 1; 25(14):1005-19.

8. Kafle G, Bhattarai I, Shrestha AK, Siwakoti M. Why do patients choose to consume Ayurvedic Medicines in Nepal? An exploratory study. International Journal of Ayurvedic Medicine. 2018 Oct 1; 9(4):250-7.

9. Ernst E. Toxic heavy metals and undeclared drugs in Asian herbal medicines. Trends in pharmacological sciences. 2002 Mar 1; 23(3):136-9.

10. Paudyal B, Thapa A, Sigdel KR, Adhikari S, Basnyat B. Adverse events with ayurvedic medicines-possible adulteration and some inherent toxicities. Wellcome Open Research. 2019; 4.

11. Centers for Disease Control and Prevention (CDC). Adult blood lead epidemiology and surveillance--United States, 2008-2009. MMWR. Morbidity and mortality weekly report. 2011 Jul 1; 60(25):841.

12. Karmakar N, Anand S. Study of the inhibitory effect of lead acetate on duodenal contractility in rat. Clinical and experimental pharmacology and physiology. 1989 Sep; 16(9):745-50.

13. Yoshinari O, Makoto K. An association between increased porphyrin precursors and onset of abdominal symptoms in lead poisoning. Toxicology letters. 1984 May 1; 21(2):219-23.

14. Matović V, Buha A, Đukić-Ćosić D, Bulat Z. Insight into the oxidative stress induced by lead and/or cadmium in blood, liver and kidneys. Food and Chemical Toxicology. 2015 Apr 1; 78:130-40.

15. Albahary C. Lead and hemopoiesis: the mechanism and consequences of the erythropathy of occupational lead poisoning. The American journal of medicine. 1972 Mar 1; 52(3):367-78.

16. Menezes G, D'souza HS, Venkatesh T. Chronic lead poisoning in an adult battery worker. Occupational Medicine. 2003 Oct 1; 53(7):476-8.

17. JENSEN WN, MORENO GD, BESSIS MC. An electron microscopic description of basophilic stippling in red cells. Blood. 1965 Jun; 25(6):933-43.

18. Ernst E. Heavy metals in traditional Indian remedies. European journal of clinical pharmacology. 2002 Feb 1; 57(12):891-6.

19. Centers for Disease Control and Prevention (CDC). Lead poisoning associated with ayurvedic medications–five states, 2000–2003. MMWR Morb Mortal Wkly Rep. 2004; 53:582–584.

20. Muzi G, Dell'Omo M, Murgia N, Curina AN, Ciabatta SI, Abbritti G. Lead poisoning caused by Indian

ethnic remedies in Italy. La Medicina del lavoro. 2005; 96(2):126.

21. Gunturu KS, Nagarajan P, McPhedran P, et al. Ayurvedic herbal medicine and lead poisoning. J Hematol Oncol. 2011; 4:51.

22. World Health Organization. Quality control methods for medicinal plant materials. World Health Organization; 1998.

23. Raviraja A, Babu GV, Sehgal A, Saper RB, Jayawardene I, Amarasiriwardena CJ, Venkatesh T. Three cases of lead toxicity associated with consumption of ayurvedic medicines. Indian Journal of Clinical Biochemistry. 2010 Jul 1; 25(3):326-9.

24. Mehta V, Midha V, Mahajan R, Narang V, Wander P, Sood R, Sood A. Lead intoxication due to ayurvedic medications as a cause of abdominal pain in adults. Clinical Toxicology. 2017 Feb 7; 55(2):97-101.

25. Porru S, Alessio L. The use of chelating agents in occupational lead poisoning. Occupational Medicine. 1996 Feb 1; 46(1):41-8.

26. Kosnett MJ, Wedeen RP, Rothenberg SJ, Hipkins KL, Materna BL, Schwartz BS, Hu H, Woolf A. Recommendations for medical management of adult lead exposure. Environmental health perspectives. 2007 Mar; 115(3): 463-71.