CASE REPORT

Case of acute lead toxicity associated with Ayurvedic supplements

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SUMMARY

Use of traditional folkloric remedies not disclosed to the physician may be difficult to identify as a source of lead toxicity. This report illustrates the presentation of a 26-year-old man who, during his 1 month vacation in India, was treated for low back pain with Ayurvedic herbal medicine. On his return to the USA, he presented to the emergency department with epigastric pain, weight loss, dark stools, nausea and vomiting. He was admitted and noted to be anaemic with a blood lead level (BLL) of 94.8 µg/dL. Peripheral blood smear demonstrated basophilic stippling. Chelation therapy with succimer was initiated. The patient became asymptomatic within months. Three years later, he remained asymptomatic with BLL <20 µg/dL. Physicians should be cognisant of potential toxicity from these Ayurvedic medications and have a heightened level of suspicion for lead toxicity in the face of anaemia and abdominal pain without obvious cause.

BACKGROUND

Lead intoxication in adults without occupational exposure is rare, accounting for <5% of elevated blood lead levels (BLL) in the USA.¹ Since the symptoms of lead toxicity are vague and non-specific, the diagnosis can be difficult to make unless there is a high index of clinical suspicion. Complementary and alternative medications, in particular Ayurvedic herbal medications, have been implicated in multiple cases of lead poisoning in India,^{2–3} the USA^{4–8} and internationally.^{9–17}

Ayurvedic herbal medicine is a traditional system that originated more than 2000 years ago in India. Ayurvedic philosophy describes a unifying theory linking the universe with all living and non-living matter.¹⁸ Approximately 80% of India's population uses Ayurveda. In Ayurveda, Rasashastra is a subdivision that deals with the study of metal and mineral. Metals, such as mercury, lead and arsenic, are used as adjuvants to the primary herbal therapy for many chronic illnesses including rheumatoid arthritis, epilepsy, insomnia and asthma. Metals are believed to exert their own therapeutic effect, enhance the potency of other medications and facilitate drug delivery to target site. Some of the indications for therapeutic Ayurvedic use of lead include treatment of diabetes and worms. It is also used as an aphrodisiac. Doses of metals used in practice are based on recommendations given in ancient Ayurvedic texts. It is estimated that roughly 35–40% of the ~6000 medicines in the Ayurvedic formulary intentionally contain at least one metal.¹⁹ For allopathic physicians who encounter

patients taking Ayurvedic herbal medicine, it can be difficult to understand and estimate the contents of these highly variable formulations.

Saper *et al* concluded that 20% of Ayurvedic herbal medicine products produced in South Asia and available in specialty stores in the Boston area had potentially toxic levels of lead, mercury and/or arsenic. Using X-ray fluorescence spectroscopy, the authors estimated a median concentration of 40 µg/g and a range of 5–37 000 µg/g of lead—far above the recommended maximum allowable lead content of 4 µg.²⁰

The following case presentation of acute lead toxicity associated with Ayurvedic herbal medicine is intended to highlight the signs and symptoms as well as outline management of lead toxicity.

CASE PRESENTATION

A 26-year-old man presented to the student health services with a 4-day history of progressive epigastric pain without radiation. He had noted 2 weeks of dark coloured stools, decreased appetite, weight loss and 1 day of nausea associated with an episode of blood-streaked emesis. He denied any significant medical history and had never had surgery. The student had travelled to India on a family visit ~3 months prior and during this trip he took Ayurvedic herbal medications to treat his low back pain. On returning from his trip to India, he began to use the herbal medications regularly. His occupational history was remarkable for his being a graduate student working in the area of Materials Science. His exposures in the laboratory included cadmium, alcohols and silicone. He reported that he performed most of his work under a hood and wore gloves in order to minimise any exposure.

INVESTIGATIONS

On initial presentation to the student health services, the patient was referred to the emergency room. His vital signs were stable. On physical examination, there were no signs of peritonitis and no neurological deficits or symptoms. Physical examination was remarkable for abdominal tenderness, especially in the epigastric area, with no rebound and no guarding. Laboratory evaluation revealed a haemoglobin level of 9.4 µg/dL with a mean corpuscular volume of 87 fL and a reticulocyte count of 3.8%. The total and indirect bilirubin and transaminases were mildly elevated. Imaging included a CT scan and an abdominal ultrasound, neither of which revealed any abnormalities. Given his blood-streaked emesis and anaemia, and in absence of another diagnosis to explain his severe

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abdominal pain and weakness, he was treated with an intravenous proton pump inhibitor. An upper endoscopy performed the following day was unrevealing. He was administered morphine and ibuprofen as needed. His abdominal pain improved over the following 2 days. Haemoglobin remained stable throughout the hospitalisation. His dark coloured stools and mildly abnormal liver function tests resolved over the course of his hospital stay. The blood-streaked emesis was thought to be from violent

Figure 1 Photo of Ayurvedic herbal medication used by patient.

Table 1 Ayurvedic herbal medication regimen per patient

Ayurvedic herbal medication	Ingredients	Frequency
Rheumo tablet	Extract of maharasnadi, salaki, mahayugaraj, sinhanad, suranjan, purified kuchla, purified vats sanabh, Samir pannag, kumum	2 tablets TID
Tryo Dashang Guggul	Garlic, ashwagandh, hawbaar, giloy, shatavri, gokharo, vidhara, ransa, fennel seed, kachoor, thymol seeds or carom with purified tryo dashang guggul	2 tablets BID
Rasnadi Guggul	Garlic, Indian gooseberry, dry ginger, pepal, black pepper, pipplamool	2–3 tablets, TID
Sutashek Hara	Copper oxide of borax, gold oxide of pearl, trikatu, chaturjata	2 tablets, BID

BID, two times a day; TID, three times a day.

retching, and did not recur subsequent to his first presentation. He was discharged after a 2-day hospital stay, on morphine as needed for pain, and on omeprazole and ondansetron, for nausea and vomiting. He was instructed to follow-up with a haematologist, gastroenterologist and primary care physician. On discharge, the patient was advised to discontinue use of his four different types of Ayurvedic medications, (figure 1 and table 1) which he did, as it was felt that they might be contributing to his symptoms.

Further work up as an outpatient included iron studies, vitamin B₁₂, folate and thyroid-stimulating hormone, all of which returned within normal limits. His peripheral blood smear, however, demonstrated basophilic stippling (figure 2) with normocytic red blood cells and no evidence of haemolysis. A BLL was subsequently performed and found to be 94.8 µg/dL (normal <10 µg/dL). The zinc protoporphyrin level (ZPP) was >350 µg/dL (normal <40 µg/dL) and a 24-hour urine assessment for cadmium revealed no elevation.

Extracts from these Ayurvedic supplements were evaluated with spectroscopy and a peak with lead was found. These analyses were limited as the results were reported as heterogeneous substances with no concentration determination of elements present in the pills.

DIFFERENTIAL DIAGNOSIS

On the basis of history, no other source of lead exposure was evident for this patient. He lived in a 19th century building without peeling paint. None of his neighbours had similar

Figure 2 Patient's peripheral blood smear demonstrating basophilic stippling.

Table 2 Selected patient laboratory values over the course of treatment

~ Weeks since first BLL	Days since first BLL	Hb (13.5–17.5 g/dL)	Blood lead level (<10 µg/dL)	ZPP (<40 µg/dL)
1	0	9.1	94.8	>350
	Treatment with succimer: round I			
	3	9.2	82.3	–
3	18	12	50.4	–
4	31	13.9	50.6	373
6	40	13.9	54.7	–
	Treatment with succimer: round II			
7	49	14.3	22.5	–
11	74	WNL	27.5	–
13	94	WNL	30.2	–
16	115	WNL	32.6	–
	Treatment with succimer: round III			
20	139	WNL	8.7	43
26	181	WNL	25	–
29	206	WNL	25.6	27
	Treatment with succimer: round IV			
35	243	WNL	15.8	27
46	322	WNL	22.6	20
56	390	WNL	23.2	23
69	480	WNL	18.8	25
83	584	WNL	22.1	29
123	858	14.8	16.4	24

BLL, blood lead level; Hb, haemoglobin; WNL, within normal limits; ZPP, zinc protoporphyrin level.

symptoms. He denied any occupational exposures to lead in his Materials Science laboratory. He also denied use of imported pottery. No environmental source of poisoning was identified.

TREATMENT

After his initial BLL of 94.8 µg/dL, the patient was briefly readmitted to the hospital in order for chelation therapy to be initiated. He was started on succimer (Chemet) 500 mg twice per day, and followed by haematology and student health services. He was later referred to the occupational and environmental clinic for treatment of elevated BLL. He was administered a total of four rounds of succimer.

OUTCOME AND FOLLOW-UP

Overall, this patient's BLL trended down over time (table 2 and figure 3). His symptoms resolved after 3 months of treatment with succimer.

DISCUSSION

Lead toxicity should be considered in the differential diagnosis for individuals presenting with normochromic anaemia and abdominal pain for whom no other diagnosis is forthcoming.⁶ The history should be sufficiently detailed to include a brief travel, occupational and environmental history as well as an inquiry regarding alternative medication, especially in our global society.

Lead concentrations >100 µg/dL almost always warrant chelation. Patients with BLL of 80–99 µg/dL with or without symptoms might benefit from therapy. Patients having 50–79 µg/dL levels with symptoms should be considered for treatment. In adults, the decision to use chelation therapy is ultimately clinical but may be guided by BLL. Chelating agents are heavy metal antagonists that form a coordination compound, preventing or reversing the binding of metallic cations to body ligands.²¹ The two chelating agents most commonly used to treat adults are oral succimer (meso-2,3-dimercaptosuccinic acid (DMSA) or Chemet) and edetate calcium disodium (CaEDTA) by injection.²² Ultimately, the decision to chelate should be made on a case-by-case basis by a medical toxicologist or occupational medicine specialist. The pace of improvement may be highly variable, ranging from weeks to years, depending on the magnitude of intoxication.²¹

BLL is the most convenient and readily interpretable of available lead biomarkers. However, BLL is not a reliable indicator of prior or cumulative dose or total body burden. Inasmuch as it is a good estimate of recent lead exposure, BLL may be in equilibrium with lead stored in bone and as such underestimate body burden. As the BLL falls as a result of chelation, it may rise again weeks later as lead is mobilised from bone. As such, it is important to measure BLL after seemingly effective treatment. ZPP is a measure of the biological effect of lead exposure.^{23 24} After exposure, ZPP elevation lags behind that of blood lead levels by ~8–12 weeks. Increasing ZPP is not usually detectable until BLL reaches 20–25 µg/dL. After stable BLLs, the ZPP plateaus in 120 days, then declines. This pattern coincides with the lifespan of erythrocytes.²⁵ The ZPP is a measure of chronic, ongoing exposure.

Figure 3 BLL and Hb trends over the course of treatment. BLL, blood lead level; Hb, haemoglobin.

This patient's BLL did not decrease linearly, but, rather, rose and fell while overall trending downwards with the chelation therapy. For example, between days 139 and 181, after being treated with the third round of succimer, his blood lead levels increased from 8.7 µg/dL to 25 µg/dL. There was no reason to suspect re-exposure to lead during this interval. However, inasmuch as lead is stored in bone, it is assumed that the levels re-equilibrated between blood and bone,²⁶ allowing this increase.

Concern regarding the use of Ayurvedic herbal medicines originates from their easy availability, increasingly international use and global reach, lack of focused scientific research and the possibility of abuse in an unregulated industry.¹⁹ This case follows similar reports in the USA of acute lead toxicity from Ayurvedic medications produced in India.⁶

Learning points

- ▶ Physicians should examine all potential sources of exposure when evaluating a potential poisoning.
- ▶ Physicians should enquire about the use of alternative medications, especially in the face of gastrointestinal or other symptoms representing an enigma.
- ▶ Use of Ayurvedic herbal medicine can result in acute lead toxicity.
- ▶ When treated with chelation therapy, be cognisant that although blood lead level is trending downwards, there may be peaks and troughs as lead may be stored in bone and re-equilibrate between blood and bone.

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