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Lead poisoning from Ayurvedic treatment: a further case

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Key words: Ayurvedic; lead poisoning; anaemia; chelation; drug safety

Summary

Purpose: *We report a case of a 30 years old Indian sailor with microcytic anemia (Hb 9.9), persistent abdominal pain, emesis, dark stool, hyperchromic urine, latent jaundice and asthenia. Lead intoxication was confirmed (blood lead value of 102 µg/dL). The patient assumed Ayurvedic medicines in the previous months. Ayurveda is an ancient form of Indian traditional popular medicine aiming to re-establish health and body function through herbal preparations, heavy metals are often added. Our purpose was to treat the patient and to establish the source of poisoning.* **Methods:** *After testing blood and urine lead concentration of other 3 crew members and analyzing over than 150 products used on the ship professional exposure was excluded. We analyzed the two Ayurvedic drugs assumed by the patient with an Inductively Coupled Plasma Mass Spectrometry. The patient underwent three chelation cycles with Calcium Disodium Ethylenediaminetetraacetic acid (EDTA) while monitoring blood and urinary lead levels.* **Results:** *The final blood lead level at discharge, after three chelation cycles, was 36.27 µg/dL. One of the two drugs contained extremely high concentrations of lead and mercury. The three different mixtures of this preparation showed lead concentrations of 12,638.54 mg/kg (Sample 2A), 23,043.02 mg/kg (Sample 2B), 21,352.97 mg/kg (Sample 2C); these levels are much higher than the highest values reported in literature for the indian soil (32 mg/kg).* **Conclusions:** *This case and similar cases raise the safety alert on complementary and alternative medicines; Ayurvedic medicine users should be carefully informed about potential risks and signs of poisoning.*

Ayurveda is a form of traditional medicine native to India which has been practiced extensively in the subcontinent for more than 2000 years (1) and is used approximately by 80% of Indians (2). Recently, Ayurveda is gaining popularity as a complementary treatment. As a result, approximately 40% of adults in the United States report using complementary and alternative medicines (CAMs) (3). Increasing numbers could probably be observed in countries where Ayurveda is not yet so practiced, due to work migration (4). Ayurvedic formulations are based on herbal products but often include heavy metals, intentionally added to restore health and normal body function, as part of Rasa Shastra (5).

Contrary to allopathic medicine, manufacturing and access to CAMs are poorly regulated. Ayurvedic medicines in Western countries are not considered as drugs. Rather, as food supplements, they

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are available without medical prescription through multiple sources including the Internet. Although even some physicians overlook possible risks associated with ayurvedic tratments, it is estimated that over 20% of ayurvedic medications distributed by U.S. and Indian companies contain toxic metals (5); some preparations have been found to contain lead and/or mercury exceeding by 100 to 10,000 times the limits set for food (6).

From 2000 to 2003, the Centers for Disease Control reported 12 cases of lead poisoning in adults associated with Ayurvedic medication intake occurring in five different states (7). Less than 20 scientific reports on lead poisoning could be found through scientific literature analysis of the past 10 years (Mesh key words: "lead poisoning" AND "Ayurvedic medication"). The contamination of herbal formulations with metals presents potential health risks. The most common diagnosis is lead poisoning, which is frequently revealed by the investigation of anaemia.

Lead is considered as an inhibitor of haem synthesis and a haemolysis promotor. Lead related anaemia can be normocytic or microcytic mainly due to the inhibition of delta aminolevulinic acid dehydratase and ferrochelatase. As a result, protoporphyrin accumulates in erythrocytes forming zinc protoporphyrin. Lead levels exceeding 30 μg/dL determine elevated blood levels of free erythrocyte protoporphyrin and zinc protoporphyrin. Anaemia develops when blood lead levels exceed 50 to 60 μg/dL. Lead has a prevalent urinary excretion, the non-excreted portion being deposited in bones. Other characteristic manifestations of lead poisoning include gastrointestinal and neurological symptoms (8).

In Western countries, industrial lead exposure control played a key role in minimizing job exposure (9) and in the last decades cases of saturnism requiring hospitalization were mostly non-occupational, due to contaminated wine (10). We recently had the chance to admit to our Department a young Indian sailor with high levels of blood lead. During a residential period in his country from 14/10/2019 to 31/01/2020 the patient presented lower back pain due to the recurrence of a pilonidal cyst, previously experienced in 2008 and 2013. In both cases, he was treated with Ayurvedic topic medications while, for this last recrudescence, his Ayurvedic practitioner (referred to as "*shaman")* prescribed an oral formulation. In February, the patient returned to Italy and rejoined his crew in Genoa (Italy) with whom he carried out different maintenance activities on board. At the beginning of March, due to persistent abdominal pain, he underwent gastroenterological examination and a few days later he presented emesis, dark stool, hyperchromic urine, latent jaundice and asthenia and was referred to Hospital Galliera in Genoa. The first blood test showed hemoglobin 9.9 mg/dL, total bilirubin 3.5 mg/dL (direct bilirubin 1.1 mg/dL), SGOT 90 mg/dL, SGPT 160 mg/dL (Table 1). Esophagogastroduodenoscopy was negative. The only finding in the chest and abdominal CT was hepatic steatosis. At the end of April, the patient underwent haematological counselling for microcytic anaemia associated with hyperferritinemia and reticulocytosis. A screening for lead poisoning showed a blood lead value of 102 μg/dL. On 8/6/2020, after passing the COVID-19 hospital prevention protocol (1), the patient came to our observation: during the previous three months the ayurvedic treatment had been withdrawn, and symptoms gradually disappeared thereafter. In April and May 2020, the patient did not undergo any blood tests.

During the first hospitalization in our department, we excluded occupational exposure. Blood and urine lead levels of other crew members were in a normal range and over 150 products used on board resulted lead free. At the admission in our department, the patient was asymptomatic, and the main haemato-chemical values were within the respective refence intervals (Table 1-2), whereas the basal lead values in blood (B-Pb) and urine samples were still high (74.61 μg/dL and 94.7 μg/L, respectively).

In consideration of the B-Pb (12, 13), a chelation protocol was initiated with the administration of Calcium Disodium Ethylenediaminetetraacetic acid (EDTA) 2 g in 500 ml of physiological solution (PS) in 12 hours for the first day, followed by four days of EDTA 1 g at the same dilution and infusion speed. Hematic and urinary lead variation during three chelation cycles is reported in Figure 1. B-Pb at discharge was 36.27 μg/dL.

The sailor referred that he used to assume an oral intake of 1 dose (about one spoon) of "product 1" mixed with 1 dose of each of the three parts of "product 2", twice a day (products 1, 2A, 2B, 2C).

Our Industrial Toxicology Laboratory analysed 0.5 g of each product sample: we added 2.5 ml of concentrated Nitric Acid to each sample and after 1h of treatment in a furnace at 80°C we made up to 25 ml, we diluted the solutions (1:1000) and used an inductively coupled plasma mass spectrometry (ICP-MS) searching for arsenic, mercury, copper, chromium, manganese, iron, nickel and lead.

Finally, we compared our values with data in the literature regarding the highest values in different soil samples of Uttar Pradesh, our patient's home region; results are summarized in Table 3 (14-16).

Conclusion

Laboratory findings confirmed the source of poisoning. The absence of mercury-related symptoms despite a high content of mercury in the samples 2A, 2B and 2C could be explained by the species of the metal, as inorganic mercury is known to be poorly absorbed by the gastrointestinal tract. A peculiar aspect of this case is that haemoglobin (Hb) usually takes several months to return to normal values in the absence of chelation while our patient had a fast normalization of Hb values in less than three months, before arrival in our hospital (Table 2). This case and similar cases of lead poisoning caused by Ayurveda practice raise the safety alert of complementary and alternative medicines. The increasing number of users of Ayurvedic drugs

Table 1 - Blood values of biomarkers of lead intoxication

	At admission (08/06/2020)	At discharge (10/07/2020)	Reference values
ALA Dehydratase, U.I./ml	11.5	20.8	20.0 – 40-0
Blood Lead Level (ICP-MS), µg/dL	74.61	42.2	0.50 – 10.0
Baseline Urinary Lead (ICP-MS), µg/dL	94.70	93.6	5.00 – 30.00
Total Hemoglobin, g/dL	12.80	13.9	14.00 – 18.00
Zinc protophorphyrin – ZP, µg/dL Hb	0.66	0.52	< 2.00
ALAU - Delta-aminolevulinic acid, mg/g creat	14.89	1.96	< 4.50
CPU – Coproporphyrin, µg/dL creat	423	3	< 100.00

Table 2 - Selected haemato-chemical values

	Initial values (11/04/2020)	At admission (08/06/2020)	At discharge (10/07/2020)	Reference values
Creatinine, mg/dL	0.9	0.93	1.04	0.60 – 1.30
Sodium, mEq/L	139	143	142	135 – 145
Potassium, mEq/L	4.6	4.4	3.8	3.5 – 5.0
Leukocytes, No.x10^9/L	9.73	6.51	5.99	4.00 – 10.00
Erythrocytes, No.x10^{12}/L	3.23	4.58	5.12	4.50 – 5.80
Haemoglobin, g/dL	8.40	13.0	14.1	13.5 – 18.00
Hematocrit, %	25.5	41.0	42.4	40.0 – 52.0
Mean corpuscular volume, fL	78.9	90	83	79 – 96
Platelet Count, No.x10^9/L	300	270	223	140 – 450

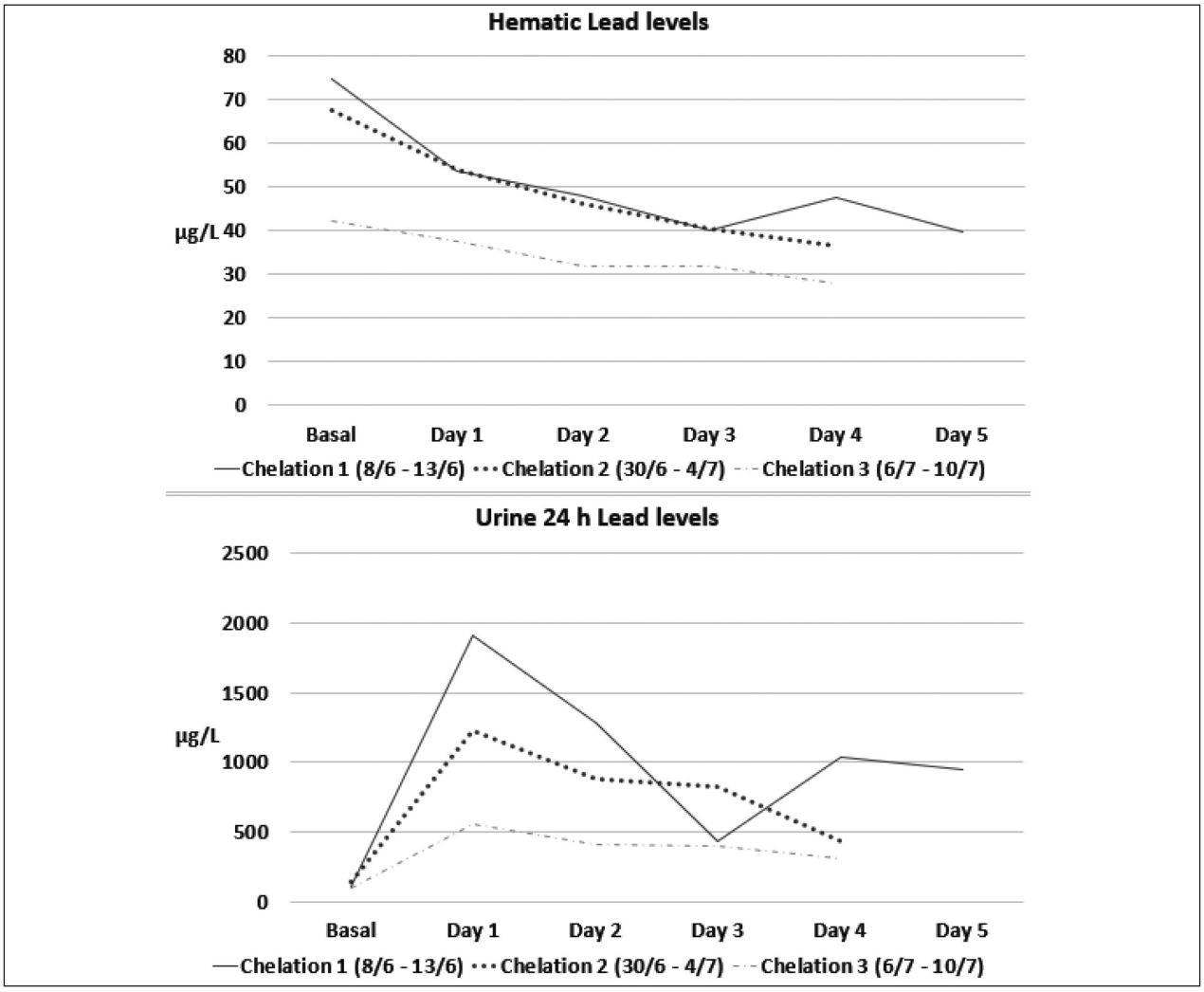

Figure 1 - Blood and urine lead levels during chelation therapy

Table 3 - Concentration of analysed elements in the environment and in the ayurvedic drug taken by the patient

	Highest soil concentration in literature (mg/kg)*	Concentration in sample product 1 (mg/kg)	Concentration in sample product 2A (mg/kg)	Concentration in sample product 2B (mg/kg)	Concentration in sample product 2C (mg/kg)
Lead	520	2.31	12,638.54	23,043.02	21,352.97
Mercury	0.49	2.54	89,076.70	126,640.27	145,710.64
Arsenic	12	0.35	134.94	103.98	122.30
Copper	323	3.96	1,511.04	2,168.79	2,356.80
Chromium	0.9	1.14	8.86	7.68	12.04
Manganese	45.1	26.34	146.74	172.53	149.75
Iron	389	288.04	14,990.34	16,498.80	15,767.59
Nickel	100	0.66	7.24	8.02	9.21

* Values referred to different sites of Uttar Pradesh region, except for mercury that is referred to whole India

worldwide calls for establishing standardized labelling and regulations of manufacturing and distribution of these treatments. Moreover, consumers should be properly informed about potential risks and clinical signs of poisoning. We believe it is important to stress these concepts and to be extremely vigilant, as the number of case reports is dwindling in the last ten years, while this work proves that the problem persists.

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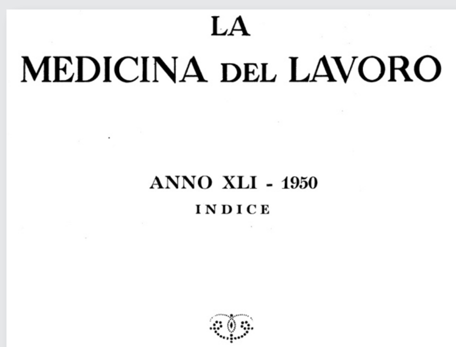

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