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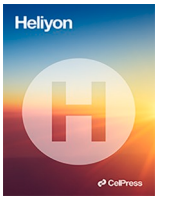

Case report

Abdominal pain caused by Tibetan medicine: A case report of lead poisoning

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ABSTRACT

Nowadays, lead poisoning in children commonly occurs, but lead poisoning caused by the administration of Tibetan medicine is rarely reported. This report describes the diagnosis and management of lead poisoning in a 16-year-old girl presented with abdominal pain, vomiting, and anemia with limb numbness, who had a childhood history of epilepsy and took Tibetan medicine intermittently to control the symptoms. After admission into hospital, Computed tomography showed high-density shadows in the gastrointestinal tract. Video-Electroencephalography showed no signs of seizure. Reflux esophagitis was observed in gastroscopy. And no obvious abnormalities in the colonic mucosa through colonoscopy. Bone marrow smear test showed basophilic stippling in the erythrocytes. The blood and urine lead levels of 626 and 75.9 μg/L, respectively. We therefore considered lead poisoning, and the patient improved after chelation therapy. Due to its atypical clinical manifestations, lead poisoning is easily misdiagnosed. Thus, clinicians should pay more attention to this disease. When abdominal pain, anemia, and neurological symptoms are present, the possibility of lead poisoning should be considered.

1. Introduction

Lead is a toxic heavy metal that is mainly absorbed through the respiratory or digestive tract [1]. Lead poisoning is often caused by occupational exposure and is very harmful to the body, especially in children, because of the underdeveloped and immature blood-brain barrier and immune system of this age group [2]. Although less common than before, lead poisoning in children remains an important health problem, especially in developing countries [3,4]. In China, cases of lead poisoning have been reported occasionally nowadays [5]. Tibetan medicine has been widely used in clinical treatments of chronic diseases, such as digestive system disease, nervous system diseases, cancer therapy and other diseases [6–8], especially for people in Tibetan areas, which is a valuable medical treasure. But the adverse effects of Tibetan medicine are often overlooked. Further, lead poisoning caused by Tibetan medicine has rarely been reported. Herein, we present the case of a 16-year-old girl diagnosed with lead poisoning due to long-term intermittent use of Tibetan medicine.

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2. Case presentation

A 16-year-old girl with retrosternal pain, abdominal pain, and vomiting for 14 days was admitted to our hospital. The symptoms started on a trip 14 days before the presentation of retrosternal pain and upper abdominal discomfort, with nausea and vomiting occurring several times. She went to a certain hospital for treatment in Shanxi and was relieved by the oral administration of Xiangsha Yangwei pills and Zuozhu-Daxi Tibetan medicine. The symptoms reappeared 6 days later. The patient then went to another hospital in Beijing for treatment, and the symptoms were relieved after the administration of oral proton pump inhibitors and liver protection drugs. However, the abdominal pain, along with vomiting, recurred 5 days later. The patient was then admitted to an affiliated hospital in Qingdao, and the examination indicated abnormal liver function indicators and moderate anemia. After treatment with oral proton pump inhibitors and spasmolytic drugs, the symptoms were temporarily relieved; however, these symptoms were still recurrent.

To determine the cause and its treatment, she was admitted to our hospital after returning to Chengdu from her trip. During her hospitalization, she presented with intermittent abdominal cramps, vomiting after eating, and scalp and limb numbness. Sixteen years previously, she had a history of epilepsy and intermittently took Tibetan medicine as a symptomatic treatment. During the treatment course, she had no episodes of epileptic seizure. The patient had no other medical history or family history of genetic disorders. The patient's vital signs were stable on admission. On physical examination, her vital signs were as follows: body temperature, 36.9 °C; blood pressure, 120/71 mmHg; heart rate, 70 beats/min; and respiratory rate, 19 breaths/min. Furthermore, abdominal examination revealed mild mid-upper abdominal tenderness without rebound tenderness, accompanied by numbness of the scalp and limbs. Neurological and chest examinations showed normal findings. Electrocardiograph results showed a sinus heart rate of 83 beats per minute. Abdominal ultrasonography showed no obvious abnormality in liver, biliary, pancreas and spleen. Routine blood analysis showed the following results: hemoglobin level, 91 g/L; red blood cell count, 3.088×10^{12} L; hematocrit level, 28.1%; reticulocyte count, 0.42%, MCV, 91.4 fl; ferritin, 594.7 ng/ml, and normal folate and vitamin B12 levels. The Coombs test showed negative findings. The liver function test showed hyperbilirubinemia (total bilirubin and direct bilirubin levels of 66.8 and 23.7 μmol/L, respectively) and a moderately abnormal aminotransferase level (alanine aminotransferase, aspartate aminotransferase, γ-glutamyl transpeptidase, and alkaline phosphatase levels of 110.2, 31.2, 172.9, and 99.0 IU/L, respectively). Urine tests were positive for white blood cells, urinary protein, urobilinogen, and ketone bodies. The stool tests yielded normal results. In the bone marrow smear test, basophilic stippling was easily observed in the erythrocytes (Fig. 1), and proliferative anemia with increased megakaryocytes was considered. Video-Electroencephalography showed no signs of seizure. The poison test report of Chengdu Borui Medical Laboratory showed blood and urine lead levels of 122.3 and 273.3 ng/L, respectively. The patient was then sent to West China Forth University Hospital for further testing and treatment, and the results showed blood and urine lead levels of 626 μg/L and 75.9 μg/L, respectively. Abdominal contrast-enhanced CT revealed hyperdensity in the appendix without obvious swelling, scattered high-density shadows in the gastrointestinal tract, and no obvious abnormalities in the liver, gallbladder, pancreas, or spleen (Fig. 2). Gastroscopy revealed grade B reflux esophagitis and chronic nonatrophic gastritis (Fig. 3). Colonoscopy revealed no obvious abnormalities in the colonic mucosa.

Based on the patient's medical history, symptoms, and auxiliary examinations, a diagnosis of lead poisoning was made. The patient immediately stopped taking Tibetan medicine and received lead chelating therapy with calcium disodium edetate (CaNa2-EDTA) at West China Forth University Hospital (CaNa2-EDTA 1g + 5% glucose 500ml for intravenous drip, continuous use for 3 days and stop for 4 days). The patient's abdominal pain, vomiting, and neurological symptoms were noticeably relieved after treatment, and the blood lead level returned to normal after two rounds of treatment.

3. Discussion

Lead poisoning is a toxic disease in which excessive lead accumulates in the body and causes multiple organ damage. The symptoms of lead poisoning are atypical and include fatigue, abdominal pain, nausea, diarrhea, anemia, and muscle paralysis or limb weakness.

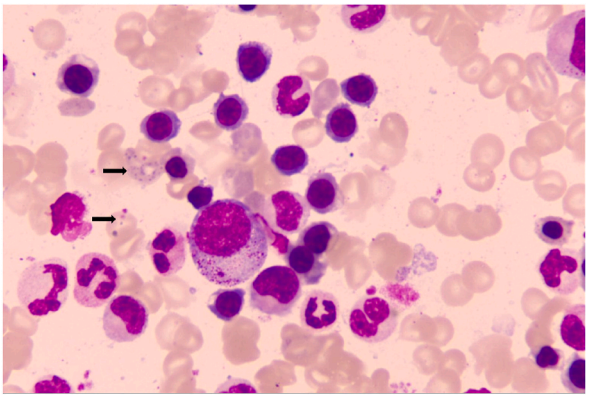

Fig. 1Bone marrow smear test showing basophilic stippling in the erythrocytes (arrow).

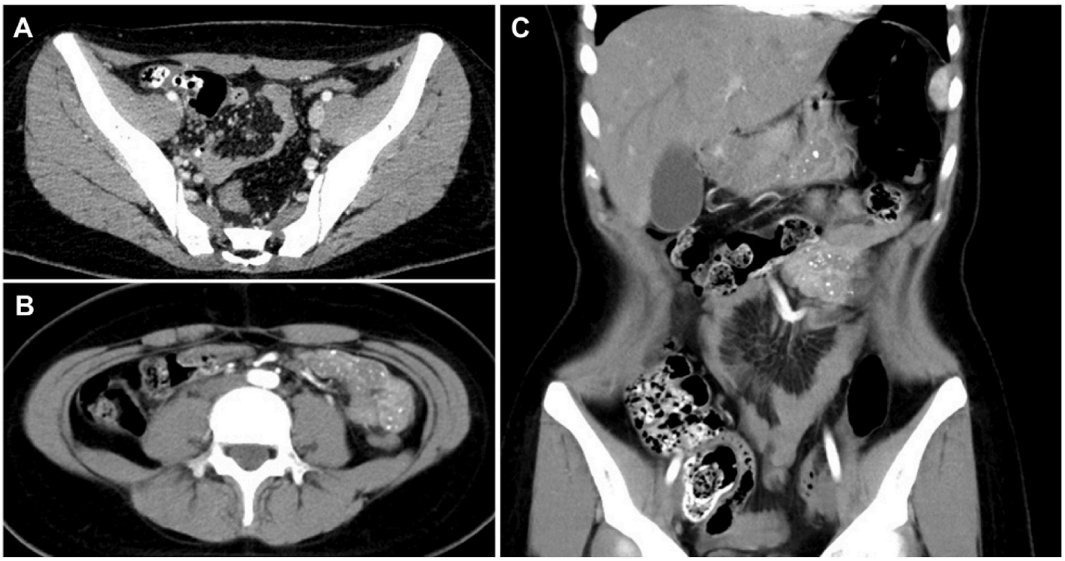

Fig. 2Contrast-enhanced computed tomography showing hyperdensity in appendix (A), scattered high-density shadows in the gastrointestinal tract, and no abnormalities in the liver, gallbladder, pancreas, or spleen (B, C).

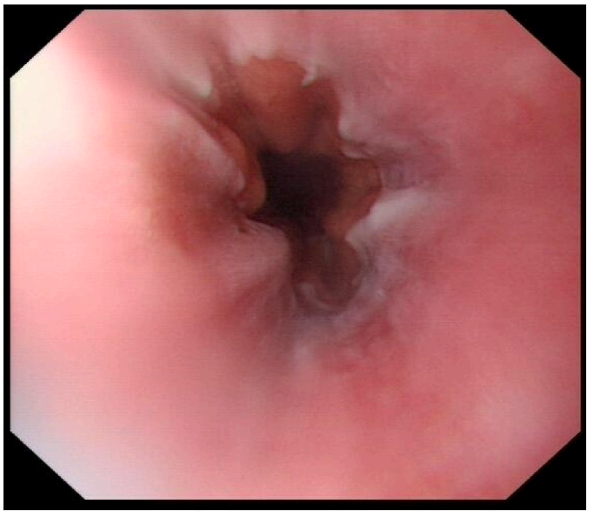

Fig. 3Gastroscopy revealed grade B reflux esophagitis.

With the progress of society, the incidence of lead poisoning has decreased [9]. Therefore, lead poisoning is often overlooked in clinical practice because of its low incidence and atypical symptoms. To the best of our knowledge, we describe the first reported case of lead poisoning caused by Tibetan medicine.

In children, lead poisoning is often caused by the intake of food with high lead levels. In the present case, lead entered the blood by taking Tibetan medicine because the patient had a history of intermittent use of Tibetan medicine to control her epilepsy symptoms. Notably, before she was diagnosed with lead poisoning in our hospital, the patient had gone to several hospitals and was administered Zuozhu-Daxi Tibetan medicine to relieve her abdominal pain. As a classic traditional Tibetan medicine, Zuozhu-Daxi Tibetan medicine has been widely used for the treatment of digestive diseases, including peptic ulcers, chronic gastritis, and gastric cancer [10]. Despite all these clinical effects, Tibetan medicine is generally high in heavy metals, which poses a certain safety hazard to patients. The Zuozhu-Daxi Tibetan medicine contains more heavy metals, such as lead and mercury [11]. Therefore, the long-term use of Tibetan antiepileptic drugs and Zuozhu-Daxi Tibetan medicine before admission were probably the simultaneous causes of lead poisoning in our patient.

Lead is present in very small amounts in the human body and is mainly distributed in bones with almost no biological function. Excessive lead intake is harmful to multiple organs, as it causes anemia, cardiovascular disease, neurotoxicity, and nephrotoxicity [12]. In the vascular system, lead can inhibit a series of enzymes involved in the synthesis of hemoglobin. The enzymes included

delta-aminolevulinic acid dehydratase (δ-ALAD), ferrochelatase, and coproporphyrinogen oxidase. The inhibition of these enzymes not only decreases red cell synthesis but also increases the fragility of erythrocytes [13]. Lead exposure has a dose-dependent relationship with anemia. In our case, the patient also had mild-to-moderate anemia. Prior to the diagnosis of lead poisoning, a bone marrow aspiration biopsy was performed to determine the cause of anemia, which revealed proliferative anemia with increased megakaryocytes. Basophilic stippling is readily observed in the bone marrow blood smears, which is an early sign of heavy metal poisoning. Its underlying mechanism is that lead inhibits pyrimidine 5′-nucleotidase, which causes the accumulation of pyrimidine nucleotide granules [14].

Lead can traverse the blood–brain barrier and cause irreversible damage to the nervous system, which is a major concern for the normal development of children [12]. Neurological symptoms, including depression, anxiety, and peripheral neuropathy, are evident when the blood lead levels are >300 μg/L. In children, obvious symptoms, including headache, vomiting, stupor, and abdominal pain, are not observed until the blood lead level reaches 450 μg/L [15]. Lead poisoning, even at low levels, can cause a decline in IQ, cognitive and executive functions, and attention span [9,16]. To identify children who are exposed to more lead, the Centers for Disease Control and Prevention (CDC) in the United States (US) has lowered the blood lead reference value to 3.5 μg/dL [17]. According to the US CDC lead poisoning classification, lead poisoning is diagnosed when the blood lead level exceeds 200 μg/L [18]. The blood lead reference value in children should be lowered to prevent the harmful effects of lead poisoning in the early stage. In the present case, the patient presented with retrosternal and abdominal pain with limb numbness, which is a manifestation of nervous system damage. Given her history of epilepsy, an electroencephalogram (EEG) was performed; however, there was no EEG specific for epilepsy. Therefore, the symptom of limb numbness may be a specific manifestation of lead poisoning.

Abdominal pain from lead poisoning is usually colic. Physiologically, lead inhibits the Ca-ATPase activity, leading to smooth muscle spasticity [19]. Our patient presented with retrosternal and abdominal pain, along with minimal physical signs, which were nonspecific. Reflux esophagitis can cause retrosternal pain, but it does not fully explain the abdominal pain. During hospitalization, the abdominal pain recurred and was not completely resolved. After excluding the organic lesions, we noted the characteristics of the long-term use of Tibetan medicine and high-density shadows in the gastrointestinal tract, especially in the appendix, which may indicate the presence of heavy metals (Fig. 2). Then, the possibility of heavy metal poisoning was considered. Thus, the diagnosis of lead poisoning was made. The available agents for chelation treatment include calcium disodium edetate (CaNa2-EDTA), dimercaptosuccinic acid, dimercaprol, and D-penicillamine [20]. The CaNa2-EDTA treatment was used for the patient, and the symptoms improved considerably after treatment. The limitation in the diagnosis and treatment is the lack of detection equipment for heavy metals such as blood lead and drugs to treat lead in our hospital, which led to the prolonged diagnosis of lead poisoning.

4. Conclusion

Owing to the low incidence and atypical symptoms, lead poisoning is easily misdiagnosed as acute abdominal disease. In addition, blood lead testing equipment is not available in every hospital, which can also delay the diagnosis and treatment to some extent. As gastroenterologists, we should comprehensively consider abdominal and systemic diseases in patients with abdominal pain. Detailed history taking is crucial for early diagnosis. Our report suggests that when common causes of abdominal pain have been excluded, lead poisoning should be considered in the differential diagnosis.

5. Ethics declarations

The authors confirm that written consent for the submission and publication of this case report, including images, clinical data and other data included in the manuscript, was obtained from the patient in accordance with COPE guidelines. And informed consent was received from participants. Authors' institution does not require ethical approval for publication of a single case report because not applicable.

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CARE checklist statement

All items in the CARE checklist were applicable in our study.

Data availability statement

This case report contains clinical data from the electronic medical record in the General Hospital of Western Theater Command. Data associated with this study has been deposited at General Hospital of Western Theater Command Data Set. http://xn120.mil.cn/. Additional information is available from the corresponding author on reasonable request from the editor.

CRediT authorship contribution statement

Liang Zhang: Writing – original draft. **Xin Yao:** Writing – original draft. **Yalun Chen:** Writing – original draft. **Ying Li:** Data

curation. **Jianping Qin:** Writing – review & editing. **Shanhong Tang:** Writing – review & editing, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

[1] S. Bouftini, J. Bahhou, B. Lelievre, J.M. de la Barca, A. Turcant, B. Diquet, et al., Screening for childhood lead poisoning in the industrial region of Fez, Morocco, Arch. Environ. Contam. Toxicol. 68 (3) (2015) 442–450.
[2] F. Chehbani, G. Gallello, T. Brahim, S. Ouanes, W. Douki, N. Gaddour, et al., The status of chemical elements in the blood plasma of children with autism spectrum disorder in Tunisia: Aa case-control study, Environ. Sci. Pollut. Res. 27 (28) (2020) 35738–35749.
[3] T.G. Hoang, Q.P. Tran, V.T. Lo, N.H. Doan, T.H. Nguyen, M.K. Pham, Blood lead levels and associated Sociodemographic Factors among children aged 3 to 14 Years living near Zinc and lead Mines in two Provinces in Vietnam, BioMed Res. Int. 2021 (2021) 5597867.
[4] Y. Liu, C. Xu, F. Liu, G. Xiao, S. Zhou, L. Huang, et al., Uneven development of the lead industry leads to regional differences in blood lead levels of children, Environ Pollut 293 (2022) 118504.
[5] H. Ma, L. Wu, Y. Zou, X. Li, Non-occupational lead poisoning associated with traditional Chinese medicine: a case report, Front. Public Health 10 (2022) 938186.
[6] Y. Shi, J. Ning, K. Norbu, X. Hou, H. Zheng, H. Zhang, et al., The Tibetan medicine Zuozhu-Daxi can prevent Helicobacter pylori induced-gastric mucosa inflammation by inhibiting lipid metabolism, Chin. Med. 17 (1) (2022) 126.
[7] C. Li, C. Niu, H. Bi, J. Zhao, J. Ivan Alvarez, F. Yuan, et al., Tibetan mineral-herbal medicine Zuotai alleviates the depressive-like behaviors in chronic restraint-stressed mice while regulating stress hormone, inflammation and monoamine, Front. Pharmacol. 14 (2023) 1098378.
[8] C. Tang, C.C. Zhao, H. Yi, Z.J. Geng, X.Y. Wu, Y. Zhang, et al., Traditional Tibetan medicine in cancer therapy by Targeting Apoptosis Pathways, Front. Pharmacol. 11 (2020) 976.
[9] D. Bunch, A.L. Pyle-Eilola, Lead poisoning: clinical and laboratory considerations, Adv. Clin. Chem. 117 (2023) 209–222.
[10] Y. Shi, J. Ning, K. Norbu, X. Hou, H. Zheng, H. Zhang, et al., The Tibetan medicine Zuozhu-Daxi can prevent Helicobacter pylori induced-gastric mucosa inflammation by inhibiting lipid metabolism, Chin. Med. 17 (1) (2022) 126.
[11] Y. Qu, J.H. Li, C. Zhang, C.X. Li, H.J. Dong, C.S. Wang, et al., Content determination of twelve major components in Tibetan medicine Zuozhu Daxi by UPLC, Zhongguo Zhongyao Zazhi 40 (9) (2015) 1825–1830.
[12] A. Lopes, T. Peixe, A. Mesas, M. Paoliello, Lead exposure and Oxidative stress: a Systematic review, Rev. Environ. Contam. Toxicol. 236 (2016) 193–238.
[13] A. Qader, K. Rehman, M. Akash, Genetic susceptibility of δ-ALAD associated with lead (Pb) intoxication: Ssources of exposure, preventive measures, and treatment interventions, Environ. Sci. Pollut. Res. Int. 28 (33) (2021) 44818–44832.
[14] P. Mitra, S. Sharma, P. Purohit, P. Sharma, Clinical and molecular aspects of lead toxicity: an update, Crit. Rev. Clin. Lab Sci. 54 (7–8) (2017) 506–528.
[15] Prevention of Childhood Lead Toxicity, Pediatrics 145 (6) (2020).
[16] H. Dapul, D. Laraque, Lead poisoning in children, Adv. Pediatr. 61 (1) (2014) 313–333.
[17] P. Ruckart, R. Jones, J. Courtney, T. LeBlanc, W. Jackson, M. Karwowski, et al., Update of the blood lead reference value - United States, 2021, MMWR Morb. Mortal. Wkly. Rep. 70 (43) (2021) 1509–1512.
[18] A.S. Ettinger, M.L. Leonard, J. Mason, CDC's lead poisoning prevention Program: a long-standing Responsibility and Commitment to Protect children from lead exposure, J. Publ. Health Manag. Pract. 25 (Suppl 1) (2019) S5–S12. Lead Poisoning Prevention.
[19] Y. Yang, S. Li, H. Wang, M. Liu, B. Tuo, H. Wu, et al., Chronic lead poisoning induced abdominal pain and anemia: Aa case report and review of the literature, BMC Gastroenterol. 20 (1) (2020) 335.
[20] S. Porru, L. Alessio, The use of chelating agents in occupational lead poisoning, Occup Med (Lond). 46 (1) (1996) 41–48.