

Two Cases of Lead Poisoning due to Herb Medicinal Pills

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We encountered two children with lead poisoning who were administered herb medicinal pills recommended by their clergyman. These patients presented anemia and severe colicky abdominal pain, but no neurologic symptoms. For this reason, they were initially misdiagnosed with gastrointestinal hemorrhagic disease. However, we got a clue that they took herb medicinal pills. Finally, based on the assay of blood lead level, we made a correct diagnosis of lead poisoning in these patients. These patients underwent chelating therapy. Subsequently, the concentration of blood lead was decreased. Finally, we drew a conclusion that the possibility of lead poisoning must be considered in children who complained of colicky abdominal pain accompanying anemia. Here, we report two pediatric cases of lead poisoning with a review of literature. (**Korean J Pediatr** 2005;48:1009-1015)

Key Words : Lead poisoning, Abdominal pain, Colic, Anemia, Chelating therapy, Herb medicinal pills

Introduction

Lead is a heavy metal that is commonly found around us. Since B.C. 3,000 or so, lead has been used for various purposes. Hippocrates once described that abdominal pain was one of the major clinical symptoms due to lead poisoning¹⁾. Historically, lead poisoning has been reported in such cases as illicit home-brewing in the 1,700s^{2,3)} and pica due to children's careless use of lead-containing paint in 1,920 or later¹⁾.

As mentioned above, lead is closely related to our daily lives. Moreover, it is normally contained as a heavy metal in food, beverage, air and soil. Lead poisoning is particularly of great concern because lead is easily ingested through inhalation. We are all susceptible to lead exposure under such circumstances as waste gas, air pollution due to the industrial smoke, cosmetics, furniture and pigments. In Korea, according to Ministry of Environment, the route of lead exposure was divided into occupational and non-

occupational one⁴⁾. With the illumination of preventive and occupational medicine since the 1980s, lead poisoning has been markedly decreased in an occupational environment¹⁾. In a non-occupational environment, however, lead poisoning remains problematic; lead is routinely ingested via the pipeline for water supply, paint, volatile oil, the contaminated soil, the combustion of waste paper, cans and food instruments. Moreover, in Asian countries including Korea, lead poisoning due to herb medicinal pills has been frequently reported. Recent studies have shown that the above cases are also prevalently seen in Asian immigrants residing in Western countries⁵⁾.

In recent years, we have encountered two related children who exhibited anemia and severe clamping abdominal pain following a 1-month administration of herb medicinal pills for the treatment of obesity. These children came nearly being misdiagnosed with hemorrhagic enteritis. However, we got a clue from their past history of herb medicinal pills. Then, we evaluated their clinical manifestations and hematologic findings; measured the concentration of blood lead; and assayed the amount of lead contained in herb medicinal pills. Finally, we made a correct diagnosis of lead poisoning.

Here, we report two pediatric cases of lead poisoning with a review of literature.

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Case Report

1. Case 1

Patient : A 13-year old male named Jung

Chief complaint(s) : A 3-week history of severe epigastric pain and vomiting

Family history : Parents got divorced. Currently, he has been raised by his mother. His mother is a carrier of Hepatitis B virus.

Past medical history : He was born by normal vaginal delivery after full-term pregnancy. Neither drugs nor illness were noted during pregnancy. He was also a carrier of Hepatitis B virus, but did not present with specific symptoms. Prior to his outpatient visit, he got administered

herb medicinal pills at a dose of approximately 30 pills a day for a month, prescribed by his clergyman. Recently, he showed a 13-kg weight loss. He was residing at a Western-style tenement house in the downtown area of Seoul. There were neither industries nor household factories nearby his house.

Present illness : Three weeks before admission, he presented with epigastric pain accompanying vomiting. On May 28, 2004, he got admissioned at department of pediatrics of our hospital. Then, he underwent gastroduodenoscopy, colonoscopy, RBC-scanning and abdominal CT scan. All these examinations were normal. On small bowel series, no specific findings were observed except for the delayed intestinal motility. He was once discharged at his mother's request. At outpatient follow-up, he presented with aggravated anemia, and confessed that he got administered herb medicinal pills. On June 14, 2004, he got hospitalized for further investigation and treatment.

Clinical findings : On admission, physical examination showed that body temperature was 36.3°C; heart rate was 72 times/min; blood pressure was 130/80 mmHg; and body weight was 100 kg (more than 97 percentile). Besides, mental status was clear; face was pale; conjunctiva was anemic (Fig. 1); no edema was found systemically; cardiac and respiratory sound was normal on chest auscultation; no abdominal distension was found; overall tenderness was present with no rebound tenderness; hepatosplenomegaly or palpable mass were not found; bowel sound was decreased; and no neurological deficits were noted.



Fig. 1. Pale-looking brothers who got administered herb medicinal pills for the treatment of obesity.

Table 1. Hematologic findings in Case 1

Date	5/28	6/5	6/14	6/22	6/25	6/30	9/25 (OPD)
Hb (g/dL)	8.1	7.9	7.9	7.0	8.4	9.4	13.4
Hct (%)	24.1	23.9	23.9	21.3	25.4	28.9	42.2
MCV (fL)	78.0	78.9	84.0	84.9	87.0	90.0	82.9
MCH (pg)	26.2	26.2	27.6	27.9	28.8	29.3	26.3
WBC (/mm ³)	5,270	6,170	4,910	4,150	5,160	6,350	4,500
Segment (%)	68.7	74.7	62.9	68.3	55.3	58.6	47.7
Lymphocyte (%)	23.5	18.6	28.2	24.8	36.2	31.0	41.3
Eosinophil (%)	0.6	1.8	2.4	0.2	2.7	3.0	2.7
Platelet ($\times 10^3/\text{mm}^3$)	242	219	236	166	265	308	224
GOT (IU/L)	60	42	28	28	23	28	16
GPT (IU/L)	39	60	47	53	36	29	19
Fe/TIBC ($\mu\text{g}/\text{dL}$)	97/292	93/239	176/262				
Reticulocyte (%)	1.89		7.5		9.06		
CRP (mg/dL)	<0.31	<0.31	<0.31	0.93		<0.31	
BUN (mg/dL)	16		19.9	9	6	7	
Cr (mg/dL)	0.8		1.0	0.9	0.7	0.7	
Coomb's test (direct/indirect)	—/—						

Laboratory findings : On admission and after discharge, outpatient follow-up hematology was summarized in Table 1. Laboratory findings associated with lead were represented in Table 2. Neither glucosuria nor proteinuria was detected on urinalysis. Both intestinal parasitology and occult blood test were negative. The blood smear showed normocytic normochromic anemia (Fig. 2A). Besides, basophilic stippling cells were noted in both bone marrow aspiration (Fig. 2C) and peripheral blood smear (Fig. 2A), in which RNA is condensed around the destroyed RBC. No specific findings were seen on chest X-ray. However, paralytic ileus was seen on abdominal X-ray. Abnormal shadow was not seen in the epiphysis of long bones. The amount of lead contained in herb medicinal pills was assayed, and was 2,612 $\mu\text{g/g}$ (the tolerance dose of crude drug is 30 $\mu\text{g/g}$). Based on these results, he was strongly suspected of having lead poisoning (Fig. 3A, 3B).

Treatment and clinical course : Their mother was reluctant to confess that our patients got administered herb medicinal pills. For this reason, patient was discharged without being diagnosed during the initial hospitalization. However, it was later disclosed that the patient got administered herb medicinal pills while visiting local clinics. During the second hospitalization, based on the laboratory findings, patient were correctly diagnosed with lead poisoning.

Initially, the concentration of blood lead was high (>70 g/dL). Edetate calcium disodium (CaNa₂-EDTA) and orally-administerable Dimercaptosuccinic acid (DMSA) are given to our patients. Then, symptoms including anemia were alleviated. The concentration of blood lead was lowered to 24.8 g/dL. At outpatient check-up, the concentration of blood lead was elevated to 45.3 g/dL. Then, DMSA was re-administered. Currently, he has been under

Table 2. Laboratory Finding Related to Lead in Case 1

Date	6/14	6/25	6/30	7/19 (OPD)	8/18 (OPD)	9/25 (OPD)	11/1 (OPD)	12/11 (OPD)	1/17 (OPD)
Basophilic stippling (Peripheral blood)	+								
Pb (Lead) ($\mu\text{g/dL}$)	72.9	31.4	24.8	29.9	45.3	41.3	52.8	33.45	38.78
ZPP ($\mu\text{g/dL}$)	200.62								
δ -ALA (24 hr urine) (mg/day)	105.9								

ZPP : Zinc Protoporphyrin, ALA : aminolevulinic acid

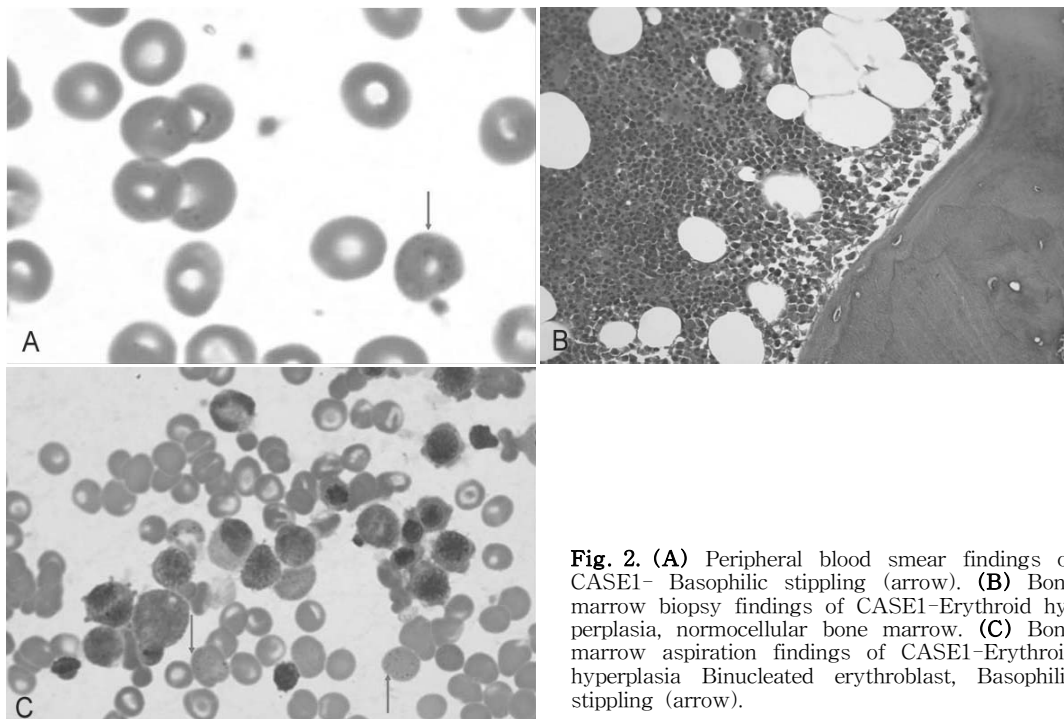


Fig. 2. (A) Peripheral blood smear findings of CASE1- Basophilic stippling (arrow). (B) Bone marrow biopsy findings of CASE1-Erythroid hyperplasia, normocellular bone marrow. (C) Bone marrow aspiration findings of CASE1-Erythroid hyperplasia Binucleated erythroblast, Basophilic stippling (arrow).

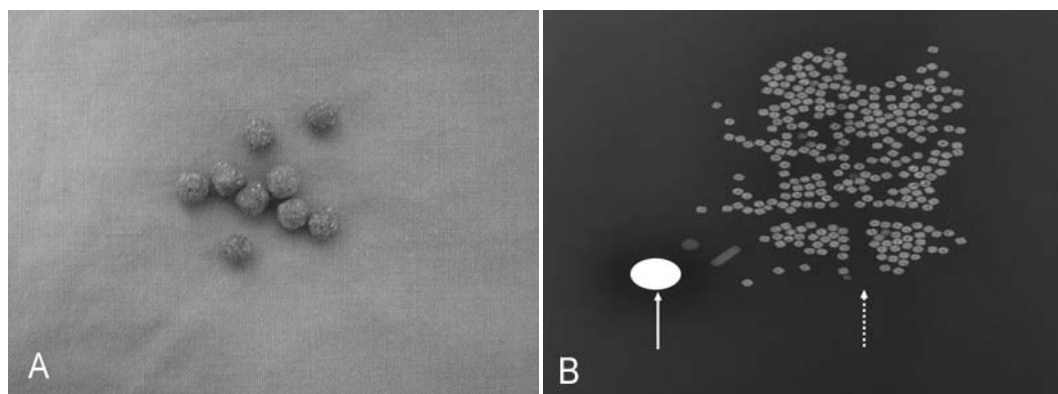


Fig. 3. (A) Herb medicinal pills. The amount of lead contained in herb medicinal pills was assayed : 2,612 $\mu\text{g/g}$ (thetolerance dose of crude drug is 30 $\mu\text{g/g}$). (B) A simple X-ray of herb medicinal pills (solid line : coin, dotted line : herb medicinal pills).

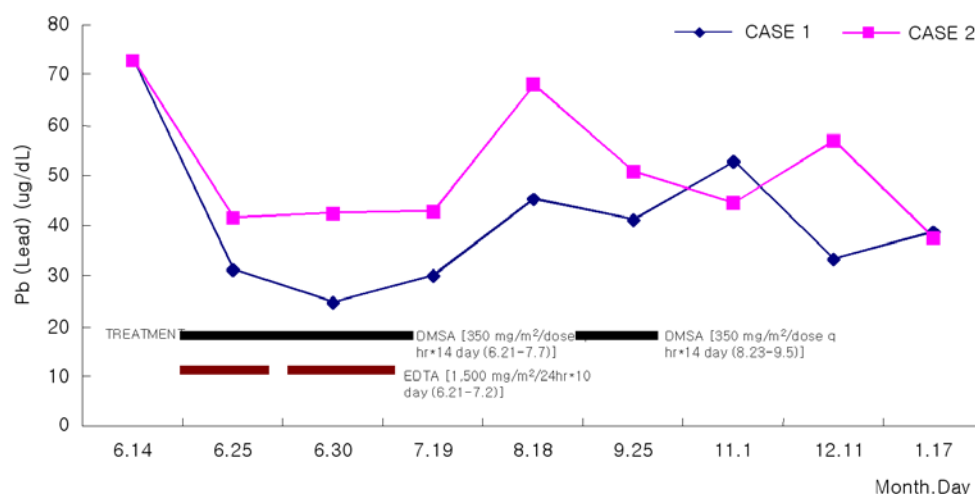


Fig. 4. The concentration of blood lead following chelation therapy. EDTA : Edetate calcium disodium, DMSA : Dimercaptosuccinic acid.

outpatient follow-up (Fig. 4). This showed that the concentration of blood lead was persistently lowered, but was still higher than normal value.

2. Case 2

Patient : A 11-year old male named Jung (younger brother of the above patient)

Chief complaint(s) : A 1-week history of severe abdominal pain accompanying vomiting. On June 14, 2004, he got hospitalized for further investigation and treatment.

Family history : Parents got divorced. Currently, he has been raised by his mother. His mother is a carrier of Hepatitis B virus.

Past medical history : He got administered herb medicinal pills with his brother. As a result, he experienced a 10-kg weight loss.

Present illness : Prior to his outpatient visit, to lose his weight, he got administered herb medicinal pills at a dose of approximately 30 pills a day for a month. He presented with a 1-week history of epigastric pain accompanying vomiting. At a local clinic, he showed the signs and symptoms suggestive of anemia. Then, he visited us with his brother for further investigation and treatment.

Clinical findings : On admission, physical examination showed that body temperature was 36.5°C; heart rate was 78 times/min; blood pressure was 120/80 mmHg; and body weight was 70 kg (more than 97 percentile). Besides, mental status was clear; face was pale; conjunctiva was anemic (Fig. 1); no edema was found systemically; cardiac and respiratory sound was normal on chest auscultation; no abdominal distension was found; overall tenderness was present with no rebound tenderness; hepatosplenomegaly or

Table 3. Hematologic findings in Case 2

Date	6/14	6/19	6/25	6/30	9/25 (OPD)	11/19 (OPD)	2/14 (OPD)
Hb (g/dL)	6.2	6.8	7.6	8.8	14.9	13.4	14.6
Hct (%)	18.6	20.1	22.7	26.5	44.8	40.3	44.0
MCV (fL)	74.2	73.4	482.8	88.5	82.7	81.4	81.0
MCH (pg)	24.7	24.8	27.7	29.3	27.5	27.1	26.9
WBC (/mm ³)	6,140	8,780	4,630	5,040	5,260	4,870	7,450
Segment (%)	59		49.9	43.8	42.1	37.6	48.8
Lymphocyte (%)	34		39.5	46.9	50.6	54.4	44.8
Eosinophil (%)	1		2.6	3.1	2.3	1.6	2.0
Platelet ($\times 10^3/\text{mm}^3$)	304	317	249	270	280	253	224
GOT (IU/L)	60			45	18	20	19
GPT (IU/L)	52		95	45	14	15	14
Fe/TIBC ($\mu\text{g}/\text{dL}$)	214/222		74				
Reticulocyte (%)	3.5		18.48				
CRP (mg/dL)	<0.31			5			
BUN (mg/dL)	21.4			0.7			
Cr (mg/dL)	0.9						
Coomb's test (direct/indirect)	-/-						

Table 4. Laboratory Finding Related to Lead in Case 2

Date	6/14	6/25	6/30	7/19 (OPD)	8/18 (OPD)	9/25 (OPD)	11/19 (OPD)	12/27 (OPD)	2/14 (OPD)
Basophilic stippling (Peripheral blood)	+								
Pb (Lead) ($\mu\text{g}/\text{dL}$)	73	41.7	42.6	43	67.9	50.9	44.45	56.8	37.45
ZPP ($\mu\text{g}/\text{dL}$)	100.2								
δ -ALA (24hr urine) (mg/day)	141.98								

ZPP: Zinc Protoporphyrin, ALA: aminolevulinic acid

palpable mass was not found; bowel sound was decreased; and no neurological deficits were noted.

Laboratory findings: On admission and after discharge, outpatient follow-up hematology was summarized in Table 3. Laboratory findings associated with lead were represented in Table 4. Neither glucosuria nor proteinuria was detected on urinalysis. Both intestinal parasitology and occult blood test were negative. The blood smear showed normocytic normochromic anemia. Besides, basophilic stippling cells were noted in both bone marrow aspiration and peripheral blood smear, in which RNA is condensed around the destroyed RBC. No specific findings were seen on chest X-ray. However, paralytic ileus was seen on abdominal X-ray. Abnormal shadow was not seen in the epiphysis of long bones. Based on the past history of herb medicinal pills, he was also strongly suspected of having lead poisoning (Fig. 3A, 3B).

Treatment and clinical course: Initially, the concentration of blood lead was high ($>70 \mu\text{g}/\text{dL}$). Edetate calcium disodium (CaNa₂-EDTA) and orally-administerable

Dimercaptosuccinic acid (DMSA) are given to our patients. Then, symptoms including anemia were alleviated. The concentration of blood lead was lowered to $41.7 \mu\text{g}/\text{dL}$. At outpatient check-up, the concentration of blood lead was elevated to $67.9 \mu\text{g}/\text{dL}$. Then, DMSA was re-administered. Currently, he has been under outpatient follow-up (Fig. 4). This showed that the concentration of blood lead was persistently lowered, but was still higher than normal value.

Discussion

In Korea, lead poisoning was first reported in an infantile case of lead encephalopathy¹⁾. The corresponding infant proved to be lactated by his or her mother who was frequently powdered for cosmetic reasons. Ha, et al⁶⁾ reported that convulsion and coma were noted in a pediatric patient who was given herb medicinal pills as a restorative. In our patients, fortunately, no neurological deficits were seen. These patients visited us with a chief complaint

of epigastric pain accompanying anemia. In cases of lead poisoning, such gastrointestinal disturbances as nausea, vomiting, the loss of appetite, constipation and diarrhea are seen to accompany severe abdominal pain. The pathophysiology of the abdominal pain, termed as 'lead colic', is not clearly understood. Janin, et al⁷⁾ said that lead colic, which is thought to be a syndrome with a multiplicity of clinical patterns and at least three possible different pathogenic mechanisms - First, it may be caused by changes in the visceral smooth muscle tone secondary to the action of lead on the visceral autonomic nervous system. Second, lead-induced alterations in sodium transport in the small-intestinal mucosa. Third, lead-induced interstitial pancreatitis. It should be considered in the differential diagnosis of abdominal pain of obscure etiology and whenever a disparity is observed between the symptoms and the abdominal findings in a patient with abdominal pain, especially in the presence of a history of exposure to lead.

In Western countries, currently, the standard concentration of blood lead was set at less than 10 $\mu\text{g/dL}$ for a screening test. In 1991, Centers for Disease Control and Prevention (CDC) defined childhood lead poisoning as cases in which the concentration of blood lead is more than 10 $\mu\text{g/dL}$. Besides, mild lead poisoning was defined as the concentration of blood lead of 10-19 $\mu\text{g/dL}$. In cases in which the concentration of blood lead exceeds 60 $\mu\text{g/dL}$, symptoms due to severe lead poisoning will occur. These symptoms include coma, convulsion, behavioral abnormalities, ataxia and persistent vomiting. Acute encephalopathy is seen in cases in which the concentration of blood lead exceeds 100 $\mu\text{g/dL}$, but is sometimes seen in those in which the concentration of blood lead is less than 70 $\mu\text{g/dL}$. Patients with acute encephalopathy present with renal dysfunction, anemia and severe lead colic. Recent studies have shown that neurological toxicity appears in cases in which the concentration of blood lead exceeds 10-15 $\mu\text{g/dL}$ ⁸⁾. Kim, et al⁹⁾ reported that long-term administered herb medicinal pills caused renal complications. Needleman, et al¹⁰⁾ have also noted that concentration difficulties, delayed language development and the lowering of IQ¹¹⁾. Cognitive and behavioral impairment due to lead poisoning are irreversible. Therefore, it is of prime importance to prevent these impairment.

Once ingested, lead persists within the body for a long-term period. Attached to the bone, lead cannot be removed even by drugs. To treat patients with lead poisoning, the

combination therapy of $\text{CaNa}_2\text{-EDTA}$ and DMSA (or BAL) along with hospitalization is recommended in cases in which the concentration of blood lead exceeds 70 $\mu\text{g/dL}$. The single use of DMSA is recommended in cases in which the concentration of blood lead ranges between 45 $\mu\text{g/dL}$ and 70 $\mu\text{g/dL}$. No specific treatment is required in cases in which the concentration of blood lead is less than 45 $\mu\text{g/dL}$. Of great importance, however, patients should not be further contaminated by being protected from the environment exposed to lead poisoning. Besides, they should be instructed by their parents, and should be under regular follow-up⁸⁾.

In our cases the concentration of blood lead was high ($>70 \mu\text{g/dL}$). $\text{CaNa}_2\text{-EDTA}$ and orally-administerable DMSA are given to our patients. The concentration of blood lead was temporarily elevated but was thereafter lowered in both cases (Fig. 4). Presumably, this might be due to the findings that lead deposited in the soft tissue and bone was redistributed to the blood.

Binding to RBC, the ingested lead mostly circulates within the blood and is then deposited in the soft tissue and bone. This elevates the intracellular Ca^{2+} level by deranging Ca^{2+} metabolism within the cells; and provokes neurotoxicity or hypertension by affecting nerve conduction or blood vessels. Moreover, lead interacts with proteins, and eventually lowers the activity of several enzymes. In particular, it causes anemia by inhibiting heme synthesis. The pathophysiology of anemia lies in the derangement of heme synthesis, in which hemoglobin is poorly synthesized, the life span of RBC is shortened and RBC destruction is facilitated. Lead is sensitive to ALA dehydratase which mediates the transformation of δ -aminolevulinic acid (ALA) into porphobilinogen at an early phase of heme synthesis. To put this in another way, lead suppresses the activity of enzymes and elevates the concentration of blood ALA. As a result, heme is poorly synthesized and the precursors are increased. Furthermore, by partially suppressing the activity of heme synthase, lead contributes to elevating the concentration of free irons and protoporphyrin within the blood¹²⁾.

As described, in children who complained of colicky abdominal pain accompanying anemia, the possibility of lead poisoning must be considered although a differential diagnosis with hemorrhagic enteritis based on endoscopy or radioisotope scanning is important. This must be followed by blood test and urinalysis.

In summary, we experienced two cases of lead poisoning due to herb medicinal pills for the treatment of obesity. Patients visited us with a chief complaint of severe abdominal pain and anemia. A correct diagnosis was made by measuring the concentration of blood lead and assaying the amount of lead contained in a herb medicinal pills.

To address the importance in considering the possibility of lead poisoning, we report our cases with a review of literatures.

한 글 요 약

환약으로 제조된 한약에 의한 급성 납중독 2례

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납중독은 가벼운 빈혈에서부터 경련을 동반한 신경장애에 이르기까지 다양한 임상증세를 나타내며, 뼈나 연부조직에 침착되어 비가역적인 장애를 남기므로 임상적으로 중요하다. 특히 소아는 소화관을 통한 흡수율이 높고 배설율이 낮아 납중독의 영향에 예민한데 혈중 농도와 개인차에 따라 심한 복통 및 지능저하, 경련 등의 비가역적인 신경계장애를 남길 수 있어 조기진단 및 치료가 중요하다. 이에 저자들은 살빼는 목적으로 비전문가에게 처방받은 환약으로 제조된 한약을 복용하여 빈혈을 동반한 심한 복통을 주소로 내원한 형제들에게 자칫 출혈성 장질환으로 여기고 지나칠 뻔 하였으나 환약복용의 과거력을 단서로 혈중 납농도 및 환약의 납 성분 분석을 통해 확진한 2례를 경험하였기에 이를 문헌 고찰과 함께 보고하는 바이다.

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