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【 CASE REPORT 】

Occupational Lead Poisoning in a Patient with Acute Abdomen and Normocytic Anemia

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Abstract:
We herein report a 24-year-old male construction worker with occupational lead poisoning who presented with acute abdomen and normocytic anemia. The levels of urinary delta-aminolevulinic acid and free erythrocyte protoporphyrin were elevated without any increase in the level of urine porphobilinogen. Detection of an elevated blood lead level of 100 μg/dL confirmed a diagnosis of lead poisoning. Chelation therapy with calcium disodium ethylenediaminetetraacetate resulted in prompt improvement of the clinical symptoms and the blood lead level. Clinicians should be aware that lead poisoning caused by occupational exposure can still occur sporadically in construction workers in Japan.

Key words: lead, occupational exposure, construction worker, abdominal colic, normocytic anemia

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Introduction

In Japan until about 1990, trilead tetraoxide (Pb_3O_4) was mixed with paint used for coating iron bridges and highway bridge girders to prevent rust. As this surface paint deteriorates, repainting is necessary every 5 to 10 years. During preparation of the surface for repainting, construction workers may be exposed to significant amounts of lead paint dust or chips in the form of particles that are scraped or sanded off. For this reason, even though lead-containing paint is no longer actively used, it still remains present on many older iron structures, so lead poisoning caused by occupational exposure may occur occasionally in construction workers (1).

We herein report a case of occupational lead poisoning in a construction worker engaged in the repainting of an iron bridge, for which he wore only a paper mask and not a sophisticated respiratory protection device. Since the symptoms of lead poisoning are vague and nonspecific, the diagnosis can be difficult unless there is a high degree of clinical suspicion. When encountering unexplained clinical symptoms in construction workers, physicians should consider the possibility of lead poisoning caused by occupational exposure and be prepared to initiate adequate chelation therapy.

Case Report

A 24-year-old man was admitted to a local hospital with a 2-day history of a fever and severe abdominal colic. He had been aware of nausea and anorexia for the past month. Until then, he had been well, with no relevant medical history. He had been employed as a construction worker for two years. On admission, he was conscious and alert, and his vital signs were as follows: body temperature, 37.6 °C; pulse rate, 82 bpm with regular rhythm; blood pressure, 122/76 mmHg; respiration rate, 12 breaths/min; and oxygen saturation, 99% (ambient air). On a physical examination, he was pale with anemic palpebral conjunctivae and had diffuse abdominal tenderness without peritoneal signs. Findings of other medical examinations were normal; in particular, no neurologic deficit was detected. A complete blood count revealed normocytic anemia; the hemoglobin level was 7.3 g/dL (normal range: 12.0-16.0 g/dL) with a mean corpuscular volume of 86.3 fL (normal range: 80.0-100.0 fL) and a reticulocyte count of 2.81×10^4/μL (normal range: 4.00-8.00×10^4/μL). The white blood cell and platelet counts were normal. The serum iron, unsaturated iron binding capacity (UIBC), folate, vitamin B12, and haptoglobin levels were

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Table. Laboratory Data for the Present Patient on Admission.

Blood cell count	Normal range		***Biochemistry***	Normal range			Normal range	
WBC (×10³/μL)	4.0-9.0	8.7	T-Bil (mg/dL)	0.2-1.2	2.1	HBsAg (COI)	0.00-0.89	0.58
RBC (×10⁴/μL)	450-510	249	D-Bil (mg/dL)	0.0-0.3	0.8	HCVAb	0.00-0.89	0.04
Hb (g/dL)	12.0-16.0	7.3	AST (IU/L)	13-33	56	CMV-Ag	(-)	(-)
MCV (fL)	85.0-105.0	86.3	ALT (IU/L)	8-42	63	CMV-IgG	<2.0	5.7
MCHC (g/dL)	28.0-36.0	34	LDH (IU/L)	100-200	182	CMV-IgM	<0.80	0.3
Ht (%)	39.0-52.0	21.5	ALP (IU/L)	115-359	254	EB VCA-IgG	<10	80
Reticulocyte (%)	0.5-2.0	1.08	GGTP (IU/L)	11-58	104	EB VCA-IgM	<10	<10
Reticulocyte (×10⁴/μL)	4.00-8.00	2.81	TP (g/dL)	6.6-8.7	6.8	EBNA	<10	80
Platelet (×10⁴/μL)	15.0-45.0	38.8	Alb (g/dL)	3.4-4.8	4.7			
			BUN (mg/dL)	5-23	18	***Immunology***		
Urinalysis			Cre (mg/dL)	0.36-1.06	0.77	IgG (mg/dL)	680-1,620	740
pH	5.0-7.5	6.5	Na (mmol/L)	135-149	137	IgA (mg/dL)	84-438	106
protein	(-)	(±)	K (mmol/L)	3.5-4.9	3.8	IgM (mg/dL)	57-288	45
sugar	(-)	(±)	Cl (mmol/L)	96-108	100	Antinuclear Ab	<40	<40
occcult blood	(-)	(-)	Ca (mg/dL)	8.1-10.4	8.6	Antimitochondrial-Ab	0.0-20	<20
ketone	(-)	(1+)	UA (mg/dL)	3.4-7.0	7.8			
urobilinogen	(-)	(1+)	Amylase (U/L)	33-120	95	***Others***		
WBC	(-)	(-)	Lipase (U/L)	13-49	29	Vitamine B12 (pg/mL)	233-914	936
			CPK (U/L)	62-287	127	Folic acid (ng/mL)	3.6-12.9	3.9
Stool			CRP (mg/dL)	0.00-0.30	0.25	Haptoglobin (mg/dL)	19-170	70
occcult blood	(-)	(-)	Fe (μg/dL)	64-187	94	Copper (μg/dL)	68-128	113
			Ferritin (ng/mL)	30.0-400.0	641.9	Zinc (μg/dL)	59-135	108
Coagulation			UIBC (μg/dL)	13-33	208	urine δ-ALA (mg/dL)	<5.0	118.1
PT-INR	0.80-1.30	1.05	TSH (μU/mL)	0.54-4.54	0.55	urine PBG (mg/day)	<2.0	4.3
APTT (sec)	24.0-36.0	32.7	fT3 (pg/mL)	2.20-4.30	3.23	FEP (μg/dL/RBC)	30-86	258
D-dimer (μg/mL)	<1	0.4	fT4 (ng/dL)	0.90-1.70	2.02	serum-lead (μg/dL)	<20	100
						urine-lead (μg/L)	<25	337.4

WBC: white blood cells, RBC: red blood cells, MCV: mean corpuscular volume, MCHC: mean corpuscular hemoglobin concentration, PT: prothrombin time, APTT: activated partial thromboplastin time, T-Bil: total bilirubin, D-Bil: direct bilirubin, AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase, GGT: γ-glutamyltransferase, TP: total protein, ALB: albumin, BUN: blood urea nitrogen, Cre: creatinine, Na: sodium, K: potassium, Ca: calcium, UA: uric acid, CPK: creatine phosphokinase, CRP: C-reactive protein, Fe: iron, UIBC: unsaturated iron binding capacity, TSH: thyroid stimulating hormone, CMV: cytomegalovirus, EB: Epstein-Barr virus, EBNA: Epstein-Barr virus nuclear antigen, δ-ALA: delta-aminolevulinic acid, PBG: porphobilinogen, FEP: free erythrocyte protoporphyrin

normal. The blood zinc and copper levels were normal, and the serum levels of C-reactive protein (CRP), lactate dehydrogenase (LDH), and creatinine were also within the normal ranges. However, the levels of total bilirubin [T-Bil; 2.1 mg/dL (normal range: 0.23-1.2 mg/dL)], aspartate aminotransferase [AST; 56 U/L (normal range: 13-33 U/L)], alanine aminotransferase [ALT; 63 U/L (normal range: 8-42 U/L)], γ-glutamyltransferase [GGT; 104 U/L (normal range: 11-58 U/L)], and ferritin 641.9 ng/mL (normal range: 30.0-400.0 ng/mL) were elevated. Serum tests for hepatitis B and C, cytomegalovirus, and Epstein-Barr virus as well as autoimmune diseases gave negative results. Fecal immunochemical testing for hemoglobin was negative. These data are shown in Table.

Abdominal ultrasound demonstrated no abnormalities. Non-contrast-enhanced whole-body computed tomography (CT) revealed multiple small, high-density areas thought to be lead particles in the stomach and small intestine, but no marked free air or ascites was noted. However, no abnormalities were detected in the respiratory tract (Fig. 1). Gastroscopy showed chronic non-atrophic gastritis, and colonoscopy demonstrated no abnormality. Wireless video capsule endoscopy revealed multiple ulcerations of the small intestine (Fig. 2). After about 30 days of symptomatic therapy, such as analgesics and fluid maintenance, the patient's clinical condition had not improved, so he was transferred to our hospital.

We then reassessed the patient's occupational history in detail and found that he had been engaged in repainting an iron bridge, involving scraping, sanding, and heat treatment with an electric iron device for two months before the onset of symptoms and had never been engaged in such work until then. During this work, he had worn a simple paper mask, and not a more sophisticated respiratory protection device. Furthermore, he had commonly smoked cigarettes at work without first washing his hands. We also reassessed the findings of the patient's physical examination and peripheral blood smear. This revealed a blue-purplish line bordering the upper gums, referred to as Burton's line (Fig. 3), and basophilic stippling of erythrocytes after May-Giemsa

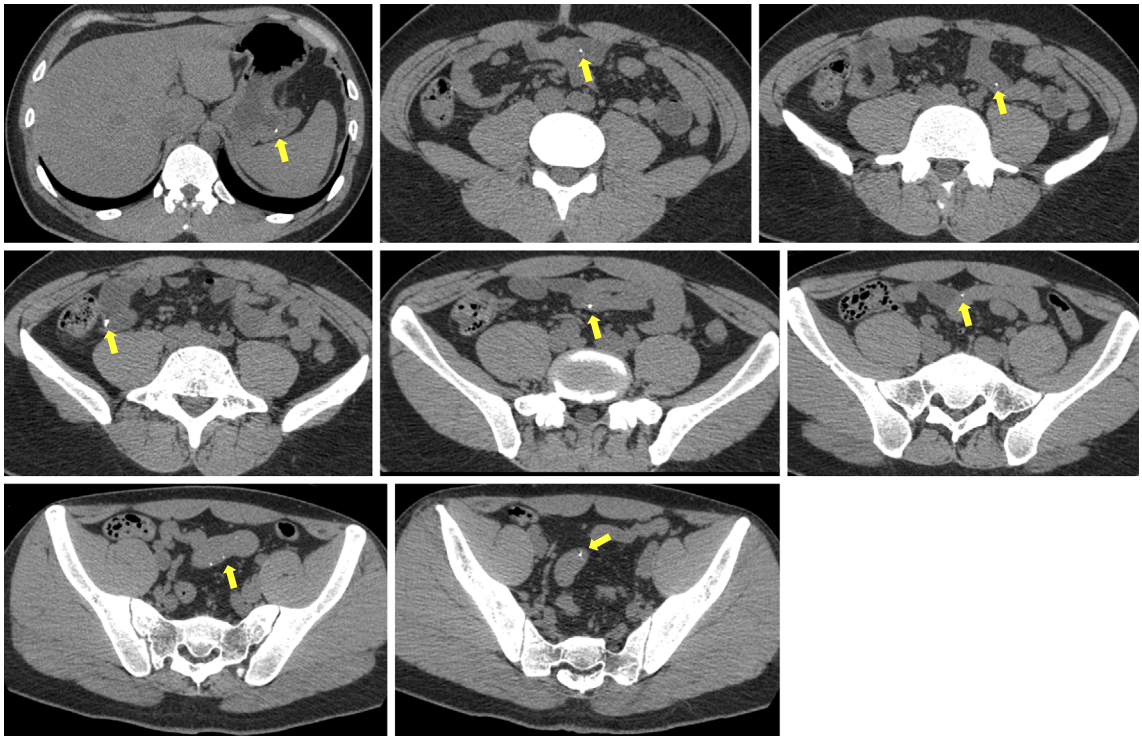

Figure 1. **Non-contrast-enhanced abdominal computed tomography showing multiple small, high-density areas in the small bowel (yellow arrows).**

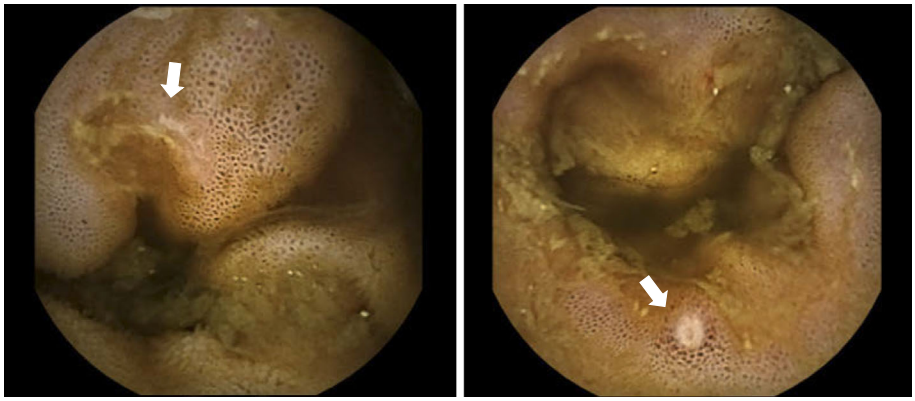

Figure 2. **Wireless video capsule endoscopy showing multiple ulcerations of the small bowel (white arrows).**

staining (Fig. 4). The levels of urinary delta-aminolevulinic acid (δ-ALA) and porphobilinogen (PBG) as well as free erythrocyte protoporphyrin (FEP) were assessed for the differential diagnosis of acute porphyria. The levels of urine δ-ALA and FEP were elevated at 118.1 mg/L (normal range, <5.0 mg/L) and 258 μg/dL/RBC (normal range, 30-86 μg/dL/RBC), respectively. However, the urine PBG level was only slightly elevated [4.3 mg/day (normal range, <2.0 mg/day)]. Occupational lead poisoning was highly suspected, so the blood and urine levels of lead were examined. This revealed an elevated blood lead level of 100 μg/dL [normal range, <20 μg/dL (values over 20 μg/dL in adults are considered toxic)] and a urine lead level of 337.4 μg/L (normal range, <25.0 μg/L) (Table).

The final diagnosis was lead poisoning due to occupational exposure, and chelation therapy was initiated immediately. Edetate calcium disodium (CaEDTA) was given orally at a dose of 2,000 mg per day for 5 days every 2 to 4 weeks. After the introduction of chelation therapy, the patient's abdominal colic and anorexia, hemoglobin level, and liver dysfunction promptly improved. The blood lead level also improved after four rounds of treatment (Fig. 5). Unfortunately, wireless video capsule endoscopy performed to evaluate the effect of treatment yielded no information.

Discussion

The present case of occupational lead poisoning, charac-

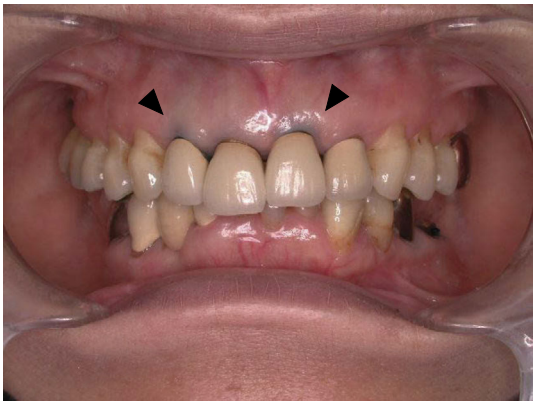

Figure 3. **Discoloration of the upper gum margin (Burton's line: black arrows).**

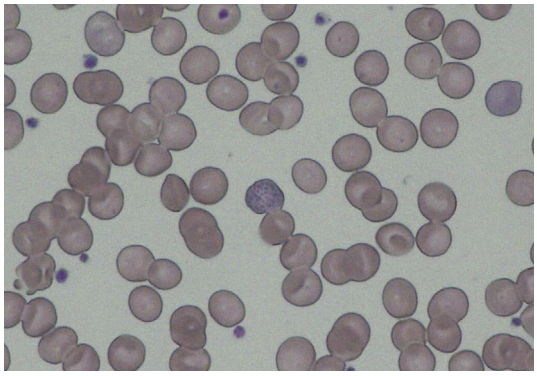

Figure 4. **Microscopic appearance of a May-Giemsa-stained peripheral blood smear. An erythrocyte with basophilic stippling is evident (×100) (black arrows).**

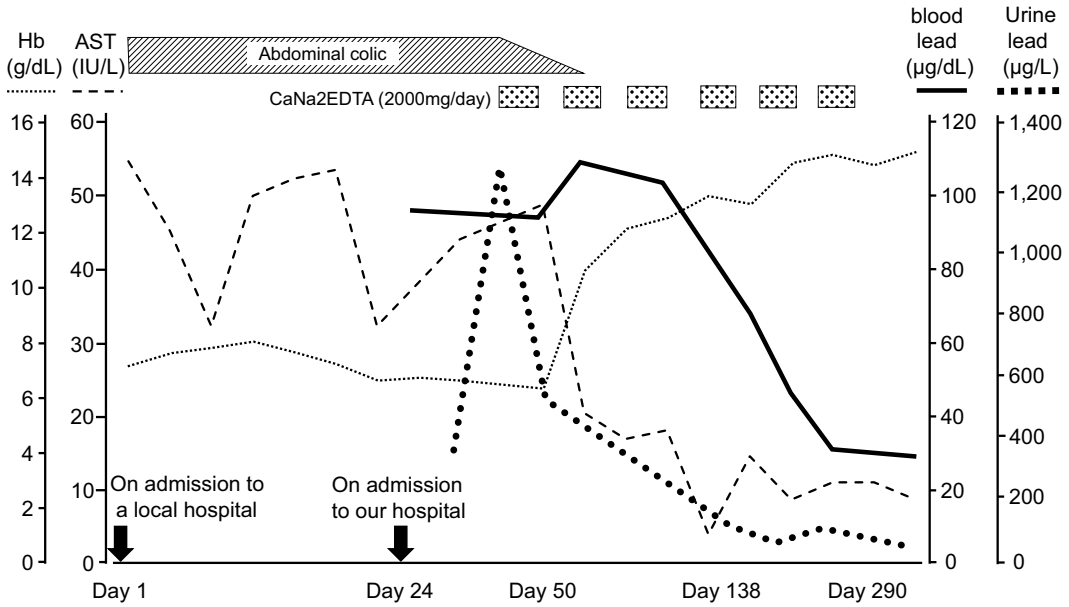

Figure 5. **Clinical course of the present patient on admission.**

terized by acute abdomen, abdominal colic, and normocytic anemia, raises several clinical and public health issues. Perhaps the most important one is that, even today, lead poisoning due to occupational exposure can still occur sporadically in construction workers in Japan. This is mainly attributable to poor compliance with recommended occupational lead exposure protection measures during maintenance work on older bridges and structures.

Acute and subacute exposure to lead in adults can produce various symptoms, including gastrointestinal (e.g., abdominal pain, constipation, and anorexia), musculoskeletal (e.g., arthralgia and myalgia), general (e.g., excessive fatigue, sleep disturbance and decreased libido), and neuropsychiatric (e.g., headache, difficulty concentrating, deficits in short-term memory, irritability, and depression) symptoms. Since the symptoms are vague and nonspecific, a misdiagnosis may occur (2-4). Proven cases of occupational illness caused by repeated exposure to chemical substances are rare in Japan in the modern era. The majority of such cases are reportedly acute intoxication resulting from accidental exposure to gases, vapors, or caustic liquids. Occupational exposure to chemicals has been greatly reduced since the early 1970s, as employers are obliged to comply with related ordinances for about 100 chemicals aimed at the fairly precise control of the work environment and practices. Compulsory measurement of the workplace concentrations of these specified chemicals based on the Working Environment Measurement Law (1975) (5) is an important factor that has contributed to the improvements seen in the last few decades. However, there are several reasons to believe that some workplaces still carry a risk of excessive exposure.

Significant exposure to lead can occur as a result of living in urban environments, consumption of produce from family gardens, renovation of homes, contact with interior lead paint dust, occupational exposure, smoking, and wine consumption. In Japan, trilead tetraoxide (Pb_3O_4) was mixed with paint to prevent rust until about 1990. Such lead-containing paints were used not only on iron bridges but

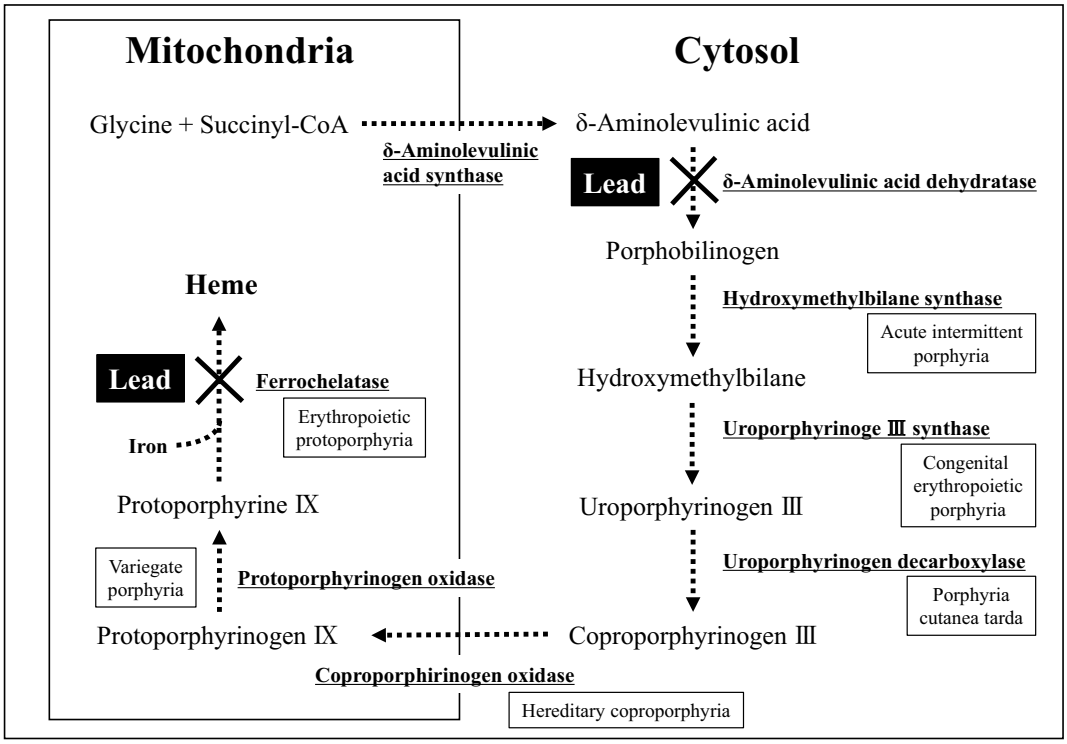

Figure 6. Effects of lead on the heme biosynthetic pathway and porphyria. Ferrochelatase and δ-aminolevulinic acid dehydratase are inhibited by lead, causing an increase in the level of free erythrocyte protoporphyrin and overproduction of δ-aminolevulinic acid with a normal level of porphobilinogen. Porphyria occurs due to the defective biosynthesis of heme, an iron-porphyrin complex that is the oxygen-carrying moiety of hemoglobin. Different types of porphyrin accumulate due to inherited defects in this biosynthetic pathway. In each specific porphyria, the activity of specific enzymes in the heme biosynthetic pathway is defective, leading to the accumulation of pathway intermediates. Each of the eight enzymes (underlined) in the heme biosynthetic pathway is associated with a specific porphyria.

also highway bridge girders and other structures, such as playground equipment in parks. In order to prevent the deterioration of paint films, repainting is required every 5 to 10 years. During surface preparation for repainting, construction workers may be exposed to significant amounts of lead paint dust or chips in the form of particles that have been scraped or sanded off. Although any construction work involving older bridges and structures carries a risk of occupational lead exposure, not all workers involved adhere to the recommended lead exposure precautions stipulated in the Ordinance on Prevention of Lead Poisoning. For this reason, sporadic cases of lead poisoning caused by occupational exposure can still be encountered in construction workers (1).

Lead is absorbed into the body through the lungs and gastrointestinal tract and, to a lesser extent, the skin. The respiratory tract is the most significant route of lead absorption in adults, while the gastrointestinal tract is more common in small children due to their tendency to place objects in the mouth. In the present case, although chest CT demonstrated no abnormality in the respiratory tract, the lead was thought to have been absorbed into the body through the lungs. However, lead absorption via the gastrointestinal tract can be a significant contributor in adults, particularly those working or eating in a lead-contaminated environment. In our patient, lead may also have been ingested, as abdominal CT revealed multiple small, high-density areas thought to be lead particles in the stomach and small intestine. In addition, wireless video capsule endoscopy demonstrated multiple ulcerations in the small bowel associated with abdominal colic, and these disappeared immediately after the start of chelation therapy. Based on these results, it was thought that, in the present case, significant amounts of lead particles had been absorbed into the body through both the lungs and gastrointestinal tract as a result of poor compliance with recommended occupational lead exposure protection. The high lead exposure he sustained despite having been engaged in repainting work for a short period of only two months was believed to have caused acute to subacute lead poisoning.

The precise details of the pathogenetic mechanism of lead-induced abdominal colic are unknown. However, three possibilities have been proposed: changes in visceral smooth muscle tone through the effects of lead on the visceral autonomic nervous system, altered sodium transport in the small-intestinal mucosa, and lead-induced interstitial pancreatitis (6). Wada et al. reported a case of lead poisoning

attributable to lead ingestion in a Japanese Black heifer with a pathologic presentation of ulceration in the alimentary canal (7). We were unable to find any other similar human case of peptic ulcer caused by ingestion of lead. Peptic ulcer formation due to direct mucosal damage following ingestion of lead might be a cause of abdominal manifestations, including lead colic.

Lead poisoning can be misdiagnosed as nonspecific abdominal pain or acute porphyria (8, 9). Both porphyria and lead poisoning can impair the heme biosynthetic pathway, potentially leading to limited heme production. High levels of lead in blood can affect the heme/hemoglobin metabolism pathway, resulting in the production of FEP and, eventually, anemia (10, 11). Furthermore, lead toxicity can cause degeneration of ribosomal ribonucleic acid in erythrocytes, leading to the appearance of basophilic stippling on peripheral blood smears (12). However, acute porphyria (characterized by a potent, variable, catalytic defect of enzymes involved in the heme pathway) is accompanied by the overproduction of heme-precursor molecules, specifically δ-ALA and PBG (13-15). In lead poisoning, the metal directly inhibits ALA dehydratase, which catalyzes the second step of heme synthesis in mammals, causing overproduction of ALA with normal PBG levels (16-18). In the present case, the elevated levels of FEP and urine δ-ALA without any increase in the level of urine PBG were useful guides for the diagnosis of lead poisoning. Testing for heme precursors, such as δ-ALA and PBG, in urine is crucial for the differential diagnosis of lead poisoning and acute porphyria (19). Heme biosynthesis and localization of characteristic enzyme defects in patients with lead poisoning or porphyria are shown in Fig. 6.

For patients who are symptomatic or have a blood lead level of ≥70 μg/dL, immediate chelation therapy is strongly recommended (20). The two chelating agents most commonly used to treat adults are ethylenediaminetetraacetic acid (EDTA) and edetate calcium disodium (CaEDTA). The rate of improvement can be highly variable, ranging from weeks to years, depending on the magnitude of intoxication (21).

In conclusion, the present case highlights the importance of taking a detailed occupational history and considering lead poisoning in the differential diagnosis of unexplained abdominal colic and normocytic anemia. Even though the diagnosis of lead poisoning may be challenging in modern Japan because of its rarity, physicians must always bear this possibility in mind for the differential diagnosis of patients with suggestive symptoms.

The authors state that they have no Conflict of Interest (COI).

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