Aggressive Approach in the Treatment of Acute Lead Encephalopathy With an Extraordinarily High Concentration of Lead

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**Objective:** To report a case of a 3-year-old child with an extraordinarily massive lead concentration, 26.4 µmol/L (550 µg/dL), following environmental exposure to lead paint in the home.

**Literature Review:** The relevant literature concerning the treatment of lead encephalopathy was reviewed during the treatment of this child and preparation of the manuscript. To our knowledge, the landmark article written by Julian Chisolm in 1968 is the only recent article that reported similarly high levels of lead concentration. This case, however, is the first in which 3 chelating agents were used for the treatment of lead encephalopathy. We also reviewed the literature on the use of whole bowel irrigation in heavy metal intoxications.

**Conclusions:** In this case, aggressive gut decontamination with whole bowel irrigation and triple chelation therapy with British anti-Lewisite, EDTA, and oral succimer was well tolerated and seemed effective for rapidly deleading the child. The extent to which her lead concentration increased while being treated with oral succimer alone necessitated further chelation with EDTA. Further evaluation is necessary to determine if triple chelation therapy is an appropriate method for severe lead intoxication, and if the use of whole bowel irrigation should be considered in heavy metal intoxication.


**Editor’s Note:** The unusually severe problem reported in this case study should serve as a stark reminder that lead poisoning might be decreasing, but it’s certainly not gone.

_Catherine D. DeAngelis, MD_

**LEAD POISONING in children remains a significant problem. Although many sources of lead (ie, gasoline, soldered seams of food and beverage cans, and seals on wine bottles, and paint) have been eliminated, lead is still present in many residences.** Buildings constructed in the United States prior to 1977 are exempt from legislation that prohibits the use of lead-based paint. The act of 1977 only restricted lead-based paint in new residential homes and paint sold in interstate commerce. Consequently, buildings constructed prior to 1980 may have a large amount of peeling or chipped paint with high lead content, putting children living there at high risk of lead intoxication. As renovations of old buildings increase, there is additional risk of exposure to lead in the dust and dirt. It is generally accepted that low-income housing areas are at high risk for lead poisoning, yet higher income areas are not immune to the risks of lead poisoning. We report a case of severe lead encephalopathy with extraordinary concentrations of lead in a 3-year-old child following environmental exposure.

**CLINICAL FINDINGS**

A 3-year-old girl was transferred to our hospital with a history of progressively worsening visual acuity, difficulty walking and speaking, abdominal pain, and vomiting. She previously had been admitted to the emergency department of a local hospital with nonspecific abdominal pain, nonbilious, nonbloody vomiting, and frequent soft bowel movements for 3 days. The child was dehydrated and her complete blood cell count revealed a microcytic, hypochromic anemia. She was given fluids by mouth and was sent home with a prescription for ferrous sulfate solution and instructions for follow-up with her primary care physician. During the next 2
days her abdominal pain and vomiting continued. She also became lethargic, sometimes difficult to awaken, and developed an unsteady gait. The mother also noticed a deviation in the child’s left eye and a deterioration in her hand-eye coordination. On subsequent evaluation at the local emergency department, she was more lethargic and had a heart rate of 60/min. Her laboratory findings included hemoglobin, 7.7 g/dL; mean corpuscular volume, 55.9 fL; red cell distribution width, 0.24; and a white blood cell count of 12.3×10^9/L, with 0.82 neutrophils. Cerebrospinal fluid analysis revealed a white blood cell count of 5.0×10^3/L, with 0.24 neutrophils and 0.62 lymphocytes; and a red blood cell count of 4.4×10^12/L. Her serum ammonia level was 38 µmol/L; alanine aminotransferase, 53 U/L. Noncontrast computed tomography of the head showed normal findings. A blood lead concentration was also drawn at this time, but was sent to an outside laboratory for testing. The child was given 1 dose of ceftriaxone disodium, 100 mg/kg, and was transferred to our facility.

The child’s medical history included one hospital admission for bronchiolitis, and the mother described behavior consistent with pica. The mother denied that the child had ingested paint chips or other lead-containing products, but did indicate that they had lived for the past 3 years in an older apartment building that had not been well maintained. The child had received limited medical care in the past and was not seen regularly by a physician.

The child was difficult to awaken and unable to walk. She opened her eyes only in response to pain. Her vital signs were temperature, 36.8°C; heart rate, 67 beats per minute; respirations, 18/min; and blood pressure, 95/31 mm Hg. Her right pupil was 4 to 5 mm in diameter and had a sluggish reaction to light. Her left pupil was 5 to 6 mm in diameter and deviated to the right. Her Glasgow Coma Scale score was 8. Her blood lead concentration was 26.4 µmol/L (550 µg/dL). An abdominal radiograph showed opaque areas that resembled paint chips throughout the gastrointestinal tract and dense areas along the iliac crest that resembled lead lines (Figure 1). Her blood smear demonstrated hypochromia and anisopoi-kilocytosis with prominent basophilic stippling.

**TREATMENT COURSE**

Because of the exceptionally high concentrations of lead in this child and other evidence indicating excessive lead exposure, it was decided by the toxicology service that the potential benefits of attempting intensive 3-drug chelation therapy and whole bowel irrigation outweighed the unknown risks. The initial chelation therapy consisted of the administration of 4 mg/kg of British anti-Lewisite (BAL) intramuscularly every 4 hours. Whole bowel irrigation (WBI) with polyethylene glycol was performed at 20 mL/kg per hour via nasogastric tube and continued for 3 days until the abdominal radiograph essentially showed no abnormalities. Calcium disodium EDTA therapy was started 4 hours after BAL, at 50 mg/kg per day intravenously, and was subsequently increased to 75 mg/kg per day on the second day and continued at this dosage through the first treatment course. When WBI was completed, oral succimer was administered at 200 mg 3 times daily for 5 days, followed by 200 mg 2 times daily for 14 days. The patient’s blood lead concentration fell from 25.4 µmol/L (550 µg/dL) to 3.38 µmol/L (70 µg/dL) during the first 5 days of the treatment course (Figure 2). It then increased sharply to 4.78 µmol/L (99 µg/dL) 2 days after the BAL and EDTA treatments were stopped. Calcium disodium EDTA treatment was restarted at 50 mg/kg per day for another 5 days, which resulted in a drop in blood lead concentration to 3.71 µmol/L (77 µg/dL) the day after completion. The administration of oral succimer was continued and the patient had serial blood lead concentrations 2 and 4 days after discontinuation of the second treatment course of calcium disodium EDTA. Blood lead concentrations were 3.18 µmol/L (66 µg/dL) and 3.96 µmol/L (82 µg/dL), respectively, and we reinstituted treatment with a third course of calcium disodium EDTA at 50 mg/kg per day for 5 days. An oral zinc sulfate supplement was also administered at 100 mg/d at this time. Blood lead concen-
trations at completion of the third course and 2 days after completion were 2.51 µmol/L (52 µg/dL) and 3.33 µmol/L (69 µg/dL), respectively. She was discharged into the care of the mother and grandmother to stay at a location approved by the Illinois Department of Public Health. Her medications on discharge from the hospital included oral succimer, zinc sulfate, and iron sulfate. The child is being monitored by her local physician without further complications.

**COMMENT**

The treatment of acute lead encephalopathy has not changed much in the last 20 years.6-11 The mainstay of treatment is chelation therapy, which is frequently limited by toxic reactions.6-12 The pharmacological action of BAL has proven useful for chelating several heavy metals, including lead.6-12 As BAL must be administered by deep intramuscular injection every 4 hours, treatment is painful and often difficult to adhere to, especially in children. Most of the other adverse effects tend to be dose limiting, but do not contraindicate the use of BAL unless the patient has an allergy to peanut oil (the diluent in which BAL is prepared) or is glucose-6-phosphate dehydrogenase–deficient.6-12 Calcium disodium EDTA (ethylenediaminetetraacetic acid) has been available for the treatment of lead poisoning for more than 50 years. Initial use revealed salt-specific problems.12 The current salt form (calcium disodium EDTA) is now the specific agent approved for use in treating lead intoxication, but it still binds other metal ions including zinc, copper, and manganese.12 Its major limiting toxicity is a dose- and infusion rate–related nephrotoxicity.13 In an effort to minimize toxic effects, we used a 5-day continuous intravenous infusion for our patient. In 1968, Chisolm10 recommended the use of BAL and calcium disodium EDTA together for the treatment of moderate to severe lead poisoning and found the combination to be superior to either agent alone in lowering the blood lead concentration. In 1992, O’Connor11 also studied the combination of calcium disodium EDTA and BAL, corroborating the results found by Chisolm in 1968 that gave us the current recommendations for the treatment of acute lead encephalopathy.6-11 Most current treatment regimens for children who are asymptomatic for chronic lead poisoning or who are asymptomatic but have blood lead concentrations greater than 3.38 µmol/L (70 µg/dL) recommend removal of the child from the source of lead and inpatient treatment with parenteral drug therapy.9 Patients who are asymptomatic with blood lead concentrations between 2.17 and 3.33 µmol/L (45 and 69 µg/dL) generally receive chronic outpatient treatments or are admitted for parenteral drug therapy with calcium disodium EDTA.9 In 1991, meso-2,3-dimercaptosuccinic acid, or succimer, was added to the treatment options for mild to moderate lead poisoning (2.17-3.33 µmol/L [45-69 µg/dL]), representing the only new agent for the treatment of lead poisoning in more than 30 years.9,12 Besunder et al13 and Graziano et al14 studied meso-2,3-dimercaptosuccinic acid in the short-term treatment of patients with low to moderate blood lead concentrations and found it both efficacious and safe. Cory-Slechta15 used meso-2,3-dimercaptosuccinic acid for long-term treatment in rats and also found it to be both safe and effective.15 She does note that it may be effective as an adjunct treatment with calcium disodium EDTA to further reduce total body lead burden.

Extraordinarily high blood lead concentrations similar to the concentration found in our patient (26.4 µmol/L [550 µg/dL]), although infrequent, have been seen in children since 1968. Until the late 1960s, death rates for patients seen with severe neurologic sequelae (ie, seizures or coma) were reported to be approximately 25%, even after the development of calcium disodium EDTA.10,16 Prior to this, Foreman17 noted that encephalopathy secondary to lead poisoning, if left untreated, had a greater than 60% mortality rate. It was not until the standard of medical practice included the concurrent administration of BAL and calcium disodium EDTA that this fatality rate started to decrease. Other factors, such as the timeliness of the diagnosis of lead intoxication and the initiation of treatment, probably also affected the percentage of deaths related to lead intoxication. Isolated case reports of child fatalities resulting from lead intoxication have been reported since 1970 (eg, Alexander and Delves18, Hugelmyer et al19), and notable features of those cases were inappropriate diagnosis, delay in treatment, or both.

Among the cases reported by Greengard et al16 in 1965, the blood lead concentrations that resulted in death

**Figure 2.** Radiographic findings of the long bones in the legs (left) and hands (right) showing areas of increased lead density of “lead lines.”
varied greatly (4.35-39.85 µmol/L [90-825 µg/dL]). It is likely that most of these deaths are related to an acute ingestion as opposed to chronic intoxication. Extraordinarily high concentrations of lead (>14.49 µmol/L (>300 µg/dL)) are most likely the result of an acute or acute-on-chronic ingestion. In light of the considerable risk of encephalopathy and death in children with very high blood lead concentrations, we elected at the outset to use a 3-drug chelation regimen. During her initial 5-day treatment course, the patient experienced a significant drop in her blood lead concentration, from 26.36 to 3.38 µmol/L (550 to 70 µg/dL), and she showed dramatic improvement in neurologic status. Even though oral succimer therapy was continued, her blood lead concentration increased substantially once calcium disodium EDTA and BAL therapy were stopped. Since her condition had improved so drastically, we decided to restart a second treatment course of calcium disodium EDTA without BAL in an effort to minimize toxic effects. Her cognitive function improved rapidly and, with the help of physical therapy, she was able to walk well again. She continued to have strabismus of the right eye, but was able to recognize objects and people. According to the family, she was close to her baseline cognitive function prior to initial presentation.

Before the third treatment course of calcium disodium EDTA was started, oral zinc supplementation was initiated. Following this, the patient’s blood lead concentration dropped significantly from 4.10 to 2.51 µmol/L (85 to 52 µg/dL). Zinc supplementation has been reported to enhance the elimination of lead when given in conjunction with calcium disodium EDTA in animals.20,21

Whole bowel irrigation has become a popular method of gross removal of toxins in the gastrointestinal tract.22,23 In this case, the use of WBI removed most, if not all, of the lead chips present in the initial kidney, ureter, and bladder, without causing any of the metabolic derangements seen with other forms of catharsis. The effectiveness of this method in removing certain toxins, especially those not bound to activated charcoal, and those found below the level of the pylorus, needs further investigation. Other forms of catharsis have been associated with significant metabolic abnormalities in fluid and electrolyte levels.22 To date, most studies and observations in the literature concerning WBI for gross removal of toxins have not been associated with significant metabolic derangement, and we found it safe, effective, and supportive of that literature.23-28 Kaczkowski and Wax29 report a case in which 44 L of polyethylene glycol at 20 to 30 mL/kg per hour for the kidney, ureter, and bladder where lead chips were present. (2) British anti-Lewisite at 4 mg/kg every 4 hours as an intramuscular injection for 3 to 5 days. (3) Calcium disodium EDTA at 50 to 75 mg/kg per day 4 hours after starting BAL therapy. (Note: We diluted the calcium disodium EDTA to a concentration of 2 to 4 mg/mL. 5% dextrose in water, and infused it intravenously over 24 hours). This was continued for a total of 5 days. (4) Once WBI was completed, we started oral succimer treatment at 10 mg/kg every 8 hours for 5 days, and then 10 mg/kg twice daily for 14 days. (Note: Oral succimer treatment was started immediately in the younger sibling, as her gastrointestinal tract was clear on presentation). (5) Zinc supplementation was started during the third course of chelation with calcium disodium EDTA.

The course of oral succimer treatment was continued after the patient was discharged from the hospital. The patient and her sister are being monitored by their pediatrician. Unfortunately, the family has relocated more than once, making follow-up more difficult. The Illinois Department of Public Health and the local police depart-
ment have been involved to ensure that the children are getting the necessary medical attention required. This situation is probably not unusual in many cases of lead intoxication. Families must often move away from the source of lead if it cannot be removed, which further confounds the efforts of the medical system to effectively treat patients.

Efforts to increase public awareness of the dangers of lead poisoning and to remove the sources of lead from the environment are clearly needed. Closer adherence to the Title X mandate “The Residential Lead-Based Paint Hazard Reduction Act of 1992” is imperative. Landrigan and Todd suggested adapting the guidelines of the Hazard Reduction Act of 1992 is imperative. Landrigan and Todd7 suggested adapting the guidelines of the Asbestos Hazard Emergency Response Act, which requires appropriate training for lead workers in the removal of lead. Without safe and appropriate removal of lead from its many sources in the environment, lead intoxication will continue to be a problem well into the 21st century.

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REFERENCES


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