Elemental Mercury Poisoning Presenting as Hypertension in a Young Child

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Abstract: Mercury intoxication is an uncommon cause of hypertension in children and can mimic several other diseases, such as pheochromocytoma and vasculitis. Mercury intoxication can present as a diagnostic challenge because levels of catecholamines may be elevated, suggesting that the etiology is a catecholamine-secreting tumor. Once acrodynia is identified as a primary symptom, a 24-hour urine mercury level can confirm the diagnosis. Inclusion of mercury intoxication in the differential diagnosis early on can help avoid unnecessary and invasive diagnostic tests and therapeutic interventions. We discuss a case of mercury intoxication in a 3-year-old girl presenting with hypertension and acrodynia, without a known history of exposure. Chelation therapy successfully treated our patient's mercury intoxication. However, it was also necessary to concurrently treat her hypertension and the pain associated with her acrodynia. Because there were no known risk factors for mercury poisoning in this case, and because ritual use of mercury is common in much of the United States, we recommend high clinical suspicion and subsequent testing in all cases of acrodynia.

Key Words: mercury poisoning/toxicity, hypertension, acrodynia, chelation therapy

(*Pediatr Emer Care* 2012;28: 812–814)

Elemental mercury intoxication is a rare cause of hypertension in children[1] but has potential for serious morbidity and can mimic several other serious conditions, including catecholamine-secreting tumors, Kawasaki disease, stimulant ingestion, and vasculitis. Elemental mercury intoxication affects, with varying degrees, the central and peripheral nervous systems, the cardiovascular system, the kidneys, the lungs, the gastrointestinal tract, and the skin, depending on the dose and chronicity of exposure.[2,3]

In the 19th and early 20th centuries in the United States, children in particular were exposed to elemental mercury in the form of laxatives and diaper and teething powders.[2] Present-day sources of elemental mercury exposure include thermometers, disk batteries, fluorescent light bulbs, sphygmomanometers, latex paint, and dental amalgams, as well as certain cultural and religious practices and industrial processes.[2–4] We present here a case of a child with elemental mercury intoxication that raises implications for the differential diagnosis and evaluation of hypertension in children and highlights the need for further evidence-based recommendations for treatment of mercury intoxication and interim management of mercury-induced hypertension and acrodynia.

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Disclosure: The authors declare no conflict of interest.
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There are no sources of support/funding for this study.

ISSN: 0749-5161

CASE

A 3-year-old girl presented with 3 weeks of intermittent abdominal pain, diaphoresis, and tachycardia. Four days before admission, she developed pain in her hands and feet. On presentation she was hypertensive, with blood pressure of 158/100 mm Hg while calm. The patient's initial examination revealed a thin, diaphoretic girl with tachycardia and a hyperdynamic precordium, a diffusely tender but soft abdomen, and a normal result in the neurological examination aside from irritability. She had warm, erythematous, edematous palms and soles with intermittently appearing papules and desquamation, as well as a pruritic, erythematous, maculopapular rash over her chest and back. Her systemic symptoms were episodic throughout the day, and she appeared anxious during the episodes. Her extremity findings were consistent with acrodynia—an idiosyncratic hypersensitivity reaction to mercury exposure.[5] On further examination of history, the patient's mother reported that there had been no fish ingestion in the last month. They also denied any broken thermometers in the house, burning of batteries or fluorescent lamps, contact with miners, steel workers, or with people working in cement factories or crematoria. They denied the patient had any recent ingestion of paint or new toys and stated that the patient did not regularly put toys in her mouth. The mother did, however, note that the family moved into a new apartment 2 months before presentation.

The patient had symmetrically elevated blood pressure in 4 extremities, unremarkable echocardiogram and electrocardiogram, and a normal result on fundoscopic examination. Her initial electrolytes, creatinine, and urinalysis were all normal and remained so on serial evaluations. Urine drug screen was negative. Thyroid function panel and levels of renin and aldosterone were normal. An abdominal plain film was unremarkable. Plasma metanephrine and plasma and urine catecholamine levels were elevated, suggestive of pheochromocytoma (Table 1). A magnetic resonance imaging (MRI)/angiography of the abdomen and MRI of the chest and pelvis showed no masses or renal artery stenosis, and an MRI of the brain and neck showed no masses or other abnormalities. Given the patient's persistent hypertension, tachycardia, diaphoresis, irritability, acrodynia, and elevated catecholamine levels without evidence of a tumor on imaging, mercury toxicity was suspected, despite absence of any known exposure. A 24-hour urine mercury sample was elevated at 60 μg (reference range, 0–20 μg/24 h).

The patient was started on oral chelation therapy with dimercaptosuccinic acid (DMSA) 16 mg/kg divided twice daily. Her hypertension was controlled with labetalol and amlodipine. One week after initiation of therapy, her urine mercury level rose to 178 μg, but after 2 weeks on therapy, it began to drop and she was continued on therapy for approximately 2.5 months (Fig. 1). Creatinine levels and results in liver function tests during chelation therapy remained normal. She required antihypertensive therapy for 2 months. At 3 months of follow-up, the patient was normotensive off medication, her acrodynia and irritability had resolved, and plasma metanephrine levels normalized.

TABLE 1. Laboratory Evaluation

Free T_4 (reference range, 0.8–1.8 ng/dL)	1.8 ng/dL
TSH (reference range, 0.35–5.5 uIU/mL)	3.85 uIU/mL
Plasma renin activity (reference range, 100–650 ng/dL per hour)	542 ng/dL per hour
Aldosterone (reference range, 2–37 ng/dL)	16 ng/dL
Plasma	
Total metanephrine (reference range, ≤205 pg/mL)	424 pg/mL
Normetanephrine (reference range, ≤148 pg/mL)	392 pg/mL
Dopamine (reference range, 0–135 pg/mL)	<20 pg/mL
Norepinephrine (reference range, 0–600 pg/mL)	1474 pg/mL
Epinephrine (reference range, 0–90 pg/mL)	149 pg/mL
24-h urine	
Total metanephrine (reference range, 0–900 μg/d)	797 μg/d
Norepinephrine (reference range, 4–29 μg/d)	119 μg/d
Epinephrine (reference range, 0–6 μg/d)	33 μg/d
Dopamine (reference range, 40–260 μg/d)	284 μg/d

T_4 indicates thyroxine; TSH, thyroid-stimulating hormone.

The state Department of Health was notified when the patient's urine mercury level returned elevated, and investigation by the Department of Environmental Management revealed elevated mercury levels throughout the home and levels above 30,000 ng/m^3 in the master bedroom, whereas a limit of 1000 ng/m^3 has been set as the safe level for occupancy. Neighbors reported that the previous tenant was a Columbian woman who practiced rituals in the home that involved the use of mercury. Such practices are well described in the literature, and elemental mercury is obtainable at community botanicas.[4]

DISCUSSION

This case report highlights the importance of including mercury intoxication in the differential diagnosis of children with hypertension, even in the absence of known exposure, and particularly when symptoms suggest pheochromocytoma. Mercury interferes with the catabolism of catecholamines by inactivating a coenzyme used by catecholamine-*O*-methyltransferase, resulting in accumulation of norepinephrine, epinephrine, and dopamine in the blood and urine.[1] This is responsible for both the pheochromocytoma-like symptoms (hypertension, diaphoresis, tachycardia) and the laboratory findings (elevated levels of plasma and urine catecholamines and metanephrines) associated with mercury intoxication. Mercury intoxication should be considered in any child in whom a catecholamine-secreting tumor is suspected.

In this particular case, with no tumor visible on MRI and before the result of the urine mercury level, the diagnosis of erythromelalgia was also considered. Erythromelalgia is a rare condition composed of episodic erythema, warmth, and burning pain in the extremities.[6] Primary erythromelalgia can begin spontaneously at any age. and new research suggests a hereditary component involving mutation in the $Na_v1.7$ voltage-gated sodium channel.[7] Secondary forms are associated with underlying illness such as myeloproliferative and autoimmune diseases. Symptoms are triggered by warm temperatures, and patients often find relief by cooling the affected extremities. Interestingly, our patient did find comfort in running her hands under cold water. The pathophysiology has yet to be fully characterized but is believed to be due to vascular shunting and reactive hyperemia.[6]

Management of this patient's hypertension was complicated by the combination of increased sympathetic nervous system activity and persistent pain resulting from this patient's acrodynia. In addition, the choice of antihypertensive agents had an impact on imaging modalities. Given that her symptoms were most suggestive of an elevated catecholamine-like state, labetalol was chosen because of its combined blockade of α- and β-adrenergic activities. Selectively blocking only α- or β-adrenoreceptors can result in overstimulation of the unblocked pathway, so it is recommended that both adrenoreceptors be inhibited. Her blood pressures were only partially controlled on labetalol. When imaging failed to demonstrate a tumor and vasculitis was suspected, calcium channel blockers (CCB)—amlodipine and isradipine—were added to her antihypertensive regimen. It was postulated that hypertension from vasculitis may result from endothelial dysfunction of the vasculature, and CCBs may inhibit this process. When no laboratory data supported a diagnosis of vasculitis, meta-iodobenzylguanidine (MIBG) scan was considered to identify any catecholamine-secreting tumor. However, labetalol and CCBs have been shown to reduce uptake of MIBG and lead to false-negative scans,[8] so there was consideration of switching her to other blood pressure agents, such as an angiotensin-converting enzyme inhibitor and a vasodilator. Fortunately, her urine mercury level came back elevated, and a MIBG scan was no longer indicated.

Hypertension resulting from mercury toxicity often requires more than 1 class of antihypertensive medication. Case reports have described the simultaneous use of up to 4 different antihypertensives.[1,5] Our report describes the successful management of this patient's hypertension with the dual therapy of labetalol 4.5 mg/kg per day and amlodipine 0.4 mg/kg per day. The emphasis placed on adequate pain management and the use of topical mexiletine to the hands and feet and oral gabapentin may have contributed to the successful control of her blood pressures.

In the literature, nephrotoxic effects from mercury exposure often present as nephrotic syndrome.[9–12] Occasionally, reversible renal tubular dysfunction has also been reported.[13] Fortunately, the patient did not develop either sign of renal toxicity. There is no specific therapy to treat the nephrotoxic effects of

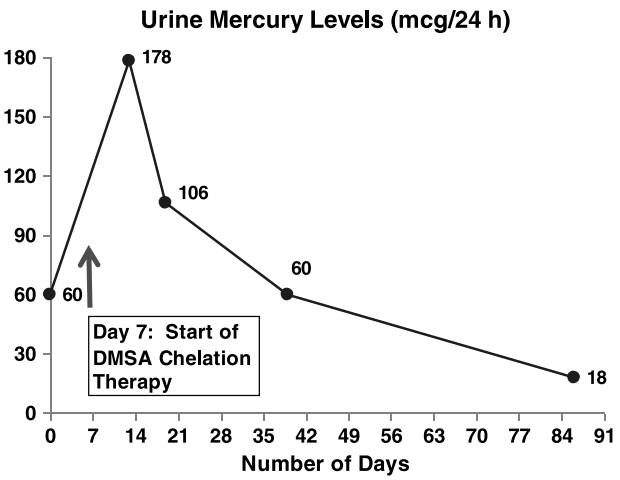

FIGURE 1. Urine mercury levels from diagnosis through treatment with DMSA.

mercury poisoning, but removal of the heavy metal by chelation can reverse the nephrotic syndrome and tubular defects.[14,15]

The patient received chelation therapy with DMSA. As expected, her urine mercury level initially rose on starting chelation therapy (Fig. 1) because the mercury was liberated from her body tissues, but then it began to drop and eventually normalized. Of note, DMSA is the most frequently used oral chelation therapy for mercury toxicity in children, but treatment remains controversial, and several studies suggest no clear clinical benefit of chelation with DMSA in people with elemental mercury poisoning.[16] Some suggest that natural clearance of mercury in the urine follows a linear 1-compartment elimination model.[17] In our case, the fact that the urine levels rose after DMSA administration implies that chelation was effective.

Clinical suspicion for mercury toxicity should remain high in the absence of risk factors. The use of mercury in religious practice is well described; however, the extent of this problem is hard to understand or measure.[18] Sale of elemental mercury from botanicas for the purposes of sprinkling about the home is not uncommon.[4,19] One screening study in New York City demonstrated that 5% of healthy pediatric volunteers had unexpected elevated urinary mercury levels.[20]

CONCLUSIONS

This case illustrates that evaluation for mercury exposure should be considered when there is presentation of hypertension and acrodynia, even in the absence of a known exposure. Selection of appropriate antihypertensive medications in the setting of increased catecholamines is challenging given the diagnostic possibilities. Management of mercury toxicity includes not only chelation therapy but also supportive care, particularly providing adequate pain control for the patient. The availability of elemental mercury at community botanicas and its use in cultural practices also represents a public health concern that warrants further attention.

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