Mercury Intoxication and Arterial Hypertension: Report of Two Patients and Review of the Literature

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ABSTRACT. Two children in the same household with symptomatic arterial hypertension simulating pheochromocytoma were found to be intoxicated with elemental mercury. The first child was a 4-year-old boy who presented with new-onset seizures, rash, and painful extremities, who was found to have a blood pressure of 171/123 mm Hg. An extensive investigation ensued. Elevated catecholamines were demonstrated in plasma and urine; studies did not confirm pheochromocytoma. Mercury levels were elevated. These findings prompted an evaluation of the family. A foster sister had similar findings of rash and hypertension. Both had been exposed to elemental mercury in the home. The family was temporarily relocated and chelation therapy was started.

A Medline search for mercury intoxication with hypertension found 6 reports of patients ranging from 11 months to 17 years old. All patients showed symptoms of acrodynia. Because of the clinical presentation and the finding of elevated catecholamines, most of the patients were first studied for possible pheochromocytoma. Subsequently, elevated levels of mercury were found. Three children had contact with elemental mercury from a broken thermometer, 2 had played with metallic mercury and 1 had poorly protected occupational exposure. All responded to chelation therapy.

Severe systemic arterial hypertension in infants and children is usually secondary to an underlying disease process. The most frequent causes of hypertension in this group include renal parenchymal disease, obstructive uropathy, and chronic pyelonephritis associated with reflux and renal artery stenosis. Less frequent causes include adrenal tumors, pheochromocytomas, neurofibromas, and a number of familial forms of hypertension. Other causes include therapeutic and recreational drugs, notably sympathomimetics and cocaine, and rarely, heavy metals. In children with severe hypertension and elevated catecholamines, the physician should consider mercury intoxication as well as pheochromocytoma. The health hazards of heavy metals need to be reinforced to the medical profession and the general public. *Pediatrics* 2000;105(3). URL: http://www.pediatrics.org/cgi/content/full/105/3/e34; *acrodynia, catecholamines, hypertension, mercury*.

ABBREVIATIONS. n, normal reference value; SAM, S-adenosylmethionine.

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Severe systemic arterial hypertension in infants and children is usually secondary to an underlying disease process. The most frequent causes of hypertension in this group include renal parenchymal disease, obstructive uropathy, chronic pyelonephritis associated with reflux, and renal artery stenosis. Less frequent causes include adrenal tumors, pheochromocytomas, neurofibromas, and an increasing number of familial forms of hypertension. Other causes are medications and drugs of ingestion or abuse, especially cocaine and sympathomimetics. Heavy metal intoxication is also implicated.[1] We present 2 patients with an infrequent cause of hypertension.

CASE REPORTS

Patient 1

A 4-year-old boy was seen at the emergency department because of new-onset seizures. History revealed headache for 1 week and no history of heavy metal exposure or toxin ingestion. He was found to have a blood pressure of 171/123 mm Hg, heart rate of 164/minute, temperature of 96°F, and respirations of 28/minute. He was anxious, irritable, diaphoretic, tremulous, and seemed to be in pain. His lips were dry, lungs clear to auscultation, and his abdomen revealed no masses or bruits. The skin was dry and rough with a scaly eczematous rash on his arms and legs, without palmar or plantar erythema. Two months before, during a physical examination for foster home placement, his blood pressure was 92/65 mm Hg. The family history was negative for chronic renal disease or hypertension. Initial evaluation revealed hemoglobin of 14.9, albumin of 5.5 g/dL. Basic metabolic studies, urinalysis, computed tomography scan of the head, and lumbar puncture all were unremarkable. A renal ultrasound was normal. Plasma renin activity was 20 ng/mL/hour, supine, (normal reference value [n]: <2.5), plasma aldosterone level 23 ng/dL (n: 3–35 supine), and urinary norepinephrine 72.1 μg/24 hours (n: 8–45). Vanillylmandelic acid was 13.6 mg/g of creatinine (n: 0–8.3). Magnetic resonance image of the head, chest, abdomen, and pelvis revealed no tumor or abnormalities. The blood lead level was <5 μg/dL (class I). The blood mercury level was 24 ng/mL (n: <9.9), and urinary mercury excretion 324 μg/24 hours (n: <10). During his inpatient stay, sodium concentration ranged from 128 to 136 mEq/L, associated with elevated fractional excretion of sodium between 1.4% and 2.5%. Plasma creatinine was .4 mg/dL and his creatinine clearance was 79 mL/minute/1.73 m.[2] His hypertension was difficult to treat, requiring 4 antihypertensive medications, including prazosin up to 1.4 mg/kg/day, isradipine up to 1.07 mg/kg/day, captopril up to 7 mg/kg/day, and labetolol up to 70 mg/kg/day.

Chelation was initiated with British antilewisite and changed to dimercaptosuccinic acid after consultation with a toxicologist. With chelation and control of his hypertension, his symptoms improved in 3 weeks. After 4 months of treatment, his urine mercury excretion decreased to 30 μg/24 hours, his plasma renin activity returned to normal, and his blood pressure normalized. His plasma sodium was 138 mEq/L and he gained 2 kg of weight. There was no neurologic sequela and his skin was normal at a 4-month recheck.

Investigation by Agency for Toxic Substances and Disease Reg-

TABLE 1. Two Children With Mercury Intoxication and Hypertension and Review of the Literature

Reference	Author	Patient's Age/Sex	Urine Mercury nmol/L	Source of Mercury	Symptoms and Blood Pressure (mm Hg)	Catecholamine Level
2	McNeil et al	14-y-old girl	2600	Elemental mercury spillage	122/98 Weight loss, anxiety, rash, pain	Not available
3	Henningsson et al	14-y-old boy	400	Playing with elemental mercury, mercury poured into an electrical coil heater	160/120 Irritability, tachycardia, sweating, tremors, rash, back pain	Plasma (nmol/L) Norepi 13.8 (n: .66–3.56) Epi 3.61 (n: <.34) Dopamine 3.29 (n: <.54) Urine (n: nmol/24 h) Metanephrine .60 (n: >6) Catecholamines 5.05 (n: <1.5)
4	Cloarec et al	32-mo-old girl	273	Broken thermometer	150/100 Tachycardia, irritability, anorexia, insomnia, rash of hands and feet	Urine (nmol/mmol creatinine) Dopamine 711 (n: 517 ± 280) Norepi + Epi 303 (n: 65 ± 43) Urine Metanephrine
5	Oliveira and Silva	17-y-old boy	1045	Manual handling of elemental Hg for extraction of gold without appropriate protection	200/130 Headache, tremors, pallor, irritability, diaphoresis, vomiting, diarrhea, weight loss, erythematous desquamating rash	2 mg/g/creatinine VMA 15 mg/24 h Dopamine 500 μg/24 h Epi 70 μg/24 h Norepi 206 μg/
6	Boudouin et al	28-mo-old girl	98	Broken thermometer	150/100 Tachycardia, irritability, polydipsia, anorexia, sweating, pain with walking, rash	Plasma (nmol/L) Norepi 14.1 (n: 1.1–1.6) Epi 1.2 (n: .15–.4) Urine (nmol/mmol creatinine) (Over 3 d) Norepi 908–2937 (n: 10–210) Epi 154–734 (n: 10–50) Dopamine 1173–1761 (n: 70–470)
7	Velzeboer et al	11-mo-old girl	62.7	Broken thermometer	130/90 Tachycardia, drowsiness, malaise, anorexia, sweating, pruritis, swollen extremities	Plasma (nmol/L) Norepi 7.52 Epi 2.81 Urine (nmol/mmol creatinine) Norepi 358 Epi 108 No normals reported
	Our patient 1	4-y-old boy	2233	Spilled elemental mercury from a pressure gauge	177/123 Tachycardia, seizures, diaphoresis, irritability, anorexia, pain, weight loss	Plasma (pg/mL) Norepi 388 (n: 70–750) Epi 29 (n: 0–110) Urine (μg/24 h) Epi 1.8 (n: .2–10) Norepi 72./1 (n: 8.0–45) Dopamine 212.1 (n: 65–400) VMA 10.1 mg/g of creatinine (n: 0–8.3)
	Our patient 2	6-y-old girl	6773.8	Spilled elemental mercury from a pressure gauge	148/78 Desquamating rash of hands and palms, erythema, tachycardia	Urine (μg/24 h) Epi 12.4 (n: .2–10) Norepi 49 (n: 8–45) Dopamine 183.5 (n: 65–400) VMA: 10.1 mg/g of creatinine (n: 0–8.3)

istry and Environmental Protection Agency found highly toxic levels of mercury in the home with liquid mercury found on the basement floor. A vacuum cleaner near this location also had high levels of mercury. A second child had hypertension, and 8 other household members had subclinical mercury intoxication. The source of the mercury was believed to be a leaking pressure gauge brought home by the father from work. The family was removed from the contaminated home.

Patient 2

A 6-year-old girl, the foster sister of patient 1, was evaluated for mercury intoxication because of the findings in patient 1. She was found to be apathetic and complaining of sore throat with erythema and desquamation of her palmar and plantar surfaces. Her blood pressure was 148/78 mm Hg and her heart rate was 114/minute. Blood mercury levels were 42 ng/mL (n: <9.9), and urine mercury excretion was 885 μg/24 hours (n: <10). She had elevated urine catecholamines levels: epinephrine of 12.4 μg/24 hours (n: .2–10), norepinephrine of 49 μg/24 hours (n: 8–45), and vanillylmandelic acid of 10.1 mg/g of creatinine (n: 0–8.3). Her blood pressure was controlled with oral captopril and prazosin at normal doses. Chelation was started and after 3 months of therapy, her blood pressure normalized, her urinary mercury excretion decreased, and she clinically recovered.

LITERATURE REVIEW

A search of Medline for mercury intoxication with hypertension produced 6 patients. Fifty percent were young children (11, 28, and 32 months old) and 50% were adolescents (14, 14, and 17 years old). All were hypertensive with pressures from 130/90 mm Hg in the 11-month-old to 200/130 mm Hg in the 17-year-old young man. Irritability, apprehension, and anxiety were found in all cases, as were dermatologic manifestations (purple hands and feet with or without desquamation). Excessive perspiration was present in 83%. Sixty seven percent of the patients had tachycardia. Fatigue, pain in the feet, anorexia, and weight loss were found in 50%. Other presenting complaints or findings in 1 or 2 patients included insomnia, tremor, back pain, headache, palpitations, generalized flushes, polydipsia, pruritis, and opisthotonos. Clinical presentations suggested pheochromocytoma. This possibility was eliminated before mercury levels were found to be elevated.

DISCUSSION

A syndrome simulating pheochromocytoma secondary to elemental mercury intoxication has been reported in 6 children since 1984. In this article, we report 2 new patients with similar findings. Our 2 patients and the 6 additional patients found in the search of Medline have acrodynia. These children, from 11 months to 17 years old, have in common hypertension, tachycardia, mental status changes, and dermatologic abnormalities. Elevated catecholamines in plasma and urine were demonstrated. Although the diagnosis of pheochromocytoma was considered in most, it was never confirmed. There was environmental elemental mercury exposure and elevated urinary mercury excretion was demonstrated. Antihypertensive medications were required and the symptoms improved with chelation. Warkany and Hubbard,[8] in their series of 28 pediatric patients published in 1953, established the link between acrodynia (erythematous rash of palms and soles, anorexia, fatigue, irritability, apathy, photophobia, polydypsia, excessive sweating, and pain in extremities) and inorganic mercury exposure. Of interest in this article is the lack of any discussion regarding the well-documented hypertension and/or tachycardia demonstrated in 21 of the 28 patients reported.

The cause of increased catecholamines in plasma and urine can be traced to the ability of mercury to interfere with the normal catabolic processing of catecholamines via the cytosolic enzyme catecholamine-O-methyltransferase.[9,10] Catecholamine-O-methyltransferase requires the use of the methyl group provided by coenzyme S-adenosylmethionine (SAM). SAM is also essential in the conversion of norepinephrine to epinephrine. Mercury inactivates SAM; as a consequence, norepinephrine, dopamine, and epinephrine accumulate in the urine in increased amounts where they can be detected. This catecholamine excess is responsible for the pheochromocytoma-like syndrome.

Mercury, a heavy metal, exists in the environment in 3 forms: organic, inorganic, and elemental. It is toxic in any of these forms.[13] Neurological manifestations involving the central nervous system are seen with chronic mercury intoxication. The largest outbreaks of mercury toxicity have occurred with the ingestion of fish and seafood contaminated with methyl mercury by industrial pollution[14] and by the consumption of grain for seeds treated with methyl mercury.[15] Accidental exposure to dimethyl mercury, a supertoxic chemical, has caused fatalities in laboratory personnel.[16] In the past, mercury was used in many approved medical products, including antisyphilitic agents, diuretics, cathartics, topical salves, teething compounds, and diaper powders, resulting in outbreaks of mercurialism in the 1940s and 1950s. These products are no longer used in the United States. Acrodynia is typically caused by inorganic mercury poisoning; however, as demonstrated in our work, new cases are being reported from exposures to elemental mercury through broken thermometers[6] or other sources. Elemental mercury, a liquid at room temperature, vaporizes easily and is able to be inhaled and absorbed by the alveolar membrane, causing pulmonary symptoms that include shortness of breath, cough, chills, fever, and radiograph findings consistent with pneumonitis.[17] Other symptoms include lethargy, confusion, stomatitis, vomiting, and colitis. These symptoms abate in ~1 week or may progress to pulmonary edema and death. Early in the disease this illness may be confused with a viral respiratory infection or flu.

In 3 of the 6 cases from the literature, the mercury exposure resulted from spillage of mercury from a broken thermometer and the younger patients were affected. Parents had no symptoms. In 1 case from Brazil, the 17-year-old patient was exposed to elemental mercury in an occupational activity. In the other 4 cases, including the 2 described by us, mercury was brought homes by individuals who were unaware of the risk involved.

Of interest in our patient 1 was the observation of hemoconcentration. This confirms a similar observation reported by Henningsson[3] in the description of his patient. It seems that these children have intra-

vascular and extracellular volume depletion. The finding of elevated renin level with normal aldosterone secretion further reinforces these impressions. Also, our patient demonstrated relative hyponatremia associated with an elevated fractional excretion of sodium. These findings are consistent with pressure natriuresis, with stimulation of dopamine receptors in the kidney.[11,12]

CONCLUSION

We conclude that in a child with severe hypertension, altered mental status, dermatological abnormalities, and elevated catecholamines, clinicians should consider pheochromocytoma as well as elemental mercury intoxication. The health hazards of heavy metal need to be reinforced to the medical profession and the public at large.

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