Mercury Poisoning as a Kawasaki Mimic: Case Report and Review of Literature

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Abstract

We present the case of a previously healthy 5 year-old male with a 2-month history of fever, tachycardia, hypertension, weight loss, and a truncal rash with cephalo-caudal progression and palmar involvement. The differential diagnosis and clinical work-up are discussed. After a negative initial workup, one of our patient’s siblings developed similar symptoms at home, prompting acquisition of additional history suggesting heavy metal toxicity. Urine mercury (Hg) level, urine Hg:Creatinine ratio, and follow-up 24-hour urine Hg studies confirmed mercury toxicity, ultimately leading to the diagnosis of acrodynia - a syndrome that includes palmar erythema with desquamation and hypertension which is often associated with exposure to elemental or inorganic mercury. Chelation with succimer (DMSA) was initiated, leading to eventual resolution of all symptoms except hypertension, which improved only mildly. It is not yet known whether this patient will have long-term neurocognitive effects. This case demonstrates the importance of keeping heavy metal poisoning in the differential diagnosis of patients presenting with signs of multisystem illness.

Key words: Acrodynia, heavy metal toxicity, mercury poisoning, chelation

Introduction

Diagnosing elemental mercury poisoning requires a high index of clinical suspicion with attention to thorough environmental, social, and family history. Due to its many nonspecific and slowly developing symptoms, the differential diagnosis is extensive and challenging. Diagnosis often requires costly laboratory and radiologic investigation to exclude other disease processes.

Case Report

A previously healthy 5 year-old male presented to his pediatrician with intermittent high fevers (Tmax 102.6°F), agitation, myalgias, and a “sandpaper-like” rash. He had a 2-month history of tachycardia, hypertension, anorexia, weight loss, and night sweats. The rash was initially a maculopapular, erythematous eruption with truncal distribution and subsequent cephalo-caudal progression...
to the buttocks, perineum, and lastly the palms and soles. His palms and soles became edematous and began to desquamate after 2 weeks (Figure 1). There was no report of conjunctival injection, cracking or swollen lips, tongue erythema, lymphadenopathy, cough, rhinorrhea, dyspnea, abdominal pain, nausea, vomiting, diarrhea, dysuria, or hematuria.

Preliminary labs including complete blood count, blood chemistry, urine studies, inflammatory markers, transaminases, and thyroid function panel failed to elucidate any clear etiology of the symptoms. Work-up for infectious etiologies including streptococcal disease, Rocky Mountain Spotted Fever, and mycoplasma was negative. Due to our patient’s characteristic rash with desquamation, palmar edema, and sustained fever, atypical Kawasaki Disease was considered most likely. However, the patient did not have any conjunctival injection, oral manifestations, or cervical adenopathy and an echocardiogram showed no coronary dilation or aneurysms.

Rheumatologic investigation including anti-nuclear antibody, C3, and C4 was unremarkable. A CT scan of the patient’s chest, abdomen, and pelvis failed to demonstrate evidence of malignancy or vasculitis. Normal plasma and urine metanephrines ruled out pheochromocytoma as an explanation for the hypertension, tachycardia, and agitation.

After a few days in our institution, we became aware that our patient’s sibling had developed similar symptoms including increased agitation and palmar desquamation. On further environmental history, we learned that the patient’s yard was being used by a family member for smelting of reclaimed copper wires. A random urine mercury (Hg) level was elevated at 21.9 mcg/L (normal 0-10 mcg/L) and urine Hg:Cr was 44.7 mcg/g (normal < 35 mcg/g). Repeat labs five days later confirmed elevated mercury levels (random urine Hg 24.2 mcg/L, urine Hg:Cr 59.0 mcg/g). Additional 24-hour urine mercury studies were performed to further characterize the extent of exposure and to monitor the progression of treatment. Our patient’s 24-hour urine Hg level was elevated at 56 mcg/d (normal range 0-15 mcg/d). Chelation with succimer (DMSA) was initiated at a regimen of 10 mg/kg/dose three times daily for 5 days (30 mg/kg/day) followed by twice daily for 14 more days (20 mg/kg/day).

The state Environmental Protection Agency performed a home mercury evaluation and discovered elevated Hg vapor levels throughout the house at 5.9 mcg/cubic meter. In one bedroom, the mercury vapor concentration was 17-22 mcg/cubic meter. The Centers for Disease Control and Prevention recommend levels be <1 mcg/cubic meter [1].

The patient tolerated chelation without complication. Following two weeks of therapy, his agitation and rash had...
significantly improved. His leg pain and myalgias resolved and his overall energy and appetite returned to baseline. Blood pressures remained intermittently elevated at time of discharge so the patient was discharged on amlodipine and labetalol. Attempts were made to establish regular appointments in the Nephrology, Toxicology, and Rheumatology clinics but unfortunately the family was lost to follow-up.

Discussion
Mercury, an important source of heavy metal toxicity, is emitted both naturally and as a result of human production. Exposure to even small amounts of mercury is a cause for concern due to its deleterious effects on normal human development [2]. Children are particularly susceptible to mercury toxicity because of their immature blood-brain barrier, developing nervous system, and high respiratory rate [3]. The heavy density of mercury vapor makes it more likely to settle, concentrating in the child’s breathing zone.

Mercury Exposures
Mercury occurs in three forms: elemental, inorganic, and organic. Elemental, or metallic, mercury (Hg⁰) exists as a liquid at room temperature. However, it readily evaporates due to its low vapor pressure, especially when heated. This makes inhalation the most common form of Hg⁰ toxicity [4]. Common environmental sources of Hg⁰ exposure include thermometers, sphygmomanometers, dental amalgams, cultural and religious practices (e.g., Ayurvedic medications), and take-home exposure from adults working in mining or smelting industries [5, 6]. Inhaled Hg⁰ vapor has an 80% absorption into the lungs, where it quickly diffuses through the alveolar membranes into the blood. Hg⁰ has been demonstrated to migrate directly from the pharynx to the brain via olfactory neurons that penetrate the cribriform plate [7].

Hg⁰ can be absorbed through the gastrointestinal tract, dermis, and respiratory tract. When ingested, Hg⁰ causes minimal systemic symptoms, owing to low (0.01%) bioavailability [8]. Similarly, a negligible amount of Hg⁰ is dermally absorbed. Hg⁰ is primarily excreted through urine and feces, though some is excreted through breath, sweat, and saliva. Its excretion is dose-dependent, with an initial rapid clearance from the blood (3-day half-life) followed by slower clearance from the rest of the body. The biologic half-life of Hg⁰ in the human body is approximately 30 to 60 days, with the half-life in the brain not well defined, but potentially up to 20 years [9,10].

Clinical Symptoms
The symptoms of patients exposed to Hg⁰ vapor can vary depending on dose and time course of exposure, but three phases of acute inhalational Hg⁰ poisoning have been described [11]. The initial phase includes flu-like symptoms lasting one to three days, including fever, headache, dry cough, and shortness of breath along with abdominal pain, nausea, vomiting, diarrhea, swollen gingiva, and salivation [10]. The intermediate phase is predominated by severe pulmonary sequelae including non-cardiogenic pulmonary edema, bronchiolitis, pneumonitis, pneumomediastinum, and pneumothorax. Death is most commonly due to progressive hypoxemia. The late phase, if the patient survives, is characterized by persistence of CNS dysfunction similar to patients with chronic low-dose Hg exposure. Post-mortem analysis of patients with acute mercury vapor poisoning has revealed erosions of the bronchial epithelium, causing a necrotizing bronchiolitis with ensuing interstitial and alveolar edema [12-15].

Chronic elemental mercury inhalation preferentially affects the central nervous system (CNS), peripheral nervous system (PNS), and the kidneys. Mercury exposure can cause erythrom, a condition characterized by mood swings, extreme shyness, anorexia, irritability, poor anger control, personality changes, memory loss, and delirium [16]. Mercury can cause a host of other neuropsychological symptoms: diminished executive and visual spatial functions as well as negative effects on learning, memory, attention, and processing speed [17]. Other CNS symptoms include tremor, ataxia, coordination disturbances, and dysdiadochokinesia [18].

The effects on the CNS can last long after urine and blood levels have normalized, as demonstrated in a 15 year-old female who was exposed to mercury for 4 days. She returned to baseline mental function 9 months after completion of chelation therapy [16]. A 10 year-old patient who was exposed for 20 days presented with acrodynia, seizures, and visual impairment, and demonstrated white matter lesions on T2-weighted-MRI that normalized after 9 months of treatment [19]. The most typical PNS symptom is peripheral neuropa-
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Several reports note an association between elemental mercury and sensorimotor polyneuropathy [20,21]. A 12-year-old male with 6 months of intermittent mercury exposure had a mixed-type polyneuropathy and idiopathic intracranial hypertension without any other CNS symptoms. He slowly improved over his 37-day hospital course [22].

The most common renal manifestation is proteinuria secondary to tubular damage; nephrotic syndrome can occur in extreme cases. Various case reports have demonstrated mercury-induced membranous nephropathy in cases of chronic mercury exposure, with renal biopsy findings showing glomerular basement membrane thickening and proliferative mesangial cells [23]. An increasing proportion of total body mercury can be found in the kidneys with each day following exposure to elemental mercury [8].

**Acrodynia**

Acrodynia, also known as pink disease, is an idiosyncratic hypersensitivity reaction to mercury that can occur following exposure to elemental or inorganic mercury, regardless of the duration of exposure [3]. It is typically seen in children, and rarely in adults. Symptoms include edematous pink palms and soles with desquamation, erythematous cheeks and nose, increased salivation, diaphoresis, photophobia, insomnia, irritability, and neuropathic pain in extremities [24]. Acrodynia is also associated with tachycardia and hypertension [25]. A majority of pediatric Hg toxicity cases present with the classic symptoms of acrodynia [26]. Acrodynia has been shown to subside with chelation therapy [27].

Acrodynia is frequently misdiagnosed as pheochromocytoma due to similar symptoms of episodic hypertension, tachycardia, and diaphoresis along with laboratory findings of elevated catecholamines [26]. The accumulation of catecholamines (norepinephrine, epinephrine, and dopamine) results from inactivation of a coenzyme used by catecholamine-O-methyltransferase [28]. Case reports have included the use of labetalol for its nonspecific blocking of α-receptors and β-receptors and subsequent dampening of catecholamines as well as amloidipine [29]. Multiple drug therapy is often necessary to control hypertension [27,28]. Tachycardia and hypertension are typically well controlled with a combination of multiple drug therapy and chelation therapy [28].

**Laboratory Diagnostics**

Blood Hg level has limited diagnostic value. It is valid only for assessment of an acute exposure to large amounts of vaporized mercury owing to the lipophilic nature of elemental mercury prior to oxidation. Due to the rapid uptake of elemental mercury and the preferential deposition of mercury into the kidney, urine measurement is recommended to help establish a diagnosis [30]. Either a spot or 24-hour urine mercury can be obtained, with a 24-hour urine collection measurement of mercury adjusted for creatinine excretion considered reliable and sensitive [31,32]. Stool, breath, and hair testing are not sufficiently accurate to guide clinical decision-making [33].

Urine mercury levels correlate poorly with severity of clinical symptoms, as noted in our patient [34-37]. For example, an 8-year-old male patient with a 4-month exposure to elemental mercury in his kitchen demonstrated severe symptoms and a urine mercury level of 12 mcg/L (compared to 24.2 mcg Hg/L in our patient) and mercury/creatinine ratio of 42.9 mcg/g (compared to 59 mcg Hg/g in our patient) [37]. This patient similarly experienced an increase in urine excretion following chelation therapy, with a urine mercury level of 48 mcg/L (compared to 118 mcg Hg/L in our patient). One comprehensive study examining children living near Hg exposed areas or working directly with Hg due to gold mining associated labor demonstrated significant symptoms in both groups compared to controls, with an average 24-hour urine Hg:Cr ratio of 36 and 80 mcg/L in each group respectively [18]. This study illustrates that symptoms and exposure level can correlate, though not with urine mercury levels.

**Treatment**

The most important and initial step of treatment is to stop (or eliminate) exposure [38]. DMSA is the most frequently used chelation therapy for children. Chelation therapy is at times ineffective in patients with elemental mercury poisoning [39]. However, after chelation therapy, our patient’s urinary excretion of mercury increased and his clinical symptoms abated, similar to other reported cases of elemental mercury exposure [16, 19, 29, 37].

**Conclusion**

While environmental Hg exposure can cause injury, disability, and multisystem disease, its onset can be insidious and...
the diagnosis not easy. Our patient, admitted for atypical Kawasaki disease, was not diagnosed until a sibling’s similar illness prompted an environmental history and subsequent testing. The environmental history should be carefully performed whenever a patient’s differential diagnosis is complicated or challenging.

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