CASE REPORT

Mercury poisoning: a rare but treatable cause of failure to thrive and developmental regression in an infant

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An infant presented with failure to thrive and developmental regression. Physical examination revealed an irritable child with swollen, erythematous extremities, and elevated blood pressure. Extensive investigations, including a metabolic work-up and neuroimaging, were unrevealing. Exposure to self-purchased medication was initially denied. The physical signs were suggestive of acrodynia. Mercury poisoning was ultimately established by measuring paired blood and urine mercury levels. On further enquiry, it was revealed that the child had been given a Chinese medicinal product for 4 months. He responded well to a chelating agent. Acrodynia is a childhood disease considered to be of historical interest only, but making a diagnosis of mercury poisoning is rewarding because the response to treatment is good. This case highlights the common misconception that alternative medicines are safe and benign.

Introduction

Mercury is a special metal. It has been used medicinally for thousands of years but its toxicity is also widely recognised as a result of medicinal applications, industrial use, and environmental disasters. Infants and small children are particularly vulnerable because of the risk of severe injury to the developing brain. Acrodynia—pink, painful oedematous swelling of the extremities with skin desquamation—is a characteristic phenomenon observed mainly in young subjects suffering inorganic mercury poisoning.[1] Elimination of mercury from the household environment and of mercury-based drugs has resulted in a marked reduction in the incidence of acrodynia, so much so that acrodynia is widely considered to be of historical interest only.[2,3] Despite its rarity, accidents involving mercury still occur and recognition of mercury poisoning is crucial. Termination of the exposure is the most important step in management. Chelation therapy may be required in selected subjects to facilitate elimination of mercury from the body. We present a case of an 11-month-old infant suffering from mercury poisoning that illustrates the importance of a good history and physical examination. This case also demonstrates that alternative medicines are not always safe.

Case report

An 11-month-old boy was referred to our hospital in May 2007 from a Maternal and Child Health Centre because of failure to thrive and developmental regression. He was born full-term after a normal spontaneous labour and had an unremarkable perinatal history. The family history was also unrevealing; there was no parental consanguinity. From the age of 5 months, he refused to take milk so was switched to a diet of congee with fish, plus vegetables and meat. From 6 months to 11 months of age, his body weight dropped from 7.1 kg (10th centile) to 7 kg (0.7 kg below the 3rd centile) and his body length dropped from the 90th centile to the 50th centile. His development was normal until 6 months of age. At 10 months he was no longer able to bear weight on his lower limbs, his head control had deteriorated with the head falling back frequently and he could no longer reach out. At 11 months he was forming no words, only babbling. His vision and hearing appeared normal but he was getting more and more irritable. He was also sleeping poorly, suffered malaise, and a lack of interest in playing. Frequent fingernail biting, scratching, and increased salivation were also noted. There was no history of fever, major illnesses, diarrhoea, or vomiting during this period and his bowel movements were normal. His mother denied giving him any self-purchased medications. A private paediatrician saw him 3 weeks before he was referred to us. Laboratory investigations were performed before referral. He was then put on multiple nutritional supplements.

Examination showed a thin and irritable infant. His body weight was below the third centile. A non-specific maculopapular rash covering the body, with some scratch marks present, was noted. Pink and swollen extremities with skin desquamation and disfigured fingernails were seen (Fig). The boy was hypotonic with decreased limb reflexes. A blood

Key words
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水銀中毒：嬰兒發育不足與發展退化的一個罕見但可治療的成因

一名嬰兒出現發育不足與發展退化的情況。生理檢查發現這名嬰兒容易暴躁、四肢浮腫、有紅斑，而且血壓偏高。進行包括新陳代謝和神經造影的全面檢查後，並未有任何發現。生理症狀顯示病人可能有肢痛症。結果，透過量度外周血和尿液水銀的水平，確定為水銀中毒。病人家屬起初否認曾服用自購藥物，進一步的查問表明，嬰兒曾服用中成藥達四個月。病人後來對螯合劑反應良好。肢痛症是一種幼兒病，被認為是一種古老並罕見的病。病人對治療的反應良好，顯示及早作出水銀中毒的判斷很重要。此外，這案例亦突顯了另類藥物安全而無害的常見誤解。

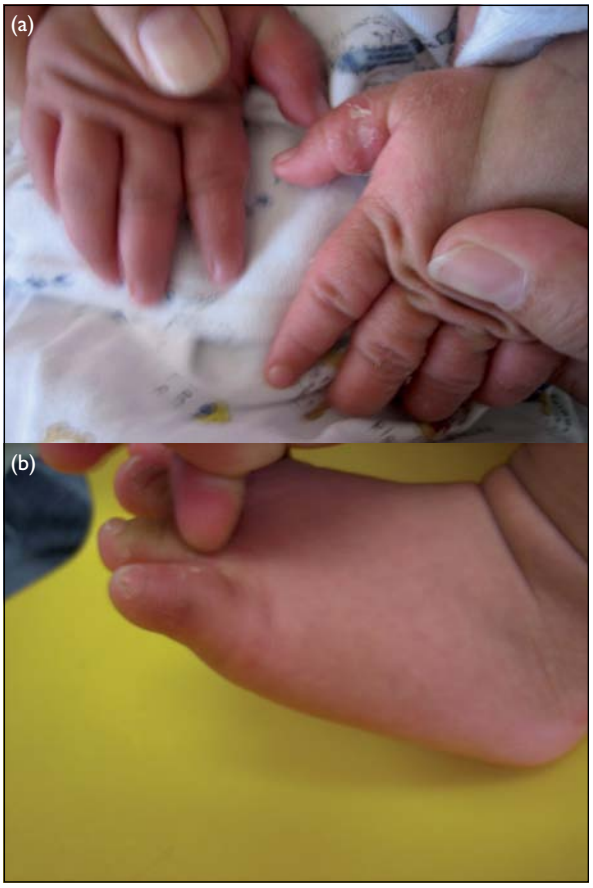

FIG. Pink, swollen extremities with desquamation

pressure of 140/100 mm Hg was recorded and his urine showed mild proteinuria. Laboratory tests results were as follows: the complete blood picture, liver function, renal function, thyroid function, and iron status were normal. Investigations for metabolic disorders including ammonia, venous blood gases, fasting glucose, lactate, pyruvate, uric acid, urine for amino acids and organic acids were all unrevealing. Nerve conduction velocities and magnetic resonance imaging of the brain were unremarkable. His urine noradrenaline was 201 nmol/mmol Cr (reference level, <120 nmol/mmol Cr) and adrenaline was 21 nmol/mmol Cr (reference level, <26 nmol/mmol Cr). A spot urine for protein-to-creatinine ratio was 0.02. His urine beta-2 microglobulin was elevated to 0.3 μg/mL (reference level, <0.2 μg/mL). His blood mercury level was 13.8 μg/L (adult reference level, <15.4 μg/L). His urine mercury was 61.6 μg/L (adult reference level, <20 μg/L) and urine Hg/Cr ratio was 150 μg/g Cr (adult reference level, <5 μg/g Cr). Results sent later by the private paediatrician showed a blood mercury of 18 μg/L, and urine Hg/Cr after a dimercaptosuccinic acid (DMSA) challenge of 340 μg/g Cr. Mercury poisoning was diagnosed.

After questioning the mother further it became apparent that the patient had been given an over-the-counter Chinese medicinal powder (Chinese name: 陳標記小兒疳積散) used for appetite improvement, from the age of 6 months. She stopped giving the baby this powder at 10 months of age after seeing the private paediatrician. Analysis of the powder showed a markedly elevated mercury concentration of 1228 ppm. The patient was treated with one course of chelating therapy, using DMSA (succimer), 100 mg 8 hourly for 10 days. Amlodipine 1.5 mg daily was started for blood pressure control.

During follow-up visits the patient showed improvements in both weight gain and development and his blood pressure returned to normal. When last seen, at 18 months of age, his body weight was on the 25th centile and height the 50th centile. He was playful, could walk independently and stoop. His pincer grip was well developed. He could build a tower with 3 bricks. He fed himself with a spoon and spoke a few single words. His blood pressure was normal as was the neurological examination. A serial decrease in his blood and urine mercury concentrations has been observed.

Discussion

The combination of developmental regression, painful, red, swollen fingers and toes in association with hypertension described in this case is characteristic of inorganic mercury intoxication. Because of its rarity today, this condition is often neglected. Other differential diagnoses are often considered before the diagnosis of mercury poisoning is reached. Achieving the diagnosis is very rewarding because, as our patient clearly illustrates, the response to treatment is good, despite the stormy presentation.

In our patient the presence of developmental regression, hypotonia, and finger biting, led to other differential diagnoses such as Lesch-Nyhan syndrome and Fabry disease being considered as well. A catecholamine-producing tumour can cause hypertension and increased catecholamine concentrations but a rash and the extremity changes seen in this baby are not features of phaeochromocytoma. The absence of fever makes

Kawasaki disease unlikely. Thyrotoxicosis was also ruled out by the physical findings and laboratory tests. Careful history taking and physical examination can help the paediatricians to diagnose mercury poisoning.

Mercury exists mainly in three forms: elemental, inorganic, and organic. Potential sources of exposure to elemental mercury include dental amalgam, accidental breakage of mercury containing thermometers and sphygmomanometers. Infant teething powder (calomel) and skin-lightening creams are well-recognised sources of inorganic mercury. Organic mercury exposure mainly comes from consumption of fish (as methylmercury), especially the large, long-lived predatory fish. Elemental mercury is absorbed mainly via inhalation. Both inorganic and organic mercury are mainly absorbed via the gastro-intestinal tract, though inorganic mercury can also be absorbed through skin and mucous membranes.[4] Its toxic effect is mainly due to its covalent bonding to sulphur and reactions with the phosphoryl, carboxyl, and amide groups. This leads to widespread dysfunction of enzymes, transport mechanisms, membranes and structural proteins. Elemental mercury is considered safe when ingested due to its negligible absorption from a healthy gut. Acute ingestion of inorganic mercury, however, could lead to gastric irritation, haemorrhagic gastroenteritis, acute tubular necrosis and shock.[4,5]

Our patient suffered from chronic inorganic mercury poisoning, which affects predominantly the central nervous system and the kidney. Patients can present with tremors, choreoathetosis, neuraesthenia, erethism, sensorimotor neuropathy, ataxia and tunnel vision.[5,6] Renal tubular dysfunction can present as nephrotic syndrome, elevated urinary excretion of albumin, transferrin, retinal binding protein, and tubular enzyme beta-galactosidase. Urine assays for N-acetyl-β-D-glucosaminidase (NAG) and β2-microglobulin can be used for early detection of subclinical mercury toxicity. Elevated β2-microglobulin was observed in our patient, indicating tubular dysfunction. Urinary assays for NAG are not available in Hong Kong.

'Acrodynia' means painful, swollen, and tender extremities, a characteristic phenomenon of inorganic mercury poisoning first observed by Feer in 1923.[1] It is less commonly observed beyond infancy due to the increase in skin thickness. Mercury combines with a co-factor of catecholamine-O-methyltransferase (COMT), causing a decrease in COMT. This causes accumulation of noradrenaline, adrenaline, and dopamine. This also explains why affected patients often also present with sweating, tachycardia and hypertension, mimicking phaeochromocytoma.[7,8] With the elimination of mercury from the household environment and of mercury-based drugs, acrodynia has become a rarity, however, cases of accidental mercury poisoning in children are still reported.[7,9]

Suspicion of inorganic mercury poisoning prompted us to further explore the child's exposure history. His mother eventually recalled giving him the Chinese powder, later found to have extremely high mercury content, for 4 months. The drug was stopped 1 month before his hospitalisation. The mother thought the drug was benign because she also took it in her childhood. The importance of history taking can never be overemphasised. There has been no good evidence to support the use of a chelation challenge test to diagnose mercury poisoning or to determine whether chelation therapy is indicated, and it may cause confusion in data interpretation.[10] Animal studies suggest that a single dose of chelating agent can cause mobilisation and redistribution of heavy metals to the more vulnerable tissues like the brain, causing more harm than benefit.[11] Both urine and blood mercury levels are validated diagnostic tools for assessing mercury exposure. The urine mercury level correlates with the severity of exposure in inorganic poisoning.[4] Measurement of blood mercury is preferred in suspected organic poisoning as this is primarily excreted in the faeces. The half-life of elemental and inorganic mercury in blood is 40 to 60 days, and about 70 days for organic mercury. Hair mercury level is not a validated diagnostic method. A recently published meta-analysis showed that the correlation of hair mercury levels with urine and blood levels was not strong enough to replace them in clinical decision-making.[12] There are no specific blood or urine levels above which treatment with a chelating agent is indicated.[10] The clinical decision to initiate treatment should be based on the duration of exposure, the patient's symptoms, and the laboratory test results.

The identification of high mercury levels in this Chinese powder has aroused significant social concern. The Hong Kong Department of Health was informed and this supplement has been withdrawn from the market.[13] Mercury poisoning is not a common condition, nonetheless, one should always consider it, especially when a patient comes to you with unexplained renal and neurological complaints, or with signs and symptoms of sympathetic over-stimulation mimicking a phaeochromocytoma.

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