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

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. 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. 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
A baby was found to have underdeveloped and delayed development. Physical examination revealed a crying baby with swollen and red fingers and toes, as well as high blood pressure. A comprehensive examination, including metabolic and neurological investigations, did not reveal any findings. The symptoms suggested the baby might have thalamic pain syndrome. Ultimately, measurement of blood and urine mercury levels confirmed mercury poisoning. The mother initially denied giving any medication, but further questioning revealed that the baby had been given a Chinese medicinal powder for 4 months. The baby responded well to chelation therapy with DMSA (succimer), and blood pressure was controlled with amlodipine. Follow-up visits showed improvements in weight gain and development, and blood pressure returned to normal. The patient was 18 months old at the last visit, with a body weight on the 25th centile and height on the 50th centile. He was playful, could walk independently, and had a good pincer grip. He could build a tower with 3 bricks, feed himself with a spoon, and speak a few single words. Blood pressure and neurological examination were normal. A serial decrease in blood and urine mercury levels was observed.

**Discussion**

The combination of developmental regression, painful, red, swollen fingers and toes associated 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. 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.

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, erythema, sensorimotor neuropathy, ataxia and tunnel vision. 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. 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. With the elimination of mercury from the household environment and of mercury-based drugs, acrodyinia has become a rarity, however, cases of accidental mercury poisoning in children are still reported.

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. 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. 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. 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. There are no specific blood or urine levels above which treatment with a chelating agent is indicated. 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. 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.
References