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Metallic Mercury Poisoning and its Neuropsychological Effects: A Case Report

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SUMMARY

Mercury is an extremely toxic heavy metal that can devastate the central nervous system. Herein we present a 15-year-old female with mercury intoxication following 4 days of exposure to elemental mercury at home. She was referred by the department of pediatrics with complaints of demonstrated emotional lability, impaired memory, disinhibition, and impulsivity. Olanzapine 2.5 mg /d was initiated. The patient's neuropsychological performance was evaluated using a neuropsychological test battery at initial examination. Impaired neuropsychological functions like interference effect and attention (Stroop Test TBAG form), verbal fluency and switching to other category (Verbal Fluency Test, (VFT)), verbal short term and long term-memory, and recognition (Auditory Verbal Learning Test, (AVLT)) was detected.

After 9 months of follow-up the patient's complaints resolved, along with the initially observed neuropsychological deficits, and her intelligence scores and ability to concentrate and sustain attention increased. Additionally, her Stroop Test TBAG Form, VFT, and AVLT scores were similar to her normal peers'. In this case report, the clinical aspects of central nervous system involvement in mercury intoxication and protection from potential toxic effects of laboratory materials like mercury at schools were discussed. School administrators should be aware of and parents and students should be given necessary protective information.

Keywords: Mercury intoxication, child, neuropsychological tests

INTRODUCTION

Mercury occurs in nature in the form of elemental mercury, inorganic salts, and organic compounds; every form of mercury is potentially toxic (Counter and Buchanan 2004). Exposure to metallic mercury is less common than exposure to organic (e.g. methyl mercury in fish) and inorganic mercury (e.g. in paint). Elemental mercury is used in many common devices, such as thermometers, barometers, batteries, pumps, dental amalgams, and thermostats. Industrial workers that handle mercury are exposed to elemental mercury at a greater degree than any other population. Children are exposed to elemental mercury via mercury brought home from such places as schools and factories (Cherry et al. 2002; Tominack et al. 2002). Due to its unique physical properties and unusual appearance, elemental mercury is very attractive to children. Older children may bring it home from school laboratories to play with and any other children that happen to be in the same environment can be exposed to toxic mercury vapor, especially when ventilation is less than adequate (Cherry et al. 2002, Gordon 2004, Tominack et al. 2002).

Elemental mercury is the only metal that is liquid at room temperature. At standard pressure and room temperature it evaporates, and as room temperature increases the vapor pressure of mercury also increases (for every 10-°C increase the vapor pressure of mercury doubles.) Mercury vapor is odorless and very toxic. Elemental mercury can enter the body via absorption through the skin, ingestion, or inhalation. The most common route of exposure causing intoxication is inhalation of mercury vapor; 80% of inhaled mercury vapor is absorbed

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via the lungs and enters the bloodstream, accumulating in the central nervous system where it manifests its neurotoxic effects. Mercury rarely has toxic effects when ingested, as <0.01% of ingested mercury is absorbed via the gastrointestinal tract. Dermal absorption is relatively minor. Elemental mercury is excreted primarily via the kidneys. The half-life of elemental mercury is 30-60 d, but the half-life of mercury accumulated in the brain may last many years (Langford and Ferner 1994).

The literature is devoid of any extensive research on the effects of elemental mercury exposure in children and adolescents. Case reports suggest that children and adolescents whose nervous system are still developing are more sensitive to the toxic effects of mercury compared to adults. The concentration of mercury is frequently reported to be higher in children than in adults, even when exposure is of a similar route (Baughman 2006). Exposure to elemental mercury can have adverse impacts on different systems such as the central nervous, immune, reproductive, respiratory, and nephrological systems, and can cause dermatological symptoms, but primarily the central nervous system and kidneys are impacted chronically (Counter and Buchanan 2004). Exposure to mercury can affect the entire central nervous system and result in erythrism (mad hatter disease), which manifests as mood swings, shyness, irritability, insomnia, anorexia, anxiety, poor anger control, and, in cases of prolonged exposure, delirium, personality changes, and memory loss (Cherry et al. 2002, Tominack et al. 2002, Yüce et al. 2012). Moreover, mercury poisoning can cause acrodynia in children. Acrodynia may involve respiratory difficulties, swelling and rashes on the hands and feet, and desquamation of the toes and fingertips (Counter and Buchanan 2004).

A meta-analysis on the neuropsychological effects of mercury poisoning reported that mercury negatively affects executive and visual spatial functions, and has a markedly negative effect on learning and memory, attention, and processing speed (Rohling and Demakis 2006). It was reported that chronic mercury poisoning impaired neuropsychological functions (attention, short-term memory, visual spatial skills, and judgment) and altered mood in 2 adolescents, and that neuropsychological dysfunction persisted even though plasma and urine mercury levels returned to normal post chelation treatment (Yeates and Mortensen 1994).

Herein we present an adolescent female that was exposed to mercury and a discussion of her neuropsychological impairment and possible preventive measures.

CASE

A 15-year-old female was referred to our clinic from the child neurology department with complaints of forgetfulness, inattention, and agitation. History of complaints and medical records revealed that the patient first presented to the hospital 3 months earlier with complaints of joint pain, tachycardia, tremors, sweating, skin rashes, headache, and fatigue. Ten days before her complaints began her 12-year-old sister had similar complaints. As the sisters had similar signs and symptoms, possible exposure of the family to a toxic substance was investigated; the investigation revealed that the younger sister had brought some mercury home from school and that the sisters had played with it 4-5 days before the younger sister developed symptoms. The girls kept the mercury in an open jar. The mercury was removed from home after the mother was informed of its presence.

During the patient's initial examination 24-h urine and plasma mercury levels were 414 μg L–1 (normal range: 0.1-20.0 μg L–1) and 19 μg L–1 (normal range: 0.6-59.0 μg L–1), respectively. As the patient had relevant symptoms and her plasma mercury level was high, both sisters were diagnosed with mercury poisoning and acrodynia by a pediatrician. The sisters were treated with DMSA (meso-2,3-dimercaptosuccinic acid) chelation therapy. Following a rapid recovery of symptoms, the younger sister was no longer followed-up. The presented patient was administered gabapentin 600 mg t.d.s., tramadol hydrochloride 50 mg b.i.d., and amitriptyline 10 mg d–1 due to acute polyarthralgia by the pain management unit. Two months later the patient presented to the pediatric emergency room with generalized tonic clonic seizure. EEG showed generalized background rhythm irregularity in cerebral bioelectrical activity and hyperventilation-induced generalized epileptiform activity. The pediatric neurology department increased the dose of gabapentin to 800 mg b.i.d. and withdrew amitriptyline due to sedation and at this time her 24-h urine mercury level was 8 μg L–1. During her ER follow-up her seizures ceased and amlodipine was started, as her blood pressure was 130/90 mmHg; 1 month later her blood pressure measurement stabilized and amlodipine was withdrawn.

Her parents reported that the patient had exhibited behavioral changes during the previous 15-20 d; she wanted to touch everything in sight and wanted to eat warm and cold foods at the same time. The patient began to collect meaningless items, such as chewing gum wrappers, and spend more money. It was reported the she would ask her friends for money and that she had mood swings, including abrupt fear, sudden outbursts of laughter, and irritability. Her academic performance declined and she had difficulty obeying rules. During her mental state examination the patient frequently paused while talking, had difficulty finding the right words with which to express herself, and could not complete sentences. Her judgment ability was impaired. Her premorbid history showed that the patient was deferent, docile, respectful, and successful. The patient and family medical histories were unremarkable.

CLINICAL APPROACH and RESULTS

The patient was prescribed olanzapine 2.5 mg d–1 due to her out-of-control behavior and disinhibition, and 15 d after her initial visit her complaints improved. A neuropsychological test battery (Table 1) was administered to the patient during her initial visit to evaluate her intelligence, learning capacity, visual spatial perception, visual perceptual organization, executive functions, verbal short- and long-term memory, visual short- and long-term memory, and recognition ability. The patient performed poorly on the Stroop Test TBAG Form, which measures the interference effect and selective attention, the Verbal Fluency Test (VFT), which measures verbal fluency and switching to other categories, and the Auditory Verbal

Learning Test (AVLT), which measures verbal short-term and long-term memory, and recognition (Table 2), whereas she performed equitably well on the remaining tests.

The patient was followed-up monthly. At the 3-month followup her psychiatric symptoms were improved, and at 6 months she was completely recovered; her academic performance, peer relationships, and behavior were at the premorbid level. The neuropsychological tests were repeated at 6 months. There was an increase in the patient's intelligence score. Her capacity to sustain attention and concentrate showed improvement. In addition, compared to the initial test results the patient's Stroop Test TBAG Form, VFT, and AVLT scores improved (Table 2). As the patient's psychiatric symptoms resolved, olanzapine was withdrawn. She continued to use tramadol hydrochloride because she experienced infrequent arthralgia. As she no longer had any symptoms and her neuropsychiatric test scores improved, the patient's follow-up was discontinued.

DISCUSSION

The presented patient manifested neuropsychological deterioration, neuropsychiatric symptoms, and organ involvement due to elemental mercury poisoning. She had acrodynia and erythrism, which was indicative of central nervous system involvement. The patient did not have any premorbid psychiatric risk factors. At the conclusion of 9 months of follow-up she had no clinical symptoms and her neuropsychological test battery scores improved. The patient's psychiatric symptoms and neuropsychological impairment persisted even though her exposure to mercury ended, and her urine and blood mercury levels returned to normal. In such mercury poisoning cases it is vital to conduct a thorough neuropsychiatric evaluation and periodic monitoring. Inhalation of elemental mercury can cause acute and chronic poisoning, and there may not always be a direct relationship between the level of mercury exposure and symptoms (Bose-O'Reilly 2010). It is thought that individual genetic differences might determine the manifestation of the toxic effects of mercury. A recent study reported that genetic indicators (serotonin transporter gene polymorphism) that are affected by elemental mercury, and related to neurobehavioral and mood dimensions are associated with an increased predisposition to mercury poisoning (Echeverria et al. 2010).

Neuropsychiatric symptoms and neuropsychological test results show that exposure to mercury vapor causes central nervous system symptoms. Compared to adults, children and adolescents exhibit more severe toxic effects following exposure to toxic substances. The toxic effects of mercury vapor in the central nervous system is inversely proportional to age and can even cause death due to respiratory failure, especially in infants (Counter and Buchanan 2004). Mercury is thought to inhibit myelination in the developing central nervous system of children and adolescents. Animal research has shown that elemental mercury accumulates in lung alveoli, the cerebral cortex, the thalamus, the corpus striatum, the mesencephalic nucleus of the trigeminal nerve, cerebral nuclei, and motor neurons of the spinal cord. Elemental mercury has also been shown to decrease the number of neurons in the cerebellum and peripheral nervous system in rats and squirrel monkeys (Counter and Buchanan 2004).

Although brain damage in patients with organic mercury poisoning has been demonstrated via cranial MRI findings, only a few case reports of metallic mercury poisoning have been published. Cortical and cerebral atrophy were reported in an adult patient with chronic mercury poisoning (Miller et al. 2003). Hyperintense lesions in the left globus pallidus, putamen and white mater of the paracentral gyrus, posterior frontal region, parietal region, and cingulate gyrus were observed via T2-weighted MRI in a 10-year-old patient with elemental mercury poisoning that manifested as acrodynia, seizures, and visual impairment (Abbaslou and Zaman 2006). It is also reported that these findings were consistent with demyelination. Following 9 months of chelation therapy the patient's clinical and radiological findings returned to normal. Similarly, the presented patient's clinical findings and neuropsychological symptoms almost totally improved after 9 months of treatment.

Abbaslou and Zaman (2006) reported that the frontostriatal pathway, originating in the frontal cortex and with sequential projections to the striatum, internal globus pallidus/ substantia nigra (GPi/SN), thalamus, and back to the frontal cortex, is affected from mercury poisoning. Orbitofrontal cortex (OFC) syndrome, which is related to the OFC (a frontostriatothalamic circuit), manifests as disinhibition, loss of social awareness, irritability, utilization behavior, impaired attention, new information learning impairment, and suppressing unsuitable ones when selecting the mental activity (Karakaş and Aydın 1999). Anterior cingulate (AC) syndrome is associated with emotional, cognitive, and behavioral dysregulation. The

primary neuropsychological test for detecting AC and OFC syndromes is the Stroop Test. Stroop Test conditions cause marked MRI signals that can be replicated not only in the OFC, but also in the right and left anterior cingulate (AC), right precuneal, left inferior frontal, and left opercular regions (Brown et al. 1999; Bush et al. 1998; Leung et al. 2000). The cognitive component of the AC plays a central role in attention processes via modulation of stimuli detection and/or modification of response detection. Dysfunction in this region contributes to poor VFT and Stroop Test performance (Bush et al. 1998, Karakaş et al. 2003). AVLT requires learning a specific list of words, ongoing processes of attention, organization and retrieval, use of various cognitive strategies, including mnemonic types and sequencing stimuli in time. AVLT performance also requires controlling the interference effect of events on themselves by the subject (Eslinger and Grattan 1994). AVLT is a learning test, in addition to a memory test, that is sensitive to the mesial temporal lobe and hippocampus, but doesn't depend on a simple learning. All these processes are associated with frontal lobe function (Fuster 1998, 1995, Tsukiura et al. 2001).

The presented patient scored lower than her peer group only on the Stroop Test, VFT, and AVLT, all of which are sensitive to the frontal and frontostriatal region for detailed neuropsychological evaluation. Behavioral and personality changes associated with the frontal lobe, including lower academic performance, difficulty following rules, and mood swings, were observed, which suggest that mercury poisoning might possibly elicit a functional response in the brain, especially in the frontal region.

Even though symptoms and signs of elemental mercury poisoning can resolve by blocking exposure to mercury and administering appropriate treatment (Abbaslou and Zaman 2006; Yeates and Morgensen 1994), patients can experience long-term loss of function. The literature is devoid of any research on the long-term effects of elemental mercury on the developing human brain. Mercury poisoning in children in Turkey is common, and most cases (88.5%) are school-age children with elemental mercury poisoning (Oto Geçim et al. 2006). Chemistry labs in schools are the main source of this exposure. An effective preventative measure would be to keep all science laboratory materials under strict control and to increase teacher awareness about the risks of mercury exposure in the school environment. Even though thermometers and barometers are thought to contain only a miniscule quantity of mercury (1 mL), a recent case report from Turkey reported that accidents that occur at school lead to increase effects of mercury by additional factors such as the use of vacuum cleaners for collecting spilled mercury (Akyıldız et al. 2012); therefore, it is essential that except alternative methods need to be put in place of using instruments such as thermometers and barometers, environmental protection law needs to be improved regarding heavy metals.

The presented case shows that mercury is a metal that causes long-term central nervous system effects and is associated with slow neuropsychological recovery. The cause of the presented patient's partial clinical improvement with pharmacological treatment remains unknown, which highlights the importance of the prevention of mercury poisoning, as its effective treatment is only possible with chelation therapy, and that it is associated with life-threatening consequences.

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