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IDENTIFYING MERCURY HEAVY-METAL POISONING MASQUERADING AS DEMENTIA AND PARKINSON'S DISEASE – RECOGNIZING NEUROPSYCHIATRIC MANIFESTATIONS AND DIETARY CONTRIBUTORS

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Abstract

Assessing older adults presenting with cognitive decline, depression or other neuropsychiatric symptoms can be challenging because the underlying causes can be multifactorial. This article describes neuropsychiatric manifestations similar to those of Parkinson's disease in an elderly man who upon examination was suspected of having an elevated blood mercury level through dietary exposure, a suspicion later confirmed by blood tests. We outline suggestions for comprehensive history taking to identify potential sources of environmental exposure and provide resources to help limit and prevent consumption of foods that can contain heavy metals.

L'évaluation des personnes âgées avec déclin cognitif, dépression ou autres symptômes neuropsychiatriques représente un défi en raison de leurs causes multiples. Cet article décrit des manifestations neuropsychiatriques semblables à celles de la maladie de Parkinson chez un homme âgé chez qui un taux sanguin élevé de mercure de source alimentaire fut soupçonné et confirmé par la suite. Nous proposons une manière de recueillir une histoire clinique exhaustive afin d'identifier les sources environnementales d'exposition, et fournissons quelques ressources visant à limiter et à prévenir la consommation d'aliments contaminés aux métaux lourds.

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neuropsychiatric symptoms, heavy-metal poisoning, older adults, environmental exposure, fish consumption

Introduction

The signs and symptoms of heavy-metal poisoning are protean, non-specific and can vary depending on the heavy metal in question, total dose absorbed, extent of exposure and route of absorption. Along with general symptoms of fatigue, pain and tingling, night sweats and metallic taste from heavy-metal exposure, organ-specific involvements can affect any system in the body but most commonly the central nervous system, peripheral nervous system, and the cardio-respiratory, renal and gastrointestinal systems. Neuropsychiatric symptoms can be a common presentation.

Mercury, a naturally occurring heavy metal in soil, rock and water, is a potent cellular toxin that decreases neurotransmitter production.[1] While the neurological, gastrointestinal and renal systems are affected by mercury exposure, this toxic metal targets the central nervous system causing mood swings, irritability, memory decline, difficulty with attention and concentration and insomnia.[1-3] In addition, mercury poisoning is associated with depression and Parkinsonian signs and symptoms, including decline in coordination, muscle tremors, ataxia and stiffness.[4] Although mercury-induced neuropsychiatric manifestations have been reported in the literature since 1926,[5] such presentations may not be recognized in the clinic and can be mistaken for Alzheimer's disease, Parkinson's disease or depression. Medications are prescribed to patients for symptomatic relief; however, blood mercury levels may not be assessed in all cases.

Case Description

Mr. S was a 70-year-old Asian male admitted to an acute care geriatric unit for evaluation of depression with Parkinsonian features. He had been experiencing psychomotor retardation associated with depression, anxiety and decreased energy for the past two years. He did not drink alcohol.

His medications on admission included venlafaxine, lorazepam, tamsulosin, finasteride, docusate sodium and senna. He had been previously prescribed levodopa/carbidopa for psychomotor symptoms, and citalopram, mirtazapine, methylphenidate and bupropion for depressive symptoms. To help alleviate his sleep difficulties he was also treated with a number of sedative agents, including chlordiazepoxide, nitrazepam, zopiclone and diazepam.

His Mini-Mental Status Examination (MMSE) score was 21/30, down from previous scores of 28/30 and 29/30, five and seven months ago respectively. The verbal reasoning subtest revealed a score of 12/20 (normal ≥16) on the Cognitive Competency Test, indicating impaired insight and judgment. Liver cirrhosis was not documented. A physical assessment revealed masked facies, mild cogwheel rigidity and bradykinesia with no resting tremor. A consultation with a neurologist suggested that idiopathic Parkinson's disease (IPD) was unlikely because his Parkinsonian features were atypical. He had a healthy appetite and consumed 450 g of fish daily, an amount suggesting that significant environmental exposure to mercury was possible. A blood test was ordered, which revealed a mercury level of 134.6 nmol/L (normal <18.0 nmol/L).

Mr. S was diagnosed with mercury poisoning with Parkinsonian features. A dietitian advised him to decrease his fish consumption along with other dietary recommendations. Following dietary adjustments, he was switched to sertraline and restarted on levodopa/carbidopa. Patients with Parkinsonian features other than those attributable to IPD may still respond to levodopa therapy, although the incidence of clinical response is lower. (Tapering levodopa could be considered at follow-up; however, clinicians should keep in mind that although patients with short-term exposure to mercury can recover, long-term exposure to this heavy metal can have lasting effects.) All other antidepressants were discontinued. Improvements were seen in his mood, sleeping time, rigidity and mobility. He was discharged two weeks later on these medications along with lorazepam 1 mg qhs for sleep. During follow-up at three months, the patient and his family reported he had more stable mood and no experienced falls. On examination, he appeared only

slightly rigid. His MMSE score improved to 28/30. He reported consuming fish only once a week. His mercury level was slightly above 20 nmol/L.

Discussion

Mercury in nature exists in three forms – elemental or metallic mercury; inorganic mercury (exposure is primarily occupational); and organic mercury, most commonly in the form of methylmercury (exposure typically is dietary).[6] In Canada most heavy-metal exposure in the general population is attributed to methylmercury from fish and seafood consumption.[7]

Numerous studies have reported that fish is high in omega-3 fatty acids, a polyunsaturated fatty acid whose consumption may protect against coronary heart disease and ischemic stroke.[8,9] Older adults are frequently encouraged to eat more fish to protect against various ailments, including cognitive decline.[9,10] However, recommending a diet high in fish can inadvertently increase the risk of cognitive impairment through heavy-metal exposure. Methylmercury can bioaccumulate in fish, but especially so in predatory fish species. Methylmercury is bioavailable, as it is absorbed through the digestive tract. It readily crosses the blood-brain barrier and has a prolonged half-time clearance of approximately 50 days in the blood.[10] While inorganic mercury comprises only 14-26% of total blood mercury, a measurement of total blood mercury is largely indicative of methylmercury from dietary sources. According to the Environmental Protection Agency and Canada's National Research Council, an acceptable blood mercury level is 28.9 nmol/L (5.8 µg/L) or lower, although individual agencies may differ in recommendations.[3,11] Physicians can test for mercury using blood, urine and hair samples, but blood tests[12] are most commonly used to measure the organic form because red blood cells have a high rate of uptake of methylmercury.[6] In a Health Quality Ontario report on testing for blood mercury levels in the general population, Lambrinos reported that hospitals in Ontario ordered 7,741 mercury tests in 2009 and 5,541 in 2010. In the community setting, 5,577 mercury tests were ordered in 2009/10 and 4,958 in 2010/11.[6]

Patients at risk of mercury toxicity include those who consume large amounts of fish, marine mammals and wild game. People from Eastern Asia, Southeast Asia, northern parts of North America, Oceania and Western Europe[13] have traditional diets that can include large quantities of fish, or large quantities at certain times of the year. Contaminated water sources can also increase risk of exposure.[14] These potential sources of mercury exposure are reasonable to investigate, especially in culturally diverse urban centres. If mercury poisoning is identified early, quick withdrawal of this neurotoxic heavy metal can enhance the brain's ability to respond to drug treatment. Early diagnosis can help ensure appropriate treatment and minimize complications.

Health Canada has prepared a food safety guide to help consumers make informed choices about fish consumption (Health Canada. Mercury in fish. www.hc-sc.gc.ca/fn-an/securit/chem-chim/environ/mercur/cons-adv-etud-eng.php),[15] as well as a resource to help assess health risks of mercury in fish and the benefits of fish consumption.[16] General recommendations suggest that individuals consume at least two servings of fish weekly.[15] However, adults, including the elderly, should consume no more than two servings weekly of fish (e.g., tuna, shark, swordfish, marlin, orange roughy, escolar) that contain higher levels of mercury. Women of childbearing age, pregnant or nursing mothers, and children should eat no more than two servings of fish per month that contain higher levels of mercury (see Table 1). The Canadian Food Inspection Agency lists common names for fish and seafood that can help consumers when shopping (Canadian Food Inspection Agency (CFIA) fish list. http://active.inspection.gc.ca/scripts/fssa/fispoi/fplist/fplist.asp?lang=e).[17]

Although this case study and paper have focused on mercury exposure from diet, clinicians should be cognizant that other heavy metals, such as lead, cadmium and arsenic, are also neurotoxic and can cause neuropsychiatric symptoms such as mood swings, irritability, memory decline, difficulty with attention and concentration and insomnia. An estimated 4 million houses in the US have lead-based paint,[18] and if the paint flakes off or is on surfaces that rub together the lead-containing dust can pose a health hazard.

Other trace elements such as selenium, zinc and manganese can also be neurotoxic from chronic exposure through diet, supplements, medications, occupational exposure or environmental contamination. A list of select heavy metals that can cause neuropsychiatric symptoms and their potential sources for exposure are presented in Table 2. (See www.ncbi.nlm.nih.gov/pmc/articles/PMC4144270/pdf/nihms414261.pdf for a comprehensive review of the environmental occurrence of heavy metals, their potential for human exposure, and molecular mechanisms of toxicity, genotoxicity and carcinogenicity.)

Heavy-metal poisoning from mercury exposure can cause symptoms similar to other diseases prevalent in older adults. The decline in memory and cognitive ability associated with methylmercury poisoning can be attributed falsely to Alzheimer's disease and the psychomotor symptoms it causes can be misdiagnosed as Parkinson's. Although it is not be feasible to order tests for all patients with neuropsychiatric symptoms or for those presenting with Parkinsonian features, blood tests should be ordered if history-taking suggests possible exposure to heavy metals or when clinically suspected even without history of exposure.
Mr. S presented with mild psychomotor retardation accompanied by depression and anxiety. Various symptomatic treatments were tried before admission, but the etiology of his symptoms remained hidden for at least two years. His multitude of medications, particularly sedatives and psychotropic medications, likely contributed further to Mr. S's significant cognitive and functional decline. Strategies for discontinuing such medications are covered in a previous article in this journal – see http://canadiangeriatrics.ca/default/index.cfm/linkservid/0844EB81-E025-AE0C-595582DFCE2E49DA/showMeta/0/.

Difficulty in recognizing heavy-metal poisoning is attributable to the insidious onset of symptoms, the non-specificity of symptoms and a lack of awareness among health care professionals. A high index of suspicion is warranted for older adults who present with persistent neuropsychiatric symptoms with no clear indication of cause. Some physical signs such as Mees lines (see www.bing.com/images/search?q=mees+lines&qpvt=mees+lines&FORM=IGRE), gum lines and discolouration of the gums or buccal mucosa (see www.haematologica.org/content/92/2/e13 for discolouration from lead poisoning) may present clues. Pattern recognition is also important. For example, a constellation of gastrointestinal symptoms (e.g., severe abdominal cramping, constipation) and neurological symptoms (e.g., dizziness, headaches, fatigue, diminished cognitive performance) and anemia (initially normocytic but later microcytic) should raise suspicion of lead poisoning. However, a history of exposure is the most critical aspect of diagnosing heavy-metal poisoning. A detailed and thorough history involving diet, occupation, hobbies and recreational activities may be especially rewarding. In our patient, Mr. S's dietary history of significant fish consumption raised a red flag for methylmercury poisoning. In other patients, suspected environmental exposure along with use of herbal medicines,[19] foods[20] and dietary supplements[21] often can lead to suspicion of heavy-metal poisoning.

Summary

Neuropsychiatric symptoms from heavy-metal poisoning can be difficult to recognize in older adults because their presentations may be similar to those of other diseases prevalent in the elderly. Increased awareness among health care professionals along with the inclusion of a detailed and thorough history during patient assessment will help promote timely identification and early treatment, and minimize negative effects of heavy-metal poisoning on a patient's health and quality of life.

Learning points

1. The most deadly form of mercury is methylmercury. It is readily absorbed through the GI tract, crosses the blood-brain barrier and has a long half-life.
2. Methylmercury is bioaccumulated in the food chain. Predatory fish or fish from contaminated waters are the most common sources.
3. A detailed dietary and exposure history is important in suspected heavy-metal poisoning cases.
4. CNS involvement is common in heavy-metal poisoning. Signs and symptoms may be neurologic, psychiatric and cognitive.
5. The mainstay of treatment is removal of the source of exposure.

Table 1. Suggested amount of fish consumption for different age groups[15]

Age groups	Suggested amount for most types of fish	*Suggested amount for types of fish that should be eaten less often[17,18]
Children aged 1–4 years	>150 g (2 servings)/week	<75 g (1 serving)/month
Children aged 5–11 years		<125 g ($1\frac{2}{3}$ servings)/month
Women who are or may become pregnant or are breastfeeding		<150 g (2 servings)/month
General population (including older adults)		<150 g (2 servings)/week
*Fresh or frozen tuna, shark, swordfish, marlin, orange roughy, escolar, etc.[17,18] See www.hc-sc.gc.ca/fn-an/securit/chem-chim/environ/mercur/cons-adv-etud-eng.php and http://www.inspection.gc.ca/active/scripts/fssa/fispoi/fplist/fplist.asp?lang=e		

Table 2. Select heavy metals with neuropsychiatric symptoms, sources of exposure, presentation and measurement

Metal	Common sources of exposure	Neuropsychiatric symptoms	Clinical sample	Method of detection
Arsenic[22-27]	Groundwater, air (coal burning), treated wood (direct or burning off), food (seafood, rice, grains), metallurgy, pesticides, pigments, traditional Chinese medicine	Acute: delirium, seizures, encephalopathy, coma, peripheral neuropathy, fasciculations, painful paresthesias, wrist and foot drop Chronic: encephalopathy resembling Wernicke's syndrome with Korsakoff's psychosis, peripheral neuropathy	Hair, nails, blood, urine	AAS, ICP-AES, ICP-MS, HPLC/MS
Cadmium[22, 24, 27-29]	Food (grain and cereal products, leafy vegetables, root vegetables, shellfish), cigarette smoke, air and drinking water if close to industry (coal and waste burning, metal smelting, batteries), phosphate fertilizers	Chronic: decreased attention level and memory loss	Urine, blood	AAS, ICP-MS

Metal	Common sources of exposure	Neuropsychiatric symptoms	Clinical sample	Method of detection
Lead[*22-24, 27, 30, 31]	Leaded gasoline (phased out in regular consumption), lead pigments (paint, putty and ceramic), lead pipes and solder, batteries, improperly canned goods, radiation shielding, lead shot	Acute: fatigue, encephalopathy, neuropathy, coma, convulsions, tremor, headaches, hallucinations, memory loss, personality changes Chronic: headache, weakness, depression, impotence, chronic encephalopathy	Blood, urine	AAS radiographic techniques, Burton lines (lead lines – see www.nejm.org/doi/full/10.1056/NEJMicm050064)
Elemental and inorganic mercury[*22-25, 27]	Air (burning of hydrocarbons), fluorescent lights, dental amalgam, batteries, thermometers	Chronic: poor appetite, headache, weakness, muscle pain, poor muscle tone, insomnia, anorexia, memory loss, drowsiness, lethargy, depression, irritability, incoordination, tremor, personality changes	Hair, nails, blood, bone, urine	AAS, ICP-AES, ICP-MS
Organic mercury[*9, 15, 22-25, 27, 32]	Food (especially predatory fish), fungicide (i.e., ethylmercury acetate), disinfectants, thimerosal[**] –containing vaccines[33]	Acute: tremor, irritability, skeletal muscle wasting Chronic: ataxia, incoordination, concentric constriction of the bilateral visual fields, paresthesias of the extremities and mouth, fasciculation, muscle pain, headache, irritability, weakness, insomnia, memory loss, depression, photophobia, muscle twitching, confusion	Hair, nails, blood, bone, urine	AAS, ICP-AES, ICP-MS

AAS – atomic absorption spectroscopy
HPLC/MS – high performance liquid chromatography/mass spectrometry
ICP-AES – inductively coupled plasma atomic emission spectroscopy
ICP-MS – inductively coupled plasma mass spectroscopy

[*]Lead and mercury tests are available in most hospitals and community labs (see LifeLabs' selected tests at www.lifelabs.com/lifelabs_bc/patients/testaz.asp as an example of a community-based lab that tests for mercury and lead). Testing for other heavy metals may require specialized labs.

[**]Thimerosal is an organomercury compound used as a preservative in vaccines, but there is no convincing evidence of health hazard from the low doses in current human vaccines.

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