Mystery of Manganism in the Mind

Lakshmi S. Kasi, BA; Neehar D. Shah, BA; Himil J. Mahadevia, MD; Jennifer B. von Ende, MD; and Jennifer M. McBride, MD

Manganism is a neurologic complication resulting from elevated serum manganese (Mn) and Mn deposition in the globus pallidi.[1] Manganism was first described by John Couper in 1837 after workers involved in grinding Mn ore developed paraplegia.[2] Early symptoms of manganism include weakness and lethargy.[3] Later symptoms include gait abnormalities, muscle rigidity, dystonia, speech disturbances, mask-like facies, hallucinations, and psychosis.[3] We present the case of a patient with altered mental status who exhibited some, but not all, characteristics of manganism. Hence, his diagnosis remained an enigma.

Case Report

Mr A presented to the emergency department with tangentiality, rambling speech, and flight of ideas. Although he was oriented to self and place, he lacked orientation to time or situation. He displayed poor insight and judgment and could not answer questions appropriately. His vital signs were within normal limits, and his physical examination revealed a mildly distended abdomen along with trace lower extremity edema.

Brain magnetic resonance imaging (MRI) showed T1 hyperintensities in the bilateral globus pallidi, suggesting Mn deposition. Advanced cerebral and cerebellar volume loss was also noted. The electroencephalogram revealed no abnormalities. Significant laboratory test results included elevated serum Mn (1.6 mcg/L; reference range: < 1.2) and low ferritin (48 ng/mL; reference range: 30–400). Throughout the patient's hospital course, the neurology, psychiatry, and gastroenterology departments were consulted. There was initial concern for delirium, and Mr A was treated with haloperidol. However, he showed no significant improvement. Neurology had an interesting perspective that iron transporters transport Mn, and iron deficiency may upregulate transporters, resulting in increased levels of Mn in various tissues including the brain.[3] Hence, Mr A was treated with ferrous sulfate and vitamin E, which prevents further oxidative stress and is neuroprotective.[4]

Wilson disease was ruled out based on ceruloplasmin and urinary copper levels within normal limits. Hepatic encephalopathy was unlikely due to absent asterixis and no improvement with treatment with lactulose and rifaximin. Porphyria was also unlikely due to no photodermatitis, abdominal pain, or family history.

Mr A's other medical conditions were treated, and he was discharged after 16 days. While he showed a slight improvement in answering questions and overall cognition, he never returned to his baseline level. At outpatient follow-up appointments, his mentation continued to be abnormal, and a subsequent MRI 2 months later was unchanged.

Discussion

Diagnosing manganism is challenging since there is no universal diagnostic criterion. The diagnosis is typically based on clinical presentation, Mn exposure (usually occupational), elevated serum Mn levels, and evidence of Mn deposition in the brain on MRI.[1] While Mr A had clinical symptoms of manganism and Mn deposition on MRI, he did not have a known exposure like mining, welding, or fossil fuel combustion.[5] Furthermore, his serum Mn level was only slightly elevated. Thus, it is unclear if he had manganism.

One possible explanation for Mr A's presentation involves decreased liver metabolism of Mn due to his history of decompensated liver cirrhosis. Liver cirrhosis may cause acquired (non-Wilsonian) hepatocerebral degeneration and result in trace dietary Mn accumulation in the brain.[6]

This case underscores the importance of establishing diagnostic guidelines, especially for nonoccupational causes of manganism. Future research may explore the interactions between Mn and hepatic comorbidities as well as investigate treatment for patients with similar presentations. A multidisciplinary approach, as demonstrated here, remains crucial.

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Author Affiliations: University of Missouri–Kansas City School of Medicine, Kansas City, Missouri (all authors); University Health, Kansas City, Missouri (all authors).

Corresponding Author: Lakshmi S. Kasi, BA, 102 W Armour Blvd, Apartment 2, Kansas City, Missouri 64111 (Lskxm5@umsystem.edu).

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ORCID: Lakshmi S. Kasi: https://orcid.org/0009-0007-2838-0630; Neehar D. Shah: https://orcid.org/0000-0003-2516-9745; Himil J. Mahadevia: https://orcid.org/0000-0002-2083-5510; Jennifer M. McBride: https://orcid.org/0009-0006-6604-0402.

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