Case in Point

Symptoms Mimicking Those of Hypokalemic Periodic Paralysis Induced by Soluble Barium Poisoning

COL (Ret) Terrence J. O'Neil, MD, FASN, USAFMC; and Badar Siddiqui, MD

An investigation of a patient who presented with apparent hypokalemic periodic paralysis instead revealed barium poisoning.

Hypokalemic periodic paralysis (HPP) is a relatively common and potentially life-threating condition that can be either sporadic or recurring and has both inherited and acquired causes.[1] Familial HPP, on the other hand, is a rare condition (1:100,000) caused by loss of function mutations leading to the disruption of membrane potential consequently making them inexcitable.[2] Appearance of symptoms is typically in the first or second decade of life (60% of cases have onset aged < 16 years) with susceptible individuals experiencing sudden onset of perioral numbness; weakness; centrifugal paralysis, often with nausea; vomiting and diarrhea; andprostration,usuallytriggeredbyhigh-carbohydrate meals and rest following sustained muscle-group use.[3]

These symptoms are common to all forms of HPP, making the differential diagnosis wide and confusing. Rhabdomyolysis is occasionally associated with many severe hypokalemic episodes.[4] Myopathy and permanent muscle weakness have been reported in HPP.[5,6] Other reported inciting factors include a drop in serum potassium caused by β-adrenergic bronchodilator treatment.[7] Clinical attacks also have been associated with diabetic ketoacidosis and combined hypokalemia and hypophosphatemia.[8] Thyrotoxicosis also causes similar muscle action potential changes but only when hyperthyroidism is uncorrected.[9-12] Less commonly, hypothyroidism has been reported to be associated with hypokalemic paralysis.[3]

Pa Ping, a condition involving hypokalemic paralysis of uncertain etiology, is geographically centered in the Szechuan region of China.[13] Cases of Bartter, Liddle, and Gitelman syndromes also have been associated with hypokalemic paralysis.[3,14] There is an association with malignant hyperthermia following or during systemic anesthesia. Patients presenting as Guillain-Barré syndrome have been found to have periodic paralysis triggered by hypokalemia from any cause.[15] Sjögren syndrome and renal tubular acidosis also are reported to have triggered symptoms of hypokalemic paralysis.[16,17]

True type 1 HPP is caused by channelopathies resulting from mutations in the calcium channel gene CACN1AS (HypoPP1), which accounts for 70% of the cases, whereas type 2 HPP is cause by sodium channel gene SCN4A (HypoPP2) mutations, which accounts for 10% to 20% of cases.[18,19] An association with a voltage-gated potassium channel KCNE3 mutation has been made but is disputed.[20,21] Females typically have less severe and less frequent attacks, and attacks lessen or disappear during pregnancy.[22]

In a small controlled trial, acetazolamide has been reported to have prophylactic benefit, although a more powerful carbonic anhydrase inhibitor, dichlorophenamide, was reported to be effective in a study after acetazolamide had become ineffective.[23,24] These treatments would not be expected to be of clinical use in hypokalemia due to barium poisoning.

Barium poisoning has been reported as a result of accidental contamination of foodstuffs with soluble barium.[25] Onset of symptoms is rapid, with nausea, vomiting, diarrhea, and malaise followed rapidly by weakness, which can include the

Dr. O'Neil is an associate physician, and **Dr. Siddiqui** is a resident physician, both at James H. Quillen/Mountain Home VAMC in Tennessee.

muscles of respiration. This little-considered but rapidly lethal poisoning event can be accidental as a result of environmental exposure due to unintentional ingestion of the toxin or deliberate criminal poisoning as in this case. Because deliberate poisoning rarely crosses the mind of the clinician, awareness of the potential similarity of barium poisoning to other forms of HPP and even familial HPP is important.

CASE PRESENTATION

A male veteran aged 45 years when treated by the authors was well until moving into a new rural home when he began to experience acute episodes of variable perioral numbness, diarrhea, paresthesias, abdominal cramping, and weakness, which ranged from mild, self-terminating extremity weakness to 3 episodes of respiratory failure that required intubation and mechanical ventilation.

All episodes were accompanied by hypokalemia in the range of 2 to 3 mEq/L, but levels varied erratically during admissions from severe hypokalemia to normo- and hyperkalemia. Over 3 years, the patient was admitted to the hospital 19 times, underwent extensive workup, and was referred to endocrinology services at Duke University, Vanderbilt University, and the Cleveland Clinic. Diagnostic efforts centered on establishing whether he had a late-presenting variant of familial HPP.

Genetic evaluations could not identify known single-nucleotide polymorphisms associated with that condition. The consensus was that he had a potassium leak somewhere between his kidneys and bladder. Recommended management was a high baseline oral potassium supplementation and spironolactone. He had a brief period of improvement after moving to a different house, but the episodes returned once he moved back to his old house despite adherence to recommended treatment. In December 2012, he experienced his worst episode, with potassium 1.8 mEq/L on admission, resulting in admission to the intensive care unit (ICU).

Following a precipitous clinical decline, the patient was intubated and mechanically ventilated. Nephrology was consulted and given the recurrent life-threatening pattern, an intensive chart review was undertaken. It was noted that a urine arsenic level that had been normal several admissions previously at 18 µg/L was elevated during a subsequent admission at 59 µg/L, and several weeks later during a later admission the level had fallen to 15 µg/L. Urine lead was undetectable on 3 occasions, and urine mercury was within normal limits.

Arsenic toxicity did not match the patient's clinical syndrome, but the pattern seemed to be consistent with the possibility of unexplained toxic exposure and subsequent clearance. Therefore, an intensive literature search for syndromes of environmental exposure or poisoning resembling HPP was undertaken. The search revealed several references in the literature to paralysis similar to HPP that involved ingestion of hair-removing soap and rat poison containing barium sulfide and carbonate. References also pointed to the similarity of the symptoms to Guillain-Barre syndrome.

As a result of that literature search, a blood barium level was collected in the ICU that revealed 14,550 ng/mL. A scalp hair sample showed 6.1 µg barium per gram of hair (reference, 0.53 µg/g to 2 µg/g). Neither the patient nor his wife reported being involved in painting, ceramic work, decorating glassware or fabric with dyes, working with stained glass, smelting, metal welding, or use of vermicides.

A U.S. Environmental Protection Agency team was sent to the house, and a detailed toxic survey of the house and the surrounding grounds was conducted with no excess barium found. Barium levels were checked by a private physician on the wife and 2 minor children. The wife's barium levels came back undetectable in a blood sample and elevated in a hair sample. One child had a very low detected level in her blood and slightly elevated in her hair, and the other child had a low level in her blood and her hair. Because the circumstances of the wife's and children's exposure could not be explained environmentally nor could the veteran's exposure source be identified, the VA Police Service contacted the Tennessee Bureau of Investigation, and they questioned the veteran and his wife.

Shortly after that the veteran received a paralyzing gunshot wound to the back, and the ensuing investigation resulted in incarceration of his wife for both attempted murder by firearm and serial poisoning after soluble barium-containing materials were found hidden in the house.

DISCUSSION

Human barium poisoning is a rarely reported toxic exposure that results in rapid onset of nausea, vomiting, diarrhea, progressive weakness that may end in respiratory paralysis and death if intubation and mechanical ventilation are not promptly initiated. Although the barium found in radiographic contrast media is highly insoluble, ingested barium carbonate and sulfide are rapidly absorbed into the bloodstream, reaching high levels quickly and altering the conductance of potassium channels. The result is erratic variation in blood potassium

and prolonged paralysis unless it is immediately suspected and hemodialysis is initiated. In this case, the suspicion level at the time of intubation was insufficient to justify initiating acute hemodialysis.

Soluble barium is available from a number of open sources. Depilatory powders and several rat poisons list barium sulfide or carbonate, both soluble forms of barium rapidly absorbed through the gastrointestinal mucosa, as a major ingredient. One celebrated 2012 case in a city near Chattanooga, Tennessee, involved allegations of barium carbonate poisoning involving rat poison mixed into coffee creamer, but no charges could be filed because the sample handling precluded definitive linkage. Another deliberate toxic poisoning in Texas was traced to soluble barium introduced into a father's food by his daughter.

The patient reported here experienced 3 years and 19 admissions with 3 episodes of mechanical intubation before his suspected variant HPP was recognized as actually being due to soluble barium poisoning.

Barium does not appear in usual heavy metal urine and blood screens and as a result may not be asked for if not thought of in the differential diagnosis. Physicians dealing with instances of recurrent suspected HPP that do not fit usual age and clinical characteristics for HPP, lack the single-nucleotide polymorphisms associated with the disease, and are not associated with other conditions causing severe hypokalemia, such as renal tubular acidosis, Bartter, Liddle or Gitelman syndrome or severe diuretic or licorice-induced hypokalemia should have soluble barium poisoning included in the differential diagnosis. Appropriately drawn blood specimens in special metal-free sampling tubes and hair barium levels should be included in the diagnostic workup. If poisoning is suspected, a chain of evidence should be obtained to protect possible future criminal investigation against compromise. ●

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