

A Case of Zinc-Induced Copper Deficiency Myelopathy in the Setting of Zinc Supplementation

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ABSTRACT

Copper deficiency myelopathy is a rare and underrecognized cause of progressive myeloneuropathy that mimics vitamin B12-related subacute combined degeneration. We describe a 45-year-old woman who presented with several months of ascending lower extremity numbness, painful paresthesia, and weakness. Her history was notable for prolonged high-dose zinc supplementation initiated for immune support following the COVID-19 pandemic. MRI demonstrated dorsal column demyelination, and laboratory evaluation revealed anemia, leukopenia, and significantly low serum copper and ceruloplasmin levels with elevated zinc, confirming zinc-induced copper deficiency. The patient was treated with intravenous copper followed by oral copper supplementation, resulting in partial symptomatic improvement. Although partial improvement was achieved, persistent neurologic deficits remained at discharge. This case highlights excessive zinc intake as a preventable cause of copper deficiency myelopathy, and it emphasizes the importance of thorough supplement history and nutrient evaluation in patients presenting with unexplained myelopathy and cytopenias. Increased clinician awareness is critical, as delayed diagnosis may lead to incomplete neurologic recovery.

Keywords

Copper deficiency myelopathy, Copper deficiency, Zinc toxicity, Zinc-induced copper deficiency, Myeloneuropathy Subacute combined degeneration, Dorsal column demyelination, Neurologic manifestations, Cytopenia.

Introduction

Copper is an essential mineral that is present in some foods and daily supplements. It is a cofactor in many enzymatic reactions and plays key roles in other processes including immune function, brain development, nervous system function, and regulation of gene expression [1]. A deficiency in this mineral can cause

many adverse effects including hematological manifestations such as anemia and leukopenia [2]. Copper deficiency-associated myelopathy is a rare finding that is characterized by symmetric demyelination of the dorsal and lateral columns in the spinal cord [3,4]. This myelopathy has the potential to involve bladder and bowel symptoms, but more frequently manifests with upper and lower limb paresthesia [2]. It closely mimics a B12-induced subacute combined degeneration and is more commonly seen in women (64%) [5]. Because this myelopathy closely mimics subacute combined degeneration due to B12 deficiency, laboratory values and relevant history become tremendously critical [6]. While B12 deficiency will have macrocytic anemia, hypersegmented

neutrophils, neuropsychiatric symptoms, and low serum B12 levels, a copper deficiency myelopathy will characteristically have cytopenia, low serum copper and ceruloplasmin, and occasionally high or high-normal zinc levels [7-10]. Though still understudied, copper deficiency-associated myelopathy is usually caused by gastric surgeries (Roux-en-Y gastric bypass), zinc toxicity, and malabsorption syndromes [11]. Myelopathy is the most common neurologic manifestation of copper deficiency, characterized by gait disturbance, sensory deficits in vibration and proprioception due to dorsal column involvement, ataxia, and gait disturbance. An associated length-dependent peripheral polyneuropathy can occur [3]. Physical examination may show a combination of myelopathic and neuropathic features with spastic paraparesis and brisk patellar reflexes in addition to decreased distal reflexes and sensory impairment that follows a glove and stocking pattern [2]. In addition to these neurological manifestations, patients may experience hematologic abnormalities including anemia and leukopenia⁵. The presence of myelopathy due to copper deficiency can be created by zinc toxicity and may be enhanced by increasing use of GLP-1 (glucagon-like-peptide-1) and GIP (glucose-dependent insulintropic polypeptide) receptor agonists [12].

Zinc is an essential trace element that serves as a cofactor for over 300 enzymes and 2000 transcription factors, playing critical roles in immune function, DNA synthesis, wound healing, protein synthesis, and cellular metabolism [13]. Copper and zinc have a competitive binding relationship with metallothionein (MT), a binding protein that has a greater affinity for copper than zinc [12]. Through an increase in supplemental zinc, metallothionein production is upregulated [12]. This upregulation creates a large increase in unbound copper binding to metallothionein. Once bound, this complex becomes stored in enterocytes, decreasing the amount of unbound copper in the serum [12]. Unlike the unbound copper and zinc, the metallothionein-zinc complex is excreted in the feces during the shedding period of cell turnover [12]. Therefore, the potential risk of copper depletion in the setting of substantially increased zinc supplementation is very high. The increased public interest in zinc supplementation during and after the COVID-19 pandemic has reinforced the importance of recognizing zinc-induced copper deficiency as a preventable cause of myelopathy, particularly in patients using over-the-counter supplements without any medical supervision [14,15].

Case Presentation

A 45-year-old female presented to Pikeville Medical Center's emergency department on December 31, 2025, with progressive bilateral lower extremity ascending numbness and weakness, more pronounced on the left. She reported numbness in her feet, with painful paresthesia described as a sensation of "stepping on needles". Symptom onset was gradual, beginning in August 2025 and progressed to painful paresthesia from the waist down. She noticed rapid exacerbation approximately one week before presentation, which prompted her to seek care. Upon initial evaluation, the patient denied recent infections, injectable drug use, recent travel, rashes, joint pain, meningismus, bowel or

bladder incontinence, or sick contacts. Her past medical history was notable for restless leg syndrome, chronic normocytic anemia, chronic leukopenia, and opioid use disorder. She had no personal or family history of autoimmune disease. She recently discontinued tirzepatide, used for weight loss, after losing 31 pounds over one year. The patient reported chronic high-dose zinc supplementation with daily intake of 200 to 300 mg initiated after a Corona Virus Disease-19 (COVID-19) infection in 2020 for immune support. She occasionally increased her dose to 300 mg whenever she felt ill. She wears dentures but denies the use of denture adhesives.

Physical examination showed intact cranial nerves and cognitive function. Motor strength was 4/5 in bilateral hip flexion, which was limited by pain. Strength was otherwise normal throughout. Sensory examination revealed a thoracic sensory level with allodynia and decreased light touch and pinprick sensation from the T5 level and below. Vibration and proprioception were preserved. Patellar reflexes were brisk (3+), Achilles reflexes were absent bilaterally, and plantar reflexes were flexor. Cardiovascular, pulmonary, and dermatologic examinations were unremarkable. Initial laboratory evaluation revealed anemia (Hemoglobin of 8.6 g/dL), leukopenia (White blood cells of $2.0 \times 10^9/L$), Varicella and Epstein-Barr virus IgG were positive, indicating a prior exposure without evidence of active infection. Other laboratory findings, including magnesium, hemoglobin A1c, vitamin B12, methylmalonic acid, folate, iron studies, thyroid function, liver and renal function, electrolytes, and immunoglobulins, were within normal limits. Cerebrospinal fluid analysis was unremarkable with two nucleated cells, glucose of 63 mg/dL, and protein of 43 mg/dL, not suggestive of infectious or inflammatory etiology. Imaging studies revealed a long segment of T2 hyperintensity in the posterior columns of the thoracic spine from T5 to T11 on magnetic resonance imaging (MRI), without contrast enhancement. Lumbar MRI demonstrated degenerative changes at L4-L5, while computed tomography (CT) scans of the head, chest, cervical, and thoracic spine were unremarkable. A suspected pineal cyst was noted on brain MRI with no other significant acute or chronic findings. Echocardiography showed normal left ventricular size and function. Intravenous (IV) methylprednisolone 1,000 mg daily was started empirically out of concern for an inflammatory or demyelinating process. Additional laboratory evaluation revealed markedly low serum copper (2 mcg/dL; range, 62-140 mcg/dL), low ceruloplasmin (<60 mg/dL), and elevated serum zinc (140 mcg/dL; range, 60-120 mcg/dL). Methylprednisolone was discontinued, and she was started on IV elemental copper 2 mg daily for four days, followed by oral copper supplementation with 8 mg daily for one week, 6 mg daily for the second week, 4 mg daily for the third week, and 2 mg daily thereafter. Pregabalin was initiated for neuropathic pain and titrated to 600 mg daily. The patient reported gradual improvement in paresthesia and some reduction in pain. However, lower extremity numbness and paresthesia persisted at discharge; her neurological recovery was limited. She was advised to discontinue all zinc supplementation and follow up neuromuscular neurology with plan for electromyography and nerve conduction studies which have not been done yet.

Discussion

Copper deficiency myelopathy is a rare, often acquired neurological syndrome that is characterized by posterior column dysfunction. The most common reported etiologies of copper deficiency include gastric surgery, malabsorption, and excessive zinc ingestion [16]. Although a history of gastric surgery is the most identified risk factor for copper deficiency, excessive zinc ingestion is widely recognized as a preventable cause of copper deficiency. Cases of overuse of zinc supplements, whether cream-based [17] or oral [18-20], leading to copper deficiency and causing myeloneuropathy are well documented. This case further reinforces that even readily available over-the-counter zinc supplements can produce a significant neurologic disease when consumed in excessive doses over prolonged periods, highlighting the importance of early recognition and prevention [18-20].

Zinc is an essential mineral that is important for immune functioning, wound healing, and DNA synthesis, which has contributed to the widespread availability and use of over-the-counter zinc supplements for immune support and management of dermatological conditions. Since the enactment of the Dietary Supplement Health and Education Act (DSHEA) of 1994, the number of dietary supplements that have been sold in the United States has increased tremendously, oftentimes without sufficient regulatory oversight or patient education [21]. Abnormal zinc levels cause an excessive upregulation of metallothionein, an intracellular ligand, and production in the enterocytes. Copper has a higher affinity for metallothionein in comparison to zinc, which results in copper displacing zinc from metallothionein. Consequentially, copper remains trapped in the enterocytes and is lost in the stool [22]. This leads to systemic copper deficiency and subsequent neurological manifestations.

Although zinc supplementation is widely available over the counter and is usually perceived as harmless and used for perceived health benefits, its use can result in adverse effects, specifically serious neurologic and hematologic complications, when used chronically without medical supervision. Since many patients do not consider vitamins or nutritional supplements to be medications, clinicians should routinely obtain a detailed history of over-the-counter supplement use when evaluating patients with unexplained neurologic symptoms [18,21,23]. This case reinforces the importance of obtaining a detailed history, as supplement use may not be disclosed unless specifically elicited.

This case uniquely shows a direct clinical impact of medical misinformation and unsupervised supplement use. Importantly, the patient's neurologic deficits developed gradually over time, illustrating how nutritional myelopathies may initially present with nonspecific symptoms before progressing to significant functional impairment. This emphasizes the importance of maintaining a broad diagnosis early in the evaluation of extremely progressive sensory and motor deficits.

The overuse of zinc supplements, especially in high doses, particularly during and after the COVID-19 pandemic, has at times

led to harmful consequences [22]. During this period, Google searches for micronutrients, specifically zinc, rose by 53%, and zinc sales increased by 415% [14,15]. These trends suggest widespread supplementation occurring usually without medical supervision, as zinc became increasingly accessible without a prescription. At the time, many believed that zinc could help support the immune system, a perception which was reinforced by studies suggesting that moderate zinc lozenges use was associated with approximately a 33% reduction of upper respiratory symptoms [24]. Although such findings seem promising, the studies did not explicitly state the dangers of zinc toxicity. Consequently, patients would seek health information from online sources, which may not have made them aware of safe zinc intake. Many health organizations, such as the National Institute of Health, Harvard T.H. Chan School of Public Health, and Mayo Clinic, indicate only to consume a range of 8 mg to 20 mg a day [13,25,26]. Even with these recommendations on how much Zinc an individual can ingest, the American Academy of Family Physicians does not recommend daily Zinc supplementation without a clinical cause, as Zinc has not been proven to be an effective treatment for upper respiratory tract infections [23]. In fact, they specifically state the risk of copper deficiency anemia and a host of other complications caused by long-term high-dose use. As access to medical information becomes easier, clinicians should be stewards of helping patients understand the consequences of online medical decision-making.

The patient's incomplete neurologic recovery in this case is typical of copper-induced myelopathy. A report evaluating 198 cases of copper deficiency myelopathy who received copper supplementation found that only 24% reported improvement in neurological symptoms, with only 5.1% returning to baseline [8]. This case also demonstrates that laboratory evaluation of unexplained myelopathy should extend beyond vitamin B12 deficiency when clinical suspicion remains high. Assessment of serum copper, ceruloplasmin, and zinc concentrations can lead to early diagnosis and treatment, which can potentially limit irreversible neurologic injury. With access to online medical information continuing to expand, clinicians must play an active role in patient education, especially about supplement use, promoting informed decision-making, and managing the unintended consequences of unsupervised health interventions.

Although hematologic abnormalities often improve following copper replacement, neurologic recovery is often incomplete, especially when the diagnosis is delayed. Because of this, early recognition is the most effective strategy for minimizing long-term neurologic disability associated with zinc-induced copper deficiency myelopathy [2,8].

Conclusion

Copper's primary role is to support cellular development and neurological functions. As seen in this case report, copper deficiency can cause debilitating myelopathic and neuropathic symptoms as well as hematological derangements including anemia and leukopenia. Zinc supplementation was an important risk factor for copper deficiency in this patient. Zinc increases

metallothionein, a protein that binds and sequesters zinc and copper. An increase in oral zinc leads to increased metallothionein, which then binds to copper, leading to copper deficiency. Early recognition, immediate discontinuation of excess zinc, and timely copper replacement may prevent irreversible neurologic injury. This highlights the importance of obtaining a detailed nutritional supplement and vitamin history in patients presenting with unexplained myelopathy.

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