Consultant360 Multidisciplinary Medical Information Network

PHOTOCLINIC

Copper Deficiency Myeloneuropathy

Volume 60 - Issue 7 - July 2020

AUTHORS:

Alina Aasim, MD

Third-Year Resident, Internal Medicine Residency Program, Flushing Hospital Medical Center, Flushing, New York

Mina Botros, MD

Second-Year Resident, Internal Medicine Residency Program, Flushing Hospital Medical Center, Flushing, New York

Anil Kapoor, MD

Neurologist, Flushing Hospital Medical Center, Flushing, New York

Karen Beekman, MD

Internist, Flushing Hospital Medical Center, Flushing, New York

CITATION:

Aasim A, Botros M, Kapoor A, Beekman K. Copper deficiency myeloneuropathy. *Consultant.* 2020;60(7):e1. doi:10.25270/con.2020.07.00001

Copper deficiency myeloneuropathy has been well studied in animal species, but the relationship with neurologic disease in humans has been identified only recently.[1] The condition is usually accompanied by hematologic abnormalities such as anemia and neutropenia. Acquired copper deficiency is most commonly associated with gastric surgery, followed by excessive zinc ingestion, among other causes. Neurologic findings of copper deficiency are often underrecognized and therefore not treated.[1,2]

CASE REPORT

A 65-year-old woman was admitted with generalized weakness, melena, and a supratherapeutic international normalized ratio (secondary to the use of warfarin and concomitant ciprofloxacin). Her

international normalized ratio (secondary to the use of warfarin and concomitant ciprofloxacin). Her

history was significant for atrial fibrillation on warfarin, coronary artery disease, type 2 diabetes mellitus, seizures, and cerebrovascular accident with residual left-sided weakness. She was admitted to the medical intensive care unit with a diagnosis of septic shock due to pneumonia and urinary tract infection (UTI), was stabilized, and then was transferred to the general medical floor.

During the course of hospitalization, the patient reported lower extremity weakness, which had been present prior to admission. She reported having fallen 8 to 12 days before admission, after which she required a walker for ambulation due to weakness. She denied recent travel, camping, tick bites, rash, and urinary or bowel incontinence. Because of her worsening functional status, a demyelinating process was suspected.

On physical examination, vital signs were unremarkable. Neurologic examination revealed intact cranial nerve function. The patient was unable to walk or stand, and bilateral quadriceps atrophy was present. Muscle strength was 5/5 in the bilateral upper extremities. However, in the bilateral lower extremities, strength was 2/5 proximally and 5/5 distally. Sensation to vibration was absent throughout. Deep tendon reflexes were absent in the biceps, triceps, and supinator muscles but 2+ in the ankles and knees. The Babinski sign was absent bilaterally.

Laboratory test findings revealed leukocytosis with a white blood cell count of 22,500/μL (reference range, 3800-11,000/μL), normocytic anemia with a hemoglobin of 10.2 g/dL (reference range, 11.5-16.0 g/dL), an elevated creatine kinase level of 23,710 U/L (reference range, 30-135 U/L), and a normal vitamin B_{12} level of 854 pg/mL (reference range, 239-931 pg/mL).

Magnetic resonance imaging (MRI) of the brain showed a chronic infarct, while MRI of the whole spine did not reveal any specific findings. Lumbar puncture results were unremarkable, showing normal cerebrospinal fluid protein level and cell count. Electromyography demonstrated findings of sensorimotor axonal peripheral neuropathy. Because of persistent high clinical suspicion for Guillain-Barré syndrome (GBS), the patient received 5 cycles of plasmapheresis over 2 weeks, without clinical response.

Because of the lack of clinical improvement, further history was reviewed with the patient. On inquiry, she reported having using zinc-based denture adhesive cream for the past 10 years. This led to suspicion for copper deficiency, which was further confirmed by a low serum copper level of 21 μg/dL (reference range, 70-175 μg/dL) and a low serum ceruloplasmin level of 4 mg/dL (reference range, 18-53 mg/dL), combined with a high 24-hour urine zinc level of 7146 μg/24 h (reference range, 100-1200 μg/24 h). The diagnosis of copper deficiency myeloneuropathy was made.

The patient was started on copper supplementation with copper gluconate oral tablets, 8 mg daily for 1 week, followed by 6 mg daily for the second week, 4 mg daily for the third week, and 2 mg daily thereafter. The patient was advised to have follow-up tests for serum copper and serum ceruloplasmin

thereafter. The patient was advised to have follow-up tests for serum copper and serum ceruloplasmin

levels in 1 month. In addition, non-zinc–based denture adhesive cream was recommended. The patient was discharged to a rehabilitation center, but she was readmitted 2 weeks later for septic shock secondary to the UTI and pneumonia and subsequently died.

DISCUSSION

Copper is an essential element involved in neurologic, hematologic, and skeletal system integrity. Neurologic deficits associated with acquired copper deficiency include gait disorders, sensory ataxia, and asymmetric weakness with electrodiagnostic evidence of denervation suggesting lower motor neuron disease.

Copper is primarily absorbed in the small intestine, mainly in the duodenum. Zinc plays a crucial role in the process of copper absorption within the lumen of the small intestine. Copper and zinc are bound by intracellular ligands, most importantly metallothionein (MT). Increased oral or parenteral intake of zinc leads to increased binding of the 2 metals. MT has a higher affinity for copper than zinc. Therefore, high levels of zinc lead to increased copper binding to MT and less overall copper absorption into the body.[3,4]

There remains a significant delay in the diagnosis of copper deficiency neuropathy/myelopathy, which is a treatable condition. The use of denture cream containing zinc should be an integral part of history-taking, and the serum copper level should be assessed in patients presenting with myelopathy with or without neuropathy, including patients presenting with vitamin B_{12} deficiency and demyelinating neuropathies such as GBS.[3,5,6]

Thorough history and assessment are important to accurately distinguish copper deficiency neuropathy/myelopathy. Clinicians should recognize the importance of timely diagnosis, since early treatment may lead to substantial improvement in neurologic symptoms.

REFERENCES:

1. Jaiser SR, Winston GP. Copper deficiency myelopathy. *J Neurol.* 2010;257(6):869-88 doi:10.1007/s00415-010-5511-x

2. Staff NP, Windebank AJ. Peripheral neuropathy due to vitamin deficiency, toxins, and medications. *Continuum (Minneap Minn).* 2014;20(5 Peripheral Nervous System Disorders):1293-1306. doi:10.1212/01.CON.0000455880.06675.5a

3. Nations SP, Boyer PJ, Love LA, et al. Denture cream: an unusual source of excess zinc, leading to hypocupremia and neurologic disease. *Neurology.* 2008;71(9):639-64 doi:10.1212/01.wnl.0000312375.79881.94

4. Hoffman HN II, Phyliky RL, Fleming CR. Zinc-induced copper deficiency. *Gastroenterology.* 1988;94(2):508-512. doi:10.1016/0016-5085(88)90445-3

5. Willis MS, Monaghan SA, Miller ML, et al. Zinc-induced copper deficiency: a report of three cases initially recognized on bone marrow examination. *Am J Clin Pathol.* 2005;123(1):125-131. doi:10.1309/v6gvyw2qtyd5c5pj

6. Kumar N, Weimer LH. Copper deficiency myeloneuropathy. MedLink Neurology. https://www.medlink.com/article/copper_deficiency_myeloneuropathy. Updated January 26, 2019. Accessed February 6, 2020.