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# Something to Chew On: Denture Adhesive-Induced Copper Deficiency Myeloneuropathy in a Patient with Suspected MS

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## Abstract

Copper deficiency myeloneuropathy is a well-described but uncommon cause of peripheral neurologic deficits. Here, we describe a case of a 60-year-old man who first presented with progressive ascending sensory loss. Physical exam revealed sensory deficits of the extremities, and initial workup was suspicious for Multiple Sclerosis (MS). However, further investigation identified severe copper deficiency presumed secondary to toxic zinc ingestion from denture adhesive overuse as the culprit. Through avoidance of anchoring bias, a misdiagnosis of MS was avoided and a rare diagnosis was made.

## Objective

Copper deficiency myeloneuropathy is a well-described but rare cause of sensory neuropathy that can mimic other more common presentations. Zinc toxicity is a common cause of copper deficiency and zinc-containing denture adhesives have been previously implicated[1][2][3][4]. We highlight copper deficiency as a rare cause of myeloneuropathy, introduce the relationship between zinc toxicity and copper malabsorption, and exemplify the risk of incomplete neurologic evaluation.

## Case

A 60-year-old male presented with 18 months of progressive ascending sensory loss of the upper and lower extremities. The patient described steadily worsening balance, inability to locate his feet under blankets, and lack of coordination in his hands, with an associated 75-lb weight loss over this time period. Past medical history was unremarkable. Physical examination revealed a symmetrical pattern of sensory deficits in vibration, proprioception, and temperature sensation in the lower extremities to the mid-thigh and upper extremities to the elbow, hyperesthesia of the plantar surfaces of the feet, and absent Achilles tendon reflexes bilaterally. The patient appeared cachectic with a body mass index (BMI) of 15, and examination of the oropharynx revealed an absence of teeth requiring the use of poorly fitting dentures fixed with large amounts of denture adhesive. Initial labs showed normocytic anemia (hemoglobin 8.6 g/dL) and normal vitamin B12 level. MRI of the brain was unremarkable, and MRI of the spine showed no compressive myelopathy or enhancing lesions. CSF studies were notable for oligoclonal bands, which, in the setting of the patient's subacute neurologic findings, raised concern for possible MS despite the absence of supportive findings on imaging. The inconsistency between his CSF studies and imaging prompted additional investigation, which yielded critically low serum copper and ceruloplasmin levels. Thus, the underlying diagnosis of copper deficiency myeloneuropathy was made.

## Case (cont.)

Notably, a serum zinc level was obtained (99 µg/100mL) and found to be within the reference range (44-115 µg/100mL). A thorough history was negative for symptomatic evidence of malabsorptive syndromes but positive for daily consumption of multivitamin supplements that contained high levels of zinc as well as significant overuse of zinc-containing denture adhesive. The patient completed five days of IV copper infusion and began to notice subtle improvements in proprioceptive fine motor control. He was later transferred to a long-term rehabilitation unit for therapy and ongoing copper replacement.

## Discussion

We describe a rare case of copper deficiency leading to bilateral ascending sensory loss, likely precipitated by zinc toxicity from denture adhesive overuse. Copper deficiency myeloneuropathy is a well-described but rare cause of peripheral neuropathy. Although its mechanism is poorly understood[5], the underlying copper deficiency is frequently attributable to malabsorption (from disease or iatrogenic causes like bariatric surgery) or zinc toxicity[6]. Zinc and copper are both absorbed via metallothionein proteins in jejunal enterocytes, and competitive binding by zinc can inhibit copper absorption[1].

Copper deficiency myeloneuropathy classically presents with lower limb paresthesia, length-dependent distribution of impaired proprioception, pain, and temperature sensation, and subacute gait disorder with sensory ataxia[7]. Leukopenia may also be present alongside microcytic, macrocytic, or normocytic anemia. The underlying micronutrient deficiency may manifest as low serum copper and ceruloplasmin levels, with or without clinically elevated serum zinc levels. Overuse of standard denture adhesive, given its high zinc content and application in the oral cavity, is a documented causative agent in zinc toxicity-induced copper deficiency[1][8]. Risk is especially high among patients with poorly fitting dentures who use more adhesive than is advised as excess adhesive is often inadvertently ingested[4]. In this patient, we suspect daily multivitamin consumption and thrice daily denture adhesive application amounted to 95 – 145 mg of inadvertent intake per day. The toxic threshold is typically considered greater than 150mg daily[9]. While this patient's zinc level was not overtly excessive, we suspect that a relatively elevated zinc level in the gut – especially in the setting of severe chronic malnutrition – was sufficient to induce copper deficiency. Additional efforts to establish the etiology of the patient's cachexia were unrevealing, as restrictive eating patterns, active infection, and indolent malignancy were not apparent. There was initial concern for MS given the patient's peripheral sensory deficits and CSF with oligoclonal bands. However, MS classically exhibits hyperintense white matter lesions on MRI which were notably absent on imaging. Thus, the presence of oligoclonal bands in the CSF of a patient with neurologic deficits concerning for MS proved to be a red herring.

## Discussion (cont.)

This differentiation was critical in preventing anchoring bias and prompted investigation into other etiologies, including tabes dorsalis, transverse myelitis, medication toxicities, and micronutrient deficiencies (Vitamin B12, Vitamin E, and copper), which ultimately led to the correct diagnosis.

Treatment of copper deficiency myeloneuropathy primarily involves discontinuation of offending agents (denture adhesive or zinc-containing multivitamins) and copper replacement[2]. A common copper replacement course is 5 days parenteral therapy followed by prolonged oral therapy with dosages ranging from 2-9 mg daily[6]. Treatment duration is variable and depends on the extent of total body copper depletion and illness chronicity. Copper replacement (monitored by serial serum copper and ceruloplasmin levels) prevents further disease progression but offers only limited long-term improvement; in a recent case report compilation, only 49% of treated cases of copper deficiency myelopathy showed any improvement and none had full neurologic recovery[6].

In summary, copper deficiency myeloneuropathy is a rare cause of peripheral sensory deficits that should not be mistaken for other more common neurologic diseases. Thorough investigation including imaging studies and serological evaluation of micronutrient deficiency should be performed, especially among patients using zinc-containing denture adhesive, in which the risk of zinc toxicity-induced copper deficiency is particularly high.

## References

[1] Nations SP, Boyer PJ, Love LA, Burritt MF, Butz JA, Wolfe GI, Hynan LS, Reisch J, Trivedi JR. Denture cream: an unusual source of excess zinc, leading to hypocupremia and neurologic disease. Neurology. 2008 Aug 26;71(9):639-43. doi: 10.1212/01.wnl.0000312375.79881.94. Epub 2008 Jun 4. PMID: 18525032.

[2] Kumar N, Gross JB Jr, Ahlskog JE. Myelopathy due to copper deficiency. Neurology. 2003 Jul 22;61(2):273-4. doi: 10.1212/01.wnl.0000073542.02761.5f. PMID: 12874423.

[3] Al-Tabbaa MM, Horvath E. Idiopathic Copper Deficiency Induced Myeloneuropathy. Cureus. 2021 Sep 20;13(9):e18130. doi: 10.7759/cureus.18130. PMID: 34692339; PMCID: PMC8528345.

[4] Cathcart SJ, Sofronescu AG. Clinically distinct presentations of copper deficiency myeloneuropathy and cytopenias in a patient using excessive zinc-containing denture adhesive. Clin Biochem. 2017 Aug;50(12):733-736. doi: 10.1016/j.clinbiochem.2017.03.005. Epub 2017 Mar 10. PMID: 28288851.

[5] Spinazzi M, Sghirlanzoni A, Salviati L, Angelini C. Impaired copper and iron metabolism in blood cells and muscles of patients affected by copper deficiency myeloneuropathy. Neuropathol Appl Neurobiol. 2014 Dec;40(7):888-98. doi: 10.1111/nan.12111. PMID: 24708542.

[6] Jaiser SR, Winston GP. Copper deficiency myelopathy. J Neurol. 2010 Jun;257(6):869-81. doi: 10.1007/s00415-010-5511-x. Epub 2010 Mar 16. PMID: 20232210; PMCID: PMC3691478.

[7] Kumar N. Copper deficiency myelopathy (human swayback). Mayo Clin Proc. 2006 Oct;81(10):1371-84. doi: 10.4065/81.10.1371. PMID: 17036563.

[8] Hedera P, Peltier A, Fink JK, Wilcock S, London Z, Brewer GJ. Myelopolyneuropathy and pancytopenia due to copper deficiency and high zinc levels of unknown origin II. The denture cream is a primary source of excessive zinc. Neurotoxicology. 2009 Nov;30(6):996-9. doi: 10.1016/j.neuro.2009.08.008. Epub 2009 Sep 2. PMID: 19732792.

[9] Prasad AS, Brewer GJ, Schoomaker EB, Rabbani P. Hypocupremia induced by zinc therapy in adults. JAMA. 1978 Nov 10;240(20):2166-8. PMID: 359844.