Acute and Bilateral Blindness Due to Optic Neuropathy Associated With Copper Deficiency

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Background: Acquired copper deficiency in adults is associated with a subacute to chronic progressive myeloneuropathy and optic neuropathy.

Objective: To describe an individual after gastric bypass surgery who developed a chronic progressive myeloneuropathy, an acute optic neuropathy, along with anemia and leukopenia.

Design: Case report.

Setting: Academic center.

Patient: A 55-year-old woman, following gastric bypass surgery 22 years earlier, developed progressive numbness, weakness, and sphincter disturbance over 6 years. She awoke one morning with bilateral blindness. Examination findings showed evidence of severe myelopathy and peripheral neuropathy.

Main Outcome Measures: Magnetic resonance imaging, optical coherence tomography, electrophysiologic studies, nerve and muscle biopsy specimens, and vision testing.

Results: Over 1 year of follow-up, copper infusion therapy seemed to stabilize the progressive myeloneuropathy and improved leukopenia and anemia. It had no effect on the optic neuropathy. Optic nerve tissue injury was observed on magnetic resonance diffusion tensor imaging and on optical coherence tomography.

Conclusions: Copper deficiency should be considered in cases of atypical optic neuropathy. Serum copper levels should be monitored in patients with a compatible neurologic syndrome who have undergone gastric bypass surgery. Although visual acuity did not improve after copper infusion in our patient, prompt recognition of copper deficiency may prevent further deterioration.

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0 at the toes and ankles and was minimally reduced to 7 at the fingers. Ankle proprioception was intact only to large-amplitude foot movements. There was no sharp or dull discrimination in the lower extremities up to the midcalf, sensation was reduced to pin over the hands and forearms, and a sensory level was present at T4-5. Finefinger movements were diminished. She required assistance to stand and walked with bilateral support, a wide-based gait, and slow shuffling steps.

Laboratory testing showed that the following results were within the normal range: white blood cell count (2500/µL [to convert white blood cell count to ×10^9/L, multiply by 0.001]), hemoglobin level (9.2 g/dL [to convert hemoglobin to grams per liter, multiply by 10.0]), and platelet count (342,000/µL [to convert platelet count to ×10^9/L, multiply by 1.0]), and platelet count (342,000/µL [to convert platelet count to ×10^9/L, multiply by 1.0]). Vitamin B₁₂, homocysteine, and methylmalonic acid levels were also normal. Her serum copper level was 15 µg/dL (reference range, 70-155 µg/dL [to convert serum copper level to micromoles per liter, multiply by 0.157]). Her serum zinc level was low normal at 72 µg/dL (normal range, 70-150 µg/dL [to convert serum zinc level to micromoles per liter, multiply by 0.153]), and iron deficiency was confirmed by an elevated soluble transferrin receptor level of 52.5 nmol/L (reference range, 8.7-28.1 nmol/L). Her serum transferrin receptor level of 106 fL (nadir of 106 fL before treatment) was less than the fifth percentile in both eyes (79.3 µm OD and 75.0 µm OS), with the thickness of the temporal quadrants measuring less than the first percentile.

This case illustrates a devastating onset of acute bilateral optic neuropathy in the setting of chronic progressive myeloneuropathy, macrocytic anemia, and leukopenia. Acquired copper deficiency is an important consideration in the differential diagnosis because early recognition and repletion may prevent further deterioration. The patient had been diagnosed years previously as having unspecified neuropathy, but myelopathy was unappreciated until examination findings revealed increased reflexes and sensory level. Although a causal relationship may be conferred by a dramatic response to copper repletion, the neurologic syndrome described herein with markedly low copper levels following gastric bypass surgery strongly implicates acquired copper deficiency. Findings from an extensive workup to exclude other causes of myelo-optic neuropathy, including demyelinating, infectious, inflammatory, and vasculitic origins, showed no abnormalities.

Treatment with copper infusion improved the patient's hematologic parameters for white blood cell count (nadir of 1200/µL before treatment and 7000/µL after treatment), hemoglobin level (nadir of 9.2 g/dL before treatment and 11.0 g/dL after treatment), and mean corpuscular volume (nadir of 106 fl before treatment and 101 fl after treatment). Although visual acuity remained unchanged during the follow-up period, her myeloneuropathy seemed to stabilize from the previous annual deterioration. Copper supplementation before the onset of visual symptoms might have prevented subsequent development of blindness.

Gastric bypass surgery is often implicated in copper deficiency, as absorption occurs in the stomach and proximal duodenum. Cobalamin requires the secretion of intrinsic factor within the duodenum for absorption in the ileum, making vitamin B₁₂ deficiency a common codependency. However, cobalamin had been continually supplemented in our patient, with normal serum and metabolite values. Acquired copper deficiency also occurs in adults with malabsorption syndromes, toxic levels of zinc, prolonged total parenteral nutrition, and medications that act as chelators (eg, ethambutol hydrochloride).

Although there are some case reports of optic neuropathy after gastric bypass surgery, 3 other case reports suggest an origin due to copper deficiency. Optic neuropathy associated with gastric bypass surgery was noted to be typically unilateral, occurring within the first few years, and more indolent than in the present case. Copper deficiency in rats leads to pathologic features consistent with demyelination in the optic nerves. The use of clioquinol, an antimicrobial agent that chelates copper, has been associated with more than 10,000 cases of subacute myelo-optic neuropathy in Japan. The patho-

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logic finding of subacute myelo-optic neuropathy has been described as symmetric demyelination of lateral and posterior columns in the spinal cord, optic nerve, and peripheral nerves.8

Optic neuropathy seems to be an uncommon manifestation of acquired copper deficiency. A case series9 of 25 patients found documentation of visual system involvement in 2 patients by visual evoked potentials. Notable observations in the present case include (1) an interval of longer than 20 years since the time of gastric bypass surgery, (2) the delay between the onset of myeloneuropathy and that of optic neuropathy, (3) and the rapidity of optic nerve involvement. Dysfunction in mitochondrial metabolism and oxidative stress may contribute to variability in the disease time course and neurologic systems involved among central nervous system functions served by copper. Neurologic manifestations may require more than 1 environmental exposure or increased individual susceptibility due to gene-environment interactions.

Copper deficiency should be in the differential diagnosis for optic neuropathy (whether acute, subacute, or chronic) and should be considered in any neurologic condition after gastric bypass surgery. Although no improvement was noted after repletion of copper in the patient described herein, her vision complications may have been avoidable had copper levels been monitored serially after gastric bypass surgery. Because neurologic effects associated with copper deficiency can be devastating, intravenous supplementation in the setting of acute neurologic dysfunction should be considered. Although only a mild response may be possible with acute repletion, even a 1-line or 2-line recovery in visual acuity could improve the patient’s level of function and independence.

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