Nutritional Optic Neuropathy Caused by Copper Deficiency After Bariatric Surgery

Yuna Rapoport, MD, MPH, Patrick J. M. Lavin, MD

Abstract: A 47-year-old woman developed severe bilateral visual loss 4 years after a Roux-en-Y gastric bypass and 24 years after vertical banded gastroplasty. Her serum copper level was 35 μg/dL (normal, 80–155 μg/dL). She was prescribed elemental copper tablets. Because her methylmalonic acid was slightly elevated, she received vitamin B12 injections as well. Five weeks later, she reported that her vision had improved and, at 10 months, her vision had recovered from 20/400 bilaterally to 20/25 in each eye. This case highlights the importance of checking copper levels in addition to the "more routine" vitamin levels, such as B1, B6, B12, E, and serum folate in patients with suspected nutritional optic neuropathy after bariatric surgery, particularly if it involved a bypass procedure.

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Copper deficiency can cause neurological and hematological disorders. Neurological abnormalities include myelopathy, myeloneuropathy, myopathy, mononeuropathy, hyposmia, hypogeusia, and cognitive impairment (1). These neurologic complications may develop insidiously decades after gastric bypass surgery (2–5). The optic neuropathy caused by copper deficiency is infrequent, or overlooked, and usually presents approximately 1.5–3 years after surgery but can occur as late as 20 years. It can be acute, subacute, or chronic (1,6). Hematological abnormalities include anemia (which may be microcytic or normocytic) and leukopenia and less often thrombocytopenia and pancytopenia (2).

The Department of Ophthalmology and Visual Sciences (YR), Vanderbilt University Medical Center, Nashville, Tennessee; and Department of Neurology (PL), Vanderbilt University Medical Center, Nashville, Tennessee.

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Address correspondence to Patrick Lavin, MD, Department of Neurology, Vanderbilt University Medical Center, A-0118 Medical Center North, Nashville, TN 37232-2551; E-mail: patrick.lavin@vanderbilt.edu

CASE REPORT

A 47-year-old woman was evaluated in the neuro-ophthalmology clinic with a 2-month history of progressive, bilateral visual loss. She also experienced formed, nonthreatening visual hallucinations and mild cognitive dysfunction. Twenty-three years earlier, she had a vertical banded gastroplasty. Three years before her visual decline, she had undergone a Roux-en-Y bypass and a partial gastrectomy to remove the band, because of regained weight (body mass index, 43.2 kg/m^2) and abdominal pain. Seven months before her visual symptoms, she had an anterior cervical spine decompression and fusion for a prolapsed disc; a month later, she developed pneumonia, and during rehydration, she aspirated and required artificial ventilation. She denied the use of alcohol or tobacco. There was no family history of ocular or neurological disease. Regular medications included estradiol, vitamin D3, a multivitamin daily, and zinc.

On examination, she was oriented but somnolent with impaired concentration and a flat effect. Visual acuity, with eccentric fixation, was 20/400 bilaterally. Color vision was decreased and confrontational visual fields demonstrated bilateral central scotomas. Pupil responses were normal and ocular motility was intact. Slit-lamp examination was significant for mild bilateral cataracts, and intraocular pressures were 15 mm Hg in right eye and 14 mm Hg in left eye. Funduscopic examination revealed mild bilateral optic disc pallor (Fig. 1). Kinetic visual fields showed generalized constriction with central scotomas in each eye. On optical coherence tomography, average peripapillary retinal nerve fiber layer thickness was normal (98 μm, right eye; 97 μm, left eye), but average macular retinal ganglion cell inner plexiform layer complex was thin (59 μm, right eye; 49 μm, left eye) (Fig. 2).

Brain computed tomography was normal. Laboratory investigations included vitamin B6: 39.5 nmol/L (normal, 20–125), vitamin B12: 1016 pg/mL (normal, 213–816),

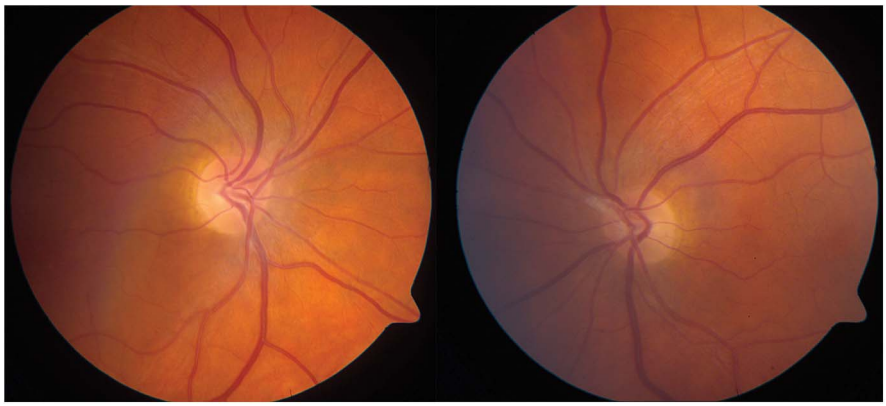

FIG. 1. The optic discs show mild temporal pallor.

methylmalonic acid: 0.43 μmol/L (normal, <0.40 μmol/L), red cell folate: 830 μg/mL (normal, 366–1356), serum copper: 35 pg/dL (normal, 80–155 μg/dL), and rapid plasma reagin nonreactive. Two months earlier, a vitamin B1 (thiamine) level was 309 nmol/L (normal, 70–180 μmol/L). The patient received elemental copper 2 mg orally daily and vitamin B12 1 mg intramuscularly initially weekly × 4, then monthly. Ten months later, she had regained acuity of 20/25 in each eye.

DISCUSSION

Our patient sought help because of formed hallucinations attributed to poor vision and mild encephalopathy. Her

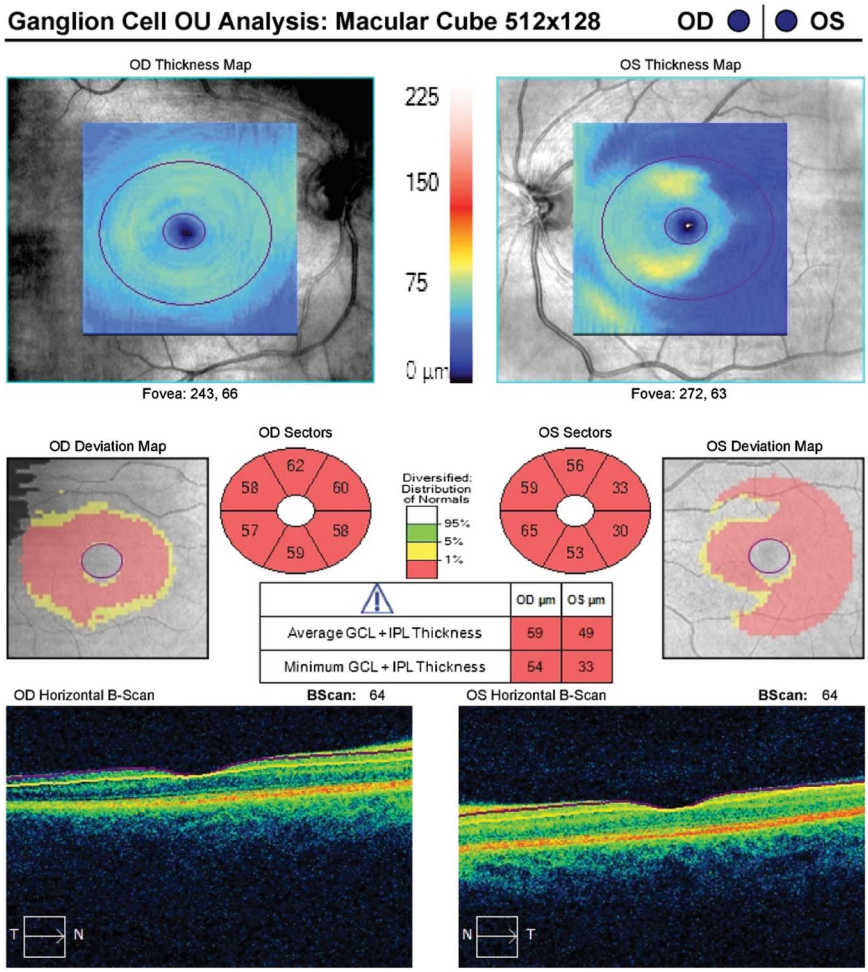

FIG. 2. Optical coherence tomography demonstrates thinning of the ganglion cell-inner plexiform layer bilaterally.

visual symptoms resolved after treatment with elemental copper tablets and vitamin B12 injections. Although nutritional optic neuropathy can be multifactorial in origin and her methylmalonic acid level was slightly elevated, we believe that the very low serum copper level had the greater role in causing her optic neuropathy and likely her mild encephalopathy.

Bariatric surgery causes weight loss by restricting food intake, limiting absorption, limiting absorption and digestion, or combinations thereof (7,8). Trace element and vitamin deficiencies vary in frequency depending on the type of surgery performed. Vitamin B12 and iron deficiencies are more common with Roux-en-Y procedures but are less common with adjustable gastric procedures (9). Overall, copper deficiency occurs infrequently with bariatric surgery (7). Procedures that are both restrictive and produce malabsorption include Roux-en-Y gastric bypass and biliopancreatic diversion with duodenal switch and are more likely to cause both B12 and copper deficiencies (6–8). Because copper is probably absorbed in the proximal duodenum (10), copper deficiency is more likely to occur with bypass procedures (11,12). Additionally, absorption of copper requires an acidic environment (13), known to be altered by partial or complete gastric resection. At 24 months, the predicted incidence and prevalence of copper deficiency after Roux-en-Y procedures are 9.6% and 18.8%, respectively (14).

Acquired copper deficiency can occur with other malabsorption syndromes including celiac disease, inflammatory bowel disease and cystic fibrosis, toxic levels of zinc with denture paste (15,16), excessive zinc therapy (17), prolonged total parenteral nutrition, fad diets (18), and chelating medications, such as ethambutol and clioquinol (19).

Optic neuropathy after bariatric surgery often is associated with copper and B12 deficiencies and typically develops 1.5–3 years after surgery (9,19). The mechanism of optic neuropathy in copper deficiency is uncertain. Copper is a component of enzymes with a critical role in the structure and function of the nervous system (3); copper deficiency may result in mitochondrial dysfunction and oxidative stress causing neuronal injury. There are few pathological studies of the neurological effects of copper deficiency. Peripheral nerve biopsies demonstrate axonal degeneration (19), and a postmortem study demonstrated degeneration in the dorsal and lateral columns of the spinal cord (20). An animal model has shown neuronal loss in the cerebellum and spinal tracts with extensive demyelination (21). Copper metabolism may be abnormal with the 5.10-methylethylenetetrahydrofolate reductase A1298C gene polymorphism, which modulates the effect of homocysteine on copper homeostasis and toxicity (1,22).

Evaluation for copper deficiency includes serum copper level, ceruloplasmin plasma level, 24-hour urinary copper, zinc levels when appropriate, and a search for other deficiency disorders.

Treatment is empirical. There are no specific guidelines for repleting copper. There are reports of 1.5–3 mg copper daily (5,23,24). In the acute phase, copper can be given intravenously (2 mg over 2 hours) initially for 5 days and then 2 mg per day orally (19). Other recommendations include 8 mg daily for a week, 6 mg daily for a week, 4 mg daily for a week, and then 2 mg thereafter. Zinc supplements should be stopped if excess ingestion is suspected; also, iron therapy can decrease copper absorption.

In evaluating patients for nutritional optic neuropathy, serum copper levels frequently are overlooked. Our protocol consists of serum vitamins B1, B6, and B12, serum folate, methylmalonic acid, homocysteine, and copper. Additional testing may include genetic studies, B2, zinc, and red cell pyruvate. After bypass procedures, patients also may be deficient in vitamin A, vitamin D, vitamin E, vitamin K, iron, calcium, magnesium, selenium, and zinc.

The complications of copper deficiency can be avoided with better preventive care, including preoperation and postoperative vitamin and mineral supplementation, frequent follow-up, and by educating patients and their families about the potential complications of deficiency disorders including visual failure.

STATEMENT OF AUTHORSHIP
Category 1: a. Conception and design: P. Lavin; b. Acquisition of data: Y. Rapoport and P. Lavin; c. Analysis and interpretation of data: Y. Rapoport and P. Lavin. Category 2: a. Drafting the manuscript: Y. Rapoport; b. revising it for intellectual content: P. Lavin. Category 3: a. Final approval of the completed manuscript: Y. Rapoport and P. Lavin.

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