Mielopathy related to copper deficiency after bariatric surgery: case report

Mielopatia relacionada à deficiência de cobre após cirurgia bariátrica: relato de caso

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ABSTRACT
Copper is an essential enzymatic cofactor in many stages of normal functioning of human body, acting mainly in hematological, vascular and neurological functions. Its deficiency is linked to some conditions as highly isolated oral zinc intake, parenteral nutrition and after bariatric surgery. Neurological symptoms due copper deficiency include gait abnormalities, sensitive ataxia and sensitive neuropathic symptoms. We present a case of copper deficiency myelopathy after bariatric surgery. Copper deficiency myelopathy is poorly diagnosed, being imperative the early recognition of the condition aiming better outcomes and neurological recovery.

Keywords: Myelopathy, Spinal dorsal cord, Copper deficiency, Bariatric surgery.
RESUMO
O cobre é um cofator enzimático essencial em várias fases do funcionamento normal do corpo humano, atuando principalmente nas funções hematológicas, vasculares e neurológicas. Sua deficiência está ligada a algumas condições como ingestão oral de zinco altamente isolada, nutrição parenteral e após cirurgia bariátrica. Os sintomas neurológicos devido à deficiência de cobre incluem anormalidades da marcha, ataxia sensível e sintomas neuropáticos sensíveis. Apresentamos um caso de mielopatia por deficiência de cobre após cirurgia bariátrica. A mielopatia por deficiência de cobre é mal diagnosticada, sendo imprescindível o reconhecimento precoce da condição visando melhores resultados e recuperação neurológica.

Palavras-chave: Mielopatia, Medula espinhal dorsal, Deficiência de cobre, Cirurgia bariátrica.

1 INTRODUCTION

It is estimated that acquired copper deficiency is a rare condition and neurological manifestations are scarcely reported. Myelopathy due to copper deficiency mimics the clinical aspects observed in vitamin B12 deficiency, being also a presentation of subacute combined degeneration of the spinal cord.

Although pathophysiology is not completely clear, it is hypothesized as result of demyelination and axonal damage in central nervous system. Treatment of copper deficiency consists in oral and parenteral supplementation. We aim to report a case of copper deficiency myelopathy after bariatric surgery, a poorly known cause, emphasizing the importance of its recognition and early treatment.

2 CASE REPORT

A 42 years old woman has looked for neurological attendance in august 2019 reporting one year of insidious presentation of cramps, muscular weakness, lower limbs paresthesia and burning pain below her knees. With time, she perceived progressive worse of gait and in the last two months was presenting urinary retention.

She has been passed through appendicitis surgery at 2 year old, being operated for bowel obstruction twice in last 20 years. Ten years ago it was performed bariatric surgery. At neurological exam presented discrete distal paresthesia, global hyperreflexia, plantar clonus, lower limbs hypoesthesia and ataxic gait.

Electromyoneurography study was normal. MRI of dorsal spine showed signal alteration of dorsal cord, compatible with dorsal cord myelopathy (Figure 1). Ancillary laboratory tests initially showed: hemoglobin 10,7 g/dL; hematocrit 34,1 million/µL;
leucocytes 8.229/mm³; neutrophils 319/mm³. B12 vitamin dosage of 6.000pg/mL, normal thyroid function, HIV, syphilis and HTLV-1/2 were negative. Inflammatory markers were normal: lupus anticoagulant, anti-Ro and Anti-La. Porphobilinogen 0.42 mg/24h (RR:< 0.2 mg/24h); Serum iron 40 μg/dL (RR: 60-180 μg/dL), ferritin 17.6 μg/dL and ceruloplasmin 14.3 mg/dL (RR: 20-60 mg/dL). It was later performed serum copper dosage, revealing hypocupremia (patient serum dosage: 33,40μg/dL; reference range: 80-155μg/dL). Treatment was initiated with elemental copper 2 grams/day and until present publishing of this report there was no recovery of neurological symptoms.

3 DISCUSSION AND LITERATURE REVIEW

Copper is a cofactor of diverse oxidative enzymes, essential for many hematopoietic, vascular and skeletal tissue functions; it participates on a structural and functional ways in nervous system, besides of acting in ion metabolism. Duodenum is the largest site of copper absorption, but it is also absorbed un lower proportion in stomach and ileum

The exact molecular pathway which copper is absorbed in intestinal mucosa is not clear. It supposedly involves Ctrl, a transporter of apical surface of intestinal epithelial cells, which allows transportation of copper to intracellular space. From there, copper combines with a intracellular protein, metallothionein, which facilitates its storage until copper interacts with copper transporter ATPase, which moves it from basal membrane to systemic circulation. Once in systemic circulation, copper acts as a cofactor in many essential reactions in liver, lungs, heart, bones, bone marrow and nervous system.

Zinc absorption also occurs in proximal gastrointestinal tract and can be affected by gastrojejunal bypass surgery. Zinc induces metallothionein, which is a endogenous metal chelant, naturally with higher affinity to copper than zinc. A raise in metallothionein thereby inhibits enteric copper absorption. Therefore, isolated oral zinc intake in patients after gastoplasty must be done cautiously because of these inhibitory effects and hypocupremia risk.

Copper deficiency is a well documented cause of hematological abnormalities, including anemia with neutropenia. Neurological manifestations mimics the myeloneuropathy observed in vitamin B12 deficiency, being also a form subacute combined degeneration of spinal cord.

Neurological symptoms are frequently severe and irreversible and may exist even in absence of hematological alterations. Desmielinization of nervous system, peripheral
Polyneuropathy and optic neuritis are known presentations of copper deficiency. Precise pathophysiology is not clear, but it is hypothesized that oxidative damage as result of superoxidase lowering leads to demyelination and axonal damage in central nervous system.

It is estimated that acquired copper deficiency is a rare condition. It is associated to bypass bariatric surgery, excessive oral zinc intake, myelodysplastic syndrome and enteral and parenteral chronic nutrition.

Copper deficiency is described as a bariatric surgery complication due to resection between 100 to 200 centimeters of proximal jejunum, site of higher absorption of copper in human. Patients after gastroplasty usually receive multivitamin supplement containing ion, zinc and B12 vitamin, but copper is not routinely supplemented. In a study, prevalence of copper deficiency in consequence of Y-en-Roux bypass bariatric surgery was 9.6% and a second study with obese women submitted to gastroplasty was 15.4%

Symptoms can appear between 2 months to 10 years after bariatric surgery. Griffith and collaborates (2009) reported two cases of patients that presented 10 years after bariatric surgery severe abnormalities in gait associated to anemia and neutropenia secondary to hypocupremia. Hematological alterations and copper levels rapidly normalized after copper intake, but neurological symptoms had only discrete better outcomes even months of following.

Magnetic resonance may not evidence abnormalities, but pathology typical alterations consists in cervical spine higher signal in T2, as presented in this case. In a study of 25 cases, 14 neuroimage workups were normal; the other 11 cases presented dorsal cord hypersignal. Neurophysiologic study indicates dorsal cord disfunction.

Treatment of copper deficiency consists in oral and parenteral supplementation until normalization of serum levels. The response to copper supplementation is variable and depends on grade an duration of depletion. There may be improvement of paresthesia, but gait abnormalities tend to remain as sequelae. Kumer and collaborates (2004) evaluated 13 patients with copper deficiency myelopathy and all of them remained with some degree of neurologic sequelae, in agreement with the present reported case.

4 CONCLUSION

Though hematological manifestation related to copper deficiency are well recognized, neurological symptoms related to hypocupremia are poorly described.
Copper deficiency myelopathy after gastroplasty is a poorly known condition, being important its recognition and early treatment.

**Picture 1**: Spinal column MRI showing dorsal cord hyperintensity in T2/STIR sequence.
REFERENCES


