ARTIGO ORIGINAL

Cooper deficiency anemia: A complication after bariatric surgery

Copper deficiency anemia after bariatric surgery

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ABSTRACT

Copper is a trace mineral essential to hematopoiesis and to the structure and function of the nervous system. Copper acts as a ligand to ferroxidase II, which oxidizes iron, allowing it to be mobilized and transported from the hepatic stores to the bone marrow to be used in erythropoiesis..Copper deficiency is a rare cause of anemia, leukopenia, and myeloneuropathy. In this report we describe a case of a 49 year-old overweight Caucasian woman who was referred June 2008 to the Obesity Outpatient Clinic at UNIFESP for evaluation of muscular pain and weakness in both legs, fatigue and chronic anemia. The past medical history included Scopinaro Surgery for severe obesity in November 2004 when her weight was approximately 180 Kg (BMI 68.6 kg/m2). She lost considerable weight after surgery, with her weight being stable around 80 kg (BMI 30). Because of clinical manifestations of sub nutrition, protein and vitamin deficiencies and severe anemia, which lead to several hospital admissions, in February 2008 she was submitted to another surgery from conversion of the gastrointestinal surgical Scopinaro procedure to that performed by Capella. She also had a history of hypothyroidism, hyperuricemia and panic syndrome, requiring specific medications, beyond parenteral iron and B12 vitamin therapies for anemia. Physical examination revealed a bilateral edema and no other abnormality. Laboratory tests revealed hypoalbuminemia and hypochromic megaloblastic anemia with normal serum levels of B12 vitamin, iron and ferritin. Due to the persistence of the neurologic symptoms and anemia in spite of adequate iron and B12 vitamin therapies, the hypothesis of copper deficiency was considered and a low serum level of 40μg/dl was found. An oral supplementation with high doses of copper resulted in evident clinical and laboratorial improvements after eight weeks of therapy. The diagnosis of copper deficiency has to be part of the differential diagnosis in patients with unexplained neurologic symptoms, anemia, and leukopenia, especially in those who underwent to previous gastrointestinal surgery.
KEY WORDS: Copper – anemia – bariatric surgery – nutritional deficiency – iron

INTRODUCTION:

Cooper is an essential trace mineral that acts as a cofactor in several vital oxidative enzymes for hematopoiesis and for the structure and function of the nervous system. Copper deficiency results in excessive iron in the liver and in the marrow bone, impairing erythropoiesis, causing anemia [1,2]. Cooper also acts on iron absorption, as a cofactor of hephaestin that when is linked to ferroportin allows to transport iron from the intestinal cell into the blood circulation.

Moreover, it is also a cofactor of cerulo-plasmin in macrophage that stores and transports iron to where hemoglobin synthesis occurs. Copper, therefore, is an essential element of the iron metabolism.

Studies with animals have suggested that the main site for copper absorption is the duodenum although part is also absorbed in the stomach and ileum [3]. Gastric juice has an important role to hinder the binding of copper to other organic complexes in the stomach which may impair

its absorption. In human beings, it is not totally known the main place of copper absorption.

Although rare, copper deficiency can occur in malnutrition, parenteral and enteral nutrition without supplementation of copper, gastrectomy, malabsorption syndromes, ingestion of chelating copper and zinc therapy suplementation [1,4-6] . The copper deficiency can cause anemia, leukopenia and mieloneuropatia, which can manifest alone or in combination. In cases of gastrointestinal surgery inducing malabsorption, copper deficiency should be considered in cases of anemia associated with leukopenia and that does not improve with conventional treatment [1,2,5].

In gastrointestinal surgeries that induce malabsorption, copper deficiency must always be considered in cases of iron deficiency anemia associated with leucopenia and with no improvement of conventional therapy.

Clinical Case:

VMB patient, 49 years old, white female, was referred to the Clinic of Obesity UNIFESP for clinical and nutritional after undergoing bariatric surgery. The first surgical procedure that used the technique Scopinaro was conducted in November 2004, when she weighed 180kg (BMI = 68.6), reaching 80 kg (BMI = 30.5) in February 2008, when this surgical procedure was changed to Capella, which induces a lower degree of malabsorption This surgery was performed because the patient had presented clinical protein deficiency with severe hypoalbuminemia, anemia and hypovitaminosis which led it to require several.

The patient presented muscular pain and weakness in the lower limb without gait difficulties, fatigue and hypochromic and megaloblastic anemia with no response to conventional therapy that had been taken for 6 months. Medications included 5000 IU of intramuscular vitamin B12 therapy once a month, endovenous administration of parenteral iron 100mg weekly, CaCO3 500 mg orally twice daily, 10000 UI of vitamin D weekly, 5000 UI of vitamin A weekly, 1000 g of Cholecalciferol weekly and a polyvitamin with reposition of microelements based on the Dietary Reference Intakes (DRIs) [7]. At Although presenting paresthesias, her clinical exam did not present sensitive disorders, muscle weakness or gait disorders.

The lack of response to the given therapy and the laboratory tests lead to suspicion of copper deficiency which was confirmed by the determination of 60 to 90 µg/dl (Table 1).

Even though copper supplementation is more used by parenteral administration, we have chosen oral administration in order to the patient had no hospitalization. An oral therapy was done with copper supplementation, 36 mg/Day (0,5 mg\kg body weight), added to the initial treatment. After two months of the supplementation, the patient referred improvement in both lower limb pain and anemia as shown in Table 1. From the second month on, copper supplementation was reduced to 10 mg/day till the 6th month when we have observed a normal level of hemoglobin, with some persistence of The decreases in serum levels of B12 vitamin, folate and A vitamin that were observed after 6 months of therapy have suggested a low adhesion to the treatment from the patient.

DISCUSSION

Bariatric surgery is the most efficient therapy available for subjects with severe obesity and the number of subjects submitted to the procedure has been drastically increasing each year [8]. The surgery responsible for gastric bypass is Roux-en-Y (RYGB) and may cause malabsorption of nutrients and may become clinically significant if they are not adequately recognized and treated.

Anemia is described in approximately two thirds of patients after bariatric surgery and its cause is usually due to low ingestion and malabsorption of iron, B12 vitamin and folic acid, and more rarely the presence of mucosa bleeding due to ulcerations [9].

Copper deficiency is the main cause of anemia among patients submitted to RYGB with a big incidence till 49%. [10,11]. Duodenum is the main site of iron absorption and in this surgery the gastrointestinal tract is excluded, creating a potential risk for nutritional deficiencies. Moreover, red meat intolerance and diminished acid gastric secretion may contribute to iron deficiencies in this group of population. Besides poor adhesion to therapy, polyvitamin supplements that are usually given may not be enough to provide suitable amount of vitamins and minerals which lead to an additional supplementation lifelong to have an ideal input of micronutrients [12].

B12 vitamin deficiency affects 12 to 33% of patients submitted to RYGB and it usually occurs after one year of surgery when there is a depletion of B12 vitamin store [13,14]. The mechanism responsible for this deficiency is achloridria which reduces the extraction of B12 vitamin from the protein intake and insufficient secretion of intrinsic factor which decreases its absorption in terminal ileum. (15). The deficiency may also occur due to a low ingestion of animal protein sources.

The folic acid deficiency is another cause of anemia in RYGB patients, affecting till 35% of patients[16]. Folate is not stored in the body because it is a hydrosoluble vitamin. The causes of this kind of anemia include low ingestion of food, B12 vitamin deficiency and exclusion of proximal segment of intestine where its high absorption occurs.

Despite patients submitted to RYGB have a higher risk to develop secondary anemia to deficiencies of iron, B12 vitamin and folate, a significant number of anemia after bariatric surgery remains without explanation [17,18]. We have reported one case of a patient with anemia that persisted even after the supplementation of iron, B12 vitamin and folate. She has presented as symptoms pain and fatigue and laboratory tests confirmed megaloblastic

In this case, anemia has become a reason of great concern, and the hypothesis of other micronutrient deficiencies less frequent were raised like copper deficiency or unbalanced zinc ingestion. The patient presented a reduced serum level of copper and oral supplementation was initiated. Two months later we have observed that oral administration of copper was associated with the improvement of symptoms, levels of copper and anemia, which presented remission after 6 months.

Copper deficiency has often been found in patients who underwent to RYGB for obesity or more rare for peptic ulcer. Several cases of copper deficiency in adults, much more severe than the patient we have observed, have been described after bariatric surgery and administration of parenteral copper has been required and malabsorption of copper in the stomach and proximal duodenum have been described too[19-22]. High ingestion of zinc may reduce the copper absorption because they compete by the same transporter [23, 24] .

In severe cases of copper deficiencies as described by Griffith et al (5) in which the serum levels were 4μg/dl and 2μg/dl, the symptoms and neurological alterations are usually presented once copper is essential to the function and structure of the nervous system [25] . The symptoms and neurological signs more commonly observed are pain in the lower limb which may be sharp, painful ability to ambulate, superficial and profound sensory ataxia [5,25,26]. In these cases, copper reposition requires an endovenous administration at the hospital. The symptoms of copper deficiency may happen decades after surgery, which is why a long term follow up of these patients is necessary to avoid this complication.

In conclusion, we have described a case of a patient that after six years of being submitted to bariatric surgery has presented a clinical feature due to copper deficiency characterized by paresthesias in the lower limb and anemia whose alterations have shown regression after two months of copper oral administration. So, copper deficiency may be part of a differential diagnosis in patients submitted to bariatric surgery and who presented neurological symptoms, anemia and leucopenia without a satisfactory response to the administration of vitamins and iron. Considering that each year an increasing number of patients will be submitted to bariatric surgery, we will have a very near future with a big population in risk to develop complex nutritional deficiencies, including copper deficiency. It is, therefore, important to be aware of it once the early detection and treatment of copper deficiency may avoid severe hematologic alterations, besides neurological deficits that sometimes are irreversible.

Conflicts of interest:

The authors affirm that they have no conflicts of interest to declare.

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Table 1: Laboratory Tests

Tests \ Days	Pre-herapy	60 days	180 days	Normal Values
Hb (gm/dL)	**7,2**	**10,1**	**12,0**	11.4 – 24.4 gm/dL
VCM(fL)	**101**	**93,1**	**94,2**	79.3–94.8 fL
CHCM (gm/dL)	**31**	**33,8**	**31,4**	33.5–35.5 gm/dL
Leucocytes (N/mm3)	**4.400**	**9.300**	**9000**	3.500–11.000N/mm3
Iron (ug/dl)	**67**	**93**	**83,0**	49-151 ug/dl
Ferritin(ng/mL)	**157**	**250**	**106,0**	9-148 ng/mL
Copper (µg/dL)	**40**	**75,4**	**113,0**	60–120 µg/dL
B12 Vitamin (ng/mL)	**361**	**361**	**105,5**	191-663 ng/mL
Folate (ng/mL)	**24**	**24**	**6,87**	4-24 ng/mL
A Vitamin (µg/dL)	**0,19**	**1,02**	**0,54**	0,35-0,75 µg/dL