Hypocupremia-related anemia and neutropenia late after Roux-en-Y gastric bypass surgery

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Introduction

The most effective and permanent method in the treatment of obesity is bariatric surgery, but the occurrence of malnutrition and nutrient deficiencies after most bariatric procedures requires close postoperative follow-up of the patients. Roux-en Y gastric bypass (RYGB) is a type of surgery that is both restrictive in food intake and malabsorptive [1]. Vitamin D, vitamin B family, calcium, iron, and zinc deficiencies can be counted as the most common vitamin and mineral deficiencies. Another deficiency that is more difficult to recognize is copper deficiency. The prevalence of copper deficiency (hypocupremia) has been reported as 10%-20% after RYGB [2]. Deficiency often affects the hematological and neurological systems. Hematological findings return within 6-12 weeks with copper replacement, but neurological findings are often permanent [3]. Although replacement stops progress, it does not improve the current situation. Copper deficiency has started to appear more frequently due to bariatric surgical procedures, which are widely applied all over the world and in our country, but it is often not recognized. In order to raise awareness on the subject, we wanted to present a patient who developed copper deficiency and secondary anemia and neutropenia after RYGB.

Case Report

A 49-year-old female patient presented with complaints of weakness, fatigue, dizziness, drowsiness, shortness of breath and palpitations. She had no known chronic disease. RYGB operation was performed 8 years ago due to morbid obesity. She went through menopause 2 years ago. Since the COVID 19 pandemic, she was using daily 50 mg of zinc sulfate and 1200 I.U. vitamin D3 regularly for about 3 years. In addition, she was using B12, iron, folic acid, and vitamin D levels were intermittently without blood analysis after bariatric surgery. She stated that he last used these vitamins 5-6 months ago. On physical examination, he appeared pale, blood pressure was 95/55 mmHg, and heart rate was 108. Heart and lung sounds were normal and abdominal examination was unremarkable. In blood tests, fasting blood glucose, lipid profile, liver, kidney and thyroid functions were within normal limits. Sedimentation and CRP were negative. In complete blood count pathologically, hemoglobin 9.3 g/dl, MCV:71 fL, iron: 15 µg/dL, ferritin: 4.4 ng/mL, neutrophil 0.48 10^3/µL was detected. Platelet count was normal. Stool occult blood was negative. B12, folic acid, calcium and vitamin D levels were

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functions and protection of skeletal health [4]. Copper is an element that is absorbed from the stomach, duodenum and jejunum. Copper is a cofactor of biologically important oxidative enzymes such as cytochrome c oxidase and superoxide dismutase. It is necessary for cellular respiration, bone marrow functions, vascular development, and removal of free radicals, central nervous system and bone marrow functions, vascular development. It is necessary for the mitochondrial enzymes responsible for oxidation. When the mitochondria of the animals with copper deficiency were examined, it was observed that the cytochrome activity was insufficient, heme synthesis could not be performed in sufficient amounts by using protoporphyrin and ferric iron, and iron accumulated in the mitochondria [10]. In addition, hephaestin and ceruloplasmin, which are copper-dependent proteins and whose task is to transport iron, cannot function adequately. Hephaestin ensures the absorption of iron from intestinal cells, while ceruloplasmin ensures that tissue iron enters the circulation [11].

Our patient also had neutropenia. In the development of neutropenia suggested etiologies have included destruction of myeloid progenitor cells the bone marrow, inhibition of

Discussion

Copper is an element that is absorbed from the stomach, duodenum and jejunum. Copper is a cofactor of biologically important oxidative enzymes such as cytochrome c oxidase and superoxide dismutase. It is necessary for cellular respiration, bone marrow functions, vascular development, and removal of free radicals, central nervous system functions and protection of skeletal health [4]. European Food Safety Authority guidelines recommend a daily copper intake of 1.6 mg for men and 1.3 mg for women [5]. Sleeve gastrectomy, RYGB and biliopancreatic diversion - Duodenal switch are the main procedures associated with nutrient deficiencies due to changing anatomy and physiology [6]. The status of micronutrients should be monitored both before and after surgery at certain periods. Calcium, vitamin D, iron, zinc, vitamin B family deficiencies may develop. These vitamins and minerals are well known and followed by clinicians. They should be followed every 3-6 months in the first year and every 6-12 months in the following years [7]. Copper, on the other hand, is an element that we want less in our routine and can be skipped in pursuit. Copper deficiency develops in 1-2 out of every 10 patients in the long term after RYGB. Although there are other conditions that cause its deficiency, the biggest reason is surgery. In a study in which 40 patients with copper deficiency were evaluated retrospectively, it was shown that 25% of the patients had bariatric surgery and 35% had gastrointestinal system surgery [8].

Another point that causes copper deficiency and which clinicians should be careful about is that excessive intake of zinc causes copper deficiency. Copper is taken up into cells via the copper transporter 1 (CTR1) located in the apical cells of the gastrointestinal tract epithelium. When copper enters the cell, it combines with a protein called metallothionain. This protein ensures that copper is stored in the cell. Metallothionain has greater affinity for copper than for zinc. Zinc increases the amount of this protein, so copper remains bound to the protein, and zinc enters the systemic circulation from intestinal epithelial cells [9]. In our case, our patient had been using zinc to keep the immune system strong for about 3 years after the COVID 19 pandemic. We think that this contributes to the development of the deficiency. A minimum of 2 mg copper intake per day is recommended to prevent deficiency after RYGB. The most important consequences of copper deficiency are related to the hematological and neurological systems. It often presents with anemia, neutopenia, less commonly thrombocytopenia and pancytopenia. Anemia can be microcytic, normocytic, or macrocytic. The main reason why copper deficiency causes anemia is the failure of the enzymes responsible for oxidation. When the mitochondria of the animals with copper deficiency were examined, it was observed that the cytochrome activity was insufficient, heme synthesis could not be performed in sufficient amounts by using protoporphyrin and ferric iron, and iron accumulated in the mitochondria [10].

Table 1. Laboratory parameters before and after treatment.

<table>
<thead>
<tr>
<th>Laboratory Parameter</th>
<th>May, 2023</th>
<th>July, 2023</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin g/dL (N: 11.6-15.5)</td>
<td>9.3</td>
<td>12.1</td>
</tr>
<tr>
<td>Mean Cell Volume (MCV) Fl (N: 80-98)</td>
<td>71</td>
<td>82</td>
</tr>
<tr>
<td>Ion (Fe) µg/Dl (N: 33-193)</td>
<td>15</td>
<td>67</td>
</tr>
<tr>
<td>Ferritin ng/ml (N: 13-150)</td>
<td>4.4</td>
<td>20.6</td>
</tr>
<tr>
<td>Neutrophil 10³/ul (N: 1.5-7.1)</td>
<td>0.48</td>
<td>2.3</td>
</tr>
<tr>
<td>Vitamin B12 pg/mL (N: 197-771)</td>
<td>328</td>
<td>90</td>
</tr>
<tr>
<td>Folate ng/ml (N: 2.2-20.6)</td>
<td>6.9</td>
<td>9.6</td>
</tr>
<tr>
<td>Calcium mg/Dl (8.5-10.2)</td>
<td>8.6</td>
<td>9.8</td>
</tr>
<tr>
<td>Vitamin D ng/ml (N: 30-80)</td>
<td>51.2</td>
<td>98.2</td>
</tr>
<tr>
<td>Copper (Cu) µg/dL (N: 80-155)</td>
<td>47</td>
<td>89</td>
</tr>
<tr>
<td>Zinc (Zn) µg/dL (N: 60-120)</td>
<td>127</td>
<td>92</td>
</tr>
</tbody>
</table>

Figure 1. Peripheral smear findings - hypochromic microcytic erythrocytes, anisocytosis, poikilocytosis, target cells.
very important to follow copper like other vitamins and minerals in patients who have undergone gastrointestinal system surgery, and also to be well aware of the clinical and laboratory findings that may occur.

References