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Persistent anemia after Roux-en-Y gastric bypass

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Abstract

Objective: We report the case of a 42-y-old morbidly obese woman who presented persistent anemia as result of Roux-en-Y gastric bypass.

Methods: The surgical procedure conducted in 1999 consisted of horizontal gastroplasty with truncular vagotomy, Roux-en-Y gastrojejunal anastomosis with an alimentary limb of 60 cm, and cholecystectomy. In 2000 a second surgery (subtotal gastrectomy, i.e., 90%, with a 50-mL gastric pouch) was performed because of failed gastroplasty. Anemia was detected approximately 1 y after the second surgery. This condition worsened significantly after an abdominal lipectomy performed in 2001. Since then, different oral iron compounds were used for treatment, but with unsatisfactory results. The subject was anemic for 4 y.

Results: The condition was corrected only after intravenous iron administration. Iron absorptions from 3 mg of iron as ferrous ascorbate and from a standardized diet that also contained 3 mg of iron were 48.4% and 39.9%, respectively.

Conclusion: Iron absorption tests provided evidence that the reduction of intestinal iron absorption capacity was the most probable cause of the persistent anemia.

Keywords: Gastric bypass; Morbid obesity; Anemia; Iron

Introduction

Morbid obesity is an increasing pathology occurring worldwide. This condition is frequently associated with comorbidities such as hyperlipidemia, type 2 diabetes, and cardiovascular disease. Surgical approaches are being recognized as the current procedures of choice for the treatment of morbid obesity [1–3].There are several alternative surgical techniques and among these the Roux-en-Y gastric bypass has shown highly satisfactory results in terms of weight loss, improvement of medical conditions, and quality of life [4]. Furthermore, the postoperative mortality rate is 0.5%. However, anastomotic leakage (2.5%) and postoperative bleeding of the gastric staple line (0.75%) are the most relevant complications of this type of surgery [4]. In terms of late adverse nutritional consequences, anemia is the most prominent finding, which usually requires the addition of iron, vitamin B12, and folic acid supplements [5–10]. Iron deficiency anemia has been reported in 33% to 49% of patients who undergo a gastric bypass [6]. Furthermore, it appears that anemia is not uncommon in morbidly obese patients before gastric bypass [7], although commonly its magnitude is lower than after the surgical procedure [6]. As a result, prophylactic use of iron supplements has been recommended for women who undergo a Roux-en-Y gastric bypass [8]. It is also known that megaloblastic anemia, indicative of vitamin B12 or folate deficiency, is less prevalent, being nearly 5% in early studies [9] and only approximately 0.8% in more recent reports [6]. In the present

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Table 1
Time course of selected iron-related parameters in a patient with morbid obesity after gastric bypass surgery

Main procedures	Hematologic parameters				
	Hb (g/L)	RBC ($\times 10^6/\mu$L)	MCV (fL)	TS (%)	SF (μg/L)
November 1999, before gastric bypass surgery	125	4.3	87.0	—	—
December 1999, gastric bypass surgery	127	3.9	95.1	—	—
October 2000, gastrectomy	115	4.1	86.0	—	—
December 2001, abdominal lipectomy	114	4.0	87.6	—	—
March 2002, hematologic control	79	3.6	71.4	11.0	—
July 2004, nutritional controls resumed	91	4.1	69	3.4	4.4
October 2004, routine nutritional control	100	4.2	75	8.8	3.0
January 2005	96	4.0	72.4	—	—
Iron absorption test					
Intravenous iron administration					
March 2005, 2 mo after intravenous iron	130	4.6	85	31.3	22.6
April 2006, 15 mo after intravenous iron	132	4.4	89	20.3	46.4

Hb, hemoglobin; MCV, mean corpuscular volume; RBC, red blood cells; SF, serum ferritin; TS, transferrin saturation

report we describe a 5-y follow-up of a female patient who had a gastric bypass. She presented with persistent iron-deficient anemia that did not respond to oral iron therapies.

Case report

The patient was a 42-y-old woman, with an initial (presurgery) body weight of 124 kg and a height of 1.55 m (body mass index, 51.6 kg/m^2). She reported that during the previous 4 y she had been receiving antihypertensive medication because of chronic arterial hypertension. The clinical history contained information related to previous surgeries, such as anterior colpoplasty, cervix amputation, and colpoperineoplasty, which were conducted in March 1986 due to cervix prolapse and hypertrophy. In addition, a trachelectomy was carried out in 1997 due to cervix elongation. The gynecologic losses were considered normal and a period of 2 y had passed from the last gynecologic surgery before the bariatric surgery was performed. Several previous attempts to reduce body weight by dietary means had failed. In December 1999 she was admitted to the Clinical Hospital of the University of Chile to undergo bariatric surgery. The Clinical Hospital is one of the country's most experienced centers in this kind of procedure. Before surgery, the subject had a hemoglobin concentration of 125 g/L and a red blood cell count of 4.3 $\times$ 10$^6/\mu$L. Unfortunately, serum ferritin, an indicator of iron stores, was not available before surgery because at that time it was not included as part of the routine tests carried out in these patients.

Surgical procedures

December 1999

Horizontal gastroplasty with truncular vagotomy, Roux-en-Y gastrojejunal anastomosis with an alimentary limb of 60 cm, and a cholecystectomy.

October 2000

Subtotal gastrectomy (90%) with a 50-mL gastric pouch. This procedure was performed because of failed gastroplasty resulting from disruption of the staple line, the presence of Barret's esophagus, and a non-bleeding gastric ulcer near the gastrojejunal stoma.

December 2001

Abdominal lipectomy and herniorrhaphy of incisional hernia.

Postsurgical evolution

Body weight was dramatically reduced as shown by the decrease in body mass index from 56.1 kg/m^2 before surgery to 34.0 kg/m^2 in 2005. Antihypertensive medication was discontinued during the first month after surgery. Anemia was detected during the first year after gastric bypass (Table 1), although a vitamin/mineral supplement had been prescribed immediately after the first surgical procedure carried out in 1999. The supplement contained 3 mg of β-carotene, 250 mg of vitamin C, 200 mg of vitamin E, 7.5 mg of zinc, 1 mg of copper, 15 μg of selenium, and 1.5 mg of manganese. In 2002, additional micronutrient supplements were prescribed: a multivitamin/mineral mix that supplied 10 mg of iron per tablet in addition to other micronutrients, a calcium/vitamin D supplement, and an intramuscular B1/B6/B12 vitamin preparation. Moderate anemia (hemoglobin level 7.9 g/dL) was detected during the hematologic control carried out in March 2002. As a result, daily iron supplements (40 mg of iron as ferric polymaltose, 109 mg of iron as ferrous sulfate, and 1 g of ascorbic acid) were indicated. During an approximately 2-y 6-mo period (2002 through part of 2004), the patient showed poor compliance to the medical and nutritional controls.

In July 2004 the patient was referred by her gastrointestinal surgeon to a nutritional specialist from our unit (C.M.)

due to the presence of malnutrition symptoms, which included anemia. At that time, a 3-d dietary recall (which included an inquiry of consumption of dietary supplements) showed daily intakes of 1545 kcal, 36.5 g of protein, 207 μg RE of vitamin A, 5.8 mg of thiamin, 1.2 mg of riboflavin, 17.8 mg of niacin, 250 μg of folic acid, 1.8 μg of vitamin B12, 225 mg of calcium, 32 mg of iron, 0.7 mg of copper, and 5.0 mg of zinc.

Nutritional intervention

A strict nutritional intervention was initiated by providing a daily micronutrient supplementation consisting of 1 mg of vitamin A, 20 mg of thiamin, 5 mg of riboflavin, 50 mg of niacin, 10 mg of vitamin B6, 0.25 mg of biotin, 5 μg of vitamin B12, 6 mg of folic acid, 1 g of vitamin C, 10 mg of vitamin E, 6.5 mg of zinc, 200 mg of iron (as ferric polymaltose), 380 mg of calcium, 625 IU of vitamin D3, 153 mg of magnesium, 1 mg of copper, 0.5 mg of manganese, 0.1 mg of molybdenum, and 24 mg of phosphorus. In addition, a monthly intramuscular supplement was administered, which contained 100 mg of thiamin, 100 mg of vitamin B6, and 10 000 μg of vitamin B12. At that time it was decided to administer iron in its ferric form because of its good tolerance and thus induce better compliance by the patient. Compliance was highly satisfactory as evaluated by the responses of the patient to unscheduled calls from the physician. After 1 mo of treatment serum folic acid concentrations were 23.7 ng/mL (normal range 5.3–14.4 ng/mL) and serum vitamin B12 concentrations were 6360 pg/mL (normal range 187–1059 pg/mL). Nevertheless, anemia and iron-related parameters remain unchanged. Therefore, it was decided to change the iron salt to ferrous sulfate supplying 80 mg of elemental iron per day. In October 2004, 4 mo after reinitiating the nutritional intervention, the hematologic parameters showed no significant improvements (Table 1).

In January 2005, an iron absorption test was performed using the double isotopic technique of Eakins and Brown [11], which uses the radioisotopes ^{55}Fe and ^{59}Fe. Iron absorption from a standard diet was 39.9%. This corresponds to the liquid diet that is routinely consumed by patients during their first month after surgery, which contains chicken breast, egg white, spinach, carrots, and potatoes and provides 3 mg of iron. Furthermore, iron absorption from an aqueous solution of 3 mg of iron as ferrous ascorbate was 48.4%. After the iron absorption test was performed, ten 100-mg iron doses, as ferric hydroxide sucrose, were administered intravenously during a 20-d period. A hematologic control was conducted 2 mo later and all hematologic parameters had reached normal values. In addition, 15 mo after intravenous iron administration serum ferritin had increased dramatically, an indication of normalization of body iron stores.

Discussion

Bariatric surgery for morbid obesity, including Roux-en-Y gastric bypass, has shown high effectiveness in promoting significant and maintained weight loss. Furthermore, correction of medical conditions such as lipid disturbances, type 2 diabetes, and hypertension can be obtained in a rather short period [4]. Nevertheless, anemia is mentioned as the most common adverse nutritional side effect of this procedure. Data from the literature show that the main determinant of anemia is iron deficiency [5–10]. In this report, we describe the hematologic changes of a patient who underwent three sequential surgical procedures, which induced an iron-deficiency anemia condition that was corrected only after intravenous treatment.

There are three critical steps that determine iron status: iron intake, iron bioavailability, and iron losses. Regarding iron intake, capacity for food intake is dramatically reduced as a consequence of the surgery. In addition, it is not uncommon for patients to report poor tolerance to certain foods, in particular red meats [12]. A substantial part of iron in meats is in the form of heme iron, which is highly bioavailable [13]. Thus, there is not only a reduction in the total amount of iron ingested but also less bioavailability. In addition, these patients have limited gastric capacity and certain components of gastric juice are necessary for the initial digestion of foods and subsequent release of iron from its protein matrix. It has been shown that gastric acid production is almost eliminated after gastric bypass from the small gastric pouch that is anatomized to a jejunal loop [14]. It is known that hydrochloric acid is important to change the oxidation state of non-heme iron from its ferric to its ferrous form and that the latter state is crucial for the incorporation of iron into the enterocyte. Iron is mainly absorbed at the duodenum and proximal jejunum.

It has been shown that iron absorption capacity is inversely related to iron status [15]. This is evidenced by the absorption of a "iron reference dose," which usually corresponds to 3 mg of iron in the form of ferrous ascorbate. Under these conditions, an iron-deficient anemic individual is able to absorb well above 80% of this dose [16]. This contrasts with the 48.3% absorption observed in our patient. Iron absorption from a meal was also less than expected. These results demonstrate that the capacity to absorb iron is reduced as a consequence of bariatric surgery.

The third main determinant of iron status is the magnitude of iron losses, which are closely related to blood losses. Blood losses are not expected to be considerable in patients after gastric bypass surgery, especially if a significant amount of time has lapsed and if the patient leads a normal life, unless additional surgical procedures take place. This was the situation of our patient. Although her regular blood losses were not abnormal, this patient had three mayor surgeries in a 2-y period. The first was a horizontal gastroplasty with truncular vagotomy, Roux-en-Y gastrojejunal anastomosis with an alimentary limb of 60 cm, and a cho-

lecystectomy. The second was a subtotal gastrectomy (90%) with a 50-mL gastric pouch. As mentioned earlier, this was performed because of failed gastroplasty resulting from staple line disruption, the presence of Barret's esophagus, and gastric ulcer. According to a recent report that compared short with long limb gastric bypass as determinants of selected outcomes, a Roux limb longer than that of the patient in the present study does not improve weight loss and may lead to an increased incidence of internal hernias [17]. Thus, in our patient the development of Barret's esophagus and gastric ulcer after the first surgery probably was not related to the limb length but rather to disruption of the staple line. The third surgical procedure, abdominal lipectomy and herniorrhaphy of incisional hernia, was followed by an important decrease in hematologic parameters.

Although oral iron supplementation was provided, the limited capacity to absorb iron could not compensate for increased iron needs, so it was necessary to use a more aggressive approach such as intravenous administration of this mineral [18]. The reversal of the gastric bypass by anastomosing the gastric pouch to the duodenal stump was not considered a means to increase iron absorption because, after 2 mo of intravenous iron, the hematologic response was satisfactory. To contribute to the recovery of the hematologic condition, oral ferrous sulfate has been reinitiated.

Fifteen months after intravenous iron administration, the clinical parameters of iron status remained in the normal range (Table 1). The substantial increase in serum ferritin during this period was noteworthy. Although the patient's problem appeared to be iron-deficiency anemia due to bypass of the duodenal sweep, where the most of the iron is absorbed, a potential development of subnormal vitamin and/or mineral status of nutrients involved in erythropoiesis could not be disregarded. Thus, we continued providing multivitamin/mineral supplements as described above (see NUTRITIONAL INTERVENTION). Our findings provide quantitative evidence of the magnitude of the reduction in the capacity to absorb iron after gastric bypass.

References

[1] Buchwald H, Avidor Y, Braunwald E, Jensen MD, Pories W, Fahrbach K, et al. Bariatric surgery. A systematic review and meta-analysis. JAMA 2004;292:1724–37.

[2] Sjostrom L, Lindroos AK, Peltonen M, Torgerson J, Bouchard C, Carlsson B, et al. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. N Engl J Med 2004;351:2683–93.

[3] Carrasco F, Klaassen J, Papapietro K, Reyes E, Rodriguez L, Csendes A, et al. A proposal of guidelines for surgical management of obesity. Rev Med Chile 2005;133:699–706.

[4] Csendes A, Burdiles P, Papapietro K, Diaz JC, Maluenda F, Burgos A, et al. Results of gastric bypass resection of the distal excluded gastric segment in patients with morbid obesity. J Gastrointest Surg 2005;9:121–31.

[5] Bloomberg RD, Fleishman A, Nalle J, Herron DM, Kini S. Nutritional deficiencies following bariatric surgery: what have we learned? Obes Sur 2005;15:145–54.

[6] Brolin RE, Gorman JH, Gorman RC, Petschenik AJ, Bradley LJ, Kenler HA, et al. Are vitamin B12 and folate deficiency clinically important after roux-en-Y gastric bypass? J Gastrointest Surg 1998; 2:436–42.

[7] Flancbaum L, Belsley S, Drake V, Colarusso T, Tayler E. Preoperative nutritional status of patients undergoing Roux-en-Y gastric bypass for morbid obesity. J Gastrointest Surg 2006;10:1033–7.

[8] Brolin RE, Gorman JH, Gorman RC, Petschenik AJ, Bradley LB, Kenler HA, Cody RP. Prophylactic iron supplementation after Roux-en-Y gastric bypass: a prospective, double-blind, randomized study. Arch Surg 1998;133:740–4.

[9] Amaral JF, Thompson WR, Caldwell MD, Martin HF, Randall HT. Prospective haematologic evaluation of gastric exclusion surgery for morbid obesity. Ann Surg 1985;201:186–93.

[10] Mason ME, Jalagani H, Vinik AI. Metabolic complications of bariatric surgery: diagnosis and management issues. Gastroenterol Clin North Am 2005;34:25–33.

[11] Eakins JD, Brown DA. An improved method for the simultaneous determination of iron-55 and iron-59 in blood by liquid scintillation counting. Int J Appl Radiact Isotopes 1966;17:191–7.

[12] Burge JC, Schaumburg JZ, Choban PS, Di Silvestro RA, Flancbaum L. Changes in patients' taste acuity after Roux-en-Y gastric bypass for clinically severe obesity. J Am Diet Assoc 1995;95:666–70.

[13] Rossander-Hulthén L, Hallberg L. Dietary factors influencing iron absorption—an overview. In: Hallberg L, Asp NG, editors. Iron nutrition in health and disease. London: John Libbey & Co; 1996, p. 105–16.

[14] Csendes A, Burdiles P, Burgos AM, Maluenda F, Diaz JC. Conservative management of anastomotic leaks after 557 open gastric bypass. Obes Surg 2005;15:1252–6.

[15] Finch CA. Regulators of iron balance in humans. Blood 1994;84: 1697–702.

[16] Cook JD, Bothwell TH. Availability of iron from infant foods. In: Stekel A, editor. Iron nutrition in infancy and childhood. New York: Nestlé-Raven Press; 1984, p. 119–45.

[17] Inabnet WB, Quinn T, Gagner M, Urban M, Pomp A. Laparoscopic Roux-en-Y gastric bypass in patients with BMI <50: a prospective randomized trial comparing short and long limb lengths. Obes Surg 2005;15:51–7.

[18] De Paz R, Hernández-Navarro F. Manejo, prevención y control del síndrome anémico secundario a deficiencia férrica. Nutr Hosp 2005; 20:364–367.