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Síndrome del intestino marrón: una rara complicación relacionada con la desnutrición después de la cirugía bariátrica

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ABSTRACT

We present the case of a 44-year-old male who presented with uncontrollable diarrhea, severe protein-calorie malnutrition and multiple vitamin deficiencies, along with peripheral neuropathy ten years after classic biliopancreatic diversion (BPD). He underwent nutritional support and had the surgery converted to a Roux-en-Y gastric bypass, with an uneventful outcome. The histopathology of the resected bowel revealed lipofuscinosis of the muscular layer compatible with brown bowel syndrome.

Brown bowel syndrome is a rare complication of malnutrition that can be observed after BPD. It is associated with vitamin E deficiency. After

recovery with nutritional support, a reoperation that elongates the common channel, and thus minimizes the degree of malabsorption, should be indicated in these cases.

Key words: Lipofuscin. Bariatric surgery. Obesity. Malnutrition. Biliopancreatic diversion.

RESUMEN

Presentamos el caso de un paciente varón de 44 años que presentó diarrea incontrolable, desnutrición proteica-calórica severa y deficiencias de múltiples vitaminas, junto con neuropatía periférica diez años después de derivación biliopancreatica clásica (DBP). Se sometió a soporte nutricional y la cirugía se convirtió en un *bypass* gástrico en Y de Roux, con un resultado sin complicaciones. La histopatología del intestino resecado reveló una lipofuscinosis de la capa muscular compatible con el síndrome del intestino marrón.
El síndrome de intestino marrón es una complicación rara de la desnutrición que se puede observar después de la DBP. Se asocia a deficiencia de vitamina E. Después de la recuperación con soporte nutricional, se debe indicar una reoperación que alargue el canal común y, por lo tanto, minimice el grado de malabsorción en estos casos.

Palabras clave: Lipofuscina. Cirugía bariátrica. Obesidad. Desnutrición. Desviación biliopancreática.

INTRODUCTION

Over recent years, overweight and obesity have reached epidemic proportions and bariatric surgery has become the gold-standard treatment option for refractory morbid obesity (1). There are several surgical modalities and techniques and also many variations within the major technical descriptions. Historically, the procedures have been classified according to their predominant mechanism of weight

loss into three major groups: restrictive, i.e., procedures that lead to weight loss by means of restriction to food intake (e.g., gastric banding, sleeve gastrectomy, and vertical banded gastroplasty); malabsorption (e.g., jejunocolic and jejunoileal bypasses); and mixed (e.g., Roux-en-Y gastric bypass, mini-gastric bypass, and biliopancreatic diversions [BPDs]). Among the mixed procedures, some are more restrictive (Roux-en-Y and mini-gastric bypasses), whereas others produce more malabsorption (biliopancreatic diversions with or without duodenal switch) (2). Among the predominantly malabsorptive mixed procedures, the classic BPD, also known as Scopinaro operation, was firstly described in the late 1970s and has been performed worldwide since then, reaching more acceptance in some European countries. It is characterized by a distal gastrectomy along with a lengthy intestinal bypass, leaving an intestinal common channel where food and biliopancreatic secretions pass through together of about 50 cm in its classic design (3). In fact, although this technique is associated with significant weight loss and resolution of obesity-related comorbidities, it has been significantly associated with ominous nutritional complications, especially severe protein-calorie malnutrition, fat-soluble vitamin deficiencies and liver failure (4). According to the last report of the International Federation for Surgery of Obesity and Related Disorders, this technique accounts for less than 1% of all proceedings performed worldwide (1).
This study aims to describe a case of malnutrition-related brown bowel syndrome in an individual who underwent a classic BPD.

CASE REPORT

We present the case of a 44-year-old male who was referred to our Bariatric Surgery outpatient service by the Clinical Neurology Department due to a refractory peripheral neuropathy of complex B vitamin-deficiency pattern. He had undergone a classic biliopancreatic diversion ten years ago at another bariatric service and had not appropriately complied with multidisciplinary consultations since then.

At surgery, his body mass index (BMI) was 59.8 kg/m^2 and he presented no comorbidites. He presented with significant complaints of asthenia along with paresthesia in both upper and lower limbs that began four months ago and progressed. He reported about nine bowel movements per day, with loose fetid stools. He also reported daily post-prandial episodes of vomiting with solid food residues. He never appropriately took vitamin supplementations following surgery. His current BMI was 23.1 kg/m^2. On physical examination, he presented with moderate cutaneous and mucous pallor, mild jaundice and severe edema in the lower limbs. Laboratory examinations revealed severe hypoalbuminemia, significant macrocytic anemia, severe deficiencies of all fat-soluble vitamins and abnormalities of transaminases and bilirubin (Table I). A contrasted gastrointestinal radiography series revealed a large gastric remnant with solid food residues, along with a significant thickening of the small bowel folds; the contrast rapidly progressed into the colon 40 minutes after intake (Fig. 1). An upper endoscopy showed a large gastric remnant and solid food residues, without other abnormalities. Bone densitometry observed a significantly decreased bone mineral density, compatible with osteoporosis. Both parenteral and enteral nutrition supports were warranted, along with parenteral iron and vitamin supplementation, oral probiotics, and pancreatic enzyme reposition. After 14 days, there were significant biochemical and clinical improvements, with a resolution of the edema and amelioration of the asthenia and neurological symptoms, along with a decrease in the bowel habit to six movements per day. His BMI was 23.3 kg/m^2; despite the improvement of the biochemical examinations, they were at borderline levels yet (Table I). A surgical intervention was then warranted, aiming at the conversion of the then current surgical technique to a less malabsorptive one, to favor the correction of the nutritional deficiencies and avoid a significant weight regain as well. At surgery, a classic BPD with a 150-cm alimentary limb and a 50-cm common channel was identified; the liver parenchyma was mildly

hardened and the bowels were thickened. The BPD was dismantled by means of a conversion to Roux-en-Y gastric bypass, with a resection of part of the gastric remnant and anastomosis along with the re-arrangement of the intestinal limbs, leading to a 100-cm alimentary limb, a 100-cm biliopancreatic limb and a 450-cm common channel. There were no postoperative complications and the patient was discharged on postoperative day 05. A diffuse perisinusoidal liver fibrosis and severe lipofuscinosis of the muscular layers of the small bowel (brown bowel syndrome) were observed in the resected specimens (Fig. 2). The individual has been regularly followed-up for 24 months since then, presenting one bowel movement per day and a current BMI of 25.5 kg/m^2. The biochemical evaluations also reached normal levels (Table I).

DISCUSSION

Occurrences of severe protein-calorie malnutrition and deficiencies of fat-soluble vitamins following BPD have been extensively reported (5,6). The design of this procedure predominantly favors the fat malabsorption, since the biliopancreatic secretions flow along with the food for a short bowel length. Moreover, the bypass of significant portions of the foregut also impairs the absorption of iron and other nutrients. However, no case of brown bowel syndrome has been reported after BPD to date. A review of the literature was conducted through an online search for the MeSH terms “lipofuscin”, “bariatric surgery” and “malnutrition” in MEDLINE (via PubMed) and LILACS (via BVS). Original studies were included that reported single cases or case series of this disease or correlated conditions. All the papers were checked according to their titles and abstracts (screening). Full papers were obtained from journals available on the Commission for Improvement of Higher Education Personnel (Comissão de Aperfeiçoamento de Pessoal de Nível Superior – CAPES) Foundation (Ministry of Education, Brazil) website. Unavailable articles were requested from their authors. Articles presenting potentially relevant

studies were read and analyzed to assess the inclusion criteria. Articles that consisted of *in vitro* or animal studies, articles in which the participants' characteristics did not match those mentioned above, poster session abstracts, review articles and other types of publications were excluded. Other papers were used for contextualization and discussion. After extensive online research, two studies were identified, both case reports. The first was reported by Evans et al. (7) and refers to a case of myometrial lipofuscinosis without confirmation of intestinal disease 21 years after a non-specified intestinal bypass. This patient presented improvement of the diarrhea and neurological symptoms after oral supplementation of vitamin E. The sole case of confirmed brown bowel syndrome observed following bariatric surgery was reported by Lee et al. (8) 26 years after a jejunoileal bypass, a procedure mostly performed during the 1970s and gradually abandoned since then, due to its ominous nutritional issues and liver failure reports. The patient underwent a reversal of the intestinal bypass along with a sleeve gastrectomy to prevent significant weight regain. Besides the predominantly malabsorptive procedure, the current case has one characteristic in common with the previously reported case, as both patients did not comply with the multidisciplinary follow-up, which is one of the pinnacles for a satisfactory and uneventful course following bariatric surgery. Besides these bariatric surgery-related cases, there were only 27 scientific reports of brown bowel syndrome correlating malnutrition and this syndrome according to a systematic review published in 2014 (11).

The brown bowel syndrome is characterized by deposits of lipofuscin in both longitudinal and circular smooth muscle layers of the small bowel; it was first reported in 1963 and is characterized macroscopically by an orange-brown appearance (9). Lipofuscin is comprised of yellow-brown granules composed of lipid-containing residues of lysosomal digestion; it is considered as a signaling pigment associated with the aging process. It appears to be the

product of the oxidation of unsaturated fatty acids and may be symptomatic of membrane damage, or damage to mitochondria and lysosomes (10).

The cause of intestinal lipofuscinosis has not been elucidated yet. It is usually thought to be caused by chronic vitamin E deficiency, which is the result of deficient enteral uptake of fat-soluble tocopherol in malabsorption syndromes such as celiac disease, short bowel syndrome, and malabsorptive surgeries. Advanced cases of brown bowel syndrome present several symptoms in addition to the signs of the underlying malabsorption disorder. They include general dystrophia, weight loss, protein deficiency edema, motility problems (e.g. vomiting, flatulence, and even pseudo-obstructions), liver cirrhosis and signs of vitamin deficiency such as severe osteoporosis, abdominal pain, diarrhea and steatorrhea (11). Another potentially harmful consequence of this syndrome that has been described is the occurrence of small bowel adenocarcinoma. The combined presence of brown bowel syndrome and small bowel adenocarcinoma has been described, although the interconnection between the two has not been clearly elucidated to date. Nonetheless, the role of vitamin E deficiency in small bowel carcinogenesis cannot be excluded and requires further study (12).

The term vitamin E is a collective name for all natural and synthetic tocol and tocotrienol derivative compounds, which qualitatively demonstrate the biological action of α-tocopherol. Tocopherol is the umbrella term for the entire class of mono-, di- and trimethyl tocotrienols. Long-term vitamin E supplementation is reportedly able to improve the malabsorption syndrome and may be accompanied by regression of the lipofuscin deposits among individuals with confirmed brown bowel syndrome (13).

For individuals who underwent malabsorptive surgeries, vitamin supplementation might not be sufficient on a long-term basis, since the absorption of fat-soluble vitamins would continue to be impaired. Moreover, in cases such as the one presently reported, abnormalities

in liver function must also be seriously evaluated. Thus, the indication of a reoperative bariatric operation in these conditions should be considered. There are several possibilities of conversion or reversion of the current technique. Usually, the predominantly adopted procedures in this context are the elongation of the common channel using the alimentary or biliopancreatic limbs or the conversion to a less malabsorptive procedure, such as the Roux-en-Y gastric bypass. The conversion to Roux-en-Y gastric bypass as described in this study is another possibility; it significantly alleviates the malabsorption and also avoids unsatisfactory weight regain (14). In extreme cases where the clinical conditions impose a rapid intervention, but do not permit complex procedures, a side-to-side anastomosis of the proximal biliopancreatic limb to the alimentary channel (“kissing X”) is also a simple possibility (15). Ideally, the operation of choice should be carefully evaluated for each case in an individual basis, since there is no consensus in the current literature.

CONCLUSION

Brown bowel syndrome is a rare complication of malnutrition that can be observed after BPD. After recovery with nutritional support, a reoperation that elongates the common channel should be indicated in these cases.

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Table I. Evolution of biochemical examinations over the course of the reported case

	Admittance	Post-nutritional support	24 months post-reoperation
Hemogram	Hemoglobin: 9.8 Mean corpuscular volume: 120 fl (nl até 100) White cell count: 2,400 Platelets: 90,000	Hemoglobin: 11.2 Mean corpuscular volume: 110 fl (nl até 100) White cell count: 4,400 Platelets: 140,000	Hemoglobin: 13.4 Mean corpuscular volume: 85 fl (nl até 100) White cell count: 6,200 Platelets: 160,000
Sodium (mg/dl)	138	137	140
Potassium (mg/dl)	4.0	4.1	4.0
Urea (mg/dl)	45	22	25
Creatinine (mg/dl)	1.2	0.8	0.8
Coagulogram	Prothrombin activity: 40%/RNI: 2.1 R: 1.9	Prothrombin activity: 98%/RNI: 1.0 R: 1.0	Prothrombin activity: 90%/RNI: 1.1 R: 1.0
Fasting glucose (mg/dl)	74	80	84
Triglycerides (mg/dl)	40	135	65
Total cholesterol (mg/dl)	90	120	120
Ferritin (ng/ml) Normal: > 15	4	19	26
Serum iron (µg/dl) Normal: > 35	26	76	69
Aspartate transaminase (U/l) Normal: < 40	90	75	40
Alanine transaminase (U/l)	95	78	43

Normal: < 40			
Alkaline phosphatase (U/l)	80	82	80
Gama-glutamyl transferase (U/l) Normal: < 60	120	90	55
Bilirubins (mg/dl) Normal: < 1.2	3.0 (direct: 1.4/indirect: 1.6)	1.0 (direct: 0.4/indirect: 0.6)	0.9 (direct: 0.4/indirect: 0.5)
Vitamin E (mg/dl) Normal: 5-20	4	12	22
Vitamin D (ng/ml) Deficiency: < 20	8	18	29
Vitamin A (mg/l) Normal: 0.3-0.7	0.2	0.4	0.6
Vitamin K (ng/ml) Normal: 0.2-2.3	0.04	0.2	1.0
Vitamin B12 (pg/ml) Normal: 210-980	122	840	340
Vitamin B1 (µg/l) Normal: 28-85	10	28	50
Vitamin B6 (µg/l) Normal: 8.7-27.2	6.4	8.1	24.5
Zinc (µg/dl) Normal: 70-120	35	71	71
Ionic calcium (mmol/l) Normal: 1.05-1.3	0.8	1.18	1.3
Total proteins (g/dl)	4.0	6.1	7.1
Globulins (g/dl)	2.0	2.9	3.1
Albumin (g/dl)	2.0	3.2	4.0
Pre-albumin (g/dl) Normal: 20-40	5.0	13.0	21
Daily fecal fat (grams per 24 hours) Normal: < 6	28	12	6

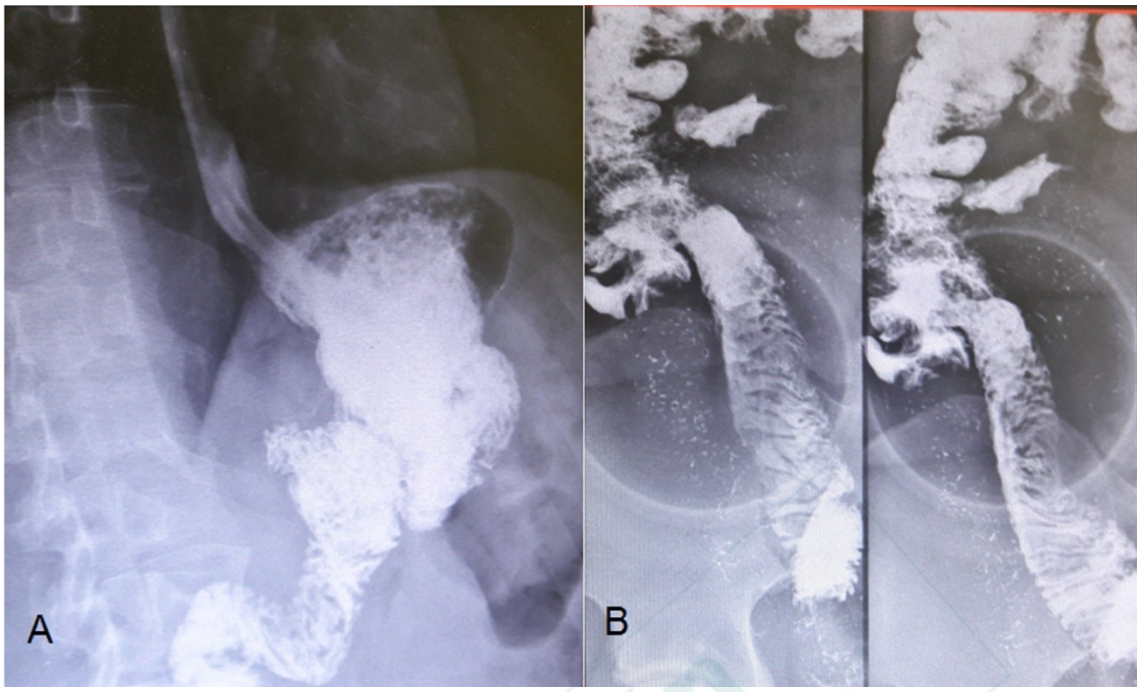

Fig. 1. Contrasted gastrointestinal radiography series. A. Large gastric remnant with solid food residues. B: Thickening of the small bowel folds.

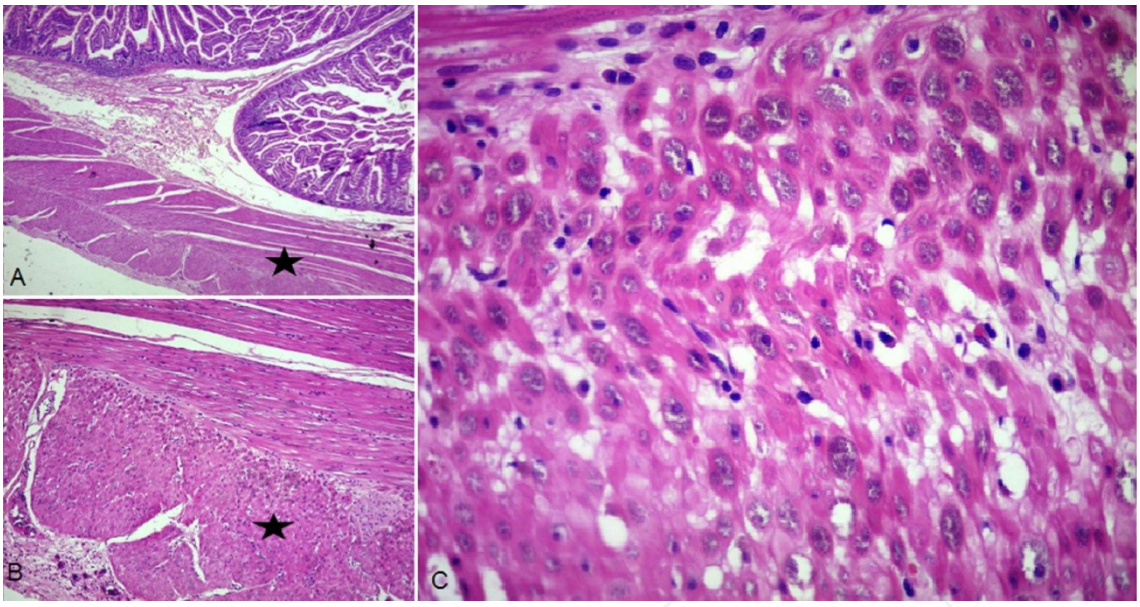

Fig. 2. Histopathological examination of the resected small bowel. The star indicates the *muscularis externa* layer. A. 40x. B. 100x. C. 400x: lipofuscin granules are visible in the upper extremity of the image.