Single Case

Brown Bowel Syndrome: An Exceedingly Rare Condition with Longstanding Malabsorption and an Unusual Cause of Colon Pseudo-Obstruction

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Keywords

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Abstract

Brown bowel syndrome (BBS) is an exceedingly rare condition usually associated with longstanding malabsorption of any etiology. As a result of vitamin E deficiency and subsequent mitochondrial degeneration due to oxidative stress induced by free radicals, lipofuscin granules accumulate in the smooth muscles of the gastrointestinal tract resulting in myopathy and dysmotility with underlying disease aggravation. The current study reports a BBS case in a 64-year-old female patient who had undergone jejunoileal bypass surgery as a bariatric procedure. The patient was admitted with signs of malabsorption and ileus in computed tomography imaging. Endoscopic workup revealed no stenosis or obstruction. The colon histologically showed periodic acid-Schiff-positive lipofuscin granules in the lamina muscularis mucosa consistent with BBS. The vitamin E level in the patient was extremely low. Moreover, clinical improvement was documented following high-dose substitution. BBS should be considered in patients with malabsorption of any cause especially with signs of gastrointestinal dysmotility. Vitamin E substitution may improve clinical status and prevent further deterioration.

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Introduction

Brown bowel syndrome (BBS) or *intestinal lipofuscinosis* is a very rare syndrome usually associated with longstanding malabsorption. Few case reports and case series were noted in the literature. The syndrome was well-described first by Pappenheimer and Victor [1] in 1946. Vitamin E plays an important role as a potent antioxidant that protects the cells from oxidative stress induced by free radicals [2]. Vitamin E deficiency results in the degradation of the lipid-containing membrane of the mitochondria with the consequence of the accumulation of lipofuscin granules in the smooth muscles of the gastrointestinal (GI) tract especially in the small and large bowel. These lipofuscin deposits lead to brownish discoloration of the intestinal wall and may cause further damage to the GI tract and worsening of the underlying disease [3, 4]. The current study reports a case of BBS in a 64-year-old female patient with postjejunoileal bypass status. The first case of BBS after such bariatric surgery reported by Lee et al. [5] in 2009.

Case Presentation

A 64-year-old female patient was admitted to our department with a marked weight loss of about 35 kg (weight 66 kg; body mass index 20.4 kg/m^2) within the previous year, recurrent watery diarrhea, as well as reduced general status. The patient reported recurrent skin abscesses and had a large abscess in the right thigh with subsequent surgical treatment 2 years previously. The patient had undergone *jejunoileal bypass* about 40 years ago. Current medications comprise L-thyroxine for known hypothyroidism, calcium, and folic acid, without other vitamin supplementation. No alcohol or drug consumption and relevant family history were noted. In addition, the patient spent a brief vacation in Tanzania approximately 1 year ago.

Clinical examination revealed cachexia, pallor, and mild peripheral edema in the lower extremities. The abdomen of the patient was markedly distended with scanty bowel peristalsis without signs of peritonitis. Moderate cognitive impairment was also noticeable.

Laboratory tests revealed marked anemia (hemoglobin 9 g/dL), elevated creatinine (1.85 mg/dL), severe hypovitaminosis, hypoalbuminemia, and hypolipidemia (Table 1). Stool culture for bacteria, viruses, and parasites was negative. HIV serology was also negative. Abdominal X-ray showed signs of ileus with massive dilatation up to 9 cm in the right colon (shown in Fig. 1). Abdominal computed tomography (CT) and magnetic resonance imaging showed marked small and large bowel dilatation with multiple (>15) intramural fatty isodense lesions in the right and transversal colon in terms of multiple lipomas (shown in Fig. 2). Gastroscopy as well as push enteroscopy showed chronic inflammatory nodular mucosa in the duodenum and proximal jejunum with markedly decreased peristalsis. Ileocolonoscopy showed a marked elongated dilated colon with absent peristalsis as well as multiple submucosal lipomas described on CT. No signs of inflammatory bowel disease or stenosis were noted. A histological examination from the duodenum and jejunum showed no signs of celiac disease, tropical sprue, parasitosis, Whipple's disease, or lymphoma. Samples from the colon showed no microscopic colitis, and periodic acid-Schiff (PAS)-positive lipofuscin deposits were noted in the cytoplasm of the smooth muscle cells in the muscularis mucosa consistent with BBS (shown in Fig. 3).

The patient initially received combined enteral and parenteral nutrition with the substitution of vitamins and trace elements. Vitamin E was substituted at a high dose of 268 mg (400 IE) bid. A significant clinical improvement was noted in the disease course. At the last follow-up about 1 year later, the patient was seen to be doing very well, did not report

Table 1. Laboratory tests

Parameter	Value on admission	Value at follow-up	Reference
Vitamin E	1.4	14.6	12–46 µmol/L
Vitamin A	0.1	–	1.05–2.8 µmol/L
Vitamin C	<1	–	5–15 mg/L
Vitamin D	36.4	37.8	50–150 nmol/L
Vitamin B1	–	76	34–102 ng/mL
Vitamin B6	1.4	4.6	≥4.4 µg/L
Vitamin B12	700	–	191–663 ng/L
Folic acid	2.7	3.8	2–15 ng/mL
Selenium	–	76	50–120 µg/L
Zink	–	844	660–1,100 µg/L
Albumin	18.2	40	35–52 g/L
Cholesterol	51	–	<200 mg/dL
LDL	14	–	<130 mg/dL
Triglyceride	61	–	<200 mg/dL

Fig. 1. **a** Sign of Ileus. Abdominal X-ray revealed massive distention in the small and large bowel, up to 9 cm in the right colon. **b** Sign of Ileus. Abdominal X-ray showed air-fluid level.

diarrhea, weighed 82 kg, and had a body mass index of 25.3 kg/m². Substituting vitamins (E, D, K, and A) had been continued in the ambulant setting intramuscularly every 4 weeks combined with the normal oral diet (Table 1).

Discussion

BBS may occur in malabsorption of any etiology and cause further symptoms in addition to the underlying disease [6]. As a result of vitamin E deficiency with subsequent mitochondrial degeneration and loss of energy source in the smooth muscles tissue of the GI tract

Fig. 2. **a** Pseudo-obstruction. Abdominal MRI showed marked distention in the stomach and small intestine. **b** Abdominal CT with multiple lipomas in the right colon (arrow). MRI, magnetic resonance imaging; CT, computed tomography.

Fig. 3. Lipofuscinosis. Tissue section from the right colon showing PAS-positive deeply purple staining lipofuscin deposits distributed within the lamina muscularis mucosae (PAS stain, original magnification, ×400). PAS, periodic acid-Schiff.

which can be described as *mitochondrial myopathy*, new symptoms could develop (e.g., dysmotility, pseudo-obstruction, and bacterial overgrowth) which may lead to significant worsening of the underlying disease [7].

Lipofuscin granules consist of lysosomal degradation products and are mainly located in tunica muscularis propria and, to a lesser extent, in the lamina muscularis mucosa. The distribution of these granules in the GI tract may sometimes be discrete and may not be visible in all bowel segments so that the brownish discoloration is not always macroscopically detectable [8]. Microscopically detecting lipofuscin granules are difficult with conventional hematoxylin-eosin stain and may require special stains (e.g., PAS). Therefore, the pathologist should always be informed of BBS suspicion. The granules appear purple with PAS stain and are resistant to diastase digestion, they also stain with Masson-Fontana and methylene blue, have yellow autofluorescence under ultraviolet light microscopy, and are detectable with electron microscopy [6, 8, 9]. The main differential diagnosis with such GI pigmentation is Whipple's

disease and melanosis coli [8, 9]. In both diseases, all granules are located almost within macrophages in the lamina propria, whereas in BBS the granules are found in the cytoplasm of the smooth muscle cells in muscularis mucosa (as in the patient of the current study) or muscularis propria. In addition, duodenal biopsies were performed in the patient of the current study without any signs of Whipple's disease. For the differential diagnosis of melanosis coli, this disease is usually associated with the chronic use of laxatives especially anthraquinone-containing laxatives (e.g., senna or aloe vera). However, the patient of the current study denied any use of laxatives.

CT and magnetic resonance imaging showed signs of ileus, however, weight loss and diarrhea, but not obstipation, are the main manifestations in the patient of the current study. The cause of diarrhea is multifactorial and may include short bowel syndrome after jejunio-ileal bypass, hypovitaminosis, and probably bacterial overgrowth due to dysmotility. However, H₂ breath test was not conducted.

As aforementioned, the patient reported recurrent skin abscesses. The susceptibility to recurrent infection is probably related to hypovitaminosis, particularly to vitamin E deficiency, which plays an important role in both cellular and humoral immunities [10]. Vitamin E deficiency may also contribute to the cognitive impairment in the patient [2].

In abdominal CT, several (>15) submucosal fatty isodense lesions in the right and transversal colon were described. These lesions were typical for lipomas (yellowish soft lesions) in colonoscopy. According to the literature survey, such findings have not been previously described in patients with BBS. Whether this is related to lipofuscin accumulation is a matter of debate. Biopsies from these lesions were not performed which is a limitation of the current study.

An association between BBS and severe lower GI hemorrhage has been described [11]. The authors supposed that the lipofuscin accumulated in the muscular layer of the vessels and this, in turn, led to vascular injury and hemorrhage. Small bowel carcinoma has also been reported in patients with BBS [12]. However, the relationship between BBS and malignancy is still unclear.

Little information regarding therapy has been noted. However, the underlying disease should be treated. Nutritional status should be evaluated and enteral or parenteral nutrition with vitamin substitution should be accordingly provided. Some authors reported clinical and histological improvement with regression of lipofuscin aggregates after underlying disease treatment and vitamin E substitution [13–15]. Moreover, vitamin E supplementation could prevent further lipofuscin accumulation and thus further deterioration of the clinical status. Usually, a high dose (150–600 mg or 250–1,000 IE) is given in the initial phase [6], and the dose should be adjusted depending on the clinical course and serum levels.

BBS is a rare condition but should be taken into consideration in patients with long-standing malabsorption especially with signs of GI dysmotility. The evaluation of nutritional status especially vitamin E level is essential in these patients.

Statement of Ethics

Written informed consent was obtained from the patient for the publication of this case report and any accompanying images. This study protocol was reviewed and the need for approval was waived by "Ethics Committee Vivantes."

Conflict of Interest Statement

The authors have no conflict of interest to declare.

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Author Contributions

Alkurdi was involved in the clinical management of the patient, performed literature search, and wrote the article. Rubin and Seelhoff were involved in the clinical management of the patient and reviewed the article. Herbst performed histologic diagnosis and reviewed the article.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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