

Right Colon Carcinoma Infiltrating the Alimentary Limb in a Patient With Biliopancreatic Diversion

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Biliopancreatic diversion (BPD) has excellent results, with the average patient losing 60% to 80% of the excess weight in the first 2 years. However, the BPD works by malabsorption and malabsorptive problems may be experienced with the operation. Therefore, monitoring is necessary for life. In the recent literature there is some debate over the possibility that this technique can increase the risk of colon cancer secondary to the action of the unabsorbed food and bile acid on colonic mucosa. We report the case of a 42-year-old patient with a previous bariatric surgery (BPD with 50 cm common channel; 300 cm alimentary limb) who developed a very aggressive right colon cancer 6 years after the operation. We also review our series of 330 patients operated on during a 14-year period to try to answer if there is any relationship between BPD and colon cancer.

Key words: Morbid obesity – Bariatric surgery – Colorectal cancer – Biliopancreatic diversion

Case Report

A 42-year-old woman who had undergone bariatric surgery in our hospital was evaluated for nonspecific abdominal pain in May 2009. She had been operated on in 2004 with a standard BPD and in 2008 she had surgery for abdominal wall eventration with cholecystectomy.

Abdominal examination was normal and she also was complaining of fatigue and weakness. We ordered a complete blood test with vitamins and to our surprise we found a highly elevated CEA (334.6 ng/mL; normal 0–3 ng/mL), CA 19–9 levels (391.9 U/mL; normal 0–35 U/mL) and mild anemia secondary to iron deficiency (10.3 g/dL; normal 12–16 g/dL). Blood chemistry and vitamin levels were within normal range. An urgent CT-scan was

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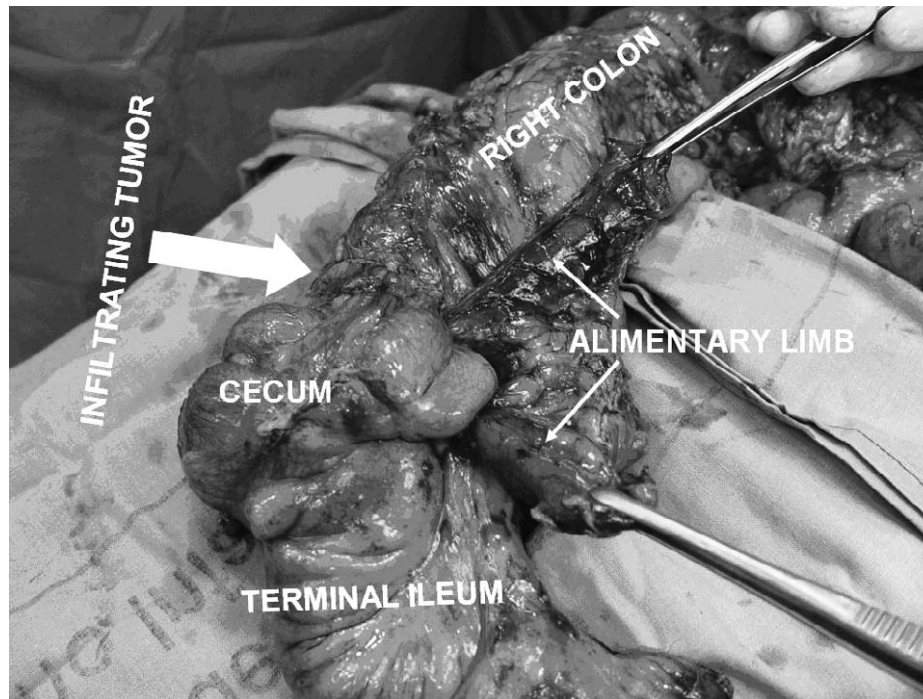


Fig. 1 Macroscopic appearance of the specimen. The tumor is infiltrating the alimentary limb. En bloc resection of the tumor was performed.

ordered, which demonstrated an infiltrative right-sided colon cancer with multiple enlarged lymph nodes in the ileocecal region and liver, as well as lung metastasis.

Colonoscopy was performed to obtain biopsy samples and to search for synchronous lesions. The mucosal biopsy specimen showed adenocarcinoma. Therefore, the patient underwent surgery.

During surgical intervention we found an ascending colon carcinoma that was infiltrating the alimentary limb close to ileocecal region (Fig. 1), multiple enlarged lymph nodes and large bilobar liver metastases that were initially unresectable.

En bloc R0 resection of the tumor was carried out with complex intestinal reconstruction of the BPD (Fig. 2). Postoperative course was uneventful and the patient was discharged on day 10.

The definitive histological examination of the specimen revealed a moderately differentiated adenocarcinoma of ascending colon infiltrating the submucosa, muscularis propria, subserosal adipose tissue, serosa, and subserosal fat tissue of jejunal segment (pT4); with 5/25 positive lymph nodes (pT4bN2aM1a; stage Iva of 7th edition of AJCC, 2010 stage criteria for colorectal cancer). Histopathology confirmed proximal, distal and circumferential negative margins.

Thirty days after the operation she started on the FOLFOX combination (leucovorin, fluorouracil, oxaliplatin) with bevacizumab and had many cycles with no biologic and radiologic response on chemotherapy. She also suffered many side effects and 5 months later she noticed many painful scalp lesions that were submitted to biopsy and proved to be metastases from intestinal adenocarcinoma. Chemotherapy was discontinued and she died 8 months after the operation.

Discussion

Bariatric surgery has gained popularity in recent years and it has grown into an increasingly popular procedure in the treatment of morbid obesity. Several different procedures are available, each with different risks, benefits, and requirements. Many of these patients have comorbid conditions, such as diabetes or heart disease, and this surgery is usually indicated in morbid patients as well as obesity (class 2) patients to cure or improve medical problems that are caused or made worse by obesity. In addition to diabetes and high blood pressure obesity surgery improved many other medical problems including hyperlipidemia, sleep apnea, gastrointestinal reflux

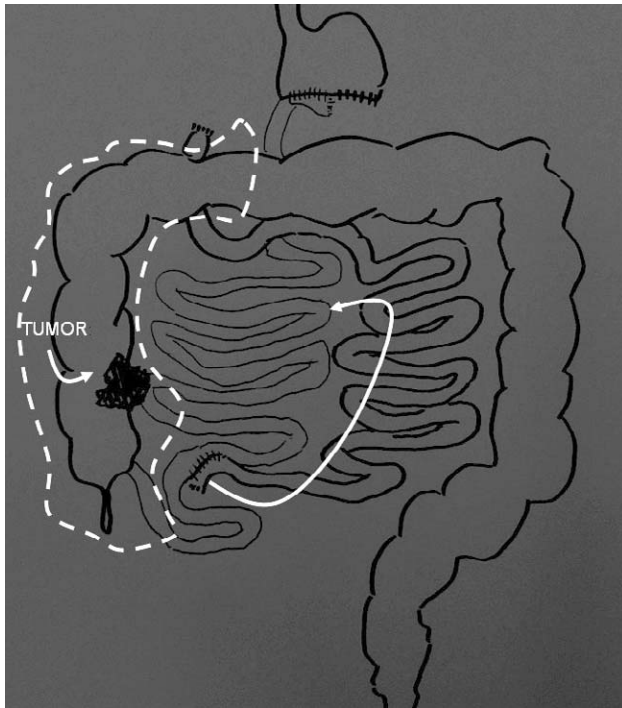


Fig. 2 Right hemicolectomy with en-bloc resection of the alimentary limb. The long arrow indicates new anastomotic site for the biliopancreatic limb and common channel in order to prevent reflux.

disease (GERD), asthma, and arthritis of weight-bearing joints.

Many studies have also demonstrated that that increased body weight is associated with increased incidence for many cancers. Abdominal obesity is associated with an increased risk of colorectal adenoma.¹ Significant positive linear trends in death rates have been observed for colorectal cancer.² Thus, there seems to be a new indication for bariatric surgery: Reduce the risk of cancer. In fact, recent evidence suggests that bariatric surgery improves the cancer outcomes in some morbidly obese patients.³

Although it has not gained wide acceptance in the United States, the BPD technique is being advocated by some European surgeons as a safe and effective treatment for the most severe obese patients. We have performed more than 300 procedures over the last 10 years with good results (not published). A recent meta-analysis has shown that BPD and the Banded RYGBP appeared to show better weight loss than standard RYGBP and LAGB at 5 years follow-up.⁴ Although at the expense of malnutrition and lifelong follow-up programs,⁵

biliopancreatic diversion is considered the most effective weight loss procedure.⁶

Due to rearrangement of the gastrointestinal tract following biliopancreatic diversion it has been speculated for many years that this surgery could lead to an increased risk of colorectal cancer caused by possible carcinogenic action of the unabsorbed food and bile acid on colonic mucosa. The role of the toxicity of bile acids to colon cell lines⁷ and gastrointestinal carcinogenesis has been studied in many papers.⁸

Deleterious effects of bile acid exposure, likely related to carcinogenesis, include: induction of reactive oxygen and reactive nitrogen species; induction of DNA damage;⁹ stimulation of mutation; induction of apoptosis in the short term^{10–12} and selection for apoptosis resistance in the long term.¹³ There is growing evidence that secondary bile acids, particularly deoxycholic and lithocholic acids, are potent colon-tumor promoters in humans. Secondary bile acids are produced in the colon from unabsorbed primary bile acids in the terminal ileum (cholic and chenodeoxycholic acids) by major bacterial reactions. In normal conditions, 1–4% of cholic and chenodeoxycholic acids (liver primary bile acids) escape from the terminal ileum to enter the colon and thus only small proportion of deoxycholic and lithocholic acids are produced.⁷ Therefore, malabsorption and rapid transfer of the bile acids to the colon in the BPD technique induce a mayor production of secondary bile acids that are potential carcinogens.

Recently, the role of alterations in the intestinal microbiota and fecal metabolite profile after malabsorptive procedures could explain increased carcinogenic risk after obesity surgery.^{14–16} Effect of postsurgical neurohormonal modulation on long-term cancer risk also requires further investigation.¹⁷

However the results obtained in Scopinaro's cohort^{18–20} provide support for the hypothesis that the incidence rate of colorectal cancer among subjects at long term following BPD is not substantially different from that observed in the general population. Our cohort of patients (330 patients with standard BPD) support Scopinaro's hypothesis. We only have detected 1 case (present case) of colon cancer with an almost 100% follow-up (0.3% incidence). Importantly, a recent retrospective study in Sweden has found that long-term risk of colorectal cancer in patients who undergo obesity surgery, including malabsorptive procedures, seems to be increased and raised concern of evaluation of

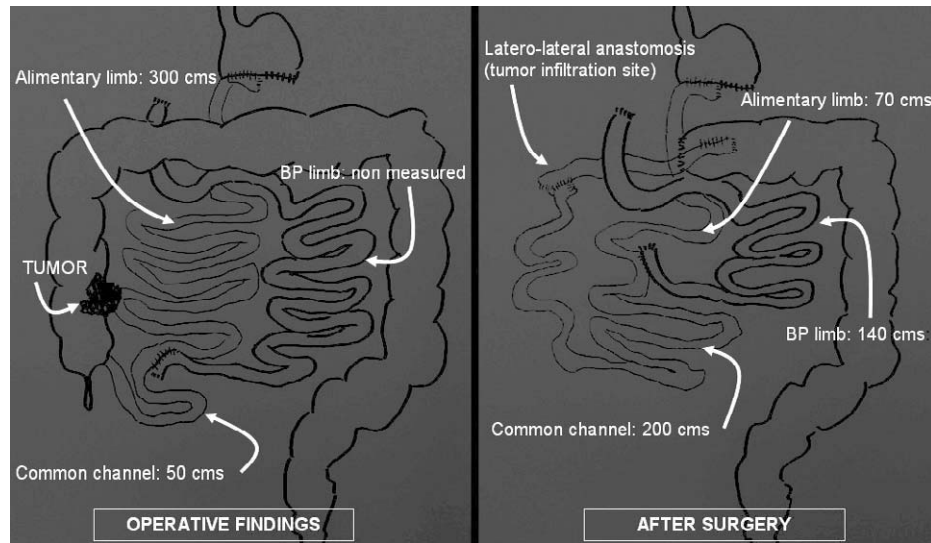


Fig. 3 Left figure shows operative findings. Right figure shows transit reconstruction after right hemicolectomy. Roux limb of 70 cm (alimentary limb; right figure) was long enough to completely prevent bile reflux in the patient.

colonoscopy surveillance for the increasingly large population who undergo this surgery. Moreover, no such increase was found for other obesity-related cancer (breast, kidney, prostate, and endometrium).²¹ On the contrary, a cohort study found a 30% decreased risk of colorectal cancer after gastric bypass compared with morbidly obese controls.²²

In some instances BPD needs to be revised as occur in the present case. Elongations and restorations are not common with this technique as shown by Scopinaro.^{23,24} Of 958 patients undergoing BPD with a minimum follow-up of 2 years, 31 (3.2%) underwent elongation of the common limb and 8 (0.8%) restoration of intestinal continuity at postoperative periods ranging from 14 to 63 months.²⁴

Both types of reoperations, common limb elongation and restoration, most commonly are not implemented to eliminate an unpleasant side effect but to correct an excess of effect of the original procedure. However, surgical reoperation is necessary in some instances, such as this case. Other less common causes of reoperation includes alcoholic or posthepatic liver cirrhosis, intolerance of intestinal gas symptoms and less commonly the diagnosis of gastrointestinal cancer.

Total restoration of intestinal continuity may be done by ileoduodenostomy or ileojejunostomy in BPD and elongation of the common limb is usually performed using the biliopancreatic limb.

Our case was complex because alimentary limb was infiltrated, so we had to improvise with our knowledge of the technique. A full understanding of

the mechanisms and physiology of the gastrointestinal tract after this technique allows any surgeon to revise the operation in cases of malignancy. Due to the infiltration of the alimentary limb we decided to elongate the common channel at expense of the alimentary limb to correct an excessive malabsorption during chemotherapy. Therefore, by increasing fat and starch absorption we reduced endogenous nitrogen loss and colonic bacteria overgrowth, resulting in a decreased protein requirement and increased protein absorption in the colon (Fig. 3).

With this type of revision we prevented diarrhea due to excessive reduction of ileal bile salt absorption and the colonic resection performed. Moreover, this type of reconstruction proved to be effective as shown by hematologic (no anemic event during chemotherapy) and serum biochemical values for blood samples obtained after surgery (normal albumin and total serum protein level).

As a conclusion, many hypotheses could explain colonic carcinogenesis after BPD: (1) Rapid intestinal transit in the colon with this technique might prevent adequate time for absorption of dietary carcinogens and production of secondary bile acids (synergic theory: both are necessary to promote carcinogenesis). (2) Altered gastrointestinal anatomy could importantly affect enterohepatic recirculation and the rate of circulating primary and secondary bile acid pool. (3) Other different theories including microbiota and gut hormones deserve more detailed studies.²⁵

Finally, the possibility that BPD can increase the risk of colon cancer does not seem to be real as shown by Scopinaro¹⁹ and our present cohort of patients. Nowadays the only truth appears to be that obesity is a risk factor for some gastrointestinal cancers¹ and BPD provides prevention of many cancers induced by weight loss.

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