Received: 1 February 2022 | Revised: 20 April 2022 | Accepted: 8 June 2022

DOI: 10.1111/ases.13099

Asian Journal of Endoscopic Surgery

WILEY

CASE REPORT

A case of familial adenomatous polyposis with protein-losing enteropathy treated by laparoscopic total colorectal resection: A literature review

Hiroki Tubakihara[1] | Hiroshi Sawayama[1] | Yoshihiro Komohara[2] | Yuji Miyamoto[1] | Katsuhiro Ogawa[1] | Mayuko Ohuchi[1] | Naoya Yoshida[1] | Hideo Baba[1]

[1]Department of Gastroenterological Surgery, Graduate School of Medical Sciences, Kumamoto University, Kumamoto, Japan

[2]Department of Cell Pathology, Graduate School of Medical Sciences, Kumamoto University, Kumamoto, Japan

Correspondence
Hideo Baba, Department of Gastroenterological Surgery, Graduate School of Medical Sciences, Kumamoto University, 1-1-1, Honjo, Chuo-ku, Kumamoto 860-8556, Japan.
Email: hdobaba@kumamoto-u.ac.jp

Abstract

Familial adenomatous polyposis (FAP) with protein-losing enteropathy is a rare disorder and is difficult to treat medically. A 74-year-old female patient was referred to our hospital with a chief complaint of anorexia. Lower gastrointestinal endoscopy showed multiple adenomas from the ascending colon to the rectum and adenocarcinoma in the sigmoid colon and descending colon. Laboratory findings showed hypoalbuminemia (albumin 1.6 mg/dl). Protein leak scintigraphy using 99mTc-HSAD found a protein leak from the colon. Although hypercaloric infusion was administered, the nutritional status was not improved and albumin transfusion was required. The patient underwent laparoscopic total proctocolectomy, ileal pouch-anal anastomosis, and temporary ileostomy. She had a good postoperative course and the hypoalbuminemia normalized in a few weeks. The patient underwent temporary ileostomy reversal. Here we report a case of FAP with protein-losing enteropathy who underwent laparoscopic total proctocolectomy, which resulted in improvement of the protein leak as well as cancer treatment.

KEYWORDS

familial adenomatous polyposis, laparoscopic total proctocolectomy, protein-losing enteropathy

1 | INTRODUCTION

Familial adenomatous polyposis (FAP) is an autosomal-dominant inherited disease characterized by multiple adenomas of the colon caused by mutations in the *APC* gene. FAP is the second-most common form of hereditary colorectal cancer, following Lynch syndrome. FAP occurs in 1 in 10,000–20,000 people.[1]

Protein-losing enteropathy is the loss of protein from the digestive tract. The causes of protein-losing enteropathy are intestinal disease, intestinal pressure, and lymphatic obstruction. Elevated intestinal pressure can also be caused by right heart stress or liver cirrhosis.[2] Although protein-leaking enteropathy associated with polyposis has been reported in juvenile polyposis with multiple polyps, cap polyposis, and Cronkhite–Canada syndrome, it is very rarely associated with FAP. This report describes the clinical course of treatment of a patient with FAP with protein-losing enteropathy. Further, we also discuss the characteristics and treatment of

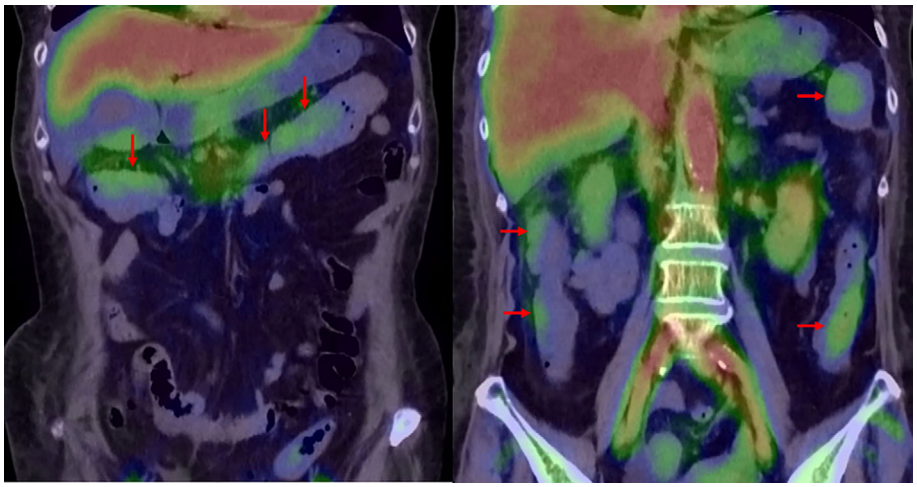

FIGURE 1 Protein leakage scintigraphy using 99mTc-HSAD

protein-losing enteropathy caused by gastrointestinal polyposis.

2 | CASE PRESENTATION

A 74-year-old woman visited a nearby doctor complaining of loss of appetite, nausea, weight loss, and abnormal nails from 3 mo ago. An upper and lower gastrointestinal endoscopy was performed and found multiple colonic polyps from the ascending colon to the rectum. Biopsy of the polyps revealed Group 5 adenocarcinoma in the sigmoid colon and descending colon, and she was referred for further examination and treatment. Her past medical history is significant for hypertension. She had no family history of hereditary polyposis or cancer. Blood tests showed hypoalbuminemia (albumin: 1.6 g/dl), renal dysfunction (estimated glomerular filtration rate [eGFR]: 38), elevated inflammatory response (white blood cell: 9700/μl, C-reactive protein: 3.34 mg/dl), and high carcinoembryonic antigen (6.6 ng/ml). Electrolytes, hepatobiliary enzymes, and the coagulation system were normal. Urinalysis showed that the urinary protein (1+) and urinary protein/creatinine ratio was normal (0.10 g/g CRE).

Endoscopic examination revealed multiple polyps in the ascending colon and rectum, and a colon tumor at 25 cm from the anal verge was found in the sigmoid colon. We performed biopsies from each site and found adenocarcinoma in two sites: the descending colon and sigmoid colon. The polyps in the other sites were tubular adenomas. Small bowel capsule endoscopy showed no obvious abnormal findings. Contrast-enhanced computed tomography (CT) examination revealed wall thickening with a contrast-enhancing effect in the sigmoid colon. No obvious lymph node metastasis or distant metastasis was observed. Protein leakage scintigraphy using 99mTc-HSAD showed increased accumulation from the ascending colon to the rectum, suggesting protein leakage. No abnormal accumulation was observed in the small intestine. There was no evidence of protein leakage from the stomach or small intestine (Figure 1). The fecal α-1 antitrypsin test was not performed.

The patient was found to be hypotrophic and dehydrated due to anorexia and protein leakage. Although hypercaloric infusion was administered to improve the nutritional status, she continued to have anorexia and the hypoalbuminemia progressed, so albumin products were administered as needed.

We performed laparoscopic total proctocolectomy, ileal pouch-anal anastomosis, and temporary ileostomy (Operation time: 6 h 34 min, blood loss: 65 ml). Tumor pathology revealed that polyps were found in the ascending colon and rectum and were dominated by adenomas and moderately-differentiated and well-differentiated adenocarcinomas, some of which contained mucinous adenocarcinoma components. Sigmoid colon cancer showed invasion into the muscularis propria. However, there was no invasion into the lymphatic vessels nor veins. Descending colon cancer remained within the mucosal intrinsic layer, and there was no vascular nor lymphatic invasion (Figure 2). The patient had a good postoperative course, and she was transferred to the hospital on the 16th postoperative day. With subsequent outpatient follow-up, hypoalbuminemia also improved over time (Figure 3), and the patient underwent temporary ileostomy reversal.

3 | DISCUSSION

In this case, the results of protein-losing enteropathy showed protein leakage from the ascending colon to

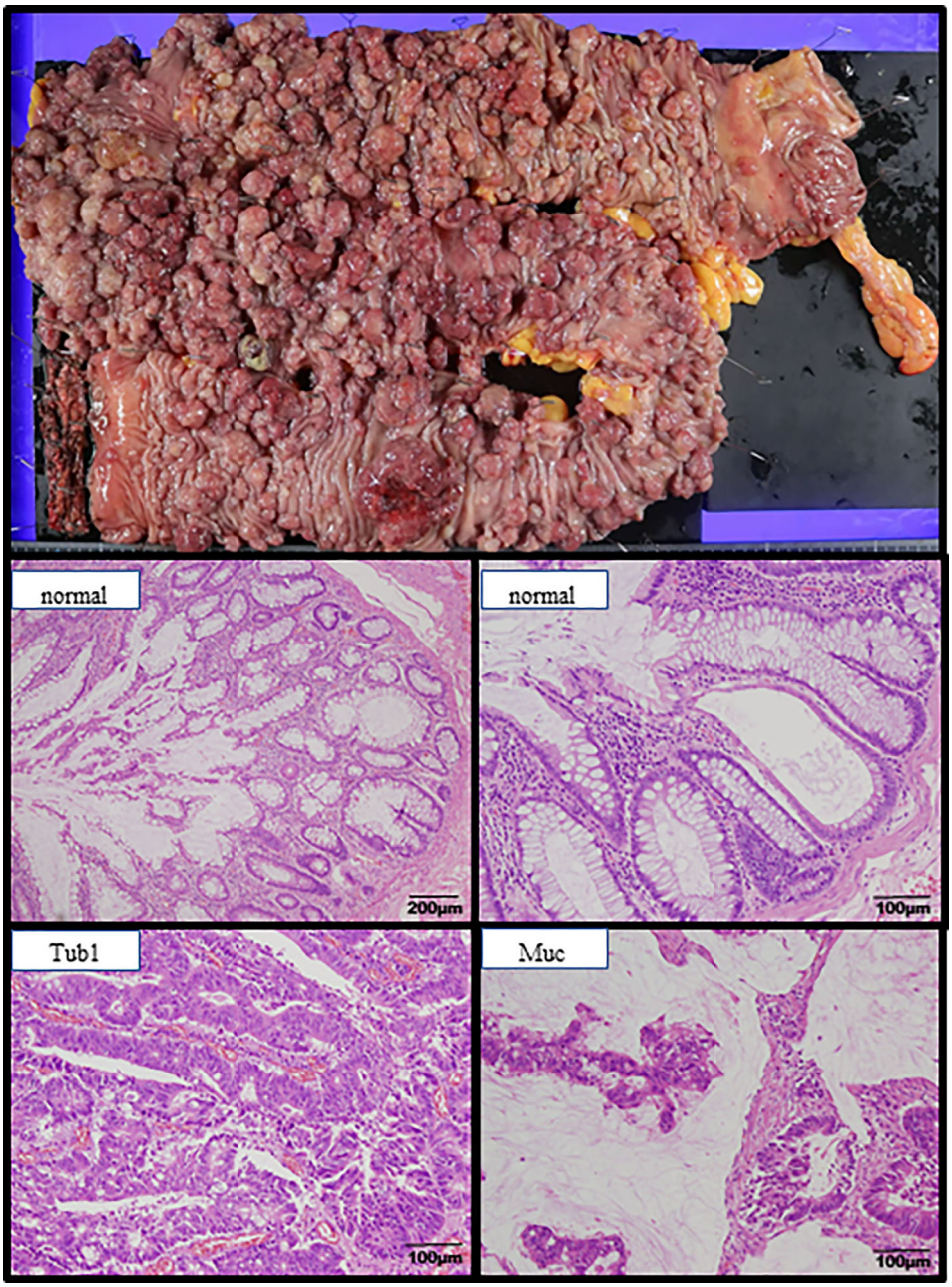

FIGURE 2 Resected specimen and pathological findings. Intestinal gland dilation and excessive mucus secretion were detected in normal mucosa. No lymphatic duct dilation was observed

the rectum, suggesting that polyposis was the cause of protein leak enteropathy. PubMed was searched for articles published in English from January 2000 to December 2021 using the terms "protein-losing enteropathy" and "polyposis" to find the relationship between protein leak enteropathy and polyposis (Table 1). In this search, the disease with the highest number of cases was Cronkhite–Canada syndrome. It has been reported that 88% of patients with Cronkhite–Canada syndrome have hypoalbuminemia, and as for treatment, in addition to supportive care such as hypercaloric infusion, there have been reports that glucocorticoids have been effective, but the dosage and treatment mechanism remain unclear.[3] A few case reports of juvenile polyposis and cap polyposis with protein-losing enteropathy were also confirmed.[4,5] These diseases have been improved by resection of the intestine with the site of protein leakage. A case of familial colorectal adenomatosis with protein leaky enteropathy has been reported. The patient had colorectal cancer and distant metastatic lesions, which were not resected. Chemotherapy is being given, and albumin has improved after chemotherapy.[6]

Protein-losing enteropathy has also been reported to be associated with advanced colorectal cancer. The mechanism of hypoproteinemia with colorectal cancer is thought to be an abnormality in the intestinal mucosal epithelium due to inflammatory changes or an increase

in intralymphatic pressure due to lymphatic invasion.[7] In this case, protein leak scintigraphy showed diffuse accumulation from the ascending colon to the rectum, suggesting that the protein leak was from multiple colorectal adenomas as well as from a malignant tumor. In a previously reported case, colonic polyps were covered with a mucin-like material, suggesting that excessive secretion of mucin-containing proteins from multiple adenomas may be the cause of the protein-losing enteropathy.[6] In the present case, although there is a possibility that the protein leakage was partially caused by colorectal cancer, the fact that the hypoalbuminemia was markedly improved by total colorectal resection suggests that the protein leakage may have been caused by a similar mechanism. In this case, since genetic analysis was not performed, we could not identify the difference in gene expression between FAP associated with protein-losing enteropathy and other types of FAP. Duplication of Exon11-13 has been previously reported in a case of FAP complicated by protein-losing enteropathy and colorectal cancer. Although several duplications of the *APC* gene have been reported in FAP, duplication of Exon11-13 has not been identified. However, this was a

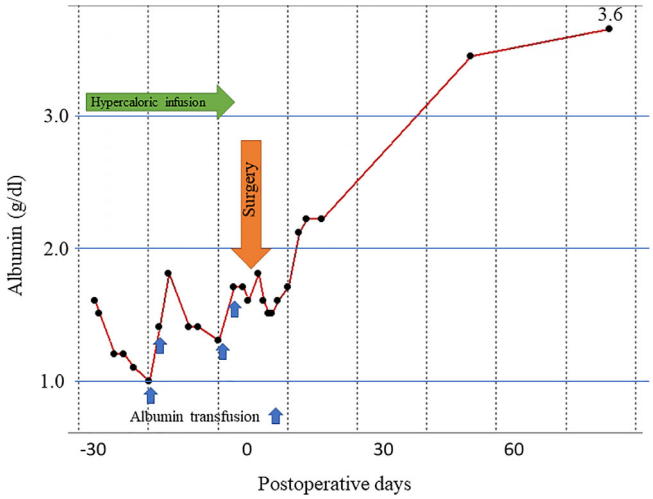

FIGURE 3 Perioperative serum albumin level

TABLE 1 Polyposis accompanied with protein-losing enteropathy

Age	Sex	Cause	Treatment	Reference
70	F	Cap polyposis	Low anterior resection (Laparoscopic surgery)	Surg Case Rep. 2018 Jul 3; 4(1):69.
54	F	Cap polyposis	Left hemicolectomy and sigmoid colectomy (Surgical approach: none noted)	Clin Nucl Med. 1998 Aug; 23(8):521–3.
55	F	Pseudomembranous colitis with cap polyposis-like features	Partial colon resection (Surgical approach: none noted)	World J Gastroenterol. 2017 Apr 28; 23(16):3003–3010.
29	F	Familial adenomatous polyposis	Chemotherapy (death after treatment 29.5 m)	Clin J Gastroenterol. 2016 Jun; 9(3):134–9.
47	F	Juvenile Polyposis Syndrome (SMAD4 mutation.)	Enterotomy with enteroscopy	Case Rep Gastrointest Med. 2015; 2015:140616.
27	F	Juvenile polyposis syndrome	Total gastrectomy (laparotomy)	J Gastrointest Surg. 2012 Mar; 16(3):669–72.
28	M	Juvenile polyposis syndrome	Total gastrectomy (surgical approach: none noted)	Intern Med. 2009; 48(5):335–8.
24	M	Generalized inflammatory polyposis	Total colectomy (surgical approach: none noted)	Clin J Gastroenterol. 2009 Jun; 2(3):156–160.
40	M	Cronkhite–Canada syndrome	Treatment response to steroid	World J Clin Cases. 2016 Aug 16; 4(8):248–52.
62	F	Cronkhite–Canada syndrome	Prednisone and nutritional support	Australas J Dermatol. 2008 Nov; 49(4):223–5.
63	M	Cronkhite–Canada syndrome	Subtotal colectomy (surgical approach: none noted)	Dis Colon Rectum. 2005 Apr; 48(4):870–3.
7 cases		Cronkhite–Canada syndrome	Nutritional supplementation ± corticosteroids (no surgical cases)	Am J Surg Pathol. 2014 Feb; 38(2):215–23.
14 cases		Cronkhite–Canada syndrome	Nutritional supplementation ± corticosteroids Four surgical resections (one partial colectomy, one subtotal colectomy, and two laparoscopic total colectomy)	Dig Dis Sci. 2012 Feb; 57(2):496–502.

single case report, and further case accumulation and investigation are needed.[6]

In terms of surgical techniques, the reports we searched included several cases that underwent total proctocolectomy for polyposis with protein-losing enteropathy, but it was not mentioned whether laparoscopically or laparotomy were performed. It has been reported that laparoscopic total proctocolectomy can be performed safely, although the operative time is longer than that of open surgery in a meta-analysis.[8] Laparoscopic total proctocolectomy is often performed on patients with ulcerative colitis who are elderly or have severe inflammation and poor general condition. Many patients with acute ulcerative colitis have poor nutritional status. A meta-analysis found that laparoscopic surgery was superior to open surgery for patients with acute ulcerative colitis in terms of postoperative fasting period, postoperative hospital stay, and overall complication rate.[9] In this case, the patient had hypoalbuminemia coursed by protein-losing enteropathy; however laparoscopic total colorectal resection was safely performed, and the patient had a good outcome. Based on a literature search using PubMed, to the best of our knowledge this is the first report of successful laparoscopic surgery for a case of FAP with protein-losing enteropathy.

In conclusion, this report describes a case of FAP with protein-losing enteropathy who underwent laparoscopic total proctocolectomy, which resulted in improvement of protein leak as well as cancer treatment.

AUTHOR CONTRIBUTIONS

Hiroki Tubakihara, Hiroshi Sawayama, Yuji Miyamoto, Katsuhiro Ogawa, Mayuko Ohuchi, Hiroki Tubakihara, Naoya Yoshida, and Hideo Baba contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Tubakihara and Sawayama. All authors have read and approved the final article.

ACKNOWLEDGMENTS

The authors thank Dr. Yoshihiro Komohara for his pathological diagnosis. We thank Editage (www.editage.com) for English language editing.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare and have received no financial support for this case report.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS APPROVAL

Ethical approval was not required for this case report. All procedures were performed in accordance with the Declaration of Helsinki.

CONSENT TO PARTICIPATE

Informed consent for publication of this case report and accompanying images were obtained from the participant.

ORCID

Hideo Baba https://orcid.org/0000-0002-3474-2550

REFERENCES

1. Jasperson KW, Tuohy TM, Neklason DW, Burt RW. Hereditary and familial colon cancer. *Gastroenterology*. 2010;138:2044-2058.
2. Nagra N, Dang S. Protein losing enteropathy. *StatPearls*, Treasure Island, FL. 2021.
3. Bettington M, Brown IS, Kumarasinghe MP, de Boer B, Bettington A, Rosty C. The challenging diagnosis of Cronkhite–Canada syndrome in the upper gastrointestinal tract: a series of 7 cases with clinical follow-up. *Am J Surg Pathol*. 2014;38:215-223.
4. Johansson J, Sahin C, Pestoff R, et al. A novel SMAD4 mutation causing severe juvenile polyposis syndrome with protein losing enteropathy, immunodeficiency, and hereditary haemorrhagic telangiectasia. *Case Rep Gastrointest Med*. 2015;2015:140616.
5. Tamura K, Matsuda K, Yokoyama S, et al. Successful laparoscopic resection for cap polyposis: case report, literature review. *Surg Case Rep*. 2018;4:69.
6. Miyamoto Y, Muguruma N, Kimura T, et al. Protein-losing enteropathy in a patient with familial adenomatous polyposis and advanced colon cancer. *Clin J Gastroenterol*. 2016;9:134-139.
7. Waldmann TA, Broder S, Strober W. Protein-losing enteropathies in malignancy. *Ann N Y Acad Sci*. 1974;230:306-317.
8. Ahmed Ali U, Keus F, Heikens JT, et al. Open versus laparoscopic (assisted) ileo pouch anal anastomosis for ulcerative colitis and familial adenomatous polyposis. *Cochrane Database Syst Rev*. 2009;1:CD006267.
9. Wu XJ, He XS, Zhou XY, Ke J, Lan P. The role of laparoscopic surgery for ulcerative colitis: systematic review with meta-analysis. *Int J Colorectal Dis*. 2010;25:949-957.

How to cite this article: Tubakihara H, Sawayama H, Komohara Y, et al. A case of familial adenomatous polyposis with protein-losing enteropathy treated by laparoscopic total colorectal resection: A literature review. *Asian J Endosc Surg*. 2023;16(1):77-81. doi:10.1111/ases.13099