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Cronkhite-Canada Syndrome Associated with Carcinoma of the Sigmoid Colon: Report of a Case

NAOKI NAKATSUBO,[1] RINICHIRO WAKASA,[1] KATSUMI KIYOSAKI,[1] KAZUHIRO MATSUI,[2] and FUMIO KONISHI[3]

[1]Department of Surgery, Himi City Hospital, 31-9 Saiwai-cho, Himi-shi, Toyama 935, Japan
[2]Department of Pathology, Toyama Medical and Pharmaceutical University, 2630 Sugitani, Toyama-shi, Toyama 930-01, Japan
[3]Department of Surgery, Jichi Medical School, 3311-1 Yakushiji, Minamikawachi-machi, Kawachi-gun, Tochigi 329-04, Japan

Abstract: Cronkhite-Canada syndrome is generally accepted as being a benign disorder. We herein present a 66-year-old-male patient with Cronkhite-Canada syndrome who had a carcinoma of the sigmoid colon along with multiple colonic polyps, which included juvenile-type polyps, adenomas, and hyperplastic polyps. In the world literature, there have been 34 cases of Cronkhite-Canada syndrome associated with colorectal carcinoma among the 280 reported cases of this syndrome. This report thus adds to the growing evidence that Cronkhite-Canada syndrome may be a premalignant condition for colorectal carcinoma. A periodic examination of the colon is therefore advised in order to detect any development of colorectal carcinoma at an early stage.

Key Words: Cronkhite-Canada syndrome, colonic cancer

Introduction

Cronkhite-Canada syndrome, first described by Cronkhite and Canada in 1955, is a rare form of non-hereditary gastrointestinal polyposis associated with diarrhea, hypoproteinemia, and ectodermal changes consisting of hyperpigmentation, alopecia, and atrophy of the nails.[1] Since this first description, a number of similar cases have been reported.[2,3] Although Cronkhite-Canada syndrome is generally accepted to be a benign disorder,[4] we herein report a case of this syndrome in which carcinoma of the sigmoid colon was found together with multiple colonic polyps.

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Case Report

A 66-year-old man was admitted to Himi City Hospital in May 1933 with a 2-month history of dysgeusia, appetite loss, scalp hair loss, and hyperpigmentation. His family history was unremarkable for bowel diseases. Physical examination revealed a thin, well-developed male with partial loss of scalp hair, generalized hyperpigmentation, and onychodystrophy. There were no abnormal signs in the chest, and there was no tenderness, nor any masses or ascites in the abdomen. Total serum protein was 5.8 g/dl, and albumin was 2.8 g/dl. The serum electrolytes blood urea nitrogen (BUN), creatinine, and liver enzymes were all normal. The immunological fecal occult blood reaction (reverse passive hemagglutination) was positive. The serum carcinoembryonic antigen (CEA) was 2.2 ng/ml, the normal being less than 5.0 ng/ml. A barium meal examination revealed multiple polyps in the stomach. The esophagus and the duodenum were normal. A barium enema examination revealed multiple polyps throughout the colon and a protruding lesion in the sigmoid colon.

On gastroscopy, numerous reddish sessile polyps with edematous mucosa were observed in the stomach. A gastric polyp was removed endoscopically and was histologically defined as a hyperplastic polyp. Colonoscopy revealed a dense growth of small sessile polyps throughout the colon. Biopsy specimens of these polyps showed histological features consistent with juvenile polyps. An ulcerated tumor was observed in the sigmoid colon. The histological findings of the biopsied specimens from the tumor of the sigmoid colon revealed adenocarcinoma.

A laparotomy was performed in July 1993. The stomach and the colon were thickened on palpation. Sigmoidectomy and lymph node dissection were carried out to remove the sigmoid colon cancer (Fig. 1). The surgical specimen revealed Dukes A well-differentiated adenocarcinoma with invasion in the muscularis propria

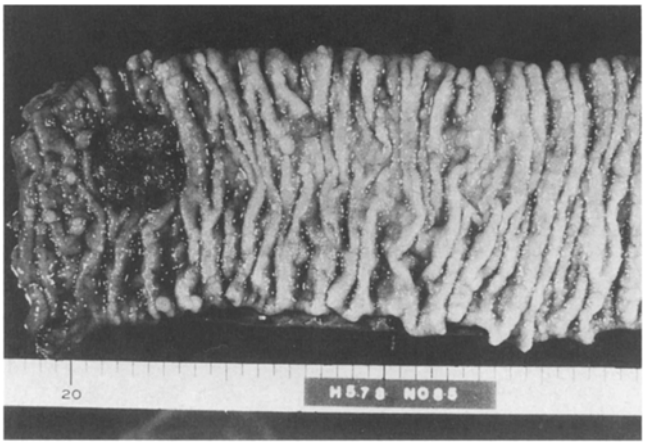

Fig. 1. Gross appearance of the resected specimen. An ulcerating tumor was observed in the sigmoid colon. Multiple polyps of varying sizes were observed in the resected sigmoid colon.

and contiguous polypoid lesions which showed histological features consistent with juvenile polyps (Fig. 2). In addition to these lesions, multiple polyps of varying sizes were also seen in the resected sigmoid colon. Histologically, these polyps were predominantly juvenile-type (Fig. 3), some were adenomas (Fig. 4), and some were hyperplastic polyps.

During the follow-up for about 5 months after the operation, the nail atrophy and dysgeusia gradually improved, and simultaneously the polyps in the gastrointestinal tract decreased in number. On colonoscopy in November 1993, four reddish sessile polyps were seen in the ascending colon. These polyps were

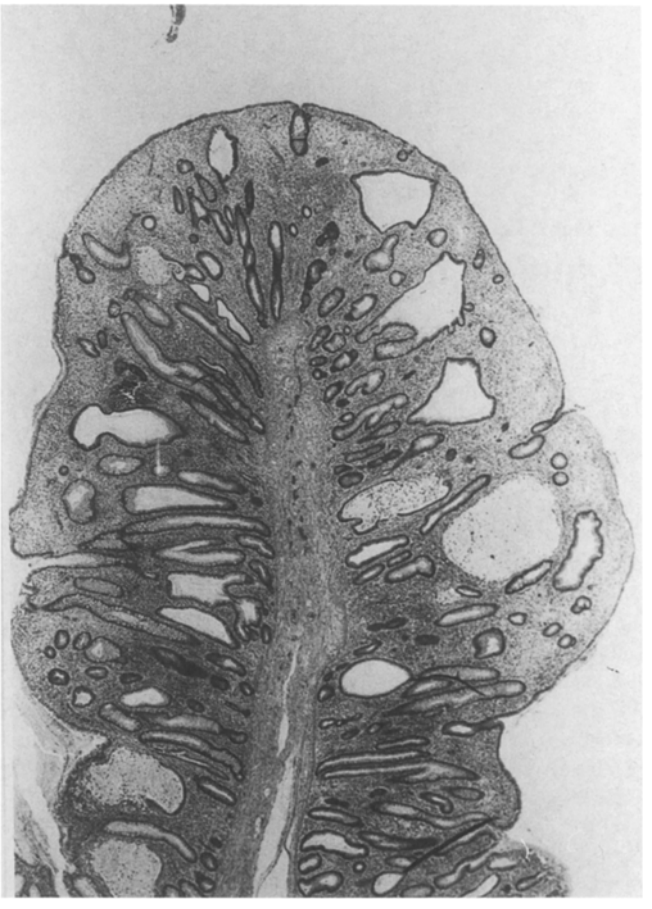

Fig. 3. Histology of a sessile polyp showed typical features of a juvenile-type polyp. (H&E, ×10)

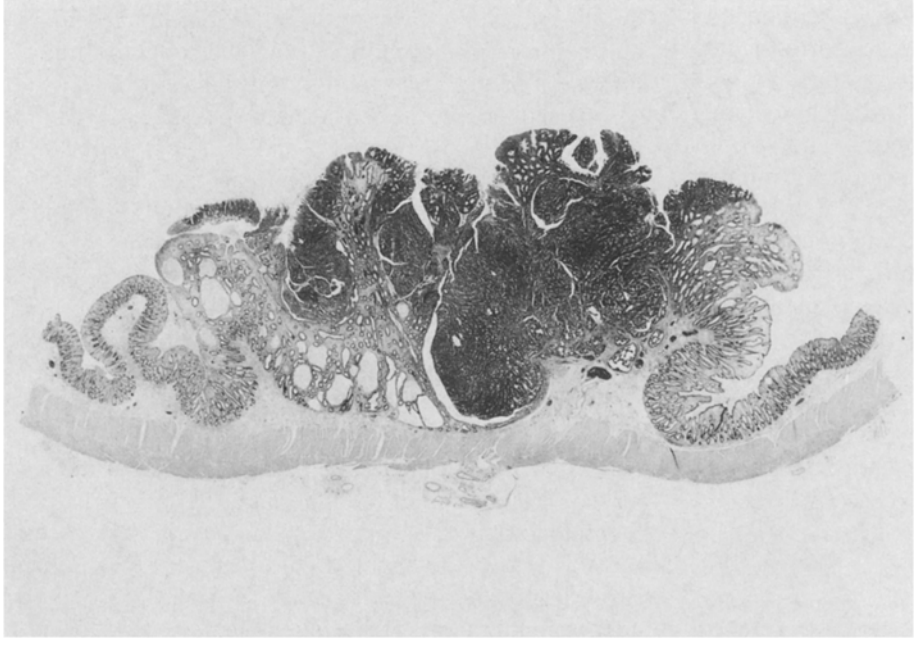

Fig. 2. Histology of the ulcerating tumor revealed well-differentiated adenocarcinoma, and contiguous polypoid lesions showed histological features consistent with juvenile-type polyps. (H&E, ×10)

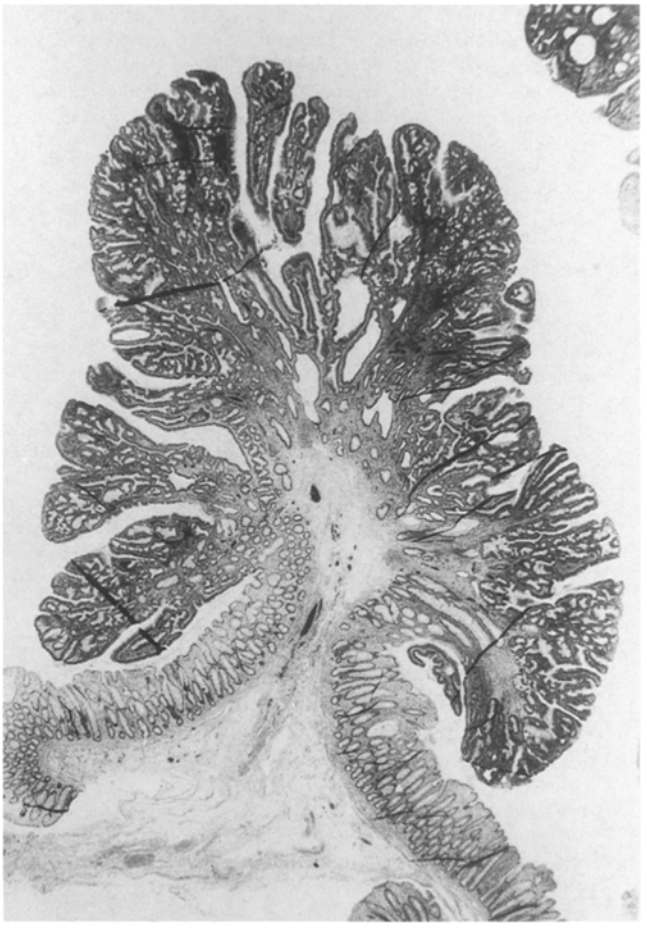

Fig. 4. Histology of a sessile polyp showed typical features of an adenoma. (H&E, ×10)

removed endoscopically and were histologically found to be adenomas. Two years after the operation the patient was alive without any recurrence of the carcinoma or exacerbation of Cronkhite-Canada syndrome.

Discussion

Cronkhite-Canada syndrome was first described in 1955 as a generalized gastrointestinal polyposis with ectodermal changes consisting of alopecia, hyperpigmentation, and onychodystrophy without any evidence of genetic transmission.[1] The major presenting symptom is watery diarrhea. Dysgeusia, anorexia, weight loss, and peripheral edema due to hypoproteinemia are also frequently present.[4] In our patient, scalp hair loss, hyperpigmentation, and onychodystrophy developed several months before admission. However, the patient did not have diarrhea, which was considered to be an exceptional clinical feature for Cronkhite-Canada syndrome. The observation that the polyps of the gastrointestinal tract which were present in our patient regressed markedly after the operation suggested that these lesions are potentially reversible.

In the original description by Cronkhite and Canada, the gastrointestinal lesions were reported to be adenomatous polyps.[1] In recent reports, however, they have been reported to be juvenile-type polyps,[2] and generally these polyps have been considered to be nonneoplastic in nature.[3] In 1976, Da Cruz reported an association of this syndrome with cancer of the colon.[5] Since then 33 cases associated with colon cancer have been reported worldwide[5–26] (Table 1). Up to the end of 1993, 280 cases of Cronkhite-Canada syndrome had been reported in the world literature.[27] The rate of association with colorectal cancer was 12.5%. We analyzed the 34 previously reported cases of Cronkhite-Canada syndrome associated with colorectal cancer. There were 28 men and 6 women ranging in age *from* 49 to 86 (mean 61.3) years. The histological types of the associated polyps in the 34 cases were juvenile-type polyp in 28 cases,[6–10,12–23,24–26] adenoma in 14 cases,[5,13–15,20,22] and hyperplastic polyp in 4 cases.[10,11,23] In our case there were three types of ployps: juvenile-type, adenomas, and hyperplastic polyps. Of the reported cases of Cronkhite-Canada syndrome with colorectal cancer, 41% showed association with ademoma or adenomatous change.[5,13–15,20,22,] In some of the reported cases, adenomatous epithelium was seen at the tip of a juvenile-type polyp and a clear transition to adenomatous proliferation and carcinomatous transformation were demonstrated.[13,14] In our case, the surgical specimen revealed Dukes A adenocarcinoma and contiguous polypoid lesions which showed histological features

Table 1. Reported cases of Cronkhite-Canada syndrome associated with colorectal cancer

Number of cases	34
Sex Male:Female	28:6
Age	49–85 (mean 61.3)
Histology of the associated polyps	
Juvenile-type	28
Adenoma	14
Hyperplastic polyp	4
Unknown	2
Site	
Rectum	12
Sigmoid	7
Transverse	7
Ascending	5
Cecum	3
Unknown	2
Depth of invasion	
Mucosa	6
Submucosa	1
Muscularis propria	13
Extramuscular layer	7

consistent with juvenile-type polyps. No histological evidence was observed, thus suggesting the process of an adenoma-carcinoma sequence in our case.

Cronkhite-Canada syndrome has been considered to be a benign condition: however, some cases may also represent a premalignant condition and thus the present report adds to the growing evidence of this possibility. We therefore recommend that patients with Cronkhite-Canada syndrome should have their colon and rectum screened carefully, so that appropriate surgical therapy can be carried out at an early stage if any malignancy should appear.

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