Squamous cell carcinoma of the rectal stump in a patient with ulcerative colitis

Report of a case and review of the literature[1]

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A 52-year-old man presented with squamous cell carcinoma of the rectal stump. Severe ulcerative colitis had developed 10 years before diagnosis and he had had to undergo subtotal colectomy and ileostomy. This tumor is a rare complication of ulcerative colitis representing 1% to 2% of all cancers complicating ulcerative colitis, a relative incidence 50 to 100 times than in the general population. It is predominantly located at the rectum, but may involve other areas of the colon. As in adenocarcinoma, squamous cell carcinoma of the large bowel is seen almost exclusively in early onset, extensive or total colitis of nine years or more duration. If treated early, long-term survival is possible. In some patients, a second primary tumor may develop either in the colon or elsewhere. It is suggested that the development of squamous cell carcinoma of the large bowel requires chronic irritation of the colonic mucosa in patients with some predisposing genetic background or disturbed immune system. The literature on squamous cell carcinoma of the large bowel associated with ulcerative colitis is reviewed.

Index terms: Case reports · Colitis, ulcerative · Rectal neoplasms

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Squamous cell carcinoma of the large bowel is a rare disease. Since its first description by Schmidtmann in 1919,[1] only a few cases have been reported.[2–10] Its prevalence is estimated to be 0.025% of all malignant tumors of the colorectum.[3–5] The tumor may arise either from normal colonic mucosa or be associated with various preexisting disorders, such as schistosomiasis,[10–11] chronic ulcerative colitis,[2–4,12,13] and colonic duplication.[6] No case in association with Crohn's disease of the colon has been reported. Previous reports of squamous cell carcinoma of the large bowel in ulcerative colitis were of patients with intact colons. We describe squamous cell carcinoma of the rectal stump that developed 10 years after subtotal colectomy and ileostomy, which had been required for the treatment of a fulminant ulcerative colitis. In addition, our patient had a transitional cell carcinoma of the bladder. We also review the literature of squamous cell carcinoma of the large bowel associated with ulcerative colitis.

Case report

A 42-year-old man was admitted to the Cleveland Clinic on August 30, 1963, with a six-week history of diarrhea, rectal bleeding, abdominal distension, and weight loss. He had enjoyed good health previously. His family history was significant in that his mother had died of gastric cancer and his father of cancer of an unknown site. His blood pressure was 100/60 mm Hg and pulse rate 100/minute. He ap-

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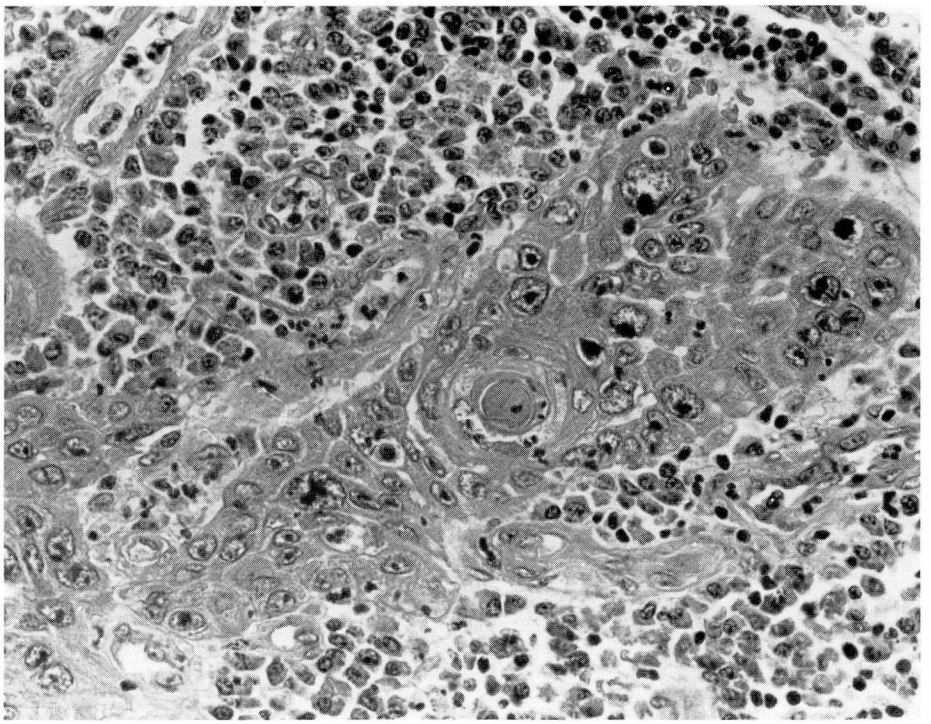

Fig. Biopsy specimen of the rectal tumor demonstrating infiltrating squamous-cell carcinoma; squamous pearl is seen in the center of the field (hematoxylin and eosin stain, ×250).

peared acutely and chronically ill, dehydrated, and stuporous. His abdomen was tender and moderately distended. At rectal examination, several polypoid masses were felt. Proctosigmoidoscopy revealed diffuse ulceration of the mucosa with numerous pseudopolyps. The chest radiograph was normal. A plain radiograph of the abdomen showed moderate dilatation of the right colon. He was treated with fluid, electrolytes, blood transfusion, and adrenocorticotropic hormone (ACTH) with no improvement. The patient had to undergo subtotal colectomy and ileostomy on October 23, 1963, for severe colitis. He did well postoperatively and was discharged from the hospital on December 3, 1963. At follow-up, he had gained 30 pounds and was complaining of a persistent foul-smelling drainage from the colectomy incision with occasional seepage of blood and mucopus from the rectal stump. He was rehospitalized on July 27, 1973, for dysuria, and continued to have intermittent discharge from the fistula. At physical examination, he appeared chronically ill, with some discharge from the incision site. Rectal examination revealed a large mass in the rectal stump, but no communication was found between the fistula and the tumor. Cystoscopy showed benign prostatic hypertrophy and a 2-mm superficial tumor posterior to the right ureteral orifice. Biopsy and fulguration of the tumor were performed. Proctoscopy revealed inactive colitis in the distal rectum and a large fungating mass about 5 cm above the anorectal line. The biopsy specimen of the rectal tumor showed invasive, moderately differentiated keratinizing squamous cell carcinoma (*Figure*). Biopsy of the bladder tumor revealed stage 0 transitional cell carcinoma. No evidence of squamous cell carcinoma in any other part of the body was found. The patient refused surgery, and received 5,000 rads cobalt irradiation of the rectal tumor in five weeks. He did not return to the clinic after radiotherapy and died in December 1974 of metastatic carcinoma. No autopsy was performed.

Discussion

Squamous cell carcinoma of the large bowel is estimated to represent 0.025% of all malignant tumors of the large bowel.[3] The incidence seems to be much higher when it is associated with ulcerative colitis: Bargen and Gage[12] found 4 cases of squamous cell carcinoma of the colon in 178 cases of colonic cancers arising in 7,000 patients with ulcerative colitis, an incidence of 2%. In our review of 1,248 cases of ulcerative colitis seen at the Cleveland Clinic, we found 82 cases of colorectal cancer, all but one (the present patient) with adenocarcinoma, an incidence of 1.2%. Therefore, the incidence of squamous cell carcinoma of the large bowel seems to be 50 to 100 times higher when associated with ulcerative colitis.

To diagnose a primary squamous cell carci-

Table. Details of reported cases of squamous cell carcinoma of the large bowel in ulcerative colitis

Author	No.	Sex	Age at Onset of Colitis	Duration of CUC to Diagnosis of Carcinoma	Site of Carcinoma	Treatment of Carcinoma	Survival	Comments
Bargen and Gage[12]	1	...	34	...	Ascending colon and other segments and rectum	...	...	Grade 3 Broders
Bargen and Gage[12]	2	...	38	...		...	...	Grade 3 Broders
Bargen and Gage[12]	3	...	41	...		...	...	Grade 3 Broders
Bargen and Gage[12]	4	...	51	...		...	...	Grade 3 Broders
Zirkin and McCord[2]	5	F	34	10	Rectum	Colectomy	2 yr	Dukes B
Hohm and Jackman[13]	6	F	26	9	Rectum	Colectomy	13 yr	Dukes B
Hohm and Jackman[13]	7	F	26	25	Rectum	Radical posterior resection	21 yr	? Dukes B
Comer et al[3] and Comer[14]	8	...	...	...	Upper rectum	Colectomy	16 yr	Dukes-Kirklin stage B1
Comer et al[3] and Comer[14]	9	...	...	...	Descending colon	Colectomy	3 yr	Dukes-Kirklin stage A
Comer et al[3] and Comer[14]	10	...	...	...	Upper rectum	Colectomy	Died 2 yr *postop*	Dukes-Kirklin stage C
Crissman[4]	11	M	21	20	Transverse colon	Colectomy	Died 6 mo postop	Dukes stage D, plus rectal adenocarcinoma
Mir-Madjlessi and Farmer	12	M	42	10	Rectal stump	Radiation therapy	Died 1 yr postop	Dukes D+ bladder tumor

CUC = chronic ulcerative colitis.

noma of the large bowel, the following requirements must be met[5]: (*a*) there must be no evidence of squamous cell carcinoma in any other organ, (*b*) the squamous cell carcinoma of the rectum should not arise from the anal squamous epithelium, and (*c*) the affected bowel should not be involved in the squamous-lined fistula tract. Our patient satisfied the first two criteria. Whether an enterocutaneous fistula contributed to the development of squamous cell carcinoma in our patient cannot be ruled out entirely, but seems unlikely because there was no apparent connection between these two lesions.

Including our own patient, only 12 cases of squamous cell carcinoma of the colorectum with preexisting ulcerative colitis have been reported to date to our knowledge.[2–4,12,13] but some details are not available for every patient (*Table*). Bargen and Gage,[12] describing 178 patients who developed colorectal cancer as a complication of ulcerative colitis, noted 4 with squamous cell carcinoma. The cancer involved "the ascending colon as well as in other segments of the large intestine, particularly in the rectum. . . ." They were 34, 38, 41, and 51 years old, respectively, and all had Broders' grade III tumors.

Zirkin and McCord[2] described a 34-year-old woman with a 10-year history of extensive ulcerative colitis who had had a fistula-in-ano operation. The patient underwent colectomy. Pathologic examination revealed a narrowed rectum, but no apparent gross tumor. However, microscopy from the rectal area revealed various degrees of change from simple nonkeratizing squamous cell metaplasia to an invasive tumor involving the submucosa and lymphatic channels.

There was also some epithelial dysplasia. The patient was alive and well two years after operation.

Hohm and Jackman[13] described 2 patients, the first, a 26-year-old woman with extensive colitis in whom squamous cell carcinoma of the rectum developed nine years after the onset of colitis. She underwent total colectomy in two stages and was well 13 years postoperatively. The second patient was a 26-year-old woman with total colitis in whom squamous cell carcinoma of the rectum developed, which also involved the vagina 25 years after the onset of colitis. She underwent a radical posterior resection and was well 21 years postoperatively. The last patient had a diverting ileostomy at the beginning of her illness, but it is not clear whether her ileostomy was ever taken down.

Comer et al[3,14] described 8 patients with squamous cell carcinoma of the colon and upper rectum (7 cm above the anorectal line). Three had had a history of ulcerative colitis, and 2 had multiple tumors. Tumors were located in the upper rectum in 2 patients and at the descending colon in 1. One patient with class C Dukes-Kirklin tumor died two years postoperatively; this patient had an adenocarcinoma of the splenic flexure, and the finding of a multicentric squamous cell carcinoma of the descending colon was incidental. The other 2 patients, one with class A and the other with class B Dukes-Kirklin tumors, were alive three and 16 years postoperatively, respectively.

Crissman[4] described 6 patients with squamous cell carcinoma of the colon, one of whom had ulcerative colitis. This 41-year-old man had extensive ulcerative colitis with a squamous cell tumor of the transverse colon, which developed 20 years after the onset of colitis. The patient underwent colectomy and died six months later. The resected colon showed a mixed squamous and glandular tumor infiltrating the muscularis propria, as well as lymphatic and vascular channels. The lymph nodes showed metastatic adenocarcinoma. At autopsy, a second primary adenocarcinoma arising from a villous adenoma was found in the rectum. The liver was involved with a mixed squamous-glandular tumor, probably metastatic. However, the author could not exclude the possibility of its being a cholangiocarcinoma arising independently.

Our 42-year-old male patient presented with fulminant colitis and had to undergo subtotal colectomy and ileostomy. Squamous cell carcinoma of the rectal stump developed 10 years after surgery. Although he had a chronic enterocutaneous fistula, no communication between the fistula and the tumor was apparent. He underwent cobalt irradiation and died one year later of metastatic carcinoma. Of note was the finding of a concomitant stage 0 transitional cell carcinoma of the bladder.

Overall, we found that squamous cell carcinoma of the colorectum developed in a group of colitis patients whose disease had started at a relatively young age, was extensive or total, and had lasted nine years or more. These features are also found when adenocarcinoma develops as a complication of ulcerative colitis.[15] Excluding the patients of Bargen and Gage[12] for lack of detailed information, the tumor was located at the rectum in at least 6 patients, descending colon in 1, and in the transverse colon in 1. Compared with the patients with squamous cell carcinoma of the large bowel, in general, we note the latter group to be older. Indeed, Williams et al,[5] in their review of 39 patients with squamous cell carcinoma of the colon found a mean age of 55 years as opposed to 35 years in our group, and the tumors were located in the following areas: rectum, 24; sigmoid colon, 5; descending colon, 1; transverse colon, 2; hepatic flexure, 1; ascending colon, 2; and cecum, 4. Biologically, these tumors behave in a manner not dissimilar from the more common adenocarcinoma. Indeed, if diagnosed early and appropriately resected, long survival may ensue.

The histogenesis of squamous cell carcinoma of the large bowel is the subject of an unresolved controversy. Basically, four theories are proposed[5] including (*a*) squamous proliferation of uncommitted reserve or basal cells following mucosal injury; (*b*) development of squamous cell carcinoma from squamous cell metaplasia of the colonic mucosa subjected to chronic irritation; (*c*) squamous proliferation of embryonal nests of ectodermal cells, which may have persisted in an ectopic site after embryogenesis; and (*d*) evolution of squamous cell carcinoma from common adenoma of the colon. Chronic irritation seems to be of particular significance as documented by the association of this tumor with ulcerative colitis with a relative incidence of 20 to 100 times higher than in the general population, as well as

schistosomiasis,[10–11] radiation exposure,[16] and homosexuality.[17] However, contact of the fecal stream with the colonic mucosa may not be necessary, as seen in our patient with squamous cell carcinoma of the rectal stump. Chronic infection or intestinal bacterial proliferation may play a more important role. Also, a high proportion of patients with this tumor have been homosexuals,[7] or are natives of India where malnutrition is widespread.[18] These findings may indicate the existence of an underlying disturbed immune system, or genetic background as a predisposing factor.

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