

CARCINOMA OF THE COLON IN CHRONIC ULCERATIVE COLITIS

Report of Two Five-Year Survivals

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IT is generally understood that carcinomas of the colon arising in the course of ulcerative colitis are highly malignant and invasive,^{1,2} metastasize early, and have a short survival period following resection. The following 2 cases are reported because the patients are alive and well, without evidence of recurrent neoplasm for 5 years.

Case Reports

Case 1. A 56 year old white man was seen for the first time at the Clinic on January 21, 1948. He had suffered from a mild chronic ulcerative colitis involving the entire colon and rectum for a period of 10 years. Frequent roentgenograms were taken of the colon and proctoscopic examinations were made during this interval. At no time had his symptoms been severe enough to warrant surgical intervention. During the preceding year he had noted frequent bleeding from the rectum, after which he submitted to examinations at closer intervals. Six months prior to admission to the hospital, several ulcerating lesions were found in the rectum. Repeated biopsies revealed adenocarcinoma. The patient was admitted to the hospital on February 10, 1948, at which time abdominoperineal resection was performed. His convalescence was uneventful.

Pathology: The open rectum and sigmoid colon revealed considerable thickening of the walls with loss of the usual mucosal folds. The mucosa was finely granular and manifested all the characteristics of chronic ulcerative colitis. Eight cm. above the dentate line the mucosal surface presented 5 rounded elevations with finely granular surfaces, the largest of which was 1.5 cm. in diameter and raised above the mucosa for approximately 1 cm. These areas were firm and sections revealed them to be papillary adenomata of the flat type with adenocarcinoma extending through the muscularis mucosa into the submucosa but without penetration of the muscularis. Eight lymph nodes were recovered from the mesentery of the rectum and sigmoid colon and none were found to be involved with secondary neoplasm.

At the present time this patient has mild symptoms of ulcerative colitis, but he has refused to undergo colectomy with ileostomy. We feel that he will in all probability develop another carcinoma in the colon, should he live long enough. He has now survived 5 years since the carcinoma was detected.

Case 2. A 46 year old white woman was seen at the Clinic for the first time on April 11, 1947. She was known to have had chronic ulcerative colitis involving the entire colon and rectum for a period of 5 years. Roentgenograms taken elsewhere were said to have revealed mild ulcerative colitis. Eight months prior to admission laparotomy was performed by the referring physician and a cecostomy was made to divert the fecal stream. After this a gain was apparent in weight and strength. However, 4 months before admission to the Cleveland Clinic Hospital she began to experience lower abdominal cramps, particularly on the left side, with an increased urge to move her bowels through the rectum and with the passage of small amounts of blood, mucus, and pus. Films of the colon made at home in July, 1946, were said to have revealed segmental ulcerative colitis of the sigmoid colon. After admission to the Clinic hospital x-rays made of the colon were reported as showing evidence of mild chronic ulcerative colitis throughout. Proctosigmoidoscopic examination revealed minimal changes in the mucosa, suggesting ulcerative colitis. Because of the severity of the symptoms, a right colectomy with end ileostomy was performed on April 23, 1947.

The right side of the colon revealed a typical nonspecific chronic ulcerative colitis with thickened and edematous mucosa. Small pinpoint ulcers were noted along the lines of the mesenteric attachment. During the patient's convalescent period there was a copious amount of blood from the rectum and the left-sided cramps were severe and continuous. Three months later she was readmitted for removal of the left colon. She stated that during the interim she had noted frequent passage of blood and mucous from the rectum and experienced a nagging pain in the left side of the abdomen. The latter persisted most of the time. On July 15, 1947, left colectomy was performed and, as the colon was rotated from the abdomen, a small papillary carcinoma was palpated in the upper sigmoid colon. Abdominoperineal resection was performed 3 months later. During the period between left colectomy and this procedure, the patient made a rapid recovery, with accompanying gain in weight, and there were no longer any symptoms to suggest either ulcerative colitis or carcinoma. The adenocarcinoma of the sigmoid colon was of the mucinous type, with but slight extension into the pericolic fat. One of 5 lymph nodes recovered from the mesentery was involved with secondary neoplasm. Sections of the colon revealed ulcerative colitis in the inactive phase. The patient was last seen in July, 1952, and has survived 5 years since the resection was performed. She is well and without evidence of metastases. We consider most of her symptoms to have been due to the carcinoma rather than to the diffuse ulcerative colitis.

Discussion

The preceding 2 cases merit attention for several reasons. First, it is rare for patients with carcinoma arising in ulcerative colitis to survive 5 years. Such neoplasms are usually highly malignant, metastasizing before operation. In addition, a neoplasm may be rather difficult to detect because the symptoms and even roentgenologic changes may be attributed to an exacerbation of the colitis, as demonstrated in case 2.

Ulcerative colitis has usually preceded the development of carcinoma by a number of years; in our series³ by an average of 16 years. The first patient reported here had ulcerative colitis for 10 years and the other for only 5 years. A 5 year history of colitis prior to the development of malignancy is relatively short and unusual. Neither patient had polyps nor pseudopolyps. While many

of the neoplasms of the colon in patients with ulcerative colitis appear to be associated with pseudopolyposis, some may develop malignancy without them. Absence of pseudopolyp or polyp, therefore, is no indication that the patient will not develop carcinoma of the colon. Although the pathogenesis of the neoplasm is believed to be chronic inflammation and irritation resulting in hyperplasia, proliferation, and finally carcinoma, the exact mechanism is unknown. However, it seems definite that chronic ulcerative colitis has a prefatory relationship to colonic cancer.

More recent reports essentially agree that the incidence of carcinoma is higher in patients with ulcerative colitis than in normal persons. Bargen⁴ has repeatedly reported a series of cases in which the incidence of carcinoma was greater than would normally be expected. He found the incidence to be 3.2 per cent in a series of 874 patients with ulcerative colitis. Jackman et al.⁵ found six instances of malignancy in 95 cases of ulcerative colitis in children. Multiple carcinomas of the colon have been reported in 7 of 27 patients by Bargen and Dixon⁶ and in 8 of 26 cases of ulcerative colitis by Sauer and Bargen.⁷ We³ found, from 1945 through 1949, that 3.8 per cent of our patients with ulcerative colitis developed cancer. The actual incidence in these patients probably is higher than the quoted figures and one needs only to follow them long enough. Since the symptoms of the two conditions can be so similar, a physician may believe that a patient has died from an exacerbation of ulcerative colitis, while actually the cause of death may have been an undetected neoplasm of the colon; only total colectomy or postmortem examination would disclose such a neoplasm. We agree with Cattell and Boehme,⁸ it would seem that as the percentage of operations increases, particularly colectomy, the number of carcinomas found would increase also. We must be conscious of the fact that carcinoma of the colon is more frequent in patients with ulcerative colitis, that the carcinoma is highly malignant, and that the symptoms of the carcinoma may simulate those of the colitis.

The question arises: What patients with ulcerative colitis are most likely to develop carcinoma? Certainly carcinoma is not apt to develop in a patient whose infection is limited to the rectum and whose disease promptly subsides on medical treatment. The development of carcinoma is dependent on three factors: the degree of infection or inflammation, the amount of colon involved, and the duration of the disease. The more severe the infection, the more extensive the involvement of the colon; and the longer the colitis has existed, the more likely that the patient will develop carcinoma. Most of the patients we have seen with carcinoma arising in ulcerative colitis have had severe involvement, usually of the entire colon. Likewise, most have had chronic ulcerative colitis for a considerable time, an average of 16 years in our series.³

Because of the highly malignant nature of the neoplasm in these patients, by the time such a lesion can be demonstrated by roentgenographic examination, the patient is usually incurable. Consequently, it is of little value to obtain yearly barium enema examinations in order to detect such a lesion at an early stage. The only way to treat carcinoma of the colon in patients with ulcerative

colitis is to prevent the neoplasm from developing by prophylactic colectomy in those patients most likely to develop malignancy. With simultaneous ileostomy and subtotal colectomy,⁹ the patient requires only 1 operation, or, at the most, if abdominoperineal resection is done subsequently, only 2 operations. The mortality of simultaneous ileostomy and subtotal colectomy in nontoxic cases since 1948 at the Cleveland Clinic has been no deaths in 50 operations. It can be seen that the operative treatment has greatly improved and the operative mortality has been reduced to the extent that the hazard of surgery is no longer a detriment.

Many patients with ulcerative colitis respond to medical treatment with healing of the ulcers and without evidence of recurrence. This is particularly true of those patients with the disease limited to the rectum and sigmoid colon. One is not concerned about these patients having a high incidence of carcinoma of the colon, and it is not our purpose to urge colectomy in every patient with ulcerative colitis. At the Cleveland Clinic¹⁰ we have operated on only 13 per cent of these patients. We believe that practically every patient should have a thorough trial on medical treatment before surgery is recommended.

Because of the increased incidence of highly malignant neoplasms in patients with ulcerative colitis, we believe that serious consideration of subtotal colectomy is indicated under the following conditions:

1. Chronic forms of colitis that have not responded to medical treatment, and have been present for a considerable length of time. Most of these patients have involvement of the entire colon. The more severe, protracted and chronic the disease, the more urgent the operation.

2. The presence of polyps or pseudopolyps. While carcinoma may develop without polyps, as in the two cases presented, neoplasm develops more frequently in those patients with ulcerative colitis who do have polyps. Colectomy is indicated in any patient with ulcerative colitis and pseudopolypsis.

References

1. Kasich, A. M., Weingarten, B. and Brown, M. L.: Malignant degeneration in ulcerative colitis; report of 7 cases. *Med. Clin. North America* 33:1421 (Sept.) 1949.
2. Lyons, A. S. and Garlock, J. H.: The relationship of chronic ulcerative colitis to carcinoma. *Gastroenterology* 18:170 (June) 1951.
3. Gleckler, W. J. and Brown, C. H.: Carcinoma of colon complicating chronic ulcerative colitis. *Gastroenterology* 14:455 (April) 1950.
4. Bargaen, J. A., Jackman, R. J. and Kerr, J. G.: Studies on life histories of patients with chronic ulcerative colitis (thrombo-ulcerative colitis) with some suggestions for treatment. *Ann. Int. Med.* 12:339 (Sept.) 1938.
5. Jackman, R. J., Bargaen, J. A. and Helmholz, H. F.: Life histories of 95 children with chronic ulcerative colitis; statistical study based on comparison with whole group of 871 patients. *Am. J. Dis. Child.* 59:459 (March) 1940.
6. Bargaen, J. A. and Dixon, C. F.: Chronic ulcerative colitis with associated carcinoma; progress in management. *Arch. Surg.* 30:854 (May) 1935.
7. Sauer, W. G. and Bargaen, J. A.: Chronic ulcerative colitis followed by carcinoma; report of 26 cases. *Proc. Staff. Meet., Mayo Clin.* 19:311 (June 14) 1944.
8. Cattell, R. B. and Boehme, E. J.: Chronic ulcerative colitis complicated by carcinoma

- of colon and rectum. *S. Clin. North America* **26**:641 (June) 1946.
9. Crile, G., Jr. and Turnbull, R. B., Jr.: The treatment of chronic ulcerative colitis. *Cleveland Clin. Quart.* **18**:239 (Oct.) 1951.
 10. Brown, C. H., Gleckler, W. J. and Jones, T. E.: Surgical treatment of chronic nonspecific ulcerative colitis. *Gastroenterology* **14**:465 (March 1) 1950.