Cancer and Ulcerative Colitis

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Summary

Ulcerative colitis is a potential precursor of cancer of the colon or rectum. In a series of patients with ulcerative colitis operated on between 1952 and 1968 seven developed carcinoma in the residual rectal stump after total colectomy and ileorectal anastomosis. After assessment of the risks of the other available forms of treatment, I believe that ileorectal anastomosis is the best operation in the majority of cases.

Introduction

Ulcerative colitis is undoubtedly a potentially malignant disease, and malignant change can progress unrecognized to an incurable stage while the patient is under medical surveillance. In theory, every patient suffering from colitis, whether diffuse or left-sided, should be advised to have an immediate panproctocolectomy with the establishment of a permanent ileostomy. Yet a balance has to be established between theory and practice, as in the treatment of other potential precursors of malignant change such as gastric ulcer or polyposis of the colon. There is morbidity and mortality after a permanent ileostomy. There is also a suicide rate, though small, among patients to whom a stoma is intolerable. Ileorectal anastomosis, too, has its risks, and, despite the potential malignancy of ulcerative colitis, medical treatment is an essential in the care of the disease.

This paper reviews those cases of ulcerative colitis in a personal series in which carcinoma developed in the residual rectal stump after total colectomy and ileorectal anastomosis. Other cases from the series are also reported and discussed in relation to the risk of malignancy developing during other forms of treatment, including medical. The series, in which total colectomy and ileorectal anastomosis was the operative objective, consists of 369 patients operated on between 1952 and 1968. These included patients with all forms of the disease—fulminating, acute, and chronic. Others were operated on in this period, but with the one exception noted below were excluded from the analysis, as some proved to be cases of Crohn's disease and in others doubt existed about the exact diagnosis after full pathological examination of the excised specimens. There were 19 operative deaths, and of the 350 survivors seven developed cancer, an incidence of 2%. The following are summaries of the case histories of these patients (Group 1).

Group 1. Cancer after Total Colectomy and Ileorectal Anastomosis

Case 1.—A man aged 20 with 16-year history at time of total colectomy and ileorectal anastomosis in 1955. Pathology: diffuse, long-standing inflammatory change with pronounced fibrous thickening of submucosa. Rectum never completely healed, stricturing developed, and biopsy confirmed suspected carcinoma. Abdominoperineal

excision in 1958. Pathology: mucus-secreting adenocarcinoma with lymph node involvement. A feature of the growth was the tendency of isolated malignant gland elements to be surrounded by fibrous tissue. Patient died 1959.

Case 2.—A man aged 30 with three-weeks history of fulminating disease. Admitted with peritonitis November 1952. Total colectomy with subsequent ileorectal anastomosis. Pathology: diffuse fulminating disease. Readmitted with rectal bleeding in 1956. Biopsy: acute proctitis. Treated with corticosteroids. Rectum strictured in 1962. Patient, living in Ireland, did not return to follow-up—corresponding only. Died in 1967 of cancer presumed due to primary in rectum.

Case 3.—A woman aged 48 with 16-year history. At her original attendance in 1954 a fibrosed stricture of the rectum was present. Panproctocolectomy was advised, but any permanent stoma was refused. After rectal dilation, total colectomy and ileorectal anastomosis was undertaken. Pathology: diffuse chronic disease. Developed the expected carcinoma of the rectum in 1960. Abdominoperineal excision carried out. Pathology: well-differentiated adenocarcinoma. Patient died in 1963 of bronchopneumonia with no evidence of secondaries.

Case 4.—A woman aged 52 with 16-year history. Developed some soft stricturing of upper rectum in 1962. Biopsy showed pronounced hyperchromatism and numerous mitotic figures, suggestive of premalignant condition. Total colectomy and ileorectal anastomosis below stricture in 1963. Pathology: diffuse chronic disease; no evidence of malignancy. Developed carcinoma of rectum in 1966. Abdominoperineal excision carried out. Pathology: poorly differentiated adenocarcinoma with lymph node involvement. Patient died in 1967. Between March 1965 and November 1966 patient failed to keep follow-up appointments. The diagnosis of carcinoma was therefore delayed.

Case 5.—A woman aged 25 with 18-month history. Total colectomy and ileorectal anastomosis for acute disease in 1955. Pathology: acute inflammatory changes in whole of colon. Rectum failed to heal. Stricturing of rectum noticed in 1962. Because of rectal bleeding abdominoperineal excision was undertaken in 1966. Pathology: moderately well differentiated adenocarcinoma extending through rectal wall. The rectal mucosa shows changes of an acute exacerbation of ulcerative colitis. Patient alive and well four years later.

Case 6.—A woman aged 51. Duration of disease 18 years. Attended in 1960 with chronic and increasing ill health. Rectal biopsy showed chronic disease with no evidence of premalignant change. Total colectomy and ileorectal anastomosis in 1960. Pathology: whole colon narrowed and affected by long-standing colitis. In the descending colon, in the constricted region, an early mucoid carcinoma present. After 1968 patient declined to attend follow-up clinics, in spite of many calls, until August 1970. Since April of that year she had had rectal bleeding and had become increasingly weak. Rectal examination showed a carcinoma. Laparotomy: carcinoma had extended in the pelvis widely. Palliative resection undertaken. Pathology: moderately differentiated mucus-secreting adenocarcinoma.

Case 7.—A man aged 57 with 12-year history at time of colectomy and ileorectal anastomosis in 1965. Pathology: acute exacerbation of chronic active colitis, with reflux ileitis, whole colon involved. During an admission for acute obstruction a nodule on postrectal wall noticed. Biopsy malignant. Abdominoperineal excision and relief of obstruction in November 1970. Patient died postoperatively from peritonitis due to dehiscence of the line of anastomosis of a resected segment of small intestine.

COMMENT

Five of the seven patients had had disease for periods varying between 12 and 18 years, and there is obviously an argument in such cases for advising panproctocolectomy. A similar high incidence of long-standing disease will be noted in those who developed carcinoma while under medical treatment. Neverthe-

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less, many patients with prolonged disease have been treated by total colectomy and ileorectal anastomosis and over a prolonged follow-up have shown no sign of the development of cancer in the rectal stump. In this category of patient, however, four-monthly visits to a follow-up clinic should replace our routine six-monthly check. This would seem to be equally important (Case 6) when a cancer of the colon has been discovered at operation or when it has been found on pathological examination of the excised specimen. However, this patient (Case 6) is the only one of the six who had potentially curable cancer at the time of operation (Group 5) and who has developed a further cancer in the rectal stump. It does not seem, therefore, that because a cancer of the colon is discovered at operation a panproctocolectomy should be carried out or, alternatively, that because a growth is discovered on pathological examination the ileorectal anastomosis should be abandoned.

In Case 4 an error was made in not taking cognizance of the suggested premalignant change existing in the preoperative rectal biopsy material. In any long-standing case preliminary biopsy specimens must be removed from representative regions of the rectum, and if any show abnormal mitoses or density of nuclear staining consideration of rectal preservation should be abandoned.

The wrong operation was carried out in Case 1. This was that of a young man who had had colitis for 16 years. He was one of our first cases and in the light of experience a similar patient would be treated by panproctocolectomy. The considerable number of young patients who, under medical treatment of many years' duration, have developed cancer have made it evident that the cancer risk is high in this group. Moreover, in this particular patient the rectum never healed and became fibrosed. It is possible, as preliminary rectal biopsy specimens were not taken, that precancerous change had already taken place at the time of the ileorectal anastomosis, and had these been examined no attempt to save the rectum would have been considered.

These experiences, surgical and medical, compel the view that in children, unless complete resolution of the disease is effected by medical treatment within a period of a year or so, operation should be recommended. Up to 1962, 16 patients under the age of 16 had been treated by total colectomy and ileorectal anastomosis. These therefore have had a minimum follow-up period of eight years. One died postoperatively, one was converted into an ileostomy because of postoperative obstruction, and a further patient required conversion because of the development of a stricture. Thirteen (80%) have a normal rectum and are in sound health. It would not appear therefore that panproctocolectomy is necessary in the treatment of ulcerative colitis in children unless the disease is of long standing.

The development of cancer in association with diffuse fibrous stricturing of the rectum (Cases 2, 3, and 5) makes it certain that, in the absence of overriding circumstances (Case 3), the preoperative presence of such a stricture is incompatible with ileorectal anastomosis, and should such a condition develop in postoperative years an abdominoperineal excision with the formation of an ileostomy should be advised.

There are two types of stricture which I do not consider to be potentially malignant. The first is that which follows the laying open of a superficial rectovaginal fistula which may complicate the disease. Firm anal fibrosis which may result from the cure of any fistula has never given rise to malignancy. The second is the occasional formation in the rectum of a thin diaphanous membrane capable of easy division. Two such cases presented and after incision of this diaphragm no further trouble resulted.

Cases 2, 4, and 6 show the imperative necessity of a follow-up of these patients. Repeated endeavour was made to arrange appointments for them, but they all defaulted and replied only by letter.

Group 2. Cancer after Ileocolonic Anastomosis

Case Report.—A girl aged 10 presented with a three-year history of diarrhoea and bleeding. Sigmoidoscopic appearances those of acute colitis. Barium enema—diffuse disease. Subtotal colectomy and anastomosis of ileum to pelvic colon in 1952. Pathology: diffuse acute disease. Patient continued reasonably well though repeated sigmoidoscopies throughout the years showed unhealed rectal and colonic mucosa. Became married and bore two children. Stricture of rectum developed in 1970. Abdominoperineal excision. Pathology: diffuse infiltrating mucus-secreting adenocarcinoma.

Comment.—This patient was the first child operated on. She was dealt with by this method as the effect on development of total removal of the colon in one of her age seemed at that time uncertain. The failure of the rectum to heal completely was probably the result of the continued presence of diseased colon. An abdominoperineal excision should have been undertaken as soon as she became adult. Every other case of the disease in childhood has been treated, when surgery was indicated, by true ileorectal anastomosis. No developmental or stature defects have been observed.

Group 3. Cancer after Simple Ileostomy

Case Report.—A woman aged 59. Thirteen years previously at another hospital an ileostomy was carried out for acute ulcerative colitis. Nine months before her admission increasing rectal discharge and bleeding was noted. Rectal examination showed a strictured rectum and biopsy specimens showed adenocarcinoma. Panproctocolectomy was carried out in 1958. Patient alive and well 12 years later.

Group 4. Cancer in Crohn's Disease after Ileorectal Anastomosis

This patient, an early one in our series, was thought to have ulcerative colitis. Pathological examination proved the presence of Crohn's disease.

Case Report.—A woman aged 31. Admitted in 1952 with 14-years history of left-sided abdominal pain associated with diarrhoea, mucus discharge, and some bleeding latterly. Lost 2 stone (12·7 kg). Previous medical treatment: Total colectomy and ileorectal anastomosis in 1952. Histological report of diffusely thickened colon states: "Diffuse chronic inflammatory reaction with atrophy of glandular elements. The inflammatory reaction spreads right through the bowel wall to the serosal surface and a few giant cell systems are seen. This histological picture is similar to that seen in regional ileitis." Patient subsequently developed anal fistulae. Recognizable cancer of rectum in 1962. Abdominoperineal excision carried out. Pathological report: "Squamous celled carcinoma arising in squamous metaplasia of lower half of rectum. I think this is metaplastic rather than congenital." Patient alive and well in 1970.

Group 5. Incurable Cancer during Medical Therapy

During the period under review 22 patients who had been under prolonged medical care were presented for operation but all had widely disseminated cancer rendering cure impossible. All regions of the colon were affected from the ascending colon to the rectum. With four exceptions, all had had ulcerative colitis over 10 years. Five had had it since childhood and 10 since early adult life. The shortest history was of five years in a patient aged 28 at the onset of the disease and the longest 26 years, the disease having started at the age of 16. Eight patients were under the age of 40 at the time of death, the youngest being 25.

In two cases the disease, radiologically, was confined to the left side of the colon and in one of these absence of colitic change was confirmed on the right side at necropsy. It is

sometimes thought that cancer can arise only in cases of total involvement of the large intestine, but this opinion is erroneous.

From a study of the records of these patients it is apparent that the onset of further symptoms of diarrhoea and bleeding were often mistakenly attributed to a flare-up of the colitis, necessitating yet another course of medical therapy. All had considerable degrees of anaemia. Repeated barium enema studies, routine sigmoidoscopic examinations, or periodic biopsies were not a feature of the follow-up of this group. So far as can be ascertained these patients were never truly fit and from a health point of view they continued for many years as second-class citizens.

Comment.—If medical therapy fails to produce a return to normal health, operative treatment of the disease should be considered. Persistence of symptoms after four years, associated with subnormal health, and particularly anaemia, may well be regarded as an indication for operation, not only in the general treatment of the patient but also as a preventive measure to the development of cancer. If for any reason a still more prolonged medical regimen is continued, barium enemas and sigmoidoscopic and other rectal biopsies should be repeated at intervals not exceeding nine months. The recognition of any stricture formation or biopsy changes of a pre-malignant type as referred to by Morson and Pang (1967) are indications for urgent operation.

Group 6. Curable Cancer during Medical Treatment

In this group were six cases, cancer having been recognized at operation in two and on pathological examination of the excised specimen in four. All were treated by total colectomy and ileorectal anastomosis. In one patient there was heavy lymph node involvement. He was operated on in 1954, when aged 52, and returned to his duties as an engine driver, and 16 years later was free of any recurrence. One patient aged 29 had three recognizable carcinomas at operation without lymph node involvement. He died six-and-a-half years later in diabetic coma with no evidence of cancer spread. Two further patients have been followed up for over five years and one for two years without any evidence of recurrence. The sixth patient is referred to in Group 1 (Case 6). One patient reported symptoms of ulcerative colitis of only two years' duration.

It would seem from a consideration of this small group, of which only one has developed further cancer and of which

two-thirds have survived five years or more disease free, that carcinoma complicating ulcerative colitis has a prognosis equal to that of carcinoma of the large intestine in the general population. It is the confusion of the symptoms with those of the disease in which it is originating, as exemplified in group 5, which delays its early recognition and thus makes it appear more lethal.

Conclusion

Medical treatment is essential in the treatment of ulcerative colitis, and if the precautions suggested are taken the risk of incurable cancer developing unrecognized are slight. With ileorectal anastomosis there is a risk of carcinoma subsequently developing in the rectal stump. This risk can be minimized by rigid follow-up and by the exercise of more courage in advising a patient whose rectum has failed to heal to undergo abdominoperineal excision—perhaps long before symptoms have developed. In the vast majority of patients followed up for many years ileorectal anastomosis has proved an ideal operation which cures the disease and restores normal health.

TABLE I—Number of Patients Treated Each Year

	Yearly Total	Cumulative Total		Yearly Total	Cumulative Total
1952-3	8	8	1961	34	200
1954	8	16	1962	22	222
1955	13	29	1963	25	247
1956	20	49	1964	26	273
1957	27	76	1965	28	301
1958	26	102	1966	22	323
1959	31	133	1967	25	348
1960	33	166	1968	21	369

TABLE II—Duration of Disease before Operation and Time Elapse between Ileorectal Anastomosis (I.R.A.) and Development of Cancer

Case No.	Duration of Disease before I.R.A.	Year of Operation	Time between Operation and Development of Cancer
1	16 years	1955	2 years
2	6 months	1952	14 years
3	16 years	1954	5½ years
4	16 years	1963	2½ years
5	18 months	1955	11½ years
6	18 years	1960	10 years
7	12 years	1965	4½ years

Reference

Morson, B. C., and Pang, L. S. C. (1967). *Gut*, 8, 423.