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Malignant Degeneration in Ulcerative Colitis:*

A Case Report

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THE PAST 20 years have seen striking advances in the understanding of histopathology of ulcerative colitis. Before this period, knowledge was scanty and reports sparse.

Yeomans,¹⁷ in 1927, discussing rectal adenomas, cited a case of carcinoma associated with ulcerative colitis. Crohn and Rosenberg⁷ later published a report on the proctoscopic appearances of chronic nonspecific ulcerative colitis in 1925, wherein they described an incidental finding of a carcinoma. To Bargen¹ belongs the credit for first linking carcinoma definitely with ulcerative colitis. Initially describing it in 1928, he has repeatedly published accounts of the association of these two pathologic entities. In 1946, Ricketts and Palmer¹⁴ reported a case of carcinoma in an 18-yearold patient who had ulcerative colitis since he was 30 months of age. Evidence of the relationship of the two diseases is revealed in a report of the American Cancer Society in 1959, wherein it is stated that there are large inclusion bodies in the cytoplasm of mucosal cells of the colon of patients with ulcerative colitis. Similar inclusion bodies have been observed in malignant polyps of the colon. Further evidence of the tendency of the disease to become complicated by malignancy is shown by the fact that in ulcerative colitis, only too frequently, carcinoma develops after the disease has been in progress for 10 years or more and usually patients are not more than 35 years of age when the cancer becomes manifest.

Incidence

The incidence of carcinoma associated with chronic ulcerative colitis has been evaluated with marked discrepancy. The basis of the calculations has varied considerably. It stands to reason that the incidence of malignancy in a series of patients with ulcerative colitis treated entirely medically differs greatly from that of patients treated surgically. It is common knowledge that, in the latter group, pathologic changes usually are more advanced and the history reveals protracted unsuccessful medical treatment. Reports based on postmortem examinations, for obvious reasons, tend to show an unusually high incidence. Medical literature reveals wide variation of authoritative opinion, ranging from categorical refusal to associate the two diseases to attaching a definite precancerous label to chronic ulcerative colitis. Streicher, 16 in 1938, reported an incidence of carcinoma in 14 per cent of 217 patients with ulcerative colitis. Clinical appraisal of 391 patients with chronic ulcerative by Lindner and associates11 revealed an incidence of carcinoma of 2.1 per cent in eight patients. In 163 patients having had chronic ulcerative colitis for 10 years or more, the incidence of carcinoma was 4.3 per cent. In 1949, Felsen and Wolarsky⁹ wrote that the alleged association of the two diseases was a myth. In their series of 855 patients, not a single case of carcinoma had occurred, and Snapper,15 in 1949, concurred in their opinion. Extreme contradiction to this view was ventured by Brooke⁴ who, in 1961, stated that ulcerative

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colitis was a precancerous condition. The occurrence of carcinoma reported in medical literature, omitting exclusively surgical or pathologic reports, showed an incidence of carcinoma of 6 to 11 per cent. Goldgraber and associates¹⁰ analyzed the records of 820 patients with ulcerative colitis, 124 of whom had undergone bowel surgery or autopsy, or both. Carcinoma was found in 24 patients (19%). Colcock⁵ found an over-all incidence of carcinoma in about 5 per cent of patients with ulcerative colitis treated at the Lahey Clinic. In those patients in whom the disease was severe enough to warrant surgical intervention, the incidence was 10 per cent. In patients who had the disease for 10 years or more, the incidence reported by him was as high as 30 per cent. Of 226 cases reported by Lyons and Garlock,¹² carcinoma developed in nine-an incidence of 3.4 per cent-but in those who had the disease for 12 years or more, the incidence of cancer was 36 per cent.

Similarly Counsell and Dukes,⁶ reporting on 63 colectomized patients, found two carcinomas in patients with less than 10 years' history of ulcerative colitis—an incidence of 3.9 per cent. However, of the 12 patients with a history of ulcerative colitis of 10 or more years' duration, five (45.5%) had cancer.

McDonald and associates¹³ estimated that the calculated risk of cancer of the colon developing in ulcerative colitis patients is 300 times greater than in the population at large, although Bargen² made a more conservative estimate of 30 times greater. Brooke³ examined the records of 500 patients with carcinoma complicating chronic ulcerative colitis and, in 286 patients studied, found the over-all age of onset of carcinoma to be 42 years, compared with 63 years in a previously normal population. In 11 patients, carcinoma was situated in a defunctioned rectum after ileostomy and colectomy, and in three it followed ileoproc-

tostomy. Recently Diethelm and Nickel⁸ reported five carcinomas in 80 patients (6.0%) with chronic ulcerative colitis.

In our series of 616 patients, of 135 who underwent resection, carcinoma was found in 14 (10.3%). Fifty had chronic ulcerative colitis five years or more and of these, 13 (27.04 per cent) had carcinoma. In patients with pseudopolypoid changes in the colon, carcinoma was found in 11 (16.3%). It is also of interest that 76.9 per cent of our patients with ulcerative colitis, with a concomitant bowel cancer, showed visual or roentgenologic evidence of pseudopolyposis. 18

Report of a Case

A 31-year-old white minister was transferred to our proctologic service on September 26, 1963, for evaluation and possible operation for what had been diagnosed as chronic ulcerative colitis. A definite diagnosis was first made in 1956, but the patient claimed to have had what he called colitis for 22 years. He had been having five to six blood-stained bowel movements daily ever since he could remember, and it had been worse since 1958. A roentgenologic examination of the colon established a diagnosis of chronic ulcerative colitis. The patient was given a course of Azulfidine® and made relatively good progress. Since January 1963 he had been hospitalized six times, the last time being in April 1963 when he was given a blood transfusion of 4 units. He had lost about 30 pounds in the previous 4 months, and for about 10 days prior to admission, had felt that his abdomen was distended; there was marked loss of appetite. About 3 days prior to admission he had several bouts of vomiting for which a nasogastric tube was inserted.

Past medical history revealed rheumatic fever at the age of seven years, and since 1955 he had arthritis of both knees. He said that his grandmother had ulcerative colitis.

He was rather cachectic and dehydrated. The abdomen was grossly distended, tense, and auscultation revealed hyperactive bowel sounds. Digital examination of the rectum revealed no abnormality. Proctoscopy to 25 cm. showed an edematous and granular mucosa, but no ulceration. There were multiple petechial hemorrhages, but no crypt abscesses.

On admission the hemoglobin was 14.3; hematocrit, 44; white blood cell count, 5,200; sodium, 136 mEq.; potassium, 5.0 mEq.; chloride, 108 mEq.; alkaline phosphatase, 9.4 King Armstrong units; total protein, 6.6 per cent; albumin, 4.2; globulin, 2.4, and albumin-globulin ratio, 1.8.

A flat film of the abdomen showed enormous distention of the small bowel consistent with low

obstruction. An attempt was made to treat the patient conservatively and decompress his bowel with the aid of a Miller-Abbott tube. After 48 hours, however, his general condition grew worse, and nasogastric suction produced larger quantities of aspirated material. Laparotomy was performed on September 28, 1963, revealing enormously distended loops of small bowel, rather inactive healed ulcerative colitis, and a large carcinoma of the cecum fixed to the posterior abdominal wall. Colectomy was performed. Four liters of fluid were aspirated from the small bowel before performing the anastomosis. The patient made an uneventful recovery and was discharged on the tenth post-operative day.

Histology: On microscopic examination, adenocarcinoma of the cecum with metastasis to lymph nodes was discovered. The colon was involved by moderately active ulcerative colitis.

Discussion

It can be stated now without fear of contradiction that there is a definite relationship between carcinoma and chronic ulcerative colitis, especially when the latter is of long-standing duration. The incidence varies inversely with age, occurring more commonly in children in whom the disease begins early. The carcinoma is less differentiated, with a high-grade malignancy, progresses rapidly, and tends to be multicentric, sometimes insheathing the whole colon (Bargen, Type 1). Counsell and Dukes⁶ found that of tumors associated with chronic ulcerative colitis, all were of Grade C classification. Multiple carcinomas were present in 33.3 per cent of our series. Inasmuch as there is no characteristic change of symptoms when malignant degeneration supervenes and radiologic signs are not pathognomonic, mitotic transformation occurs insidiously and often is beyond control before it is detected. Increased vascularity of the bowel favors early spread of the disease. In our series, 53.8 per cent of patients had evidence of metastasis. The mortality rate is extraordinarily high; the 5-year survival rate is dismally low. Of 286 patients reported on by Brooke,4 221 died before five years had elapsed. Only 13 (4.2%) survived longer than 5 years. He estimated that the best possible figure ap-

peared to be 18.6 per cent. The underlying process of progression to cancer is poorly understood. The expected sequence of events would be ulcerative colitis-mucosal tags-pseudoadenomatous polyps-adenoma -carcinoma. Not all specimens of carcinoma and ulcerative colitis, however, show pseudopolyps; nor does a carcinoma present itself with significant frequency in specimens with pseudopolypoid changes. The genetic factors of ulcerative colitis and cancer have been explored, but there have been no unequivocal conclusions. The constant destructive and reparative process with deepithelialization and proliferation sets the stage for a disorderly and bizarre pattern with uncontrolled mitoses resulting in a columnar-cell and, rarely, a squamous-cell carcinoma.

Summary and Conclusions

A case of carcinoma of the colon complicating chronic ulcerative colitis of long duration in a 31-year-old patient has been presented. It has been stated once more that there is a much higher incidence of cancer in patients with this disease than in the normal population. The incidence becomes extremely great as the duration of the disease increases. The virulence of malignant disease in chronic ulcerative colitis has been stressed and the poor prognosis emphasized. It is the authors' considered opinion that the patient with ulcerative colitis should have periodic proctoscopic and roentgenologic examinations and that surgery should be performed whenever localized changes are revealed on roentgenologic examination after the patient has harbored the disease for 5 years or more.

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time career in a field to which he has made many notable contributions.

Cancer of the Colon, Rectum and Anal Canal consists of 18 comprehensive chapters, 956 pages, and 343 illustrations, from which students and teachers, as well as practitioners in the fields of medicine and surgery, have an invaluable source of information. It includes several thousand references to which any physician can turn when he desires information concerning reports in medical literature on the subject of diseases of the colon, rectum and anal canal.

A master of surgical anatomy and physiology, Dr. Bacon has devoted more than 50 pages of his book to a detailed explanation and clarification of these important topics.

Chapter 4, with its 12 subdivisions, deals in a most comprehensive manner with polypoid disease in all its forms, including benign and potentially malignant lesions, juvenile polyps, villous adenoma, familial polyposis, PeutzJeghers syndrome, Gardner's syndrome, syndrome of polyposis, pigmentation, alopecia and onychotropia, syndrome of polyposis of the colon and multiple hereditary cartilaginous exostosis, the syndrome of familial polyposis of the colon and malignant tumors of the central nervous system, pseudopolyposis, and malignant disease superimposed on benign anorectal disease.

Chapters 5 through 14 deal exhaustively with the over-all subject of malignant disease of the colon, rectum and anal canal, throughout which, repeatedly, the superlative knowledge and capabilities of the author, without premeditation, are brought into focus.

In Chapter 15 the subjects of colostomy and ileostomy are covered comprehensively, and Chapter 16 tells a complete and interesting story of the incidence, prevention and management of surgical and postoperative complications encountered by the author while performing 1,846 resections on 2,160 patients; the mortality rate was 3.6 per cent.

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