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CARCINOMA OF THE COLON IN CHILDREN*

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The symptoms, histology, extent and course of disease in 16 adolescents with colorectal carcinoma who were admitted to Hacettepe University Children's Hospital between 1972 and 1990 are presented. Most patients presented with vague abdominal complaints. Twelve of the 16 patients had mucin-producing adenocarcinoma. Extensive disease at diagnosis and unresponsiveness to medical management were determined. Only one patient survived free of disease four years after diagnosis. Nine of the patients died between one day and one year following the initial surgery. The remaining six patients were very ill when they were discharged from the hospital, after which time no information was received concerning them. *Key words: colorectal carcinoma, childhood tumors.*

Carcinoma of the large bowel is rare in individuals under 20 years of age[1]. Colonic cancer is more common in the Western world than in rural Africa[1]. This difference is thought to be related to the longer transit time of fecal material in the bowels of persons consuming relatively low-fiber diets[1,2].

Although there are approximately 145.000 new cases of colorectal carcinoma in adults annually[1], the Surveillance, Epidemiology, and End Results (SEER) data suggest that only about 80 cases of colorectal carcinoma occur annually in the United States in individuals under 20 years of age, since the incidence of this tumor is approximately one per million in this group[1]. In children and adolescents, these tumors may occur at any site in the large bowel and are not usually associated with a family history of large-bowel cancer[1].

During the period from 1972 to 1990 at Hacettepe University Hospital, there were 4.749 nonleukemic, malignant tumors encountered in patients from birth to age 17. Nineteen of them originated from the gastrointestinal tract (0.4%). There were

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two malignant neoplasms of the stomach and one malignant tumor of the pancreas. The remainder were 16 carcinoma of the colon and rectum, and these are presented in this report. Thus, colonic neoplasms represented 0.33 percent of all cancers seen in roughly the first two decades of life at Hacettepe University Hospital during the study period.

Material and Methods

For the 16 subjects, the age at diagnosis ranged from 11 to 16 years, with a median age of 13 years (Table I). There were nine boys and seven girls in the patient group. Each year from 1972 to 1990, one or two patients were diagnosed. There was no increase in the number of patients according to years.

Table I: Characteristics of Patients with Colorectal Carcinoma

Pt.	Age	Sex	Primary Site	Histology*	Stage at Diagnosis	Documented Metastases at Diagnosis	Operation	Survival
1.	13 yr	M	Rectum	Mucoid	D	Mesenteric nodes, peritoneum	Abdomino-Perineal resection	Died in 6 months
2.	14 yr	F	Rectum	Non mucoid	D	Liver	Refused operation	Died in 1 month
3.	13 yr	F	Recto sigmoid	Non mucoid	C	Iliac nodes (+)	Abdomino-perineal resection	Died in 6 months
4.	11 yr	M	Transverse colon	Non mucoid	D	Intra-abdominal diffuse metastases to liver, abdominal wall, peritoneum	Exploratory laparotomy; biopsy	Died first postoperative day
5.	14 yr	F	Rectum	Mucoid	D	Peritoneum	Exploratory laborotomy; transverse loop colostomy	No follow-up
6.	13 yr	M	Rectum	Non mucoid	D	Peritoneum	Abdomino-perineal resection	Died in 9 months
7.	12 yr	M	Sigmoid	Mucoid	D	Omentum, peritoneum	Exploratory laparotomy; biopsy	No follow-up
8.	13 yr	M	Cecum	Mucoid	C	Mesenteric nodes	Ileocecal resection; ileocolic anastomoses	Followed 4 yrs, no follow-up further
9.	16 yr	M	Hepatic flexure	Mucoid	C	Mesenteric nodes	Ileocecal resection; ileocolic anastomoses	Died in 1 year
10.	15 yr	F	Decending colon	Mucoid	D	Mesenteric nodes, peritoneum, omentum	Transverse loop colostomy	Died in 6 months

Pt.	Age	Sex	Primary Site	Histology*	Stage at Diagnosis	Documented Metastases at Diagnosis	Operation	Survival
11.	11 yr	F	Recto sigmoid	Mucoid	D	Mesenteric nodes, peritoneum	Rectosigmoid resection; colostomy	Died in 8 months
12.	16 yr	M	Sigmoid	Mucoid	D	Omentum, peritoneal carcinomatosis	Exploratory laparotomy; biopsy	No follow-up
13.	14 yr	F	Rectum	Mucoid	D	Peritoneall carcinomatosis	Colostomy	No follow-up
14.	13 yr	M	Sigmoid	Mucoid	C	Mesenteric nodes	Sigmoid colon resection, colostomy	No follow-up
15.	14 yr	M	Hepatic flexure	Mucoid	D	Omentum, mesenteric nodes	Ileocecal resection	Died in 12 days
16.	13 yr	F	Transverse colon	Mucoid	D	Omentum, mesenteric nodes	Exploratory laparotomy, biopsy	Died in 1 month

* All histopathologic diagnoses were adenocarcinomas.

There was no history of ulcerative colitis, familial polyposis or any other precancerous lesion in any of the patients.

The primary tumors were located throughout the large bowel. One primary tumor arose in the cecum, two in the hepatic flexure, two in the transverse colon, one in the descending colon, three in the sigmoid, two in the rectosigmoid, and five in the rectum (Fig. 1).

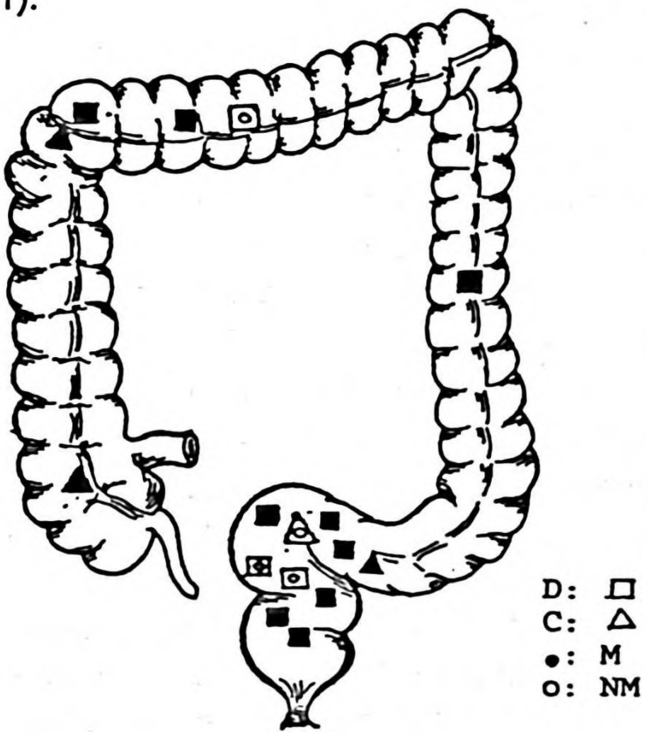

Fig. 1: Distribution, histologic features and stages of colon cancer.
D : Dukes' stage D. C : Dukes' stage C.
M : mucinous type of adenocarcinoma. NM : nonmucinous histologic findings.

The most common presenting symptom was abdominal pain, which was observed in 11 of the 16 patients. This was followed by rectal bleeding, abdominal distention, weight loss, nausea, vomiting, anorexia and intestinal obstruction. Palpable abdominal mass, diarrhea and constipation were also seen. No particular site was found to be associated with any specific symptom, although all patients with rectal or sigmoid primary tumors presented with rectal bleeding, and one complained of rectal pain.

The duration of symptoms prior to diagnosis ranged from two weeks to two years (median three months).

Four patients (patients 2, 3, 4 and 6) had nonmucinous adenocarcinoma. The remaining patients had mucin-producing carcinomas.

Most of the subjects were seen with extensive disease at diagnosis[3] (Table I). In six patients abdominal ultrasonography and in seven patients barium enema colon graphy was performed. Although there are several staging systems for colorectal carcinoma, using the modified Dukes' staging system (Table II) four patients had stage C disease, and 12 had stage D disease.

Table II: Modified Dukes' Classification Colorectal Carcinoma[3]

Stage	Description
A	Lesion confined to bowel wall
B	Direct extension to serosal fat without lymph mode involvement
C	Lymph node involvement
D	Distant metastases (may include extranodal intraabdominal tumor, lung, brain, bones, etc.)

The clinical follow-up of all patients illustrated the nature of the disease (Table I). In addition to the extensive intra-abdominal tumor, involvement of distant organs such as the lungs was detected in one patient. Adjacent invasion, tumor seeding and metastases to the intraabdominal organs were found during surgery in all of the stage D patients.

Surgical procedures were categorized according to the extent of initial surgical resection. In four patients laparotomy revealed an unresectable lesion or widespread intra-abdominal disease, and only incisional biopsies were performed. In another group of three patients, palliative colostomies were performed. Segmental resection was defined as resection of the involved segment along with margins of less than five centimeters. Two patients had resection and colostomy of the rectosigmoid area. Another group of three patients had resection and anastomoses of the right colon. Complete resection of the rectum was performed in three patients by abdominoperineal resection. The procedure included resection of a wide segment of the colon and its mesentery. One patient refused surgery and only rectal biopsy was performed.

Most patients had significant residual tumor after the initial surgical procedure. The chemotherapy used to treat six of these patients consisted of 5-fluorouracil. Another six subjects received 5-fluorouracil and cyclohexylnitrosourea (CCNU), and a group of three subjects received 5-fluorouracil. adriamycine and mitomycine. None of the patients could be followed up to determine the long-term survival and the effects of chemotherapy. The only long-term survivor of this entire group (patient 8) had a primary cecum tumor, was treated with ileocecal resection and ileocolic anastomoses, and received 5-fluorouracil and CCNU for 14 months. He was followed in continuous remission for four years. No information concerning him was received after this period.

Discussion

It is not known whether there is an increasing rate of colon cancer in young individuals or whether the median age of all individuals with colon cancer is decreasing.

The differences in duration of symptoms, primary site, pathologic findings, stage and prognosis between adults and children are striking[4, 5]. A continuing problem affecting prognosis in children is the delay in diagnosis. The initial and most common symptoms of vague abdominal pain coupled with constipation and diarrhea are not indicative of malignancy. Anemias are treated routinely without arousing the physician's suspicions. Adolescents generally do not wish to relate rectal bleeding with cancer, and are unlikely to volunteer this information. Screening methods as used for adults are not feasible in children except in those instances of predisposing conditions[3, 6-8]. An awareness that colorectal cancer can occur, and more detailed attention to symptoms, could conceivably increase the rate of earlier diagnosis. In our patients the most common symptoms were abdominal pain and rectal bleeding.

The predominant histologic pattern noted in 12 of the 16 patients was that of mucin-producing adenocarcinoma. This subtype occurs in five to 15 percent of adult patients[5, 9] but has been reported for most of the tumors of children and adolescents[1, 4, 7, 10, 11]. Tumors may grow to huge sizes because of the pooling of mucin.

Although no sex predominance has been reported among adults[12-14], there is a notable preponderance of males among young patients[13, 15, 16]. Nine of 16 patients in this series were boys.

Regarding the primary tumor site, 60 percent of adult patients are found to have their primary located within 25 cm of the anus. The rectum and sigmoid are also common primary sites for mucinous adenocarcinoma in adults, occurring in 33 and 27 percent of cases, respectively[9]. This preponderance has not been found in young subjects. In 79 children reviewed by Anderson and Bergdahl[15],

the most common site was the transverse colon (39%), compared with two of 16 in this series (12.5%). In our patients the most common primary site was the rectum (31%).

The survival of our patients was influenced by the very advanced stage of disease at presentation, which was the most important clinical aspect of these adolescents with colorectal carcinoma[13]. Prolonged duration of symptoms and delay in diagnosis may have contributed significantly to the poor outcome for these patients. In this series, 12 of the 16 patients had widespread intraabdominal disease at the time of diagnosis; all had extension of the primary tumor beyond the bowel wall. The only long-term survivor in this group (patient 8) had no residual tumor following definitive surgery. We could not follow our patients for a long period. One of them died on the first post-operative day, while eight died between 12 days and one year after the initial surgery. The remaining seven patients were very ill when they were discharged from the hospital. No information concerning them was received after that time. The median survival time was six months in the patients who were able to be followed.

The survival pattern for our patients corroborates the results of the series reported by Andersen and Bergdahl[15] in which only two of 38 patients who underwent "curative" surgery survived more than five years, and the results of the series reported by O'Brien[17] in which only three of almost 200 patients survived five years or more. Delayed diagnosis, locally invasive, aggressive metastatic behavior and poor responsiveness to nonsurgical modalities of treatment were major determinants in the poor prognosis for these young patients. These data are in marked contrast to the data that have been reported for adult patients with colorectal carcinoma[18]. For 120 adults with mucinous carcinoma, as reported by Symonds and Vickery[9], the five-year survival was 53 percent.

Current therapy is unsatisfactory for several reasons. Colorectal carcinomas are detected after development of disease extension in adolescents[1, 16, 19]. Colon carcinoma is one of the most unlikely diagnoses for a teenager and is therefore unsuspected by the pediatrician, in ternist or surgeon examining a patient with diffuse abdominal discomfort or a mass. Another reason for concern is that surgery is the only modality known to be effective in providing cures. Adjuvant chemotherapy extends the life of individuals during childhood. Few patients who present with extensive metastatic disease are cured with chemotherapy[20]. Radiation has little to offer this tumor except when the tumor involves the rectosigmoid or anal areas.

Future considerations include determination of the implications of the DNA labeling index for the response to chemotherapy, refinement of the tumor cloning assay for prediction of the response to treatment, determination of the impact of specific histologies for the response to various chemotherapeutic agents, and greater integration of new therapeutic modalities in the management of these uncommon childhood tumors[1].

In conclusion, cancer of the colon should not be excluded from a clinical diagnosis in childhood on the basis of age alone. However, symptoms in children with abdominal pain are generally associated with mesenteric lymphadenitis, gastroenteritis and appendicitis, whereas in adult patients cancer of the colon would be considered.

It is suggested that barium enema x-rays be performed more frequently in children who have abdominal pain or vague abdominal symptoms persisting more than three weeks. Rectal bleeding is another symptom which has to be taken into consideration in the diagnosis of colorectal malignancies in childhood.

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