Adenocarcinoma of the Colon in Children Presenting as Abdominal Pain: Report of Two Cases

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Adenocarcinoma of the colon is an unusual disease in patients under 30 years of age, and generally presents as advanced disease because of a lack of awareness of its occurrence, especially in the pediatric age group. The authors report on 2 cases of colon cancer in children less than 17 years old, whose initial presentations were abdominal pain of unclear etiology and non-specific abdominal complaints. No other abnormal laboratory results were found except that 1 patient had anemia. Barium studies revealed the typical colon lesions in both patients, and colonoscopic pathologic examination disclosed mucinous adenocarcinoma. The first patient was rather unusual in that 2 separate tumors were found simultaneously in the large intestine. The therapeutic approach included surgery and adjuvant chemotherapy, but both patients ultimately died due to poor response and early recurrence. Survival obviously depends on the extent of the disease at diagnosis; the earlier the diagnosis is, the better the prognosis will be. Clinical characteristics, diagnosis, and treatment of colon cancer in pediatric patients are discussed. *(Chang Gung Med J 2002;25:349-54)*

Key words: children, abdominal pain, colon adenocarcinoma.

Colorectal adenocarcinoma is a common visceral malignancy in adults and is the third leading cause of cancer mortality in Taiwan.[1] Although a rare disease in patients younger than 30 years of age,[2,3] carcinoma of the colon in children and adolescents usually has a poorer prognosis than in adult patients and often escapes early diagnosis because of a lack of awareness. Contrary to adult patients in whom a predisposing history of familial polyposis, ulcerative colitis, or colorectal cancer in relatives can be sought, most pediatric patients develop de novo carcinoma in a previously normal colon.[4-8] This report presents 2 adolescent patients with carcinoma of the colon, and the literature is briefly reviewed to emphasize the clinical diagnostic clues of this serious disease. Colon cancer should be included in the differential diagnosis in teenagers with abdominal pain of unknown etiology.

CASE REPORTS

Case 1

A 13-year-old boy was seen in the pediatric outpatient clinic with a 1-month history of a poor appetite, abdominal fullness, and right lower quadrant pain, without obvious body weight loss. There was no family history of colon cancer or polypoid diseases. General physical examination revealed a healthy-appearing pubertal male. There were no palpable abdominal masses, but tenderness was found on abdominal and rectal palpation. The child had a normal hematocrit and a normal white blood count.

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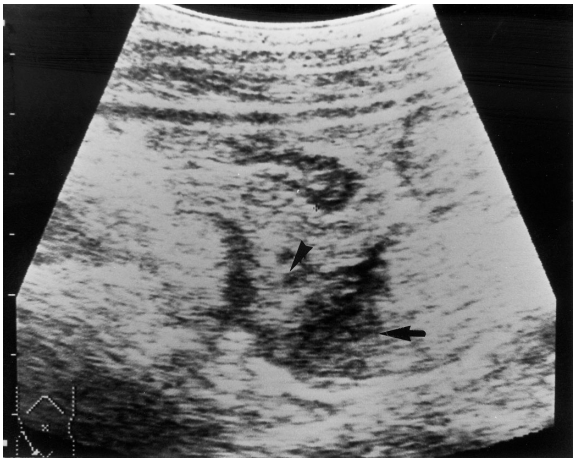

Fig. 1 Abdominal ultrasound in Case 1 showing a target-like lesion of thickened bowel wall with protrusion toward the serosal layer (arrowhead). Localized ascites can also be noted (arrow).

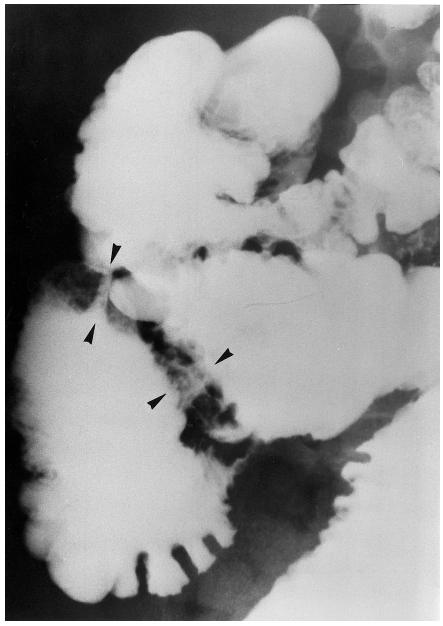

Fig. 2 Upper gastrointestinal series in Case 1 with small bowel follow-through studies showing "apple-core" annular lesions (arrowheads) in the ascending colon.

Stool guaiac test was negative. Abdominal ultrasound showed a target-like lesion on the thickened segmental bowel wall with a protrusion of the serosa, which was surrounded by localized ascites in the lower abdomen (Fig. 1). An upper gastrointestinal barium series with small bowel follow-through study revealed 2 "apple-core" annular lesions in the ascending colon; thus carcinoma of the colon was suspected (Fig. 2). The carcinoembryonic antigen (CEA) level was within normal limits (< 5.0 μg/l). Colonoscopic examination revealed friable polypoid mucosal lesions in the ascending colon. Laparotomy revealed 2 separate tumors approximately 2 cm in diameter within the ascending colon and hepatic flexure of the colon, with a segment of normal colon 7 cm long between them. The masses were tightly adherent with infiltration into the anterior muscular wall of the descending duodenum, gallbladder, stomach, and liver edge. Regional mesenteric lymph nodes were enlarged. The tumors were dissected free from the adjacent organs, then a right hemicolectomy with tumor-free margins was performed. Pathologic examination disclosed a poorly differentiated adenocarcinoma of the mucinous type, with mainly signet ring tumor cells (Fig. 3) extending through the muscularis onto the serosal surface and surrounding soft tissue. Regional lymph nodes and the duodenal wall contained metastatic adenocarcinoma. The cancer was classified as Dukes' D stage.

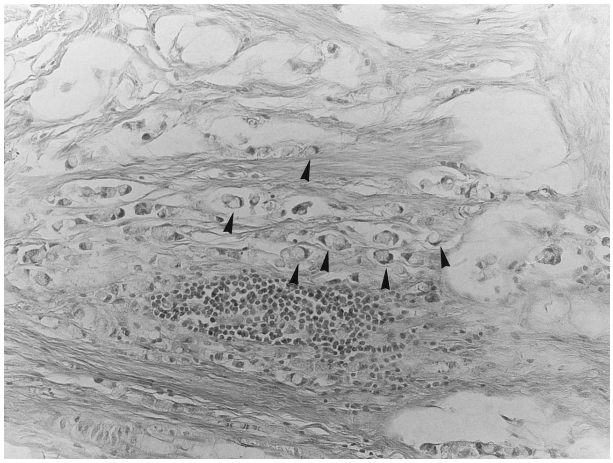

Fig. 3 Pathologic examination revealing colon adenocarcinoma of the mucinous type. Original magnification shows multiple signet ring tumor cells (arrowhead) in a fibrous stroma (H & E, 50 ¡).

The immediate postoperative course was uneventful. The patient was placed on a chemotherapy protocol consisting of 5-fluorouracil, leucovorin,

levamisole, and cisplatin. Unfortunately, this patient experienced complications of tumor recurrence and intractable intestinal obstruction. Ultimately, the patient died of complications of acute renal failure and gastrointestinal bleeding 1 year and 5 months after the diagnosis.

Case 2

A 15-year-old boy had epigastric pain and decreased appetite for 1 month. Postprandial vomiting and mild watery diarrhea occurred in the week prior to admission with a 2-kg weight loss. Physical examination showed a chronically ill, mildly pale-looking adolescent male. Epigastric and periumbilical tenderness was found on percussion and deep palpation. Rectal examination revealed negative findings. Laboratory results showed anemia with a hemoglobin level of 8.7 mg/dl, but stool guaiac test was negative. Under an impression of peritonitis and chronic anemia, abdominal computed tomography was performed which documented ascites, punctuated calcification, and edematous swelling in the right side of the mesenteric roots. Intestinal obstruction ensued 2 days later. A colon barium enema study revealed a stenotic lesion at the hepatic flexure, and carcinoma of the colon was suspected. Colonoscopic examination showed a giant ulcerative tumor in the transverse colon, measuring 7.0 ¡ 1.5 cm, which was located 85 cm proximal to the anal verge. An elevated CEA level (38.2 μg/l) was obtained. Laparotomy with palliative ileosigmoidostomy bypass was performed to relieve the intestinal obstruction due to diffuse abdominal carcinomatosis spreading onto the liver surface, diaphragm, and pelvic cavity. Pathologic examination confirmed the lesion to be an adenocarcinoma of the mucinous type. The patient showed poor response to chemotherapy and died of cachexia and sepsis 1 month after the operation.

DISCUSSION

Colorectal cancer is a common visceral malignancy in adults, with a peak incidence occurring in the sixth decade. In the first 2 decades, less than 1% of all cancers are colorectal cancers in the US.[2,3] The incidence of colonic carcinoma in children under 20 years of age was estimated to be 1.3 per one million in the US.[4] In Japan, about 1-3 colon carcinomas were identified annually among approximately 700 pediatric malignant solid tumors.[5] However, the incidence of colorectal cancer in Taiwanese children has not been reported before. According to an official report in 1997, there were 15 children with documented colorectal cancer in Taiwan (Department of Health, Taiwan, R.O.C. data, pers. commun.). The prevalence of childhood colonic carcinoma in Taiwan therefore can be estimated as 2 in one million (based on a population of children under 20 years of age of about 7.5 million in Taiwan). In general, colon cancer accounts for the most-common primary carcinoma of the gastrointestinal tract in children. The gender distribution of colon cancer is equal in adults, but there is a predominance of males in the pediatric group with a ratio of 2:1.[1-8] Middelkamp et al.[6] reported that 67 of the 71 (94.3%) cases of childhood colon cancer, like our patients, occurred in late childhood and adolescence (9 to 17 years old). The youngest reported child in the literature was a 9-month-old infant with a mucin-secreting adenocarcinoma.[9]

Symptoms of colon cancer in children are nonspecific and include chronic persistent abdominal pain (90%), vomiting, constipation/diarrhea, weight loss (77%), occult blood in the stool with chronic anemia (60%), changes in bowel habits, tenesmus, and a palpable abdominal mass.[5-8] Unfortunately, many colon cancers cause periumbilical and epigastric pain which is often indistinguishable from the non-organic recurrent abdominal pain commonly found in about 10% to 15% of school-aged children.[10,11] Furthermore, non-specific abdominal pain in children is usually considered to be insignificant and to have a non-organic symptomatology, leading to delays in diagnosis of months and even years. However, physical examination such as rectal digital examination, which can detect the signs of rectal tenderness, bleeding, or a palpable mass, may be helpful in evaluation but it is not absolute. Our 2 cases were diagnosed early after a 1-month history of abdominal pain because of positive warning signs, such as rectal tenderness and intestinal lesions on abdominal ultrasound in Case 1, and body weight loss and anemia in Case 2.

In addition to history taking and physical examination, the combination of ultrasound, barium studies, and endoscopic examinations is useful in reach-

ing a correct preoperative diagnosis. Lutz[12] and Bluth and colleagues[13] described how "pseudokidney" or "target" signs on abdominal ultrasound were highly suggestive of a mass of gastrointestinal origin. On barium studies, early colon carcinoma usually appears as a small polypoid mass, indistinguishable from benign tumors. Advanced lesions appear as an "apple-core" annular lesion with luminal narrowing where the transition from normal bowel to the tumoral area is usually abrupt,[14] characteristics found in both of our patients. Computed tomography is recommended for preoperative staging and postoperative follow-up.[8] In our first case, ultrasound revealed a target-like bowel lesion with ascites; the diagnosis was later supported by the barium study and confirmed by colonoscopy. The second patient also had a positive barium study, mesenteric involvement on computed tomography, and colonoscopic confirmation. The CEA determination possesses neither sensitivity nor specificity to enable its use as a screening test for suspected colorectal cancer in children.[15,16] The clinical utility of CEA in the management of patients with colorectal cancer emphasizes that increased preoperative CEA levels may be correlated with a higher rate of relapse.[15,16] Only 1 of our patients had an increased CEA level (38.2 μg/l) in whom diffuse abdominal carcinomatosis had developed and primary tumor resection was impossible. To enhance diagnosis of early colorectal cancer in children, we suggest that a non-invasive abdominal ultrasound examination and barium enema studies are necessary diagnostic tools in children suffering from persistent abdominal pain with any warning signs, like weight loss, anemia, and positive abdominal or rectal tenderness. Colonoscopy may be reserved for confirmation or exclusion of possible colon neoplasms in suspected children. In addition, monitoring of CEA levels is recommended during postoperative follow-up.[17]

Although patients with ulcerative colitis and familial polyposis are particularly predisposed to development of carcinoma of the colon, colon carcinoma in children mostly arises de novo without a contributory history.[6-9] Neither of our 2 patients had a history of preneoplastic diseases. In adults, most carcinomas of the colon come from the left-side colon, especially the sigmoid colon and rectum, where a sigmoidoscopic examination can establish a diagnosis. However in children, there appears to be an equal distribution between the right and the left sides of the colon. About half of the colon cancers in children arise from the transverse colon and ascending colon.[2,4-7,17,18] Locations of these neoplasms include the cecum, and ascending and descending colon, in descending order of frequency.[18,19] Colonoscopic examinations in our patients documented the tumors arising from the ascending colon and transverse colon, which are common sites for colon cancers in children. Hence, a full-course colonoscopic examination is preferred rather than merely sigmoidoscopy in such children.

In general, complete resection is the cornerstone of management for colonic carcinoma to improve the survival time and rates.[18] An extended right hemicolectomy is indicated for right-side tumors, and a subtotal colectomy is recommended for left-side tumors. Resection of metastases in the lung or liver, if technically possible, is also advised for advanced diseases. In patients with either rectal or rectosigmoid lesions, preoperative radiotherapy may be a valuable adjunct. The use of adjuvant chemotherapy and immunotherapy remains controversial.[17-20]

The prognosis of colonic carcinomas in adults improves with early diagnosis, surgical resection, and adjuvant therapies. However, the prognosis remains conversely very poor in children.[19] In large-group follow-up studies, the 5-year survival rate was worse in adolescents than in older patients (51% vs. 75%).[8,10] Two factors may contribute to this unfavorable prognosis in children. First, the diagnosis is not made early because of nonspecific gastrointestinal complaints leading to a low index of suspicion. Delay in diagnosis results in advanced disease at presentation with up to 60% of patients having intestinal obstruction as opposed to 18% in adults.[2,8] A cure is possible only when the cancer is diagnosed and treated at Duke's stage A or B. However, a majority of childhood cases are diagnosed late at Duke's stages C or D, with a poor 5-year survival of 10% to 20%.[8,10] Second, more than 50% of colon cancers in young patients are mucinous adenocarcinomas, while in adults the frequency is only 5%.[2,8,16] Mucin-producing adenocarcinomas grow more rapidly and thus has a short clinical course from the onset of the disease to advanced, metastatic disease.[14] The signet ring cell subtype has the worst prognosis.[8] The disease

in our 2 patients also belonged to the mucinous type adenocarcinoma which responds poorly to surgery and chemotherapy.

In conclusion, adenocarcinoma of the colon is relatively rare in children, and the prognosis is consistently poor for advanced disease. In order to improve outcomes, a high index of suspicion should be kept in mind and mandatory diagnostic modalities such as abdominal ultrasound, barium studies, and/or colonoscopy should be carefully performed in children presenting with persistent abdominal pain of unknown etiology, especially that associated with any warning signs.

REFERENCES

1. Tang R, Wang JY, Lo SK, Hsieh LL. Physical activity, water intake and risk of colorectal cancer in Taiwan: a hospital-based case control study. Int J Cancer 1999; 82:484-9.
2. Andersson A, Bergdahl L. Carcinoma of the colon in children: a report of six cases and a review of the literature. J Pediatr Surg 1976;11:967-71.
3. Gupta SK, Caballes RL. Adenocarcinoma of colon in a child. J Pediatr Gastroenterol Nutr 1986;5:973-6.
4. Culter SJ. Proceedings: report on the Third National Cancer Survey. Proc Natl Cancer Conf 1973;7:639-52.
5. The Committee on Malignant Tumors, The Japanese Society of Pediatric Surgeons: Japanese Tumor Registry of Pediatric Tumors in 1984. Jpn Pediatr Surg 1986; 22:125-71.
6. Middelkamp JN, Haffner H. Carcinoma of the colon in children. Pediatrics 1963;32:558-71.
7. Taguchi T, Suita S, Hirata Y. Carcinoma of the colon in children: a case report and review of 41 Japanese cases. J Pediatr Gastroenterol Nutr 1991;12:394-9.
8. Brown RA, Rode H, Millar AJW. Colorectal carcinoma in children. J Pediatr Surg 1992;27:919-21.
9. Kern WH, White WC. Adenocarcinoma of the colon in a 9-month-old infant: report of a case. Cancer 1994;74: 1979-89.
10. Goldthorn JF, Powars D, Hays DM. Adenocarcinoma of the colon and rectum in the adolescent. Surgery 1983; 93:409-14.
11. Doraiswamy NV, Ahmed J. Carcinoma of the rectum in pre-teen girl. Pediatr Surg Int 1987;2:124-6.
12. Lutz HT, Petzoldt R. Ultrasonic patterns of space occupying lesions of the stomach and the intestine. Ultrasound Med Biol 1976;2:129-31.
13. Bluth EI, Merritt CRB, Sullivan MA. Ultrasonic evaluation of the stomach, small bowel and colon. Radiology 1979;133:677-80.
14. Lamego CMB, Torloni H. Colorectal adenocarcinoma in childhood and adolescent-report of 11 cases and review of the literature. Pediatr Radiol 1989;19:5048.
15. Wanebo HJ, Rao BN, Pinsky CM. Preoperative carcinoembryonic antigen level as a prognostic indicator in colorectal cancer. N Engl J Med 1978;299:448-51.
16. Wolmark N, Fisher B, Wieand S. Prognostic significance of preoperative carcinoembryonic antigen levels in colorectal cancer: Results from the NSABP clinical trials. Ann Surg 1984;199:375-81.
17. Donaldson MH, Taylor P, Rawitscher R, Sewell JB Jr. Colon carcinoma in childhood. Pediatrics 1971:48:307-12.
18. Rao BN, Pratt CB, Fleming ID. Colon carcinoma in children and adolescents. Cancer 1985;55:1322-6.
19. Rao NB, Pratt BC, Fleming DI. Colon carcinoma in children and adolescents: a review of 30 cases. Cancer 1985; 55:1322-6.
20. Cremin BJ, Brown RA. Carcinoma of the colon: diagnosis by ultrasound and enema. Pediatr Radiol 1987;17:319-20.

以不明原因腹痛表現之小兒大腸腺癌：二病例報告

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大腸腺癌在小於三十歲年紀的病人是少見的疾病。因爲容易忽略它的發生所以常常發現時已是疾病後期併發嚴重症狀表現，特別是兒童期大腸腺癌。本文報告二例罹患大腸腺癌的青少年，他們最初都以不明原因腹痛或非特異腹部症候表現；除了一個病人有貧血症狀外，其他實驗室檢驗如糞便常規檢查並無異常。經由超音波和鋇劑檢查而發現大腸病灶，大腸鏡病理報告確診指出爲大腸黏液腺癌，尤其第一例病人更爲罕見的同時發現升結腸內有二個分別的腫瘤。治療方法包括手術和輔助的化學治療，案例一因早期腫瘤復發，案例二因無法開刀切除而最終死亡。小兒大腸黏液腺癌臨床上高度惡性，早期診斷不易。本文將就兒童大腸癌的臨床表現，診斷和治療作一探討。(長庚醫誌 2002;25:349-54)

關鍵字：兒童，不明原因腹痛，大腸腺癌。

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