RESEARCH COMMUNICATION

Colorectal Carcinoma in Children - Experience at a Tertiary Care Cancer Centre in Pakistan

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Abstract

Background: Colorectal carcinoma in the pediatric population is extremely rare. We report our experience with this disorder presenting in children and adolescents. Procedure: A retrospective review was conducted of medical records of all patients aged 18 years and less who were registered at Shaukat Khanum Memorial Cancer Hospital & Research Centre (SKMCH & RC), Lahore, Pakistan, with a diagnosis of colorectal carcinoma between 1st January 1995 and 1st January 2006. Results: Of a total of 2,142 pediatric patients with non-hematologic malignancies registered at SKMCH & RC in the specified time period, 29 (1.35%) had colorectal carcinoma. Ages ranged from 7 to 18 years, with a median of 15 years. There were 25 males and 4 females. All were Pakistani in origin, 22/29 belonging to rural areas of the country. Family history of gastrointestinal malignancy was found in only 1 patient. The commonest presenting complaints were constipation and bleeding from the rectum. There was a site predilection for the rectum (16/29). Histopathology showed high grade adenocarcinoma in 17/29, signet ring carcinoma was prominent amongst this group, 9/17 (52.9%). Some 25 of 29 (86.2%) presented at TNM stages III or IV - 12 patients were fit only for palliation at presentation, the remaining 17 were given multi-modality therapy using surgery, radiotherapy and chemotherapy. A total of 15 of 29 (51.7%) patients have expired, 4/29 were lost to follow-up, 10/29 are still alive but of these 5 have uncontrolled disease while 5 are alive with no evidence of disease. Of the 5 who are in complete remission (CR), 1 remains free of disease 4 years post treatment, 2 are in CR more than 2 years and 1 remains in remission 1.5 years after treatment of metastatic adenocarcinoma colon. The 5th patient went into remission with treatment of adenocarcinoma colon but developed glioblastoma multiforme immediately afterwards and is currently on treatment for GBM. Conclusions: Our clinical experience with these patients corresponds to other reports in literature that show a marked predominance of high grade lesions, advanced stage at diagnosis, and poor responses to treatment in this age group. Our data suggest that colorectal cancer in children may be more common in our local population compared to figures from developed countries. Pediatricians and pediatric oncologists need to have a higher index of suspicion for colorectal carcinoma in patients presenting with chronic gastrointestinal symptoms to allow early diagnosis and better clinical outcome in this age group. Future studies should concentrate on etiologic factors especially the role of environmental pollutants and possible influence of dietary and social habits.

Key Words: Colorectal carcinoma - children - clinical parameters - aetiology

Asian Pacific J Cancer Prev, **10**, 789-792

Introduction

In the United States colorectal carcinoma is one of the four most common cancers in adult men and women (Jemal et al., 2004), and the second leading cause of death after lung cancer in men and breast cancer in women (Cancer Facts and Figures, 2003). It is generally thought to be a disease of advanced age with the highest prevalence in the eighth decade of life (Ries et al., 1994; Keswani et al., 2002). In the pediatric age group, however, it is rare and is seen in only 1 person per 1 million younger than 20 years in the United States annually (Chantada et al., 2005). We found several reports in literature, from surgical or oncologic centers, describing colorectal carcinoma in individuals less than 40 years of age (Keswani et al., 2002; Liang et al., 2003; Griffin et al., 1991; Kam, 2004) but within these reports the number of patients under 18 years of age is very few (Table 2). Shaukat Khanum Memorial Hospital and Research Center (SKMCH & RC) is a tertiary care cancer referral centre in Pakistan. We describe our experience with an unusually high number of cases of colorectal carcinoma in the pediatric population treated in this institution over a period of 11 years.

Between 1st January 1995 and 1st January 2006 this hospital registered a total of 3,213 cancer patients under 18 years of age. Of these 2,142 had non-hematologic malignancies and amongst them 29 (1.37%) had colorectal carcinoma.

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Materials and Methods

We included all patients 18 years of age and younger who were registered at SKMCH & RC with histologically proven colorectal carcinoma between 1st January, 1995 and 1st January, 2006. Data were extracted through retrospective review of hospital records of each patient and the presenting signs and symptoms were described. The statistical software, Statistical Package for Social Sciences (SPSS), version 10, was used to obtain the descriptive results and run the survival analysis. Counts and percentages were obtained for gender, stage, tumor site, histopathology, treatment type and its outcome, and patient status. To look into the age distribution, mean age at presentation, age range, and standard deviation were determined. Survival analysis was conducted using the Kaplan-Meier method. Follow-up time was defined as the interval between diagnosis and last contact. Death was taken as the outcome of interest.

Results

Epidemiology

There were a total of 2142 pediatric patients registered at SKMCH & RC with non-hematologic malignancies in the given period of time. Of these 29 (1.4%) had colorectal carcinoma. There were 25 males (86.2%) and 4 females. Ages ranged from 7 to 18 years with a median of 15 years and a mean of 14.5 years (SD=2.9). They were all Pakistanis, 22 of 29 had a rural origin and 7 came from an urban background. There was only 1 patient with a strong family history of gastrointestinal malignancy; he later developed intracranial malignancy and was therefore thought to have Turcot Syndrome. One patient had multiple gastrointestinal polyps and was thought to be an index case of Familial Adenomatous Polyposis (FAP) but the parents declined screening of the rest of the family.

Clinical features

The commonest presenting signs and symptoms were constipation, bleeding per rectum and abdominal pain (Table 1); other symptoms included diarrhoea, weight loss, vomiting, abdominal mass and anaemia. All patients had more than one complaint at diagnosis. The primary site of disease was rectum in the majority (16 of 29) patients, sigmoid colon in 5, recto-sigmoid in 3, cecum in 2. In 3 patients other parts of the colon were involved, including one suspected FAP who had hamartomatous polyps in the entire length of his colon. Using the TNM staging system, 9 were stage IV, 16 stage III, 3 stage II and only 1 had stage I disease at diagnosis (Table 1). Histopathology showed adenocarcinoma in all patients, 17 had high grade lesions (signet ring=9, mucinous=7, and poorly differentiated=1) and 12 had low grade histologic features (moderately differentiated=9, well differentiated=3).

Treatment

Twelve patients had very advanced disease at presentation and were offered palliation only. The remaining 17 were treated with multimodality therapy using combinations of surgery, chemotherapy and/or radiotherapy. Surgery was total colectomy in 3 of these 17 patients, anterior pelvic resection (APR) in 4, resection anastomosis in 3, right hemicolectomy in 3, low anterior resection (LAR) in 2 and left hemicolectomy in 1, while 1 patient & his family refused to undergo definitive surgery so he was treated with chemoradiotherapy. The 12 palliative patients had only temporary bypass procedures done. The chemotherapy regimens employed were 5-Fluorouracil (5-FU)+Leucovorin (LV) in 14 of 29 patients, 5-FU alone in 5 patients, 5-FU+LV+Irinotican (CPT 11) in 2 and 5-FU+LV+Oxaliplatin in 3 while 5 patients received no chemotherapy. Radiotherapy was used in combination with surgery or chemotherapy or both in 12 of 29 patients.

Table 1 Features of Colorectal Cancer in Children

Features		Count (N=29)	Percentage
Gender	Male	25	86.0
	Female	4	14.0
Age at presentation (years)			
	Mean	14.5	-
	Median	15	-
	*Mode	18	-
	Range	7-18	-
	Standard deviation	2.9	-
Stage	I	1	3.4
	II A	2	6.9
	II B	1	3.4
	III B	7	24.1
	III C	9	31.0
	IV	9	31.0
Site	Rectum	16	55.2
	Sigmoid colon	5	17.2
	Rectosigmoid	3	10.3
	Cecum	2	6.9
	Transverse colon	1	3.4
	Colon	2	6.9
Histopathology			
	Low grade, m[1]	9	31.0
	Low grade, w[2]	3	10.3
	High grade,signet ring	9	31.0
	High grade, mucinous	7	24.1
	High grade, p[3]	1	3.4
Intent of Treatment			
	Curative	17	58.6
	Surgery+chemo+radio	5	-
	Surgery + chemo[4]	10	-
	Surgery only	1	-
	Chemo + Radio	1	-
	Palliative	12	41.4
	Surgery+chemo+radio	5	-
	Surgery + chemo	2	-
	Surgery only	3	-
	Surgery + radio	1	-
	Chemo only	1	-
Outcomes	Expired	15	51.7
	Alive with disease	5	17.2
	Alive without disease	5	17.2
	Loss to follow-up	4	13.8
Total		29	100

*Seven patients (24%) were 18 years old; [1]moderately differentiated; [2]well differentiated; [3]poorly differentiated; [4]One patient refused to undergo surgery

Table 2 Literature Review for Comparison

Author	Study period	Age group	No. of cases reported	
Odone et al (1982)	16 years	< 20 years	24	< 18 years = 19
Petrek et al (1984)	10 years	< 40 years	50	< 20 years = 1
Behbani et al (1985)	11 years	< 40 years	56	< 18 years = 0
Rao et al (1985)	20 years	< 30 years	30	< 20 years = 29
Steinberg et al (1988)	20 years	< 20 years	9	
Lewis et al (1990)	25 years	< 20 years	8	< 18 years = 7
La Quaglia et al (1992)	39 years	< 21 years	29	< 18 years = 13
Minardi et al (1998)	21 years	< 40 years	37	< 20 years = 3
Keswani et al (2002)	10 years	< 40 years	24	< 18 years = 0
Kam et al (2004)	12 years	< 30 years	39	< 18 years = 0
Chantada et al (2005)	13 years	< 30 years	21	< 18 years = 14

Outcome

All 12 patients given palliation have expired. Of the 17 who received definitive treatment, four got lost to follow up at various stages of treatment and three have expired. Of the remaining 10, 5 relapsed or progressed on therapy and are alive with uncontrolled disease at the time of submission of this report. 5 of 29 (17.3%) patients are still alive without disease, 1 remains free of disease 4 years post treatment, 2 are in CR more than 2 years and 1 remains in remission 1.5 years after treatment of metastatic adenocarcinoma colon. The 5th patient went into remission with treatment of adenocarcinoma colon but developed glioblastoma multiforme (GBM) immediately afterwards and is currently on treatment for GBM.

Survival Analysis

Of a total of 29 cases, 9 cases with only one visit were removed from the Kaplan-Meier survival study. Analysis was conducted on the remaining 20 cases (Fig. 1). Of these 20, death of 12 children had been recorded at the hospital. Eight cases were censored as they did not reach the endpoint of interest, i.e. death. Accordingly, the median follow-up time was computed to be 10 months (95% confidence interval 4.53, 15.47). One-year cumulative probability of survival was 37% and 3-year was 28%.

Discussion

Although colorectal carcinoma is one of the most common cancers in persons over 40 years of age, it is not commonly diagnosed in younger individuals. Patients aged less than 40 years account for 2–8 % of all cases of colorectal cancer (Enblad et al., 1990; Heys, 1994), whereas in patients younger than 20 years the incidence of colorectal cancer in the United States is reported to be 1:1,000,000 (Chantada et al., 2005).

We reviewed literature reports of colorectal carcinoma in patients less than 40 years of age (Table 2). Nearly all of these reports are hospital based from surgical or oncology units of tertiary care hospitals and majority of them report only occasional patients under 18 years of age (Minardi, 1998; Keswani et al., 2002; Kam, 2004). Our experience shows a substantially higher number, 20 patients in 11 years' span, who were 18 years of age or younger at the time of diagnosis. This apparent high number may be due to the fact that SKMCH & RC is the only tertiary care cancer hospital in the country. However the possibility of a true high incidence cannot be ruled out. Majority of our patients belonged to rural areas of the country and the potential etiologic role of industrial pollutants like pesticides and commercial fertilizers could be worth looking into in future studies.

The predominant histologic type in our patients was high grade, (17 of 29 (58.6%)) suggesting aggressive disease, in contrast to adults where high grade lesions especially mucinous variety comprise no more than 5–15 % of all colorectal carcinomas (Symonds, 1976; Rao et al., 1985; Minardi et al., 1998). We saw 7 of 29 (24.1%) high-grade lesions consistent with mucinous adenocarcinoma, which is associated with a higher rate of local recurrence (Rao, 1985; Keswani et al., 2002) presumably because mucin facilitates intramural spread of the tumor (Keswani et al., 2002). Interestingly, we also saw a very high numbers of the signet ring lesions, 9 of 29 (31.0%), in our patients compared to the experience reported in literature where high-grade lesions in adolescents have mostly been of the mucinous variety (Symonds, 1976; Rao et al., 1985; Steinberg, 1988; Minardi, 1998). The fact that 86.2% (25 of 29) patients presented with advanced stage also correlates with histopathologically aggressive disease, although delay in diagnosis due to non-specific symptoms in the younger age group and higher threshold of suspicion may be additional factors.

We saw a notable preponderance of males, 25 of 29 (86.2%). This may be reflective of our social setup where males are given more preference than females and so chronic symptoms are less likely to be ignored in boys than in girls. However, this observation has been reported in the younger age group in several other studies (Keswani et al., 2002; Kam, 2004; Rao et al., 1985; Odone, 1982; Steinberg, 1988; Lewis et al., 1990; Minardi, 1998), in contrast to adult literature where no gender predisposition has been defined.

The distribution of carcinoma within the colon in our patients was predominantly in the rectum (16 of 29) followed by sigmoid (5/29), recto-sigmoid (3/29), cecum (2/29) and other parts of the colon 3/29. This is similar to the reported distribution in other studies (Lewis et al., 1990; Griffin, 1991; Kam, 2004), which show a predominance of left-sided lesions as in adults.

Only 1 of our patients showed a potential predisposing disorder as he had multiple hamartomatous polyps in his large gut, he was suspected of having familial

adenomatous polyposis (FAP) but the family declined screening. Family history of gastro-intestinal (GI) malignancy was found in only 1 patient who additionally had history of non-GI malignancies in first-degree relatives. This same patient later developed a second primary intracranial tumour, glioblastoma multiforme (GBM) for which he is receiving treatment, his colon carcinoma is presently in CR.

The natural history and prognosis of colorectal cancer in young patients are controversial, however most studies report a worse outcome in this age group (Odone et al., 1982; Rao et al., 1985; Steinberg, 1988; Lewis et al., 1990; Minardi, 1998). Amongst our cohort, only 5 of 29 (17.3%) patients are alive without disease at the time of preparation of this report. The poor survival is mostly attributed to delay in diagnosis resulting in advanced disease (Odone et al., 1982; Rao et al., 1985; Steinberg et al., 1988; Lewis et al., 1990). In addition, a high proportion of high-grade lesions, advanced stage at presentation and poor response to treatment also contribute to poor outcome.

As others have reported, colorectal carcinoma may be diagnosed late in children and adolescents mainly due to low index of suspicion on the part of the clinicians and also because of the vague nature of symptoms at onset that often are disregarded. Physicians caring for children and adolescents should aggressively evaluate chronic gastrointestinal complaints especially rectal bleeding.

Acknowledgement

Preliminary study presented as a poster at the 36th Congress of the International Society of Pediatric Oncology, Oslo, Norway. 16-19 September, 2004.

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