COLORECTAL CANCER IN THE YOUNG ADULT

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ABSTRACT

Out of 964 patients presenting with primary colorectal cancer (CRC) to the Department of Colorectal Surgery, Singapore General Hospital between April 1989 until December 1992, there were 57 (5.9%) aged 40 years or less.

These younger patients were significantly more likely to have a family history of cancer, particularly CRC; a tumour situated more proximally; and tumours displaying certain characteristic histopathologic features. There were no adverse findings for clinicopathologic staging at presentation, curative resection rate, and systemic recurrence rate within the early follow up period.

With proper management, the young adult with CRC enjoys the same outlook as his older counterpart. But, in view of the likely operation of inherited genetic factors, follow up surveillance of the patient and the provision of advice and screening are vital elements in optimising outcome. Furthermore, advice and screening should be available for first degree relatives as well.

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INTRODUCTION

Stimulated by recent advances in the understanding of the genetic basis of colorectal cancer[1], most notably with the identification of the APC gene involved in familial adenomatous polyposis (FAP)[2] and the gene of hereditary non-polyposis colorectal cancer (HNPCC)[3], there is a growing interest in the plight of subjects in their first four decades of life who develop colorectal cancer (CRC). This is because these individuals and their immediate relatives are more likely to have an inherited, as distinct from acquired, genetic predisposition and are most likely to benefit from specific preventive measures such as polyp surveillance[4], dietary advice[5], and screening[6].

Although there have been anecdotal reports of young Asian adults presenting with CRC not related to familial adenomatous polyposis[7-9], the incidence and characteristics of this entity in the South East Asian setting have not been the subject of systematic study.

The accumulated experience of the Department of Colorectal Surgery, Singapore General Hospital since its establishment in April 1989 provided the opportunity to ascertain the incidence, clinicopathologic features, and outcome of the management of young adults with CRC.

METHODS

Computerised audit and follow up data, case records and pathologic reports of all new patients undergoing treatment for colorectal cancer (CRC) in the Department of Colorectal Surgery, Singapore General Hospital from 1 April 1989 until 31 December 1992 were reviewed. Information about the incidence, demographic details, clinical and family history, operative details, pathologic details, and follow up outcomes were recorded and analysed.

Where appropriate, analysis of variance and testing for significance ($\alpha<0.05$) between unpaired groups using a non-parametric statistical test (Chi-squared, χ^2, test) were performed.

RESULTS

There were 964 patients who presented with primary colorectal cancer (CRC) to the Department of Colorectal Surgery, Singapore General Hospital between 1 April 1989 and 31 December 1992. Table I sets out in summary form the main clinicopathologic findings. Out of the total number, 57(5.9%) were aged 40 years or less, three of whom had familial adenomatous polyposis (FAP).

The male:female ratio of subjects aged 40 years or less did not differ significantly from that of their older counterparts.

Whereas a personal history of non-CRC cancer(s) was uncommon in the patients as a whole, there was a significantly greater family history of cancer including CRC ($\chi^2=7.07$, $p=0.03$) in the young patients.

The index tumour was likely to be sited more proximally in the colorectum of those aged 40 or less ($\chi^2=13.26$, $p=0.02$).

Both the clinicopathologic staging at presentation of, and the proportion of patients able to undergo a "curative" operative strategy for the tumour were not influenced by the age of the patient. This was despite there being a higher incidence of poor differentiation ($\chi^2=8.53$, $p=0.01$) and either mucinous, colloid, or signet cell components ($\chi^2=13.01$, $p<0.001$) of the tumour in the younger subjects.

At 22 months median follow-up (range 1 - 48 months), there was no significant difference in the incidence of distant metastases for those aged more than 40 years and those aged less than 40 years respectively.

DISCUSSION

The relatively low proportion (5.9%) of young adults in all cases of colorectal cancer (CRC) managed by us is very similar to that reported in countries of high incidence, characteristically Western ones, and is consistent with the

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Table I - Clinicopathologic details of patients grouped according to age

	>40 [yrs]		≤40 [yrs]		x^2	dof	p
	no.	(%)	no.	(%)			
No.	907	(94.1)	57	(5.9)			
Gender							
Male	521	(57)	35	(61)			
Female	386	(43)	22	(39)	0.20	1	ns
Personal Past History							
Other cancer	12	(1)	1	(2)	0.10	1	ns
Family History							
Colorectal cancer	59	(7)	8	(14)			
Other cancer	31	(3)	4	(7)	7.07	2	0.03
Operation outcome							
Curative	498	(71)	43	(75)			
Palliative	202	(29)	14	(25)	0.29	1	ns
Colonic site							
Caecum	37	(5)	6	(11)			
Ascending	45	(6)	6	(11)			
Transverse	107	(14)	6	(11)			
Descending	37	(5)	1	(2)			
Sigmoid	194	(25)	19	(37)			
Rectum	364	(46)	19	(37)	13.26	5	0.002
Dukes' stage							
A	78	(9)	5	(9)			
B	268	(30)	18	(32)			
C	323	(36)	22	(39)			
"D"	240	(26)	12	(21)	0.81	3	ns
Histology							
Differentiation:							
Well	53	(6)	6	(11)			
Moderate	742	(85)	40	(70)			
Poor	81	(9)	11	(19)	8.53	2	0.01
Mucinous/colloid or signet cells	31	(4)	8	(14)	13.01	1	<0.001
Distant recurrence (curative resections)							
Liver/lungs/peritoneum	37	(7)	5	(12)	0.48	1	ns

χ^2: Chi-squared test; dof: degrees of freedom; ns: not significant (p>0.05)

observed upward trend of the disease in Singapore[10]. The relative proportion of young adults out of all those contracting CRC in any study population varies widely from 5.4% in New Zealand, a country with a high incidence overall, to 23% in Saudi Arabia, a country with low incidence[11]. The relatively low incidence of young sufferers with CRC in a population of high overall incidence is due to the dilution effect of the large numbers of sporadic cases of CRC occurring in the older age groups as a result of the operation of as yet imperfectly understood environmental, as distinct from inherited genetic, factors. Thus the percentage of young adults out of the total CRC incidence is an approximate and inverse guide to the overall incidence of the disease in any population under scrutiny. This study provides indirect evidence that in Singapore there is an increasing representation of the older age groups having the sporadic type of the disease. This is probably a reflection on the changing lifestyle, particularly dietary, of the inhabitants of this modern bustling Asian city-state. Recently, a reduction in the incidence of CRC occurring in the younger generations in a population of high overall incidence has been reported[12]. This has been attributed to public health initiatives, similar to the current one in Singapore, in publicising the desirability of a more healthy lifestyle, particularly diet and exercise.

The specific syndrome of FAP (only 3 cases in our study) aside, a significantly increased family history of cancer in general and CRC in particular was found in the young adults. This is consistent with the well known fact that although there is a graduated increased risk of CRC in relatives according to the age of the index patient [13,14], it is the first

degree relatives of the young patient who are most at risk[15]. The most extreme forms of this familial tendency are seen in the two Lynch syndromes of hereditary non-polyposis colorectal cancer[16], but in this series, only 2 of the 57 young adult patients would fulfil the strict criteria to be labelled as such. The important implication of the above is that all young adults with CRC are deserving of close follow up and their first degree relatives of screening[6,17], ideally through the availability of a dedicated Colorectal Cancer Family Advisory Service[18] and according to a rational protocol[19]. Preemptive colonoscopic removal of polyps has recently been proved to reduce the incidence of CRC[4].

The tendencies of tumours to be right-sided in situation and exhibit mucinous, colloid or signet ring forms are well known characteristics of CRC in the familial setting where a strong genetic predisposition exists[20]. It is therefore not surprising that the tumours of the young adults in this study exhibited significantly more of these features than those of their older counterparts. The significantly greater incidence of mucin, colloid and signet ring morphology in, and poorer differentiation of, the tumours of the younger patients might be expected to be associated with a poorer prognosis. However, up to the present time of follow up, this was not apparent. First, there was gratifyingly no significant tendency for the younger subjects' tumours to be more advanced at presentation. Second, there was no difference between the two age groups when two important measurements of outcome were compared: (1) the curative resectability rate at primary surgery was similar for both age groups, and (2) in the early follow up period within which most recurrences would likely occur, there was no significant difference in the systemic recurrence rates.

It is thought by some[21] that CRC in the young adult is more advanced at presentation, more aggressive in behaviour, and has a correspondingly worse prognosis. However at this early stage in the follow up of our patients, this bad reputation of the disease in young adults is not confirmed by our study and this is in agreement with an emerging consensus fuelled by other reports[22,23] that, with modern advances in surgical technique[24] and adjuvant therapies[25,26], young adult sufferers are not disadvantaged by the fact of their tender years *per se*.

CRC occurring in young adults poses challenges in the primary management and follow up of patients; and mandates the provision of appropriate advice and screening for relatives. In themselves however, both the young age of the patient and the associated inherited genetic risk for CRC, give no particular grounds for pessimism over a good outcome for patient and family alike.

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