



RESEARCH ARTICLE

HISTOMORPHOLOGICAL SPECTRUM OF TUMORS OF LARGE INTESTINE

Kavita, G.U¹., Shashikala, P¹., Gurubasavaraj, H² and Vijayanath, V³

¹Department of Pathology, S.S.Institute of Medical Sciences & Research Centre,
Davangere, Karnataka

²Department of Pathology, J. J. M. Medical College, Davangere, Karnataka

³Department of Forensic Medicine and Toxicology, S. S. Institute of Medical Sciences and
Research Centre, Davangere, Karnataka

ARTICLE INFO

Article History:

Received 7th October, 2010

Received in revised form

12th November, 2010

Accepted 30th December, 2010

Published online 31st March, 2011

Key words:

Large intestine tumors,

Polyps,

Colorectal cancers.

ABSTRACT

Colorectal cancer is the most common gastrointestinal malignancy in the developed world. India is a vast country consisting of people of different customs and traditions. Hence pattern of large intestinal malignancy varies in different parts of the country. The present study of two years was undertaken to know the spectrum of tumors and tumor like lesions of the large intestine, in and around Davangere district, which is situated in the central part of Karnataka. Relevant data regarding the cases were obtained from the request forms. Large intestinal tumors constituted 0.44% of the total specimens received for histopathology. Females were more frequently affected than males and commonest location was rectum (57.78%). Majority of them showed exophytic (53.13%) growth and adenocarcinoma was the commonest malignancy (93.34%) encountered. Tumors constituted 76.27% and tumor like lesions constituted 23.72% of the total (59) specimens studied. The role of pathologist remains important in evaluation, diagnosis, grading and staging so as to help the clinician in proper management of the disease.

© Copy Right, IJCR, 2011, Academic Journals. All rights reserved.

INTRODUCTION

Colorectal cancer is the most common gastrointestinal malignancy in the developed world. In UK, for example, there are approximately 16,000 deaths and 20,000 new cases per year. In developed societies, life time risk of developing cancer of large bowel is approximately 4% (Taylor, 1990).

The introduction of fiberoptic colonoscopy has now made it possible to take biopsies from any part of the large bowel including even terminal ileum and thus helps in early detection and prevention (Morson and Dowson, 1979). India is a vast country consisting of people of different customs & traditions. Hence pattern of gastrointestinal cancer varies in different parts of the country (Kalyani *et al.*, 2010). Surgical specimens from patients with tumors of colorectum continue to be among the

*Corresponding authro: drvijayanath@gmail.com

tissue specimens most frequently examined by pathologists. The way in which this examination is done, and the final reporting of the results, plays an important role in assessing the prognosis (Qizilbash, 1982). The aims and objectives of the study to identify and study the histomorphology of the tumors of large intestine and the incidence of tumors and tumor like lesions of large intestine in and around Davangere.

MATERIALS AND METHODS

A descriptive study of malignancies of large intestine (colorectal tumors) was undertaken for a period of two years. Material consisted of resected and biopsied specimens from patients with suspected tumors and tumor like lesions of large intestine, which were received for histopathology. These patients were admitted in various hospitals in and around Davangere. All histopathology cases related to large intestine, reported as malignancy and those reported as tumor like lesions were included for the study. Operated and biopsied specimens were examined in detail for gross and microscopic features, for confirmation of clinical diagnosis and for histological typing and grading. Relevant clinical data regarding age, sex, of patients with confirmed microscopic diagnosis of malignancy were obtained from the records and cases were analyzed according to the histopathological type and compared with similar studies.

RESULTS

This is a descriptive study on histomorphology of tumors and tumor like lesions of the large intestine over a period of two years. During the period a total of 10,216 specimens were received in the department for histopathological examination. Large intestine and anal canal specimen constituted 127 (1.24%) of the total specimens received. These were either resected segments or biopsy specimens. Of these 59 (46.45%) were tumors and tumor like lesions which were taken for study. Rest of the specimen with various inflammatory and neoplastic diseases and lesions of the anal canal were excluded. The 59 specimen were divided into two groups viz. tumors and tumor like lesions based on

histopathology which included 45 (76.27%) tumors and 14 (23.72%) tumor like lesions.

Tumors of the large intestine

This group included 45 tumors, that is, 76.27% of the specimen studied. 31 patients (68.89 %) were above 40 years of age and 14 patients (31.11%) were less than 40 years. The youngest patient encountered was 14 yrs old. 19 patients (42.22 %) were males and 26 patients (57.78%) were females. The commonest location of tumors encountered was rectum, seen in 26 patients (57.78%). Of the 45 cases of tumors of large intestine, 32(71.11%) were resected specimen and 13(28.89%) were biopsy specimens.

Morphology of tumors of large intestine in resected specimens

Analysis of the gross appearance of 32 tumors of large intestine in resected segment revealed the following features: Morphologically, 17(53.13%) of the tumors were of ulcero proliferative type. When tumors were analyzed based on their size and growth pattern of endophytic or exophytic nature, 23 (71.87%) were found to be exophytic and 9 (28.125%) were endophytic (Table 1).

Table 1. Morphology of tumors of large intestine in resected specimens

Nature of lesion	Right colon	Transverse colon	Left colon	No. of cases	Percentage
Polypoidal	2	1	3	6	18.75
Ulcerative	3	--	2	5	15.63
Ulceroproliferative	4	--	13	17	53.13
Constrictive	1	--	2	3	9.37
Limitus plastica	--	--	1	1	3.13
Total	10	1	21	32	100

Microscopy

Microscopically, all these 45 tumors studied were malignant. The microscopic types and incidence of these tumors were as follows

Adenocarcinoma of large intestine

Adenocarcinoma constituted 93.34% of the tumors of large intestine. Age of the patients ranged from 14years to 85 years with 12 patients in the age group of 51-60 years. Seventeen (40.48%) patients were males and 25(59.52%) patients were females

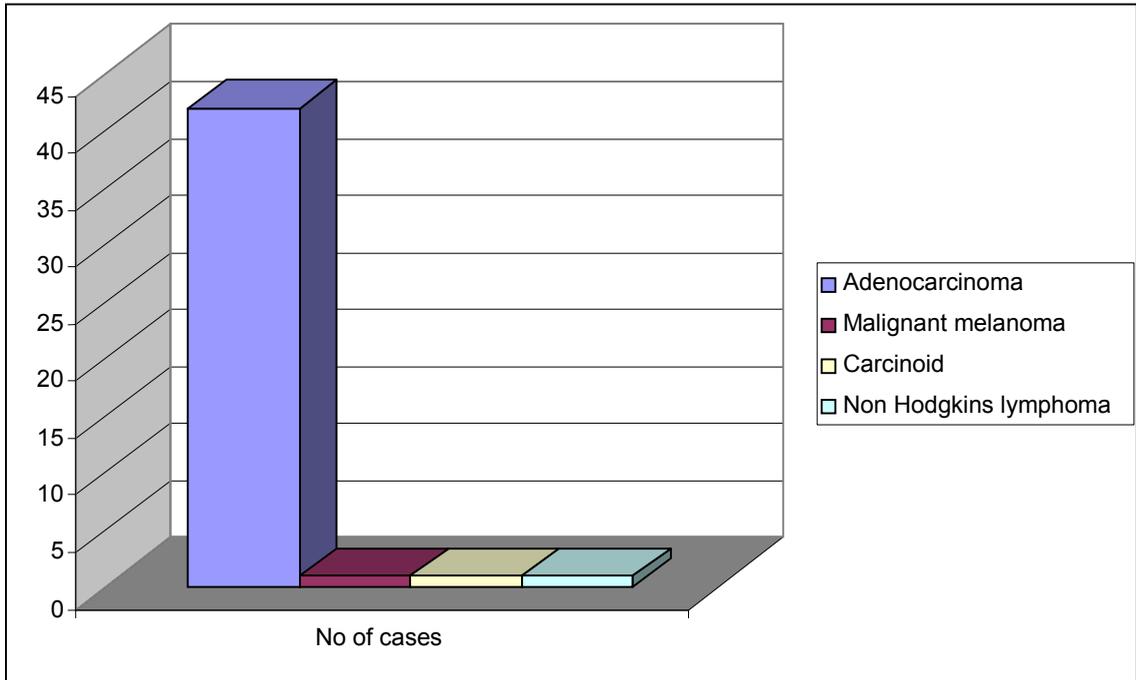


Figure 1: Incidence of large intestinal tumors

Majority of these tumors 24(57.14%) were located in the rectum. Morphologically, 17(40.48%) tumors were of ulcero-proliferative type. Cut section of the tumors was grey-white, with areas of necrosis. Mucin was observed grossly in 4 tumors. All these tumors showed infiltration into the wall of the intestine.

Lymph nodes were isolated in 18 specimens. The size of which varied from 0.5cm -1cm. The number of lymph nodes isolated varied from 1 to 12. Cut section of these lymph nodes was grey-white and four showed tiny areas of mucin. Of the lymph nodes isolated from 18 specimens, 11 showed metastatic deposits. Adenocarcinoma was further divided into two groups, based on mucin production into mucinous and non mucinous adenocarcinoma. The criteria to include a tumor under mucinous was presence of mucin comprising >50% of the tumor. Mucin in these tumors appeared pale blue with H & E stain and was seen intracellularly, extracellularly or both, with intracellular mucin giving a signet ring appearance to the cells. The mucin was highlighted with special stains like PAS and mucicarmine. Of the 42

adenocarcinomas, 9 (21.42%) were mucinous adenocarcinomas.

Histological grading of adenocarcinoma

The degree of differentiation of the tumor was recorded according to three grade system. Non mucinous adenocarcinomas were divided into three grades: well differentiated adenocarcinoma consisting of entirely of well formed glands, moderately differentiated carcinomas with solid sheets of malignant cells comprising at least 25% of the tumor, mixed with glands and poorly differentiated consisting of solid sheets of malignant cells with < 25% of recognizable glands. Of the 9 mucinous adenocarcinomas, one tumor had a preponderance of tumor cells with intra cytoplasmic mucin, pushing the nucleus of the cell to the periphery, giving the appearance of signet ring and this tumor was categorized as signet ring cell carcinoma. Of the 31 resected segments with adenocarcinoma lymph node metastasis was seen in 11(35.48%) (Table 2). These tumors showing lymph node metastases in resected specimens of

Table 2. Lymph node metastasis

Type of adenocarcinoma	No of cases with lymph node metastases	Percentage
Well differentiated	1	9.09
Moderately differentiated	4	36.37
Poorly differentiated	1	9.09
Mucinous adenocarcinoma	5	45.45
Total	11	100

adenocarcinoma were of different histological grades.

Stromal inflammatory infiltrate: Of the total 45 colorectal malignancies studied, 9(20%) had inflammatory infiltrate consisting predominantly of lymphocytes.

Resected margins: Resected margins in all 31 colorectal adenocarcinomas was >5cms on either side or microscopically and macroscopically free of tumor.

Malignant melanoma: Of the 45 colorectal malignancies, one (2.22%) tumor was diagnosed as malignant melanoma on a biopsy from the rectum of a 50 year old man who presented with bleeding per rectum. The tumor showed a biphasic pattern with presence of melanin pigment.

Carcinoid: Of the 45 colorectal malignancies, one (2.22%) tumor was diagnosed as carcinoid of sigmoid colon in a 45 year old man who presented with pain abdomen.

Microscopically: There was ischemic necrosis of wall with many dilated blood vessels. Sections from necrotic segment showed small viable area with features of carcinoid tumor, one lymph node isolated was normal.

Non Hodgkin's lymphoma: Rectal mucosal biopsy of a 70 year old man presenting with pain abdomen showed Non-Hodgkin's lymphoma accounting for 2.22% of the colorectal malignancies. Microscopically, sections showed rectal mucosa with ulceration. There was diffuse infiltrate of non cohesive cells. These cells were uniform, had scant cytoplasm, large nuclei with irregular contours and small nucleoli.

Tumor like lesions: The number of tumor like lesions encountered in the present study was 14 constituting 23.72% of the 59 specimens studied. The various types of tumor like lesion encountered were 12(85.71%) juvenile polyps and one (7.14%) each of hyper plastic polyp and inflammatory polyp.

Table 3. Incidence of various tumors and tumor like lesions of large intestine

Tumors	Histological type	No of cases	Total cases
Epithelial tumors			
Benign	--	Nil	
	Adenocarcinoma	32	
Malignant	Mucinous adenocarcinoma	9	
	Signet ring cell carcinoma	1	45
Carcinoid tumors	Carcinoid	1	
Non epithelial tumors	--	Nil	
Hematopoietic and lymphoid neoplasms	Non Hodgkin's lymphoma	1	
Unclassified tumors	Malignant melanoma	1	
Secondary tumors	--	Nil	
	Juvenile polyp	12	
Tumor like lesions	Hyperplastic Polyp	1	14
	Inflammatory polyp	1	
Total			59

DISCUSSION

Geographic variation in the incidence of colorectal cancer has been well documented in different parts of the world and this variation has been ascribed to multiple environmental factors (Dajani *et al.*, 1980). Large intestinal malignancies in the present study constituted 6.81 % of the total (660) malignancies reported during the study period . In west midlands, annual incidence between 1957 – 1981, was 24.5 per 1,00,000 population for colonic cancer and 18.4 per 1,00,000 for that of the rectum (Allum *et al.*, 1994). However in the present study, the prevalence of colorectal carcinoma was 0.44%, which represents only a hospital based statistics.

Age: Colorectal cancer becomes more frequent with increasing age, but is by no means a disease of extreme old age. The mean age at diagnosis is

around 60 years (Jass, 1992). The mean age of patients with colorectal carcinoma in the present study was 48.8 an observation consistent with the Jordanian study reported by Dajani *et al.*, 1980.

Sex: In men rectal cancer ranks 7th in Bhopal and Bangalore Cancer registry. In women rectal cancer ranks 8th in Bombay and Madras, while colon cancer ranks 8th in Bangalore and Bhopal. Luthra and Jain, 1992, Cancer of colon is more common in women than men in a proportion of 2:1 (Dowson and Morson, 1979). In the present study, the number of females with colonic cancer were more (26 patients, 57.77%) than males. The F: M being 1.38:1 Rectal cancer is more frequent in males and difference increases with age (Morson and Dowson, 1979; Jass, 1992; Jass, 1987). This was not substantiated in the present study, where M: F was 1:1. About 50% of all carcinoma occur in the recto sigmoid area although their relative incidence seems to be decreasing (Jass, 1987; Rosai, 1996). Tumors showed a predilection for left side similar to other studies (Qizilbash, 1982; Dajani *et al.*, 1980).

Morphology of tumors in resected specimens of large intestine

It is said that tumors of the proximal colon tend to grow as exophytic masses leading to intestinal obstruction, whereas tumors of the distal colon tend to be annular encircling lesions that produce so called napkin ring constrictions of the bowel.¹¹ Most cancers of colon and rectum are ulcerating tumors with raised everted edges (Joss, 1987). This fact was observed in the present study, where 22(68.75%) tumors had ulcerated surface.

Microscopy

Adenocarcinoma was the most common type of malignancy encountered in the large intestine accounting for 93.33% of the tumors, a finding consistent with the study by various authors (Joss Qizilbash, 1982; Dajani *et al.*, 1980; Osime *et al.*, 1988). Incidence of large intestine adenocarcinoma varies widely from 5– 55 per 1,00,000 population (Dajani *et al.*, 1980; Owen and Kelly, 1990).

Table 4. Incidence of adenocarcinomas in various studies

Studies	No of cases Adenocarcinoma/ Total malignancies	Percentage
Qizilbash Al (1982)	244/247	94.94
Osime, Morgan, Guirguis (1988)	73/76	96.05
Present study	42/45	93.33

However, in the present study adenocarcinoma of large intestine constituted 0.41% of the total specimens received which represents only a hospital based statistics. Between 10 and 15% of colorectal cancers are mucinous, implying that substantial quantities of mucin are retained within the tumor (Joss, 1987). This was also the finding in the present study where mucinous adenocarcinomas constituted 22.22% in contrast to low incidence reported by Osime, Morgan, Guirguis as well as Qizilbash Al H (Qizilbash, 1982; Osime *et al.*, 1988). Two main growth patterns of mucinous adenocarcinoma were encountered. Glands filled with mucin together with interstitial mucin and chains or clumps of cells surrounded by mucin. It is true that grading of all mucinous adenocarcinoma is made rather inaccurate by the presence of large amounts of secretions which compresses and obscures the cytological elements and tumors composed only of signet ring cells are rare in those countries with a high incidence of colorectal cancers but are definitely more frequent in low risk areas. In the present study, only a single case of signet ring cell carcinoma with predominant signet ring cells was encountered.

Histological Grading

About 50% of the tumor were well differentiated, and degree of differentiation varies widely (Morson and Dowson, 1979; Joss, 1987). Twenty percent of the tumors showed local inflammatory infiltrate in contrast to other studies. Spratt Spjut graded the inflammatory reaction around the cancer from none to severe and demonstrated doubling of the five year survival in lesions associated with severe reaction. Similarly Murray et

al found a 46% five year survival in patients with Duke's B carcinoma without local inflammatory reaction and an 89% five year survival in those cases associated with such a reaction (Qizilbash, 1982).

Lymph node metastasis

Eighteen tumors measured more than 4cm of which 8 (44.44%) showed regional lymph node metastasis. Among these 3 (37.5%) were mucinous adenocarcinomas.

Malignant melanoma

Malignant melanoma invariably arises in the transitional zone above the dentate line and is therefore classified among the malignant melanomas of the mucus membranes. Pigment is not always obviously present on macroscopic observation. As with squamous cell carcinomas of the anal canal, malignant melanomas show preferential upward submucous spread, which is the reason why they present clinically as growths of the rectum (Joss, 1987). The present case of malignant melanoma was encountered in the rectum Nicholson *et al.* (1992) also reported five cases of malignant melanoma in the rectum.

Carcinoid tumors

Carcinoid tumors of the colon are rare entities constituting approximately 2.5% of all gastrointestinal carcinoids and less than 1% of colorectal neoplasms. Incidence of colonic carcinoids varies in different age groups as reported by Ballantyne *et al.* (1991) and other studies (Ballantyne *et al.*, 1992; Rosenberg and Welch, 1985; Federspiel *et al.*, 1989; Kaura *et al.*, 1997). The single case encountered in the present study was in the sigmoid colon and accounted for 2.22% of all colorectal cancers. Although a rare entity, carcinoid tumors of the colon, when encountered, represent a challenge to the colorectal surgeon. These lesions may be observed in any age group including the pediatric population. In addition, these patients require evaluation of the entire gastrointestinal tract for evidence of coexisting malignancy (Ballantyne *et al.*, 1992).

Lymphoma

Though gastrointestinal tract is the most common site for extra nodal non Hodgkin's lymphoma, large intestine is rarely involved accounting approximately 0.2 to 1% of all colorectal malignancies. This feature was observed in the present study where Non Hodgkin's Lymphoma (NHL) constituted 2.22% of all colorectal malignancies. Lymphomas of the colon have been reported by various authors in their studies (Gloekner *et al.*, 1999; Nirmala *et al.*, 1981; Lavergne *et al.*, 1994; Yatabe *et al.*, 1998; Isaacson *et al.*, 1984). It is important to determine whether the lymphoma is primary or secondary in the colon because of the known tendency of these tumors to remain localized and therefore, amenable for radical excision. Recently much attention has been directed to the morphologic and phenotypic similarities between malignant and benign lymphoreticular cells. This has resulted in great advances in the classification and understanding of non Hodgkin's lymphomas.

Conclusion

The results of careful and systematic examination of surgical specimens from patients with tumors of the large intestine play an important role in patient care and the assessment of prognosis. The pathology report should include information on the site or sites of tumor, the size, configuration and circumference of the bowel wall involved, obstruction, distance of resected margin from the tumor, depth of infiltration tumor grade, tumor margin, local inflammatory reaction, lymph node involvement and location and venous and perineural invasion. With the overwhelming success of chemoradiation, multidisciplinary cancer care and application of new concepts in radiology, chemotherapy and basic research for the treatment of tumors of the large intestine, the role of pathologist remains important in evaluation, diagnosis and staging so as to help the clinician in proper management of the disease.

REFERENCES

- Allum W. H. *et al.*, 1994 "Cancer of the colon and rectum in the west Midlands. *Br J Surg.*, 81: 1060-63.

- Ballantyne G.H. *et al.*, 1992. Incidence and mortality of carcinoids of the colon. *Cancer*, 69 : 2400-2405.
- Behbehani A. *et al.*, 1985 "Colorectal carcinoma in patients under age 40", *Ann Surg* , 202: 610-14.
- Crawford J M. 1999. The Gastrointestinal tract" Chapter 18 in Pathologic basis of disease, 6th edn, Cotran, R.S. Kumar V. and Collin T., Philadelphia: Ws Saunders Company, 775-844.
- Dajani Y. F. *et al.*, 1980 " Colorectal cancer in Jordan and Nova Scotia. *Cancer*, 46: 420-6.
- Federspiel, B.H. *et al.*, 1989. Rectal and colonic carcinoids. *Cancer*, 65 : 135-40
- Gloekner, K. *et al.*, 1999. Colonical primary large cell lymphoma with maginal zone growth pattern presenting as multiple polyps. *Am J Surg Pathol.*, 23 (9) : 1149-52.
- Isaacson P. *et al.*, 1984. Extranodal malignant lymphoma arising from mucosa associated lymphoid tissue. *Cancer*, 53 . 2515-2524.
- Jass J.R. 1992. Epithelial and mesenchymal tumors of the small and large bowel," CHAPTER 16.16 in Oxford Textbook of Pathology, McGee James O. P., Isoason P G and Wright N.A., New York : Oxford University Press, 1258-1269.
- Joss J.R. 1987. Alimentary Tract", Systemic Pathology, 3rd edn. Morson B.C, Symmers St C.W., New York : Churchill Livingstone, 353-416.
- Kalyani, R., Subhashish Das, M L. and Harendra Kumar, 2010. Spectrum of gastrointestinal cancers- a ten years study. *J. Indian Med. Assoc.*, 108 : 659-62
- Kaura A.N. *et al.*, 1997. Carcinoid tumours of the rectum. *Cancer*, 79 : 1294-98.
- Lavergne A. *et al.*, 1994. Multiple lymphomatous polyposis of the gastrointestinal tract", *Cancer*, 74 : 3042-3050.
- Luthra U.K. and Jain D.K. 1988. National Cancer Registry Programme, Biennial Report, 1988-89, Population based cancer registries- An epidemiological study. New Delhi, ICMR, 1992, 12.pp.
- Morson B.C. and Dowson I.M.P. 1979. Gastrointestinal Pathology, Oxford, London: Blackwell Scientific publications, 607-755.
- Nicholson, A.G. 1993 "Primary malignant melanoma of the rectum. *Histopathology*, 22 : 261-264.
- Nirmala V., Thomas J.A. and Anthony A J. 1981. Primary malignant lymphoma of colon. *Indian J Cancer*, 18 : 47-50.
- Osime U., Morgan A. and Guirguis M., 1988 "Colorectal Cancer in Africans" *J Indian Med Assoc*, 86: 270-272.
- Owen D. A. and Kelly J.K. 1990. Large intestine and Anus", chapter 56 in Andersons Pathology, 10 th edn. Damnajov I . Linder J., St Louis Missouri: Mosby Year Book Inc; 1741-78.
- Qizilbash, A.H. 1982. Pathologic studies in colorectal Cancer. *Pathol Annu*, 23:27-66.
- Rosai J. 1996. Gastrointestinal tract", Chapter 11 in Ackerman's Surgical Pathology, 8th edn, New York, Mosby Year book Inc., 729- 814.
- Rosenberg J.M. and Welch J.P 1985. Carcinoid tumours of colon. *Am J Surg.*, 149 : 775-79.
- Taylor I., 1990. Colon polyps and colon cancer." *Medicine International*, 80: 3300-3304.
- Yatabe Y. *et al.*, 1998. Multiple polypoid lesions of primary mucosa associated lymphoma of colon. *Histopathology*, 32 : 116-25.
