Original Research

ScopeMed

Spectrum of intestinal neoplasms: A study of 400 cases

Aminder Singh, Bhavna Garg, Neena Sood, Harpreet Kaur Puri, Vikram Narang, Sumit Grover

Department of Pathology, Dayanand Medical College & Hospital, Ludhiana, Punjab, India

Address for correspondence:
Aminder Singh, Assistant Professor, Department of Pathology, Dayanand Medical College & Hospital, Ludhiana - 141 001, Punjab, India.
Phone: +91-8968966550,
E-mail: dramisingh@gmail.com

ABSTRACT

Objective: The present study is a five-year analysis of all the tumors of small and large intestine received in the Pathology Department of Dayanand Medical College and Hospital, Ludhiana. **Methods:** All the cases were grossly and microscopically examined and were staged according to Astler Coller Staging and classified and subtyped according to WHO classification. The important differences between the small and large intestine tumors were also analyzed. **Results:** There were 400 cases out of which 356 were in large intestine while 44 were in the small intestine. There were only 56 benign neoplasms while 344 were malignant tumors. Adenomas were the most common benign tumors while majority of malignant tumors were adenocarcinomas. Lymphomas, mesenchymal tumors, and carcinoid tumors were much more common in a small intestine as compared to large intestine. Majority of adenocarcinomas were located in the large intestine with most of them being moderately differentiated having Astler Coller Stage B II. Mucinous carcinomas had the worst prognosis as compared to adenocarcinomas. Anal canal had mainly squamous cell carcinomas. **Conclusions:** Tumors of large intestine were much commoner than of small intestine. There was a higher incidence of tumor in males with M:F ratio of 2.2:1. Mean age of presentation of benign tumor was younger, i.e., 32.6 years when compared to 54.5 years for malignant tumors. Tubular adenoma was the most common benign tumor and adenocarcinoma the commonest malignant neoplasm.

KEY WORDS: Adenocarcinomas, Astler Coller staging, small and large intestine

INTRODUCTION

Intestinal tumors are extremely common these days, and there is a general tendency to study these tumors according to their site, i.e., whether of a small intestine, large intestine or anal canal. Small intestinal tumors comprise of only 3-6% of all gastrointestinal neoplasms. One of the enigmas of medicine is a low incidence of malignant neoplasms in the small intestine. The ones occurring are usually related to genetic syndromes like familial adenomatous polyposis (FAP). Lymphomas and endocrine tumors are fairly common in a small intestine. On the other hand, colon and rectum are leading sites for cancer. Both environmental and genetic factors play a role in the etiology with adenomas and chronic inflammatory conditions like ulcerative colitis being the main precursor lesions. Cure is strongly related to the anatomical site, microscope grading of the tumor and staging, which is related to the extent of invasion of bowel wall and lymph node metastasis. Hence in this study, incidence of tumors according to their site was ascertained, and the differences between small and large intestinal tumors were studied. Also, pathological features of all the tumors were noted and their grading was done.

MATERIALS AND METHODS

The present study was a 5-year study conducted in the Pathology department. In this study, all the tumors of small and large intestine were analyzed with reference to light microscope findings with special emphasis on histological type and grade of tumors. In each patient; clinical findings (age, sex, clinical presentation and operative findings) were noted. All the pathological findings were recorded by examination of hemotoxylin and eosin stained slides. The cases were histologically classified and subtyped according to WHO classification [1,2] of tumors of a small intestine, large intestine, and anal canal. Their site, size, gross features, histological type and grade of the tumor were noted. The depth of penetration, vascular, perineural and lymphatic invasion along with the presence of lymph node and mesenteric deposits were also noted. The tumors were graded, and a comparison was done between large and small intestinal tumors. Other associated significant disease like inflammatory bowel diseases, polyps etc. were also taken note of.

RESULTS

Total number of cases analyzed were 400 out of which majority were present in large intestine [Table 1]. The most common clinical presentation was bleeding per rectum in 25% cases followed by obstruction in 22.2% patients, perforation in 2.5% patients, altered bowel habits and jaundice in a few other cases. The rest, i.e., 41% were asymptomatic.

Large intestinal tumors comprised of the major chunk (90%) of tumors. The most common age group affected by the tumors was between 50 and 59 years (23.75%) with age ranging from 1 year to 92 years. The tumors were broadly classified into benign and malignant. The number of benign tumors was 56 while malignant constituted 344 cases. In benign tumors, the mean age of presentation was 32.6 years while in malignant tumors it was 54.4 years. There were 275 males and 125 females with a male to female ratio of 2.2:1.

Out of the 56 cases of benign tumors; tubular adenomas were commonest (23 cases) closely followed by juvenile polyps (21 cases). There were 3 cases each of Peutz Jeghers polyps and villous adenoma. 2 cases each of hyperplastic polyps and FAP were encountered. There was one case each of tubulo-villous adenoma and lipoma. Only two of these cases were located in the small intestine; rest of them were in the large intestine.

In the malignant category 285 cases were of adenocarcinoma, 28 cases were of mucinous carcinoma, Non-Hodgkin's lymphoma (10 cases), gastrointestinal stromal tumor (GIST) (7 cases), squamous cell carcinoma (5 cases), carcinoid tumor (3 cases), metastatic carcinoma (2 cases), malignant mesenchymal tumor (2 cases) and 1 case each of signet ring cell carcinoma and undifferentiated carcinoma.

Further analyzing the small intestinal tumors; we made the following observations [Table 2]. There were only two cases of benign neoplasms; both of which were Puetz Jeghers polyps. Majority of adenocarcinomas were located in the duodenum and all of them presented as polypoidal growths ranging in size from 1 to 3 cm. Microscopically, out of 18 cases; 17 were moderately differentiated, and 1 was of well-differentiated type. About 79.4% cases had regional lymph node involvement. No distant metastasis was seen. There were 5.42% cases with perineural invasion and 11.1% cases with vascular invasion.

Nine cases of Non-Hodgkin's lymphomas were found with the majority being located in the ileum [Figure 1]. All the cases had diffuse thickness of the wall. Their mean age of presentation was 51 years with M:F ratio of 1.8:1. All these cases were of MALToma's and were graded as high and low grade as per

Table 1: Distribution of tumors according to site

Site	Total number of cases	Percentage of cases
Small intestine	39	9.8
Large intestine	356	89
Anal canal	5	1.2
Total number of cases	400	100

WHO Grading of MALToma's. There were 6 cases of low-grade lymphomas and 3 of high-grade ones. Seven cases of GIST were encountered majority of which were in jejunum. They were seen as subserosal nodular growths ranging in size from 1-10 cm. The mean age of presentation was 53 years with M:F ratio of 6:1. They were categorized into high and low-risk types on the basis of tumor size, mitotic activity, etc. There were 5 cases of high-risk category while 1 case each was of intermediate and low risk. There were 3 cases of carcinoid tumors as well [Figure 2].

We also analyzed in detail 356 cases of large intestinal tumors; out of which 148 (41.5%) were located on right side of colon, 110 (30.8%) on left side and 98 (27.6%) cases were located in the rectum. In benign cases mean age of presentation was 32.6 years while in malignant tumors it was 54.5 years. Out of 356 cases, 54 were benign tumors while 302 belonged to the

Table 2: Division of malignant small intestinal tumors according to anatomical site and morphological type

Site	Type of tumor	Total number of cases	Percentage of cases
Duodenum	Adenocarcinoma	17	43.6
	Non-Hodgkin's lymphoma	3	7.7
	Carcinoid	2	5.1
Jejunum	GIST	5	12.8
	Non-Hodgkin's lymphoma	2	5.1
Ileum	Non-Hodgkin's lymphoma	4	10.3
	GIST	2	5.1
	Mucin secreting	2	5.1
	Recurrent adenocarcinoma	1	2.6
	Carcinoid	1	2.6
Total number of cases		39	100

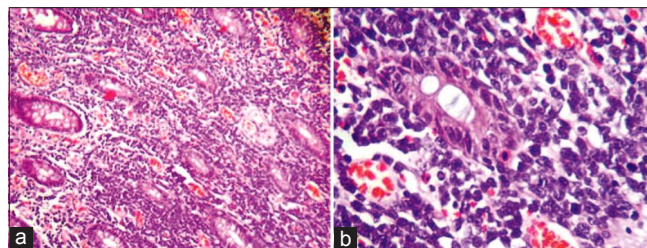GIST: Gastrointestinal stromal tumor

Figure 1: (a) Diffuse sheets of small round cells of Lymphoma present in between the intestinal glands (H & E, ×100). (b) High magnification showed that lymphomatous cells are surrounding and infiltrating the intestinal glands (H & E, ×400).
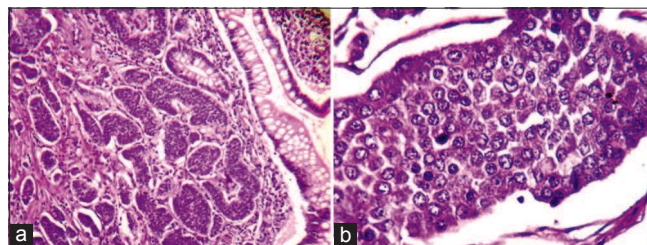

Figure 2: (a) Well-formed Zell Ballen (Nesting) pattern by tumor cells of carcinoid (H & E, ×100). (b) High magnification showed classical salt and pepper chromatin pattern of carcinoid tumor cells (H & E, ×400).

Table 3: Malignant tumors of large intestine

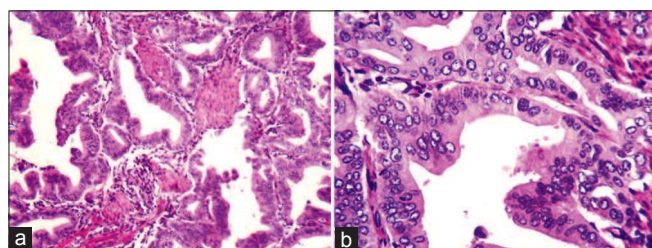| Type of tumors	Total number of cases	Percentage of cases
Adenocarcinoma	267	88.4
Mucinous carcinoma	28	9.3
Metastatic carcinoma	2	0.7
Malignant mesenchymal tumor	2	0.7
Signet ring cell carcinoma	1	0.3
Non-Hodgkin's lymphoma	1	0.3
Squamous cell carcinoma	1	0.3
Total number of cases	302	100

Figure 3: (a) Well-formed glandular pattern of adenocarcinoma of large intestine (H & E, ×100). (b) High magnification showed nuclear hyperchromasia and stratification without any intervening stroma (H & E, ×400)

malignant category. Out of the benign neoplasms there were 23 cases of tubular adenomas, 3 of villous adenoma and 1 case of tubulovillous adenoma. 21 cases of juvenile polyps, 2 cases of hyperplastic polyp and 1 case of Peutz Jeghers polyp were encountered. There was 1 case of lipoma and 2 patients had FAP.

Adenocarcinoma [Figure 3] was the commonest tumor of a large intestine comprising 267 cases [Table 3]. The mean age of presentation was 54.5 years with M:F ratio of 2.5:1. 86 cases had exophytic growth, 57 ulcerative and 24 had infiltrative growth patterns. 240 cases were moderately differentiated, 22 poorly differentiated and 5 were well differentiated. The staging was done according to Astler Collar staging system. The most common stage was B II (52.7%) followed by C II (46.7%) implying that the nodal metastasis was noted in 46.7% cases. Mucinous carcinoma was second most common malignant tumor after adenocarcinoma. In them most common stage was C II (64.7%) followed by B II (35.7%); hence lymph node metastasis was even more in this subgroup. 2 cases each of malignant mesenchymal tumor and metastatic tumor were identified. There was 1 case each of signet ring cell carcinoma, non-Hodgkin lymphoma, and squamous cell carcinoma.

There were 5 cases having anal canal tumors, out of which 4 were squamous cell carcinomas, while 1 case was of undifferentiated carcinoma. All these cases presented with infiltrative growth ranging in size from 2-3.5 cm. All squamous cell carcinoma were moderately differentiated.

DISCUSSION

The present study included all the case of neoplasms of small and large intestine and anal canal which were received in the Department of Pathology. These were analyzed both grossly and microscopically. The tumors' were classified according to WHO guidelines [1,2]. In our analysis tumors of a small intestine were much less (only 9.8%) as compared to tumors of a large intestine, which constituted 91.8% of the cases. This low incidence was also encountered by Chew *et al.* [3] who also found that small bowel tumors were 40-60 times less common than large bowel tumors. A higher incidence was seen in males irrespective of the type and site of tumors with M:F ratio 2.2:1. This correlated with study done by Thomas *et al.* [4] who also found M:F ratio of 2:1 in their analysis of gastrointestinal tumors over a period of 5 years. Most common age group affected was between 50 and 59 years with a mean age of presentation being 54 ± 2.4 years. We broadly classified the tumors as benign and malignant with the number of malignant tumors being far more than benign tumors. Also, the mean age of presentation of benign tumors was 32.6 years while that for malignant ones was 54.4 years; indicating that benign tumors occurred almost two decades earlier than the malignant ones. This is corroborated by Kumar *et al.* [5], who also found that benign tumors occurred at a younger age group. In our study, tubular adenoma was commonest benign tumor which was also reported by Rudy *et al.* [6], who reported that tubular adenomas constituted 83% of all benign tumors. On the other hand, the most common malignant tumor encountered by us was adenocarcinoma. Berg *et al.* [7] also found that adenocarcinoma is the commonest malignant tumor of the gastrointestinal tract. Neuguet *et al.* [8] and Chew *et al.* [3] suggested that high incidence of adenocarcinomas in duodenum and colon was due to similar risk factors for cancer i.e., alcohol intake, smoking, inflammatory bowel disease and FAP, etc. in these regions.

In the small intestine; duodenum was the most common site affected by tumor, followed by ileum and jejunum. Chew *et al.* [3] also found the similar trend. However, Ionnis *et al.* [9] had most of the tumors in ileum followed by duodenum and jejunum in his study. This disparity could be explained by the fact that in their study maximum cases were of lymphomas while in the other, adenocarcinoma predominated. Adenocarcinomas (46.2%) were the commonest tumors followed by non-Hodgkin's lymphomas (23%), GIST (17.9%) and carcinoids (7.7%). Almost all adenocarcinomas were located in the duodenum especially near ampulla of Vater whereas lymphomas and carcinoids were more commonly seen in the ileum; whereas GIST's were more in jejunum. This similar distribution pattern was also reported by chew *et al.* [3]. 99% of our patients with adenocarcinoma of a small intestine presented with jaundice 95% of all. Adenocarcinomas were moderately differentiated with lymph node metastasis in 79.4% cases. All these tumors had penetrated the entire wall thickness. The second most common tumor in a small intestine was non-Hodgkin's lymphoma, i.e. 23% cases. This is in contrast with a large intestine where there were only 0.3% cases of lymphomas. All the cases were of MALToma's and ileum were the commonest site of involvement. Issca *et al.* [10] also encountered lymphomas primarily in the ileum which were mainly MALToma's. Next common tumor of a small intestine was GIST constituting 17.9% of all cases. Miettinen *et al.* [11] also reported that GISTs were common in a small intestine constituting 14% of all small intestinal tumors. Taking into account tumor size and mitotic activity we graded these GISTs

and majority of them turned out to be of low risk category. Miettinen *et al.* [11] and Franquemont *et al.* [12] also had similar results. There were 3 cases of carcinoid and 2 cases of Peutz Jegher's polyps.

The large intestinal tumors were also divided into benign and malignant categories. The benign tumors constituted 15.2% of the cases while malignant were 84.8%; hence malignant were 5 times more common than the benign ones. This high incidence of adenocarcinomas in colon was also reported by Potler *et al.* [13] according to whom the vast majority of adenocarcinomas were due to adoption of western lifestyle, high intake of non-vegetarian diet, smoking and alcohol consumption. In the category of benign tumors adenomas topped the list with the majority being tubular adenomas whose size ranged from 0.3 cm to 1.2 cm. Villous and tubulo-villous adenomas accounted for 5.5% and 1.8% cases, respectively. There were 2 cases of FAP who had more than 100 polyps in the colon ranging in size from 0.5 cm to 2 cm. Both the cases were males with mean age of presentation being 27 years.

Adenocarcinomas were the commonest malignant tumors with a mean age of presentation being 54.5 years. The youngest case was a 14-year-old boy. Higher incidence of adenocarcinoma was seen in the proximal colon (55.6%) as compared to distal colon (44.4%). Demere *et al.* [14] also reported the same findings and he reported that contact time of fecal stream was higher in proximal colon as compared to distal colon and rectum that is why there is a higher incidence of adenocarcinoma in the proximal colon. 2.3% of adenocarcinomas had synchronous presence of tubular adenomas which is concordance with study done by Eide *et al.* [15] who reported that large bowel specimens with carcinomas had higher incidence of polyps than those without carcinomas. Only 7% of adenocarcinomas showed association with inflammatory bowel disease, i.e. ulcerative colitis in our group.

The commonest grade encountered was moderately differentiated accounting for 89.9% of all adenocarcinomas followed by grade 3(8.2%) and grade 1(1.9%). This is also collaborated by WHO [1,2] which identified moderate differentiation as the commonest grade. Staging was done according to Astler Coller staging system [1]. 52.7% cases were of stage B II category followed by C II (46.7%) and B I (0.6%), i.e., lymph node involvement was there in 46.7% cases. Thomas *et al.* [4] also had 50% cases with regional lymph node deposits at the time of presentation. Mucinous carcinomas were the second commonest malignancy of the colon in our study. This similar incidence was also reported by Atkins *et al.* [16]. 64.3% of cases of mucinous carcinoma were of stage Astler Coller C II. Perineural invasion was seen 8.9% cases and vascular invasion in 11.2% cases. This advanced stage and more aggressiveness of mucinous carcinoma was also noted by Younes *et al.* [17] who stated that mucinous carcinoma carried a worse prognosis. Signet ring cell carcinomas formed <1% of all malignant tumors of the intestine. Also, lymphomas and GISTs were very less in incidence as compared to those in a small intestine. There were only 5 cases of tumors

of the anal canal, and this low incidence was documented by Winawer *et al.* [18] also. Out of these majority of the cases ie, 4 were squamous cell carcinoma while one case was of undifferentiated carcinoma.

To summarize, we concluded from our study that tumors of a large intestine were much commoner than of a small intestine. There was a higher incidence of tumor in males with M:F ratio of 2.2:1. Mean age of presentation of benign tumor was younger, i.e. 32.6 years as compared to 54.5 years for malignant tumors. Tubular adenoma was the commonest benign tumor and adenocarcinoma the commonest malignant neoplasm.

Lymphomas and mesenchymal tumors occurred more commonly in a small intestine while large intestine mainly had adenocarcinomas. In small intestine duodenum harbored majority of adenocarcinomas while jejunum had more mesenchymal tumors and ileum had lymphomas especially MALToma's. We encountered carcinoids only in a small intestine. Adenomas were commonest benign tumor of a large intestine, followed by juvenile polyps. Adenocarcinomas were extremely common in large intestine with majority being moderately differentiated. Lymph node metastasis was seen in 46.7% cases. Stage B II was commonest. Mucinous carcinoma had a higher stage. In large intestine, GISTs and lymphomas were very rare.

REFERENCES

1. Astler VB, Coller FA. The prognostic significance of direct extension of carcinoma of the colon and rectum. Ann Surg 1954;139:846-52.
2. Wright NH, Howe JR, Solun LH. Pathology and Genetics of Tumour of Digestive System. World Health Organization Classification of Tumour. Lyon: IARC Press; 2000. p. 69-145.
3. Chow JS, Chen CC, Ahsan H, Neugut AI. A population-based study of the incidence of malignant small bowel tumours: SEER, 1973-1990. Int J Epidemiol 1996;25:722-8.
4. Thomas RM, Sobin LH. Gastrointestinal cancer. Cancer 1995;75:154-70.
5. Kumar V, Abbas AK, Fausto N. The gastrointestinal tract. In: Pathologic Basis of Disease. 7th ed. Philadelphia: Elseveir Inc.; 2004. p. 797-876.
6. Rudy DR, Zdon MJ. Update on colorectal cancer. Am Fam Physician 2000;61:1759-70.
7. Berg JW, Howell MA. The geographic pathology of bowel cancer. Cancer 1974;34:807-14.
8. Neugut AI, Jacobson JS, Suh S, Mukherjee R, Arber N. The epidemiology of cancer of the small bowel. Cancer Epidemiol Biomarkers Prev 1998;7:243-51.
9. Hatzaras I, Palesty JA, Abir F, Sullivan P, Kozol RA, Dudrick SJ, *et al*. Small-bowel tumors: Epidemiologic and clinical characteristics of 1260 cases from the connecticut tumor registry. Arch Surg 2007;142:229-35.
10. Isaacson PG, Spencer J. Malignant lymphoma of mucosa-associated lymphoid tissue. Histopathology 1987;11:445-62.
11. Miettinen M, Sarlomo-Rikala M, Lasota J. Gastrointestinal stromal tumors: Recent advances in understanding of their biology. Hum Pathol 1999;30:1213-20.
12. Franquemont DW. Differentiation and risk assessment of gastrointestinal stromal tumors. Am J Clin Pathol 1995;103:41-7.
13. Potter JD. Colorectal cancer: Molecules and populations. J Natl Cancer Inst 1999;91:916-32.
14. Demers RY, Severson RK, Schottenfeld D, Lazar L. Incidence of colorectal adenocarcinoma by anatomic subsite. An epidemiologic study of time trends and racial differences in the Detroit, Michigan area. Cancer 1997;79:441-7.
15. Eide TJ. Prevalence and morphological features of adenomas of the large intestine in individuals with and without colorectal carcinoma. Histopathology 1986;10:111-8.

16. Sasaki O, Atkin WS, Jass JR. Mucinous carcinoma of the rectum. Histopathology 1987;11:259-72.
17. Younes M, Katikaneni PR, Lechago J. The value of the preoperative mucosal biopsy in the diagnosis of colorectal mucinous adenocarcinoma. Cancer 1993;72:3588-92.
18. Winawer SJ, Fletcher RH, Miller L, Godlee F, Stolar MH, Mulrow CD, *et al.* Colorectal cancer screening: Clinical guidelines and rationale. Gastroenterology 1997;112:594-642.