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Clinicopathological study of colorectal malignant neoplasm with special emphasis on vascular invasion as prognostic factor.

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Abstract

Colorectal cancer is the fourth most common cancer in the world and fifth most common cancer in India. We conducted 4 year cross sectional study to find various morphological spectrum of colorectal cancer, its clinical presentation and to study the association of vascular invasion with grade and stage of colorectal cancers. We included total of 35 cases in the study which were fitting our eligibility criteria. Biopsy samples, lack of data about anatomical location and presence of other histopathological types were excluded from the study. The specimens were received in 10% formalin & thorough gross examination was done. The gross details were noted and sections were taken from tumour including tumour border and adjacent mucosa, non-neoplastic mucosa, proximal and distal margin of resection. Special stains for e.g. elastic stain were done wherever necessary. For old cases H&E stained slides were retrieved from pathology archives, took extra sections and screened for vascular invasion. Data was collected, compiled, and analyzed using Epi Info version 7.2. Vascular invasion, peri neural invasion, tumour budding, tumour necrosis and inflammatory response are some prognostic factors studied in colorectal cancers. We also noted vascular invasion and its association with the grading and staging of the colorectal cancers. The most common location noted in our study was descending colon. In our study vascular invasion was present in 40% of the patients. In our study we found the significant association of vascular invasion with grading and staging of the tumour based on Astler Collar staging. As the staging and grade increases, the proportion of the vascular invasion also increases significantly. Vascular invasion thus is a vital marker to be noted that will assist the clinician making

decisions of the management of the tumour and predicts the prognosis.

Keyword: Colorectal carcinoma, vascular invasion, prognostic factor.

Introduction

Colorectal cancer is the fourth most common cancer in the world with 1.3 million new cases each year. In India, it is the fifth most common cancer following breast, cervix, oral cavity, and lung cancer [1–3]. The TNM classification provides the strongest prognostic information for patients with early stage disease and patients with advanced disease [4]. For patients with intermediate levels of disease, it is less able to predict the outcome of disease. In patients with tumours of the same pathologic stage may experience considerably different clinical outcomes.

Ideal histopathological 5 prognostic markers are readily assessable on routine histopathological examination. These markers facilitate patient counselling and clinical decision making with respect to follow-up scheduling and administration of adjuvant therapy [4–6]. Colorectal cancer disseminates as invasive tumour cells that can either enter the lymphatic system to be transported to regional lymph node or enter into the blood vessel. Vascular invasion is a biologic manifestation of aggressive behaviour in colorectal cancer. With this background we conducted a study to find various morphological spectrum of colorectal cancer, its clinical presentation and to study the association of vascular invasion with grade and stage of colorectal cancers.

Material and methods

A cross sectional study was conducted on the histopathologically diagnosed colorectal cancer specimens which were referred to department of pathology of a tertiary care hospital in Maharashtra. The data collected was of four years in total i.e. two years retrospective data (September 2014 to September 2016) from records and 2 years prospectively (September 2016 to September 2018). So, we included total of 35 cases in the study which were fitting our eligibility criteria. Biopsy samples, lack of data about anatomical location and presence of other histopathological types were excluded from the study. An ethical committee clearance was taken before the start of the study.

Data was collected in a predesigned case record form. The case record form has demographic details like age, gender, address etc. and details of gross and histopathological examination. The specimens were received in 10% formalin & thorough gross examination was done. Gross examination was done according to standard grossing techniques [7]. The gross details which were noted were type of specimen, length of specimen, tumour characteristics, size, pattern (infiltrating, polypoidal, ulcerative, proliferative) and presence of lymph nodes. Sections were taken from tumour including tumour border and adjacent mucosa, non-neoplastic mucosa, proximal and distal margin of resection. The specimen was subjected to routine processing, paraffin blocks were prepared, cut & stained with routine haematoxylin & eosin stain. Special stains for e.g. elastic stain were done wherever necessary. For old cases H&E stained slides were retrieved from pathology archives, took extra sections and screened for vascular invasion. Standard techniques were used for staining the slides [8]. Astler collar staging system was used to stage the carcinomas and was used as one of reference prognostic indicator in our study [9].

Statistical analysis: Data was collected, compiled, and analyzed using Epi Info version 7.2. The qualitative data was expressed using percentages. The quantitative data was expressed in terms of mean and standard deviation. The difference between the two proportions was analyzed using chi square test. For assessing the association of vascular invasion with prognosis, chi square for trend was applied. All analysis was two tailed and the significance level was set at 0.05

Results

We included 35 specimens in our study.

Table 1: Demographic characteristics of the patients

Demographic characters	Frequency	Percentage
Age group (in years)		
31 to 40	8	22.85
41 to 50	8	22.85
51 to 60	9	25.71
61 to 70	9	25.71
>70	1	2.80
Gender		
Male	18	51.43
Female	17	48.57

The mean age of the subjects were 52 ± 13 years with minimum age of 31 years and maximum of 76 years with male: female ratio of 1.05: 1.

Table 2: Distribution of the patients of colorectal cancers based on chief complaints

Chief complaints	Frequency	Percentage
Pain in abdomen	26	74.28
Anorexia	24	68.57
Weight loss	20	57.14
Altered bowel habits	16	45.71
Malena	11	31.43
Lump in the abdomen	5	14.29

The most common presenting complaint noted was pain in abdomen (74.28%) followed by anorexia (68.57%) and weight loss (57.14%)

Table 3: Specimen characteristics

Specimen characteristics	Frequency	Percentage
Location of tumour		
Ileocaecal junction	4	11.43
Ascending colon	6	17.14
Transverse colon	3	8.57
Descending colon	12	34.29
Recto sigmoid junction	2	5.71
Rectum	8	22.86
Pattern of Growth		
Ulceroproliferative	10	28.57
Ulcerative	9	25.71
Polypoidal	7	20.00
Infiltrative	7	20.00
Circumferential	2	5.71
Lymph node		
Present	22	62.86
Absent	13	37.14
Longitudinal mucosal resection and margins involved		
Present	6	17.14
Absent	29	82.86
Doughnuts		
Yes	6	17.14
No	29	82.86
Vascular invasion		
Present	14	40.00
Absent	21	60.00

The most common location of the tumour we noted was descending colon (34.29%) of the cases and ulceroproliferative growth (28.57%) was the most

common pattern of growth noted. We had 22 cases in which lymph node was also present as a part of specimen, about 17.14% had both longitudinal and mucosal margins involved, about 17.14% had doughnuts and 40% of the total cases had vascular invasion.

Table 4: Correlation of vascular invasion with staging of cancer (Prognosis)

Astler collar staging	Vascular invasion				Total	
	Present		Absent			
	Number	%	Number	%	Number	%
Stage A	0	0	1	100.00	1	2.86
Stage B1	2	16.67	10	83.33	12	34.29
Stage B2	4	40.00	6	60.00	10	28.57
Stage C1	3	60.00	2	40.00	5	14.29
Stage C2	5	71.43	2	28.57	7	20.00
P Value	0.0231					
Chi square for trend	5.34					

Majority of the subjects were in stage B1 (34.29%) followed by stage B2 (28.57%) and stage C2 (20.00%). We found the significant association between the vascular invasion and staging of the tumour based on Astler Collar staging. As the staging increases, the proportion of the vascular invasion also increases significantly.

Table 5: Correlation of vascular invasion with grading of tumour

Astler collar staging	Vascular invasion				P Value
	Present		Absent		
	Number	%	Number	%	
Well differentiated	1	7.14	13	61.90	0.0024
Moderately differentiated	5	35.71	1	4.76	
Poorly differentiated	8	57.14	7	33.33	

If we see total number of vascular invasion, poorly differentiated adenocarcinoma had more percentage of vascular invasion then well differentiated adenocarcinoma. However moderately differentiated adenocarcinoma showed more number of vascular invasions, which was not clear. There was significant association between the differentiation and vascular invasion ($p<0.05$).

We tried to contact patients with diagnosed colorectal cancer for follow up. Out of 35 cases only 5 cases were possible to trace in which 2 patients with vascular invasion died and 3 patients came with recurrence.

Discussion

Vascular invasion, peri neural invasion, tumour budding, tumour necrosis and inflammatory response are some prognostic factors studied in colorectal cancers [6, 10–13]. We conducted a cross sectional study to evaluate the characteristics of colorectal cancer specimens which were referred to the department of pathology in a tertiary care hospital in Maharashtra. We

also noted vascular invasion and its association with the grading and staging of the colorectal cancers.

The most common presenting complaint noted was pain in abdomen in our study. A study conducted by Quddus MA et al [14] reported that abdominal pain, anorexia, altered bowel habits; per rectal bleeding and abdominal lump were the cardinal features. A study conducted by Farzana T et al [15] reported that abdominal pain was the most common symptom followed by altered bowel habits and diarrhoea and bleeding per rectum. A study conducted by Kantilal M et al [16] reported that abdominal pain was the most common symptom followed by bleeding and weight loss in their study.

The most common location noted in our study was descending colon (34.29%). A study conducted by Ghazi S et al [17] inferred that recto sigmoid junction was the most common area involved in their study. Another study done by Quddos MA et al [14] found that rectum was common site. A study done by Patra T et al [18] reported that the most common location of the tumour was rectum followed by transverse colon. A study conducted by Farzana T et al [15] reported rectum to be the most common location of the tumour when compared to other sites. A study conducted by Kantilal M et al [16] reported rectum to be the most common site in their study. Hajmanoochehri F et al [19] reported that rectum was the most common site followed by sigmoid colon in their study. Komori K et al reported sigmoid colon followed by lower rectum to be the most common location of the tumour in their study.

In our study vascular invasion was present in 40% of the patients. We studied extramural and intramural vascular invasion but extramural vascular invasion was less so we are not drawing any conclusion. A study conducted by Betge J et al [23] had 23% of the cases with vascular invasion. In which extramural invasion was prognostically significant. A study conducted by Ghazi S et al [17] inferred that the vascular invasion was present in 22.22% and 37.3% in elective and emergency cases involved in their study and this difference was statistically significant. This means that those with emergency surgery on colorectal cancers had higher vascular invasion indicating the need for vascular invasion as soon as the histopathological diagnosis is made. Ashwini K et al [20] reported 45.6% of cases had vascular invasion. Komori K et al [21] reported 34.4% of the cases to have vascular invasion in their study. Fuji T [24] and workers reported that 47.45% of cases had vascular invasion.

In our study we found the significant association of vascular invasion with grading and staging of the tumour based on Astler Collar staging. As the staging and grade increases, the proportion of the vascular invasion also increases significantly. A study conducted by Betge J et al [23] had a significant association with tumour classification, AJCC staging of the tumours, tumour differentiation and pattern of invasion in their study. Further, they studied that extramural and intramural invasion was significantly associated with AJCC classification of tumours. Fuji T and workers [24] reported that vascular invasion and depth of invasion were poor prognostic factors for the overall survival of the colorectal cancers. Based on Kaplen Meier curves, the cases with vascular invasion had shorter survival when compared to those who did not and this was significant. Akagi Y et al [22] found a significant association between the invasion and the disease stage in their study. A study conducted by Chang SC et al [25] reported that the 5 year disease free survival with lymphovascular invasion was 60% and without it was 93.4% and this difference was significant. This

indicates that the cases with invasion are projected to survive less when compared to those without invasion. Lim SB and workers [26] reported that the cases with lymphovascular invasion were having poor disease free and overall survival based in Kaplen Meier curves studied. Sugai T et al [27] reported that vascular invasion to be the independent predictor for the prognosis of the patients with colorectal carcinomas after adjusting to all the confounding variables. Xu B et al [28] reported that vascular invasion is the predictor for the prognosis of the colorectal carcinomas.

Conclusions

In our study, colorectal cancers were more common in the age group of 51 to 70 years with male preponderance. Abdominal pain was the most common symptom noted. We found about 2/5th of our specimens to have vascular invasion on histopathological examination and this was associated with the staging of the disease (Prognosis) and differentiation of tumour. Vascular invasion thus is a vital marker to be noted that will assist the clinician making decisions of the management of the tumour and predicts the prognosis.

Legends Figures

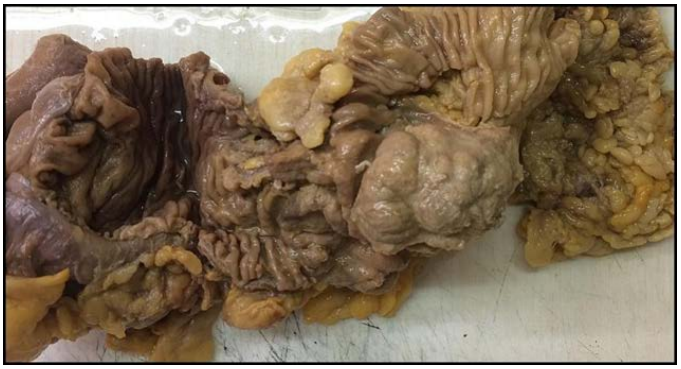

Figure 1: Gross photograph of colon with polypoidal mass

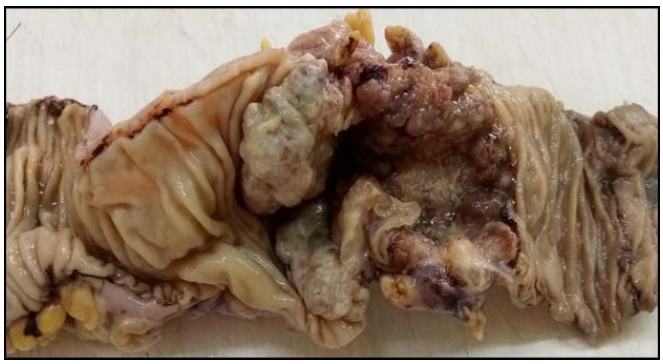

Figure 2: Gross photograph of colon with ulcerative mass

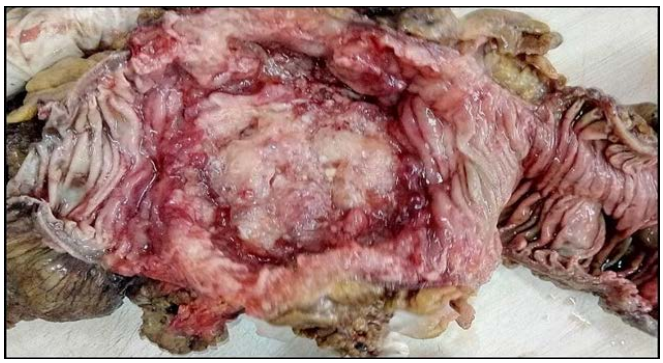

Figure 3: Gross photograph of colon with ulceroproliferative mass

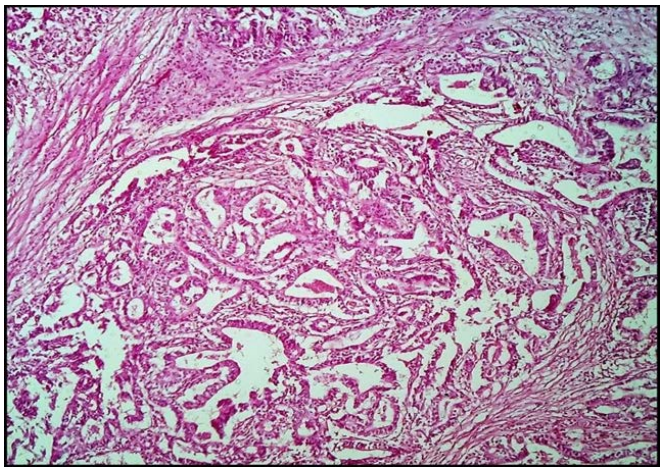

Figure 4: Photomicrograph of moderately differentiated adenocarcinoma H&E 10X

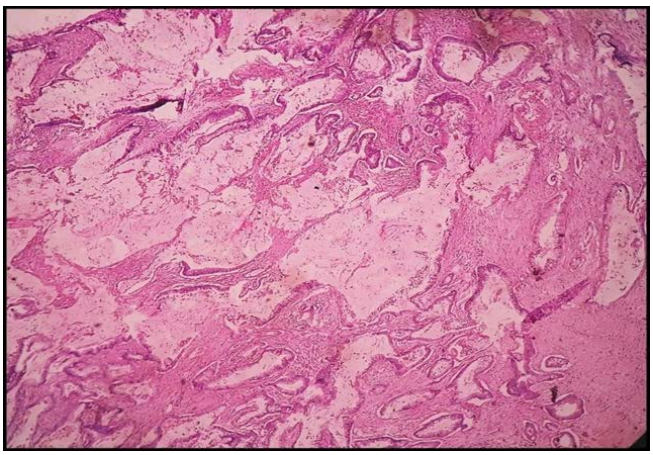

Figure 5: Photomicrograph of mucin secreting adenocarcinoma of colon with mucin pool H&E 10X

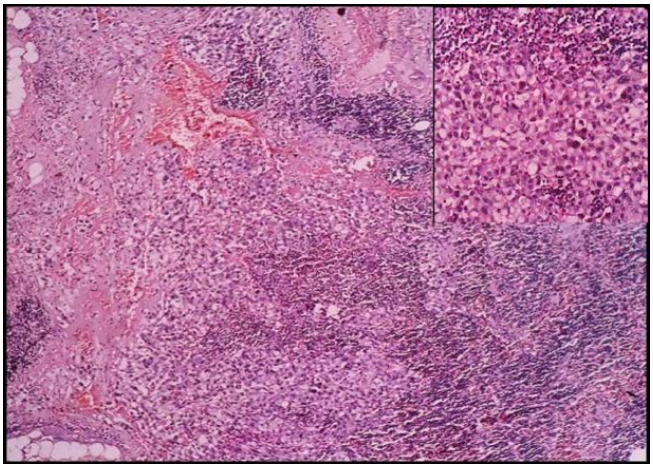

Figure 6: Photomicrograph of lymph node with metastasis of poorly differentiated adenocarcinoma colon H&E 10X

Inset – tumour cells with lymphocytes

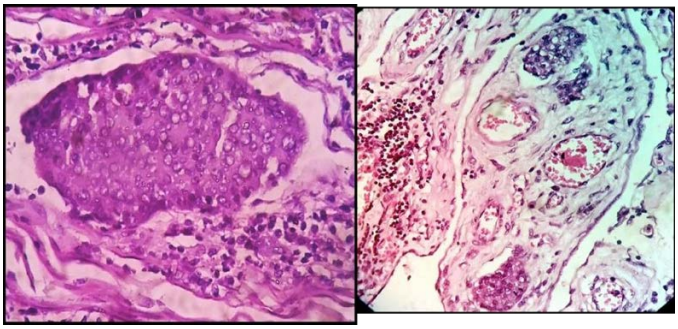

Figure 7 and 8: Photomicrographs of vascular invasion- tumour cells lined by endothelial cells in vascular lumen H&E 40X

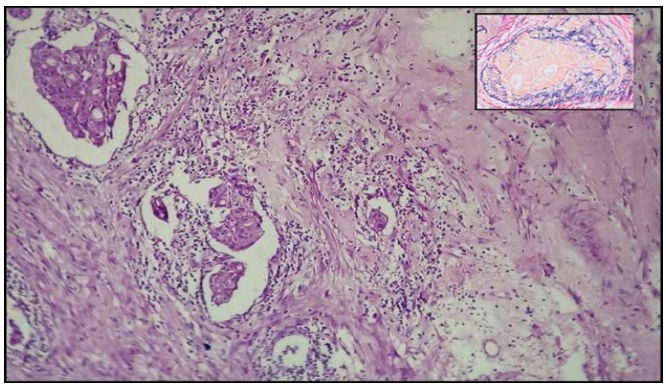

Figure 9: Photomicrograph of vascular invasion in H&E 10X Inset- vascular invasion in elastic stain

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