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Original Research Article

A study on histopathological examination of colorectal carcinoma with special reference to expression of CK20 in colorectal adenocarcinoma at a tertiary care centre

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ABSTRACT

Background: Colorectal carcinoma is the third most common cancer worldwide, over 1.8 million new cases are estimated in the year 2018. In terms of mortality, colorectal carcinoma ranks second with estimated 881,000 deaths in 2018. Histopathological study plays a central role for diagnosis and definitive treatment of colorectal carcinoma. In present time, immunohistochemical markers with adjunct to morphology helps in diagnosis and also in prognosis and treatment. Therefore, in colorectal carcinoma, along with morphology, many such immunohistochemical markers are being studied.
Methods: This study was carried out in the Department of Pathology at a tertiary care health centre in the southern part of Assam for a period of 1 year from June 2018 to May 2019. 52 cases of colorectal carcinoma diagnosed by histopathological study were included in the study. All patients were analysed for age, gender, type of growth and location of growth. Immunohistochemical staining of cytokeratin (CK) 20 was done and expression was studied and correlated with age, location of tumour, grade and tumour stage.
Results: Out of total 52 patients, 33 were male and 19 were female. Average age of presentation was 48.46±15.51 years. On gross examination rectal tumours were the most common and maximum tumours had polypoidal type of growth. On immunohistochemical study CK20 expression was detected in 82.7% out of 52 cases of colorectal adenocarcinoma and negative in 17.3% cases.
Conclusions: The correlation between CK20 expression and grading and tumour stages of colorectal adenocarcinoma was statistically significant. Further, large scale population-based studies with more number of cases and follow-up of these cases need to be done for better assessment of this immunohistochemical marker in colorectal adenocarcinoma that can be used for assessment of prognosis.

Keywords: Colorectal carcinoma, Immunohistochemistry, Cytokeratin, Grading, Tumour stage, Prognosis

INTRODUCTION

Colorectal carcinoma is the third most common cancer worldwide, over 1.8 million new cases are estimated in the year 2018. In terms of mortality, colorectal carcinoma ranks second with estimated 881,000 deaths in 2018.[1] In India, annual incidence rates for colon cancer in men is 4.4 and that of rectal cancer is 4.1 per 100000 population.[2]

Histopathological study plays a central role for diagnosis and definitive treatment of colorectal carcinoma. In present time, immunohistochemical markers with adjunct to morphology helps in diagnosis and also in prognosis and

treatment. Therefore, in colorectal carcinoma, along with morphology, many such immunohistochemical markers are being studied.

Cytokeratins (CKs) are the intermediate sized filaments present in the cytoskeleton. Total 20 subtypes of cytokeratin filaments are found which have different molecular weights and show differential expression in different cell types.[3] CK20 are low molecular weight cytokeratins.[4] CK20 expression is shown in gastrointestinal (GI) epithelium, urothelium, and Merkel cells. The pattern of expression is dependent on histological features, differentiation, lymph node metastasis and anatomical location of colorectal adenocarcinoma.[4] Hence study of expression profile of CK20 is important in case of colorectal adenocarcinoma.

METHODS

This study was carried out in the Department of Pathology at a tertiary care health centre in the southern part of Assam for a period of 1 year from June 2018 to May 2019. 52 cases of colorectal carcinoma diagnosed by histopathological study were included in the study.

Inclusion criteria: all cases irrespective of age and sex, clinically diagnosed or suspicious of colorectal carcinoma that has undergone colonoscopic biopsies and/or colectomy operation conducted in the department of surgery from June 2018 to May 2019.

Exclusion criteria: non epithelial tumours, benign epithelial tumours and anal carcinoma cases were excluded from the study.

Detailed clinical history and routine investigations were done after taking consent from the patients. Macroscopic examination of the colorectal growth was done and growth types were recorded as per colonoscopy reports and by gross examination of the specimens. Microscopic examination of H and E stained sections were done. Immunohistochemistry was performed on paraffin embedded tissue in histopathologically diagnosed colorectal carcinoma cases. Antibody to CK20 (Monoclonal Mouse Anti human, clone Ks20.8, Dako) was used.

The positive control used for CK20 was normal colonic mucosal tissue. The negative control used were sections of the study tissues with no primary antibody incubation.

Positive immunostaining for CK20 was identified in cytoplasm, cell membrane or both tumour cell components. Cases that stained >5% of tumour cells were considered positive.[10] For statistical analysis Chi-square test and Fisher's exact test were used. A p value of less than 0.05 was considered statistically significant.

RESULTS

Age of the patients included in the study ranged from 19 years to 85 years with a mean age of 48.46±15.51 years. The most common age group was found to be 46 - 60 years (38.5%), followed by 31-45 years (32.7%). (Table 1)

Table 1: Distribution of cases according to age.

Age (years)	Number of cases	Percentage
16- 30	7	13.5
31- 45	17	32.7
46-60	20	38.5
61-75	5	9.6
>75	3	5.7

Table 2: Distribution of cases according to location of tumours.

Location of tumour	Number of cases	Percentage
Rectum	23	44.2
Sigmoid colon	9	17.3
Descending colon	8	15.5
Ascending colon	6	11.5
Caecum	5	9.6
Transverse colon	1	1.9

Table 3: Distribution of cases according to gross appearance of tumours.

Macroscopic appearance	Number of cases	Percentage
Polypoidal	24	46.1
Ulceroproliferative	17	32.7
Ulcerative	9	17.3
Annular	2	3.9

It is seen that of the 52 cases, 33 cases (63.5%) were males and 19 cases (36.5%) were females; the male to female ratio being 1.7:1.

On gross examination, it was observed that rectal tumours were the most common (44.2%), followed by tumours of the sigmoid colon (17.3%), tumours of the descending colon (15.5%) (Table 2) and that maximum cases had polypoidal type of growth (46.1%), followed by ulceroproliferative type of growth (32.7%) and ulcerative growth (17.3%). (Table 3)

On microscopy it was evident that in our study all cases were colorectal adenocarcinoma (100%) out of which most cases were of moderately differentiated adenocarcinoma (50%), followed by well differentiated adenocarcinoma (38.5%) and the least number of cases were poorly differentiated adenocarcinoma (11.5%). (Table 4)

Table 4: Distribution of cases according to histopathological differentiation.

Differentiation status	Number of cases	Percentage
Well differentiated	20	38.5
Moderately differentiated	26	50
Poorly differentiated	6	11.5

Table 5: Distribution of cases according to pathological tumour stage.

Pathological tumour stage	Number of cases	Percentage
T1	12	23.2
T2	21	40.3
T3	18	34.5
T4	1	2

Table 6: Expression of CK20 in cases of colorectal adenocarcinoma.

CK20 expression status	Number of cases	Percentage
Positive	43	82.7
Negative	9	17.3
Total	52	100

According to location, CK20 expression was the highest in transverse colon (n=1, 100%) followed by rectum (91.3%) and descending colon (87.5%). The positivity of CK20 was the least in caecum (60%) and ascending colon (66.7%). (p=0.47, Not Significant) This finding was statistically significant (p=0.014). CK20 expression was more in cases of colorectal adenocarcinoma which have lymph node metastasis (86.9%). However, this finding was not statistically significant (p=0.46). (Table 7)

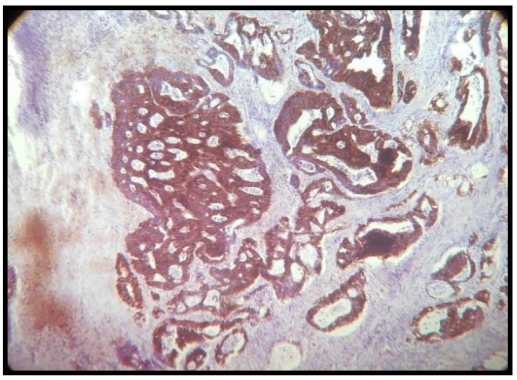

Figure 1: CK20 positive in colorectal adenocarcinoma.

It is observed that expression of CK20 was more in low grade adenocarcinoma (89.1%) than that of high grade colorectal adenocarcinoma (33.3%). The correlation between CK20 expression and grading of colorectal adenocarcinoma was statistically significant (p=0.004). In our study CK20 positivity was overall higher in all tumour stages. But loss of expression of CK20 was more in tumour stages of T3 and T4 (36.8%) than that of stages T1 and T2 (6.1%).

Table 7: Expression of CK 20 in different grade, tumour stage and lymph node metastasis.

		CK20 positive	CK20 negative	Total	P value
Grade	Low	41 (89.1%)	5 (10.9%)	46 (100%)	
	High	2 (33.3%)	4 (66.7%)	6 (100%)	0.004
Tumour stage (t)	T1, T2	31 (93.9%)	2 (6.1%)	33 (100%)	
	T3, T4	12 (63.2%)	7 (36.8%)	19 (100%)	0.014
Ln Metastasis	Absent	23 (79.3%)	6 (20.7%)	29 (100%)	
	Present	20 (86.9%)	3 (13.1%)	23 (100%)	0.46

In our study most cases were of T2 (40.3%), followed by T3 (34.5%), T1 (23.2%), and T4 (2%). Maximum cases showed no lymph node metastasis (55.8%) and 44.2% cases showed lymph node metastasis. (Table 5)

On immunohistochemical study CK20 expression was detected in 82.7% out of 52 cases of colorectal adenocarcinoma and negative in 17.3% cases. (Table 6) It is observed that expression of CK20 is slightly more in age group of ≤45 years (83.3%) than that of >45 years of age (82.2%). But this finding was not statistically significant. (Figure1)

DISCUSSION

In the present study, maximum cases were observed in the age group of 46-60 years (38.5%) which was also seen in studies by Halder et al.[5] In a study by Virk et al, it was found that 70% of cases were of more than 65 years of age.[6]

Table 8: Expression of CK20 in different studies.

Studies	CK20 positive	No. of cases
Bayrak et al [4]	81.1%	196
Al-Maghrabi et al[12]	62.5%	144
Gheini et al[13]	90.38%	52
Present study	82.7%	52

There is significant male preponderance in our study with the male to female ratio being 1.7:1, as similar to other studies by Laishram et al, Rasool et al and Haleshappa et al.[8,9]

In our study, on gross examination polypoidal type of growth was the most commonly found which is in accordance with study done by Peedikayil et al, and Ibrahim et al.[10,11]

CK20 expression was detected in 82.7% out of 52 cases of colorectal adenocarcinoma and negative in 17.3% cases. The percentage of CK20 positivity in various studies done earlier is listed in the table. (Table 8)

In a study by Al Maghrabi et al, and in another study by Park et al, they found no significant association between expression of CK20 in different age and sex of the patients.[12,14]

Bayrak et al, in their study in 2011 found positivity of CK20 was more common in rectum and desending colon carcinoma than in proximal colon carcinomas which was statistically significant.[4] Hernandez et al, in their study compared expression of CK7 and CK20 in rectum, sigmoid colon and other parts of colon.[15] There was no significant association between the expression and location of tumour (p=0.68).

Bayrak et al found that there was statistically significant association between CK20 expression and histological grades of colorectal adenocarcinoma (p<0.001).[4] CK20 positivity was more common in low grade colorectal adenocarcinoma (85.1%) than in high grade adenocarcinomas (47.6%). In their study they also found that there was no significant association between expression of CK20 and tumour stages of colorectal carcinoma (T). However CK20 expressions were higher in stage T2 tumours, 87.5%.

Park et al, in their study compared the expression of CK20 in colorectal carcinoma with tumour stage. But they found no significant association between them.[14]

CONCLUSION

Expression of CK20 was more common in low grade colorectal adenocarcinoma and early tumour stage (T1, T2). The correlation between CK20 expression and grading and tumour stages of colorectal adenocarcinoma was statistically significant. Further, large scale population-based studies with more number of cases and follow-up of these cases need to be done for better assessment of this immunohistochemical marker in colorectal adenocarcinoma that can be used for assessment of prognosis. Also, cytokeratin 20 can be used along with other cytokeratin markers for evaluation of accurate site of origin in cases of some metastatic tumours where routine histopathology may be challenging.

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