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Original Article

Pathology Section

Clinicopathological Significance of Tumour and Stromal CD10 Expression in Colorectal Adenomas and Adenocarcinomas and Its Association with Dysplasia: A Cross Sectional Study

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ABSTRACT

Introduction: Colorectal cancer commonly develops through the adenoma-carcinoma sequence, and identification of biomarkers involved in tumour progression and tumour-stroma interaction is essential for risk stratification. CD10 is a zinc-dependent transmembrane metallopeptidase implicated in extracellular matrix degradation, tumour invasion, angiogenesis, and modulation of the tumour microenvironment. Evaluation of CD10 expression in tumour cells and stroma may provide insight into its role in colorectal carcinogenesis.

Aim: To evaluate tumour and stromal CD10 expression in colorectal adenomas and adenocarcinomas and to assess its association with the grade of dysplasia in adenomas.

Materials and Methods: This cross-sectional study was conducted at the Department of Pathology, Pushpagiri Institute of Medical Sciences and Research Centre, Tiruvalla, Kerala, India, from April 2024 to October 2025. It included 40 cases each of histopathologically confirmed colorectal adenomas and adenocarcinomas selected by consecutive sampling. Clinicopathological parameters (age, gender, tumour location, tumour type, histological grade and CD10 expression with its correlation to grade) were recorded. Histomorphological evaluation was followed by Immunohistochemical (IHC) staining for CD10. Tumour cell and stromal CD10 expression were assessed separately and correlated with dysplasia grade in adenomas using appropriate statistical tests such as the Chi-square test or Fisher's-exact (including Fisher–Freeman–Halton test for larger contingency tables) test where appropriate, and the association was evaluated using p-values, and a p-value <0.05 was considered statistically significant.

Results: A total of 80 cases (40 adenomas, 40 adenocarcinomas) were studied. Most patients were >55 years (adenomas: 85.0%; adenocarcinomas: 97.5%) with male predominance (60.0%). Adenomas commonly involved the rectum and transverse colon (22.5% each), while adenocarcinomas were most frequent in the rectosigmoid region (27.5%) (p=0.002). Low-grade dysplasia was seen in 60.0% and high-grade dysplasia in 40.0% of adenomas, with the tubulovillous type being most common (50.0%). Tumour CD10 expression was comparable in adenomas (80.0%) and adenocarcinomas (77.5%) (p=0.785). Stromal CD10 expression was significantly higher in adenocarcinomas (p<0.001). Tumour CD10 positivity was significantly associated with higher dysplasia (66.7% vs 100%; p=0.0096), while stromal expression was not (p=0.124).

Conclusion: CD10 expression was associated with features of the adenoma-carcinoma sequence. Increased tumour CD10 expression is associated with higher grades of dysplasia in adenomas, while significantly increased stromal CD10 expression in adenocarcinomas highlights the role of tumour-stroma interaction in colorectal carcinogenesis. CD10 expression was associated with tumour progression-related histopathological features.

Keywords: Colorectal cancer, Dysplasia, Immunohistochemistry, Neoplasia, Tumour stroma

INTRODUCTION

Colorectal cancer (CRC) is a major cause of cancer-related morbidity and mortality worldwide. Most colorectal carcinomas arise through the adenoma-carcinoma sequence, characterised by progressive histomorphological and molecular alterations [1]. Identification of biomarkers involved in tumour progression and tumour-stroma interaction is essential for better understanding of colorectal carcinogenesis and improved risk stratification [2,3].

CD10 (neutral endopeptidase) is a zinc-dependent transmembrane metallopeptidase that plays a role in extracellular matrix degradation, tumour microenvironment modulation, angiogenesis, and tumour invasion [4,5]. Its expression has been documented in both tumour cells and stromal fibroblasts in colorectal neoplasms, with emerging evidence suggesting a significant role of stromal CD10 in tumour progression [6].

However, existing literature shows inconsistent findings regarding the differential expression and prognostic significance of tumour versus stromal CD10 in colorectal adenomas and adenocarcinomas. Furthermore, limited studies have evaluated its association with the grade of dysplasia in adenomas and its role in the adenoma–carcinoma sequence [3]. This highlights the need for further studies to clarify the role of CD10 in colorectal tumourigenesis.

Hence, the present study aimed to evaluate tumour and stromal CD10 expression in colorectal adenomas and adenocarcinomas and to assess its association with the grade of dysplasia in adenomas. The objectives were to assess the frequency of expression of CD10 in colorectal adenoma and adenocarcinoma and to determine the association between the expression of CD10 and the grading of dysplasia in adenoma.

MATERIALS AND METHODS

This was a cross-sectional observational study conducted in the Department of Pathology, Pushpagiri Institute of Medical Sciences

and Research Centre, Tiruvalla, Kerala, India from April 2024-October 2025, after obtaining approval from the Institutional Ethics Committee (IEC No: PIMSRC/E1/388A/12/2024).

Sample size estimation: A total of 80 histopathologically confirmed cases comprising 40 colorectal adenomas and 40 colorectal adenocarcinomas were included by consecutive sampling. Sample size estimation was based on the study by Bhavana GR and Clement Wilfred D [7]. which reported stromal CD10 positivity rates of 41.3% in adenomas (P1=41.3%) and 63.4% in colorectal carcinomas (P2=63.4%). Assuming a 95% confidence level (α=0.05) and 90% power (β=0.10), the required sample size was calculated using the formula for comparison of two proportions described by Charan J et al., [8] No inflation for attrition or exclusion was applied. However, owing to the retrospective nature of the study, all eligible archival cases available during the study period and fulfilling the inclusion criteria were included, yielding 40 cases in each group.

Inclusion criteria: Biopsy or resection specimens diagnosed as colorectal adenoma or adenocarcinoma, and adequate tissue for IHC analysis were included.

Exclusion criteria: Poorly preserved tissue, cases with inadequate material for IHC and patients who had received chemotherapy and/or radiotherapy prior to tissue sampling were excluded.

Study Procedure

Histopathological evaluation: Haematoxylin and Eosin (H&E) - stained sections were reviewed for confirmation of diagnosis. Adenomas were graded as Low-grade Dysplasia (LGD) or High-grade Dysplasia (HGD).

Immunohistochemistry (IHC): Immunohistochemical staining for CD10 (monoclonal mouse anti-human CD10 antibody, clone 56C6) was performed on formalin-fixed, paraffin-embedded tissue sections using standard protocols. Tumour cell and stromal CD10 expression were evaluated separately. Tonsillar tissue is taken as control where germinal centre B cell show CD10 positivity.

Tumour CD10 expression was scored as positive or negative by comparing with the colour intensity of the control used [3].

Stromal CD10 expression was graded according to a 4-point scale based on the percentage of positively stained area [3].

Score 0: 0-10% positive stromal cells

Score 1+: 11-20% positive stromal cells

Score 2+: 21-50% positive stromal cells

Score 3+: >50% positive stromal cells

Clinicopathological parameters (age, gender, tumour location, tumour type, histological grade, and CD10 expression with its correlation to grade) were recorded.

STATISTICAL ANALYSIS

Data were analysed using appropriate statistical software, Statistical Package for Social Sciences (SPSS) version 24.0. Categorical variables were compared using the Chi-square or Fisher's exact test (including Fisher-Freeman-Halton test for larger contingency tables) where appropriate. A p-value<0.05 was considered statistically significant.

RESULTS

A total of 80 cases were included, comprising 40 colorectal adenomas and 40 adenocarcinomas. The majority of cases in both groups were observed in patients aged >55 years (adenomas: 34/40, 85.0%; adenocarcinomas: 39/40, 97.5%), while those aged ≤55 years accounted for 6/40 (15.0%) and 1/40 (2.5%) respectively, indicating a strong association with increasing age [Table/Fig-1].

Variables	Category	Adenoma n (%)	Adenocarcinoma n (%)
Age group (years)	≤55	6 (15.0)	1 (2.5)
	>55	34 (85.0)	39 (97.5)
Gender	Male	24 (60.0)	24 (60.0)
	Female	16 (40.0)	16 (40.0)

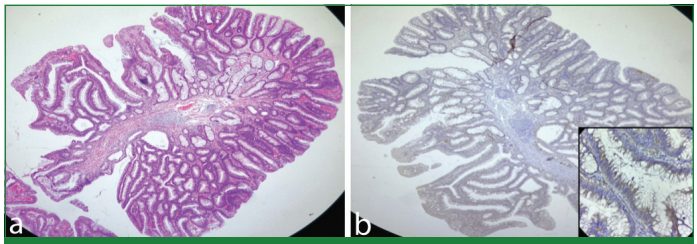
[Table/Fig-1]: Demographic distribution of adenoma and adenocarcinoma cases (N=80).

Male predominance was noted in both groups 24/40 (60.0%), with females constituting 16/40 (40.0%) [Table/Fig-1]. In adenomas, the rectum and transverse colon were most commonly involved, 9/40 each (22.5%), followed by descending colon 8/40 (20.0%) and sigmoid colon 7/40 (17.5%). In adenocarcinomas, the rectosigmoid region was most common, 11/40 (27.5%), followed by descending colon, 8/40 (20.0%) and both sigmoid and ascending colon, 7/40 each (17.5%), with rectal involvement in 5/40 (12.5%) (χ^2=20.361, p=0.002).

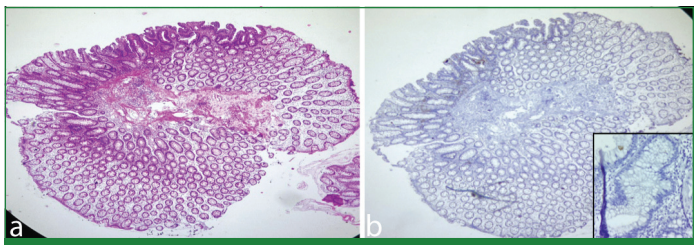
Among adenomas, LGD was seen in 24/40 (60.0%) and HGD in 16/40 (40.0%) [Table/Fig-2]. Tubulovillous adenoma [Table/Fig-3] was the most common type, 20/40 (50.0%), followed by tubular 17/40 (42.5%) [Table/Fig-4,5] and villous adenoma 3/40 (7.5%) [Table/Fig-6,7].

Variables	Category	n (%)
Grade of dysplasia	Low-grade dysplasia	24 (60.0)
	High-grade dysplasia	16 (40.0)
Histological type	Tubular adenoma	17 (42.5)
	Tubulovillous adenoma	20 (50.0)
	Villous adenoma	3 (7.5)

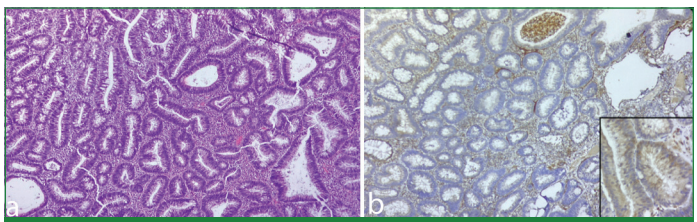
[Table/Fig-2]: Grade of dysplasia and histological types of adenomas.



[Table/Fig-3]: a) Tubulovillous adenoma with LGD (H&E,4x), b) CD10 tumour score positive (inset figure) and CD10 stromal score 2+ in tubulovillous adenoma with LGD (4x).



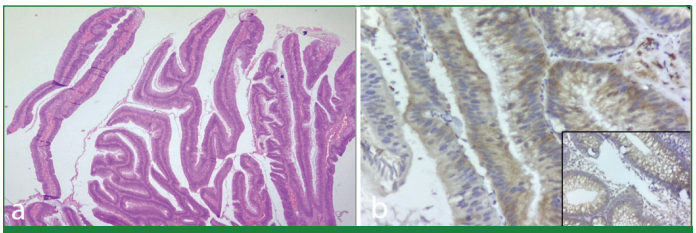
[Table/Fig-4]: a) Tubular adenoma with focal LGD (H&E stain,4x), b) CD10 tumour score negative (inset figure) and stromal CD10 score 0 in tubular adenoma with LGD (4x).



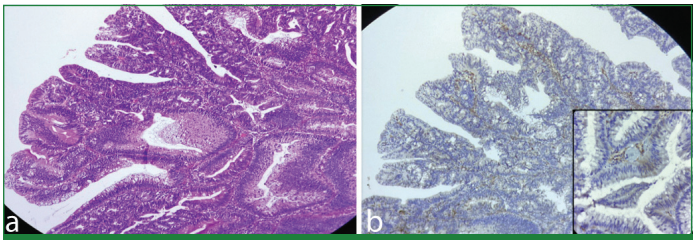
[Table/Fig-5]: a) Tubular adenoma with HGD (H&E,10x), b) CD10 tumour score positive (inset figure) and stromal CD10 score: 2+ in tubular adenoma with HGD (10x).

Tumour CD10 expression was positive in 32/40 (80.0%) adenomas and 31/40 (77.5%) adenocarcinomas [Table/Fig-8] (χ^2=0.075, p=0.785). Stromal CD10 expression showed significant variation,

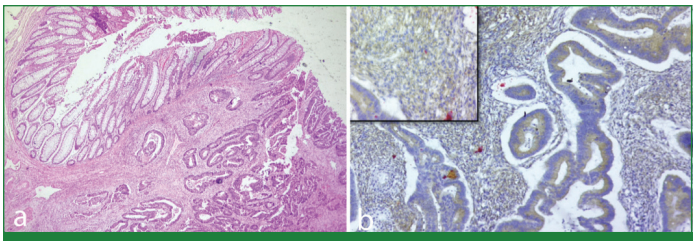
with adenomas predominantly showing score 1+ (24/40, 60.0%), while adenocarcinomas showed higher expression [Table/Fig-8], including score 2+ (17/40, 42.5%) and score 3+ (7/40, 17.5%) (χ^2=17.101, p<0.001) [Table/Fig-9].



[Table/Fig-6]: a) Villous adenoma with LGD (H&E,10x), b) CD10 tumour score positive and stromal CD10 score 2+ (inset figure) in villous adenoma with LGD (40x).



[Table/Fig-7]: a) Villous adenoma with HGD (H&E,10x), B: CD10 tumour score positive (inset figure) and stromal CD10 score 2+ in villous adenoma with HGD (10x).



[Table/Fig-8]: a) Adenocarcinoma colon moderately differentiated (H&E, 4x), b) CD 10 tumour score positive and CD10 stromal score 3+(inset figure) in Adenocarcinoma colon moderately differentiated (10x).

CD10 expression	Category	Adenoma n (%)	Adenocarcinoma n (%)	χ^2	df	p-value
Tumour CD10	Positive	32 (80.0%)	31 (77.5%)	0.075	1	0.785
	Negative	8 (20.0%)	9 (22.5%)			
Stromal CD10	Negative	6 (15.0%)	8 (20.0%)	17.101	3	<0.001*
	1+	24 (60.0%)	8 (20.0%)			
	2+	10 (25.0%)	17 (42.5%)			
	3+	0	7 (17.5%)			

[Table/Fig-9]: Association of tumour and stromal CD10 expression with tumour type. *Statistically significant.

Tumour CD10 positivity was significantly associated with dysplasia grade, being present in 16/24 (66.7%) low-grade and 16/16 (100%) high-grade adenomas (Fisher's exact test, p=0.0096). Stromal CD10 expression was higher in high-grade dysplasia but not statistically significant (χ^2=4.757, p=0.124) [Table/Fig-10].

CD10 expression	Category	LGD n (%)	HGD n (%)	Test used	p-value
Tumour CD10	Positive	16 (66.7%)	16 (100%)	Fisher's exact test	0.0096*
	Negative	8 (33.3%)	0		
Stromal CD10	Negative	6 (25.0%)	0	Fisher-Freeman-halton Exact test	0.124
	1+	13 (54.2%)	11 (68.7%)		
	2+	5 (20.8%)	5 (31.3%)		

[Table/Fig-10]: Association of tumour and stromal CD10 expression with grade of dysplasia in adenomas.
*Statistically significant

DISCUSSION

The present study evaluated both tumour and stromal CD10 expression in colorectal adenomas and adenocarcinomas, highlighting their differential roles in colorectal tumourigenesis. Tumour CD10 expression was found to be comparably prevalent in adenomas and adenocarcinomas, suggesting that its expression in tumour cells may represent an early event in the adenoma-carcinoma sequence [9,10]. This observation is in concordance with earlier studies, such as those by Jang TJ et al., and Yao T et al., which demonstrated CD10 expression in premalignant colorectal lesions, indicating its involvement in early neoplastic transformation [5,11].

A significant association was observed between tumour CD10 expression and higher grades of dysplasia in adenomas in the present study, supporting its role in neoplastic progression. Similar findings have been reported in study done by Ogawa H et al., where increased CD10 expression correlated with dysplastic changes and malignant potential in colorectal epithelium [3]. These studies suggest that CD10 may contribute to tumour progression by modulating peptide-mediated signalling pathways and promoting cellular proliferation.

In contrast, stromal CD10 expression showed a statistically significant increase in adenocarcinomas compared to adenomas, with higher stromal scores predominantly observed in invasive carcinomas. This finding is consistent with previous reports by Ogawa H et al., and Zheng J et al., who demonstrated increased CD10 expression in stromal fibroblasts during colorectal tumour progression and highlighted the contribution of tumour-associated stromal cells to tumour invasion and progression [2,3]. The increased stromal expression in carcinomas underscores the importance of tumour-stroma interactions in colorectal carcinogenesis.

CD10, a zinc-dependent metalloproteinase, is known to degrade various bioactive peptides and is implicated in extracellular matrix remodelling [7,12,13]. Previous studies by Ogawa H et al., and Zheng et al., demonstrated progressive upregulation of stromal CD10 expression during colorectal tumour development and highlighted the role of CD10-positive tumour-associated fibroblasts in facilitating tumour progression [2,3]. Furthermore, Raposo TP et al., reported an association between CD10 expression and advanced-stage colorectal cancer [9]. The present findings further support this concept, as higher stromal CD10 expression was associated with invasive carcinoma.

Although stromal CD10 expression appeared more frequent in adenomas with high-grade dysplasia in the current study, the association did not reach statistical significance. This is in contrast to some studies that have reported a significant correlation between stromal CD10 and dysplastic progression [3,5]. The lack of statistical significance in the present study may be attributed to the relatively small sample size and limited number of high-grade dysplastic adenomas. Larger cohort studies are required to better elucidate this relationship.

Overall, the findings of the present study suggest that tumour CD10 expression may serve as an early marker of neoplastic transformation, whereas stromal CD10 expression appears to play a more prominent role in tumour invasion and progression. These observations are in agreement with the multistep model of colorectal carcinogenesis, emphasising both epithelial alterations and stromal contributions in tumour development.

Limitation(s)

The present study had a relatively small sample size, which may have reduced the statistical power of the analysis and limited the ability to detect subtle associations between CD10 expression and clinicopathological parameters. As this was a single-centre study, the findings may reflect local patient demographics and Institutional practices, thereby limiting the generalisability of the results to other populations. The cross-sectional design of the study did not allow for

longitudinal follow-up of patients, making it difficult to assess changes in CD10 expression over time or its role in disease progression. In addition, no prognostic or survival analysis was performed; therefore, the clinical impact of CD10 expression on patient outcomes such as overall survival or disease-free survival could not be determined. Interobserver variability in IHC interpretation may have influenced the consistency of results, particularly in borderline or weakly positive cases. Another limitation is the lack of a standardised scoring system for CD10 expression, which may affect reproducibility and make comparison with other studies challenging. Finally, there was an unequal distribution of adenoma and carcinoma subtypes in the study population, which could have introduced bias and influenced the observed associations.

CONCLUSION(S)

CD10 plays a significant role in the adenoma–carcinoma sequence of colorectal neoplasia. Increased tumour CD10 expression is associated with higher grades of dysplasia in adenomas, while enhanced stromal CD10 expression in adenocarcinomas underscores the role of tumour-stroma interaction in colorectal carcinogenesis. CD10 may serve as a useful adjunct marker in understanding tumour progression.

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REFERENCES

[1] Żurawski J, Talarska P, de Mezer M, Kaszkowiak K, Chalcarz M, Iwanik K, et al. Evaluation of CD10 expression as a diagnostic marker for colorectal cancer. Gastroenterol Hepatol Bed Bench. 2022;15(1):24-31.
[2] Zheng J, Zhu Y, Li C, Li Y, Nie Q, Zhu Z, et al. Expression of CD10 in tumour-associated fibroblasts of cancerized or recurrent colorectal adenomas. J Zhejiang Univ Med Sci. 2016;45(4):335-41.
[3] Ogawa H, Iwaya K, Izumi M, Kuroda M, Serizawa H, Koyanagi Y, et al. Expression of CD10 by stromal cells during colorectal tumour development. Hum Pathol. 2002;33(8):806-11.
[4] Hirano K, Nimura S, Mizoguchi M, Hamada Y, Yamashita Y, Iwasaki H. Early colorectal carcinomas: CD10 expression, mucin phenotype and submucosal invasion. Pathol Int. 2012;62(9):600-11.
[5] Jang TJ, Park JB, Lee JI. The expression of CD10 and CD15 is progressively increased during colorectal cancer development. Korean J Pathol. 2013;47(4):340-47.
[6] Fujimoto Y, Nakanishi Y, Sekine S, Yoshimura K, Akasu T, Moriya Y, et al. CD10 expression in colorectal carcinoma correlates with liver metastasis. Dis Colon Rectum. 2005;48(10):1883-88.
[7] Bhavana GR, Clement Wilfred D. CD10 expression in colorectal adenoma and carcinoma and its association with pathological prognostic factors. Iran J Pathol. 2024;19(4):441-446.
[8] Charan J, Kaur R, Bhardwaj P, Singh K, Ambwani SR. Sample size calculation in medical research: A primer. Ann Natl Acad Med Sci (India). 2021:57(2):75-80.
[9] Raposo TP, Comes MS, Idowu A, Agit B, Hassall J, Fadhil W, et al. CD10 inhibits cell motility but expression is associated with advanced stage disease in colorectal cancer. Exp Mol Pathol. 2018;104(3):190-98..
[10] Ilie DS, Mitroi G, Pa˘un I, Ţenea-Cojan TS¸, Neamt¸u C, Totolici BD, et al. Pathological and immunohistochemical study of colon cancer: Evaluation of markers for colon cancer stem cells. Rom J Morphol Embryol. 2021;62(1):117-24.
[11] Yao T, Tsutsumi S, Akaiwa Y, et al. Expression of CD10 in colorectal neoplasms and its association with tumor progression. Pathol Int. 2004;54(6):392-398.
[12] Maguer-Satta V, Besançon R, Bachelard-Cascales E. Neutral endopeptidase (CD10): a multifaceted environment actor in stem cells, physiological mechanisms, and cancer. Stem Cells. 2011;29(3):389-96.
[13] Wang S, Xiao Y, An X, Luo L, Gong K, Yu D. A comprehensive review of the literature on CD10: its function, clinical application, and prospects. Front Pharmacol. 2024;15:1336310.

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