Immunohistochemical Expression of Carbohydrate Antigen CA19-9 in Colorectal Tumors

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ABSTRACT

Background and Objectives: Carbohydrate antigen 19-9 (CA19-9) is one of the most representative tumor markers in colorectal carcinomas. Colorectal cancer is one of the leading causes of cancer-related mortality in the world. The objective of this study is to investigate the expression of CA 19-9 in colon tumors and its correlation with pathological prognostic factors (age, gender, tumor site and histological grade).
Methods: A total of 47 colonic tissues were selected from Razgary teaching hospital from the period January, 2007 to January, 2009 consisting of 20 colonic adenocarcinoma, five tubular adenoma,12 retention polyp, four ulcerative colitis and six normal colonic mucosa.
Results: CA19-9 expression found in 18 out of 20 colonic adenocarcinoma, 2 out of 5 tubular adenoma and one out six normal colonic tissues .
Conclusions: It was concluded that high expression of CA19-9 is seen more frequently in colonic adenocarcinoma with higher grade tumor in comparison with benign tumor and normal tissue. There was also high CA19-9 expression in old age patient (>50 years) and in male gender.
Key words: Colon adenocarcinoma, CA19-9.

INTRODUCTION:

The CA 19-9 antigen is a monosialosyl Le blood group antigen which has been shown to be a useful tumor-associated antigen for the diagnosis of gastrointestinal cancers[1]. Colorectal cancer is the 7th among the commonest ten cancers in Iraq[2]. Colorectal carcinomas are one of the most frequent neoplasms in Western society, in USA it is by far the most common and most curable carcinoma of the gastrointestinal tract. Males and females are affected equally, the mean age of incidence is 62years[3, 4]. The cause and pathogenesis of colorectal carcinoma are related to both environmental (is mainly dietary by fat and protein intake)and genetic factors (represented by high predisposition for colorectal carcinoma in patients with familial polyposis)[3,5]. CA19-9 is a cancer-associated carbohydrate antigen that plays process of tumor progression as an adhesion molecule and has been found to be associated with colorectal carcinoma[6]. Carcinoembrionic Antigen (CEA) and carbohydrate antigen 19-9 (CA 19-9) are the most commonly used tumor-associated antigens in the management of patients with colorectal cancer[7].

PATIENTS & METHODS:

A retrospective study of fourty seven cases of surgical lesions (total colectomy and excisional biopsies) were investigated. These cases were retrieved from Razqari teaching Hospital Laboratory during the period January, 2007 to January, 2009 ,including 20 colonic adenocarcinoma ,five tubular adenoma, 12 retention polyp ,four ulcerative colitis and six normal colonic tissue. For each case representative sections were stained with haematoxylin (H) and eosin (E) and others

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immunohistochemically and examined for the type of tumor and histological grading. Data were subjected to statistical analysis using chi square.

RESULT:

The expression of CA19-9 was positive in 18 out of 20 (90%) colorectal carcinoma cases (Figures 1 and 2). Two out of five tubular adenoma cases (40%) were CA19-9 positive. Three out of 12 retention polyp (25%) were CA19-9 positive (Figure 3). One out of four ulcerative colitis cases (25%) were positive .One out of six normal colonic tissues (16.7%) was positive. Statistical analysis (Table 1) revealed a significant difference ($P < 0.05$) regarding CA19.9 expression . The expression of CA19-9 with diffuse pattern of staining was seen in 16 out of 18 positive cases (66.7%) in colorectal carcinoma .While in normal mucosa the pattern of staining was occasional. Statistical analysis (Table 2) revealed a significant difference in relation to Pattern of staining ($P < 0.05$). Fifteen out of 25 (75%) positive cases observed in patients of more than 50 years old group and 6 of the 25 (24%) positive cases for patients of less than 50 years old group were observed. Table (3) showed no statistical significant difference in relation to age groups of CA19.9 expression.Regarding the site, 12 out of 20 (60%) colonic tissues were positive for CA19-9 expression. However, no statistical Significant difference ($p \geq 0.05$) were observed (Table 4). The expression of CA19-9 was positive in 3 out of 4 (75%) in well differentiated carcinoma, 9 out of 10 (90%) in moderate differentiated carcinoma and 6 out 6 (100%) of poor differentiated carcinoma showed CA19.9 expression. Statistically there was no significant difference regarding CA 19.9 expression in relation to tumor grading (Table 5). The expression of CA19-9 was positive in 16 out of 27 male genders (59.3%) and 9 out of 20 female genders (45%), there was no statistical significant difference were observed (Table 6).

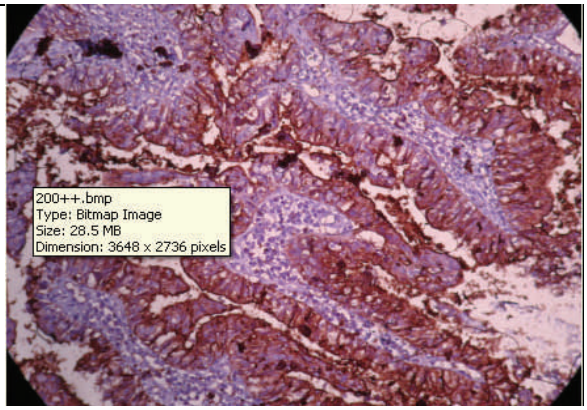

Figure 1: Colonic adenocarcinoma shows positive reactivity for CA19-9. The cytoplasm stains with brown color. (X 200) (Immunohistochemical staining).

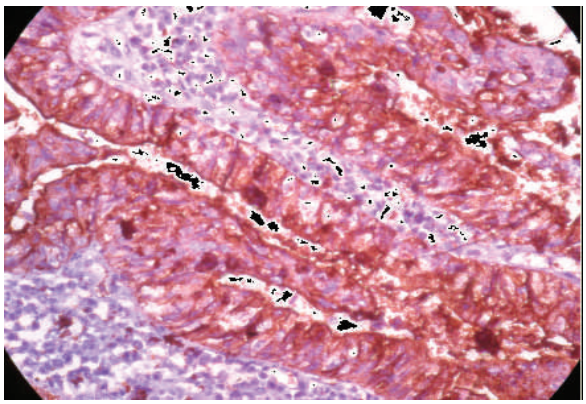

Figure 2: Colonic adenocarcinoma shows positive reactivity for CA19-9. The cytoplasm stains with brown color. (X 400) (Immunohistochemical staining).

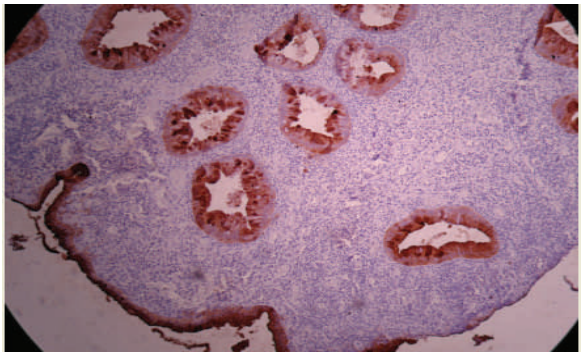

Figure 3: Retention polyp shows positive reactivity for CA19-9. The cytoplasm stains with brown color. (X 100) (Immunohistochemical staining).

Table 1: CA19.9 expression in colonic tissue .

Type	CA19.9		Total
	+ve	-ve	
Adenocarcinoma	18 (90%)	2(10%)	20
Tubular adenoma	2 (40%)	3(60%)	5
Retention Polyp	3 (25%)	9(75%)	12
Ulcerative colitis	1 (25%)	3(75%)	4
Normal colon	1 (16.7%)	5(83.3%)	6
Total	25	22	47

Significance difference (P < 0.05).

Table 2: CA19.9 expression according to Pattern of staining.

Type	Pattern of staining of CA19.9			Total
	Occasional	Focal	Diffuse	
Adenocarcinoma	2(11.1%)	4(22.2%)	12(66.7%)	18
Tubular adenoma	1 (50%)	1 (50%)	0	2
Retention Polyp	2 (66.7%)	(33.3) 1	0	3
Ulcerative colitis	1 (100%)	0	0	1
Normal colon	1 (100%)	0	0	1
Total	7	6	12	25

Significant difference (P < 0.05)

Table 4: Ca19.9 expression according to the site.

Site	CA19.9		Total
	+ve	-ve	
Colon*	2 (60%)	8 (40%)	20
Sigmoid colon	3 (37.5%)	5(62.5%)	8
Rectum	10(52.6%)	9 (47.4%)	19
Total	25	22	47

No significant difference (p ≥ 0.05)
***Colon : including ascending, descending and transverse colon.**

Table 5: CA19.9 expression in relation to grading system

Grade	CA19.9		Total
	+ve	-ve	
Well differentiated	3 (75%)	1 (25%)	4
Moderate differentiated	9(90%)	1(10%)	10
Poor differentiated	6 (100%)	0	6
Total	18	2	18

No significant difference (p ≥ 0.05)

Table 6: CA19.9 expression in relation to the gender

Gender	CA19.9		Total
	+ve	-ve	
Male	16 (59.3%)	11(40.7%)	27
Female	9(45%)	11(55%)	20
Total	25	22	47

No significant difference ($p \geq 0.05$)

DISCUSSION:

Many immunohistochemical studies have investigated the relationship between immunohistochemical characteristics and histopathological findings in colorectal tumors. The relationship between the immunohistochemical characteristics of the neoplasms and the clinicopathologic parameters is of significant importance [8, 9.] Carbohydrate antigen 19-9 (CA19-9) is one of the most representative tumor markers in colorectal carcinomas. We studied the immunohistochemical expression of CA19-9 in primary colorectal carcinoma to identify its significance as a prognostic factor. The staining pattern of CA19-9 is an apical and/ or cytoplasmic , 90 % stained positively in colorectal adenocarcinoma and less in adenoma (40%) and lesser in normal colonic mucosa (16.7%) this is similar to other results[10-14]. It was concluded that the positive staining rate, especially the rate of diffuse pattern for the antibody, correlated with the degree of atypia (differentiation) of the colorectal neoplastic lesion, and this is also agreed by others [15]. It was found in this study that there was a slight increased CA19-9 expression in male gender and in patients older than 50 years old.

REFERENCES:

1. Steven H. Itzkowitz, Mei Yuan, Yasuo Fukushi, Han Lee, Zuorong Shi, Vincent Zurawski, Jr., Sen -itiroh Hakomori. Immunohistochemical Comparison of Lea, Monosialosyl Lea (CA 19-9) and Disialosyl Lea Antigens in Human Colorectal and Pancreatic Tissues. Cancer Research. 1988. 48, 3834-3842.
2. Results of Iraqi Cancer Registry. Ministry of Health. 2001.
3. Rosai, J. Rosai and Ackerman's Surgical Pathology. 9th ed., Mosby. 2004.
4. Ponz de Leon M, Di Gregorio C. Pathology of colorectal cancer. Dig Liver Dis. 2001. 33(4):372-88.
5. Weisburger, J.H. Causes relevant mechanisms and prevention of large bowel cancer. Semin. Oncol. 1991. 18:316-336.
6. Nakayama, T., Watanabe, M., Teramoto, T. Kitajima, M. CA19-9 as a predictor of recurrence in patients with colorectal cancer. J. Surg. Oncol. 1997. 66(4):238-43.
7. Reiter, W., Stieber, P., Reuter, C., Nagel, D., Lau-Werner, U., Lamerz, R. Multivariate analysis of the prognostic value of the CEA and CA19-9 serum levels in the colorectal cancer. Anticancer Res. 2000. 20:5195-8.
8. Lorenzi, M., Vindigni, C., Minacci, C., Tripodi, S. A., Iroatulam, A., Petrioli, R., Francini, G. Histopathological and prognostic evaluation of immunohistochemical findings in colorectal carcinoma. Int. J. Biol. Markers. 1997. 12(2):68-74.
9. Kijima, H., Ueyama, Y., Osamura, Y. Histopathology and tumor markers Rinsho Byori. 2003. 51(12):1203-15.
10. Tucci, G. F., Grande, M., Stroppa, I., Federico, F., Farinon, A. M. Tissue expression of CA 19-9 in adenomatous lesion of the colorectum. Grotowski M. Antigens (CEA & CA19-9) in diagnosis and prognosis colorectal cancer.
11. Pol. Merkur Lekarski. 2002. 12(67):77-80Grotowski, M. , Antigens (CEA & CA19-9) in diagnosis and prognosis colorectal cancer. Pol Merkur Lekarski. 2002 Jan;12(67):77-80
12. Igarashi, K. Value of SLX & CA19-9 in the serum and tissue in colorectal cancer including the relation to Lewis blood type. Nippon Shokakibyo Gakkai _Zasshi. 1989. (10):2394-403.
13. Mauricio, Z., Cynthia, Cohen and Momin, T. Siddiqui. Immunohistochemical expression of SMAD4, CK19, and CA19-9 in fine needle aspiration samples of pancreatic adenocarcinoma: Utility and potential role. Cytojournal. 2007. 4:13. Published online 2007 June 22. doi: 10.1186/1742-6413-4-13.
14. Wolf, B. C., Salem, R. R., Sears, H. F., Horst, D. A., Lavin, P. T., Herlyn, M., Itzkowitz, S. H., Scholm, J. and Steele Jr., G. D. The expression of colorectal carcinoma-associated antigens

in the normal colonic mucosa. An immunohistochemical analysis of regional distribution. Am. J. Pathol.1989. 135(1): 111–119.
15. Taguchi T., Kijima, H., Mitomi, T., Osamura, R.Y. Immunohistochemical study of colorectal adenocarcinoma and adenoma with antibodies against CEA, CA19-9, Keratin, alpha-tubulin and secretary component (sc) Gastroenter Jpn. 1991. 26(3):294-302.