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Histopathological and Immunohistochemical Study of the Prognostic Significance of Cox2 and CDX2 Expression in the Available Cases of Colorectal Carcinoma

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Abstract

Background: Colorectal cancer is the third most common cancer worldwide. In Egypt, the relative frequency of colorectal cancer is about 9-12% with high male predominance 3:1. Several proteins are associated with the development and progression of colorectal cancer including Cox2 and CDX2 proteins. However, it is still controversial whether Cox2 and CDX2 expression can be regarded as prognostic factors for colorectal cancer patients.

Aim of Study: The purpose of this study is to detect the immunohistochemical expression of Cox2 and CDX2 in colorectal carcinoma and correlate their expression with the available clinicopathological parameters to illustrate their prognostic role.

Material and Methods: Fifty cases of colorectal carcinoma in colectomy specimens were collected retrospectively. They were stained by H & E, Cox2 and CDX2 for immunohistochemical study. The relations between their expression and the available clinicopathological parameters were evaluated.

Results: Cox2 expression in colorectal carcinoma showed statistically significant relation with depth of tumor invasion, lymph node status, distant metastasis and tumor stage. CDX2 expression showed statistically significant inverse relation with histopathological grade, depth of tumor invasion, lymph node status, distant metastasis, tumor stage and vascular invasion. There was statistically significant relation between the immunohistochemical expression of Cox2 and CDX2 in colorectal carcinoma.

Conclusions: Expression of Cox2 and loss of CDX2 are usually related to poor outcome and metastasis in colorectal cancer.

Key Words: *Cox2 – CDX2 – Colorectal carcinoma – Immunohistochemistry – Prognosis.*

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Introduction

COLORECTAL cancer is the third most common cancer worldwide [1]. It is a very common malignant tumor of the digestive tract, with about 1.2 million new cases and 600,000 deaths worldwide each year [2]. Colorectal cancer is the third most commonly diagnosed malignancy in males, after lung cancer and prostatic cancer and the second in females, after breast carcinoma [3]. It is the second most frequent cause of death by cancer [4].

Colorectal cancer is the 7th most common cancer in Egypt, representing 3.47% of male cancers and 3% of female cancers [5,6]. In Egypt, the relative frequency of CRC is about 9-12% with high male predominance [7]. It is the third most common tumor in males after urinary bladder and lymphohemopoietic malignancies, and in females it ranks fifth after breast, lymphohemopoietic, cervical, and urinary bladder cancers. Recently, interest in Egyptian colorectal cancer has been raised when clinical studies revealed a high incidence of the disease among the young Egyptian population [8]. In Egypt, colon cancer was commonly diagnosed in elder people with a mean age about 53 year-old, which is still more than a decade younger than the corresponding age in the USA (69 in men and 73 in women) [6,9]. Alterations and changes in the traditional Egyptian diet, introduction of new types of foods and eating habits such as consumption of processed or semi-processed, tinned or cooked meats, fried potatoes, hamburger, and pizza are taking place. Fast foods became popular as well as physical inactivity and smoking which might lead to increasing CRC among Egyptian population [7].

Certain molecular markers involved in CRC tumorigenesis have verified prognostic and predictive impact in addition to conventional TNM staging classification which is considered the major prognostic indicator [10].

Several epidemiological researches reported a 40-50% decrease in the relative risk of colorectal cancer in persons chronically using Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) indicating that these drugs might have a chemoprotective and possibly chemotherapeutic effect [11,12]. The best known targets of NSAIDs are cyclooxygenase (Cox) enzymes [13]. Many studies have focused on the role of Cyclooxygenase 2 (Cox2) in tumor development and progression [14]. It is a rate-limiting synthase which catalyzes the metabolism of Arachidonic Acid (AA) to PGs. Cox2 is an inducible enzyme and is associated with inflammatory diseases and carcinogenesis [15]. It is encoded by the gene located on chromosome 1 at q31.1 [16]. Overexpression of Cox2 plays a central role in intestinal tumorigenesis. In fact, elevated levels of Cox2-derived PGE2 are associated with resistance to apoptosis [17]; stimulation of cell proliferation; simulation of cell migration and angiogenesis [18].

Caudal-related homeobox transcription factor 2 (CDX2) is an intestine-specific transcription factor essential for intestinal development and differentiation [19,20]. It is encoded by CDX2 gene which is a member of the caudal-related homeobox gene family [21] that maps to the ParaHox gene cluster [22] in chromosome 13q12 [23]. The expression of CDX2 in adults is restricted to the intestine, from the duodenum to the rectum. CDX2 is regarded as a specific marker of the intestinal epithelial cells that can be utilized for identifying the colorectal origin of metastatic adenocarcinomas [24]. The role of CDX2 protein during CRC development remains controversial, as different studies suggest both negative and positive modulation of tumourigenesis [23]. CDX2 has been proposed as a tumor suppressor in colon cancer [24,25], but CDX2 expression is seldom lost in colon cancer tissue, and the gene is rarely mutated [26,27]. Furthermore, several studies have found that CDX2 gene is often amplified in colon cancer, suggesting a lineage survival oncogene function in some tumors [28,29].

Material and Methods

This study was carried out on 50 cases of colorectal carcinoma in the form of colectomy specimen. These cases were collected retrospectively from the archives of Pathology Department, Faculty of Medicine, Tanta University and from some private laboratories during the period of the research from February 2016 to December 2017 and patients' data were obtained from files of surgery and oncology reports. Approval from Research Ethics Committee (REC), Faculty of Medicine, Tanta University was taken antecedent to conducting study.

Cases were classified microscopically according to the 4th edition of the World Health Organization (WHO) classification system, 2010 [30,31]. Cases were graded traditionally using the three-tiered system into well differentiated (Grade 1), moderately differentiated (Grade 2) and poorly differentiated (Grade 3) carcinomas according to the WHO criteria which was based on the extent of glandular differentiation as the following [32]:

Grade 1: Showing more than 95% of gland formation.

Grade 2: Gland formation ranged between 50% and 95%.

Grade 3: Gland formation was lower than 50%.

Pathological staging of the studied colorectal carcinomas was determined according to the recommendations of the 8th edition of AJCC, Cancer Staging Manual, 2017 by using the TNM staging system [33].

Immunohistochemical staining was performed on 10% formalin fixed, paraffin embedded tissue blocks for evaluation of Cox2 and CDX2 expression. Sections were immunohistochemically labeled, using primary antibodies to Cox2 (Ready to use Rabbit monoclonal antibody, Thermo Fisher Scientific, USA) and CDX2 (DAK-CDX2 clone, ready to use mouse monoclonal antibody, DAKO, Egypt). Cox2 expression was mainly cytoplasmic in the tumor cells [34]. Immunostaining evaluation was performed using a semi-quantitative scoring system by estimating the percentage of the tumor cells stained and staining intensity [35]. The extent of staining was graded as follows: 0-staining in less than 1% of tumor cells; 1-staining in 1-20%; 2 - staining in 20-50%; and 3-staining in more than 50%. Overall intensity of staining was also assessed as follows: 0 no staining; 1 weak staining; 2 moderate staining; and 3 strong staining. Final scores (range from 0 to 9) were obtained by multiplying staining extents and intensities. Final scores were described as follows: 0, no expression; 1 to 3, weak expression; 4-6, moderate expression; and 7-9, strong expression. For statistical analysis, no expression and weak expression were combined and

described as negative for expression, and moderate and strong expression were combined and described as positive for expression [14]. Nuclear CDX2 were scored as the percentage of positive tumor cells [24]. The tumor was considered to be positive for CDX2 when it showed at least 20% of positive cells [24,36].

Chi-square test was used as a test of significance to evaluate the association between categorized variables and p-value <0.05 was considered statistically significant. Statistical analyses were performed using SPSS software, Version 12.0.

Results

The clinicopathological characteristics of the studied cases were summarized in (Table 1). We immunohistochemically evaluated 50 cases of colorectal carcinoma specimens for Cox2 and CDX2 expression and correlated with different clinicopathological characteristics (Tables 2,3).

Out of 50 studied colorectal carcinoma cases, 38 cases (76%) were Cox2 positive including 23 cases (46%) of moderate expression and 15 cases (30%) of strong expression, while 12 cases (24%) were Cox2 negative including 11 cases (22%) of weak expression and one case (2%) of no expression. There was a statistically significant correlation between Cox2 expression and the depth of tumor invasion (p-value=0.024), lymph node status (p-value=0.009), distant metastasis (p-value=0.035) and TNM stage (p-value=0.001). Cox2 expression was not significantly correlated with histopathological type, histopathological grade, vascular invasion and perineural invasion (p-value=0.091, 0.405, 0.385 and 0.329 respectively).

Out of 50 studied colorectal carcinoma cases, 39 cases (78%) were CDX2 positive, while 11 cases (22%) were CDX2 negative. There was a statistically significant inverse correlation between CDX2 expression and histopathological grade (p-value=0.005), depth of tumor invasion (p-value= 0.001), lymph node status (p-value=0.001), distant metastasis (p-value=0.001), TNM stage (p-value= 0.002) and vascular invasion (p-value=0.001). CDX2 expression was not significantly correlated with histopathological type and perineural invasion (p-value=0.097 and 0.248 respectively). The relation between Cox2 immunohistochemical score and CDX2 immunohistochemical staining in the studied cases was statistically significant (p-value= 0.035).

Table (1): Clinicopathological characteristics of the studied cases.

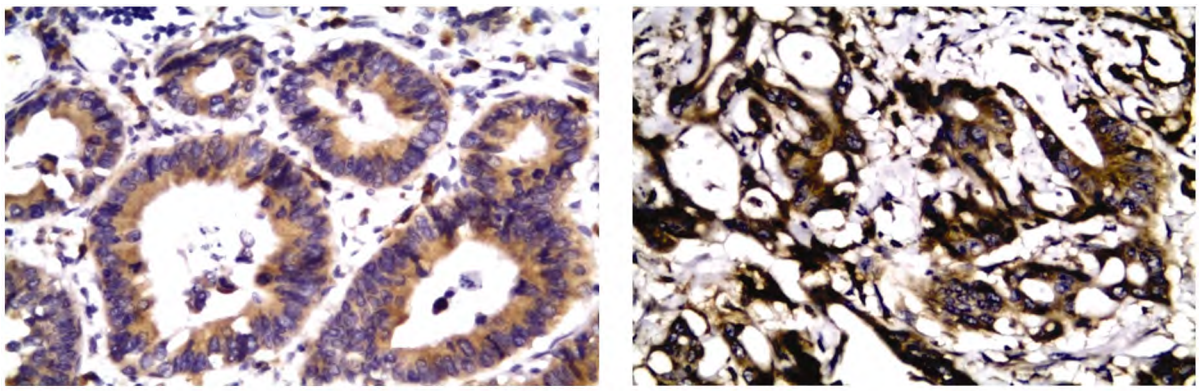
Clinicopathological characteristics	No.	%
Age:		
• <40	14	28.0
• 40-60	18	36.0
• >60	18	36.0
Sex:		
• Male	26	52.0
• Female	24	48.0
Tumor location:		
• Right colon	17	34.0
• Left colon	20	40.0
• Rectum	13	26.0
Tumor size:		
• <5cm	23	46.0
• ≥5cm	27	54.0
Gross appearance:		
• Fungating	17	34.0
• Ulcerating	17	34.0
• Infiltrating	16	32.0
Histopathological types:		
• Conventional adenocarcinoma	30	60.0
• Mucinous carcinoma	10	20.0
• Signet ring carcinoma	3	6.0
• Adenocarcinoma with neuroendocrine differentiation	2	4.0
• Medullary carcinoma	1	2.0
• Adenosquamous carcinoma	1	2.0
• Small cell carcinoma	1	2.0
• Large cell carcinoma	1	2.0
• Papillary adenocarcinoma	1	2.0
Histopathological grade:		
• Grade I	5	10.0
• Grade II	25	50.0
• Grade III	20	40.0
Vascular invasion:		
• Present	12	24.0
• Absent	38	76.0
Perineural invasion:		
• Present	8	16.0
• Absent	42	84.0
Depth of invasion:		
• T1	2	4.0
• T2	4	8.0
• T3	26	52.0
• T4	18	36.0
Lymph node status:		
• N0	20	40.0
• N1	16	32.0
• N2	14	28.0
Distant metastasis:		
• M1	11	22.0
• M0	39	78.0
TNM staging:		
• Stage I	6	12.0
• Stage II	14	28.0
• Stage III	19	38.0
• Stage IV	11	22.0

Table (2): Correlation between Cox2 immunohistochemical score and different clinicopathological parameters.

Variables	n.	COX2 immunohistochemical score				χ^2	MC_P
		Positive		Negative			
		n.	%	n.	%		
Type:							
• Conventional adenocarcinoma	30	20	66.7	10	33.3	13.675	0.091
• Mucinous carcinoma	10	10	100.0	0	0.0		
• Signet ring carcinoma	3	3	100.0	0	0.0		
• Conventional with neuroendocrine differentiation	2	2	100.0	0	0.0		
• Medullary carcinoma	1	0	0.0	1	100.0		
• Adenosquamous carcinoma	1	1	100.0	0	0.0		
• Small cell carcinoma	1	0	0.0	1	100.0		
• Large cell carcinoma	1	1	100.0	0	0.0		
• Papillary carcinoma	1	1	100.0	0	0.0		
Grade:							
• Grade I	5	3	60.0	2	40.0	1.809	0.405
• Grade II	25	18	72.0	7	28.0		
• Grade III	20	17	85.0	3	15.0		
The depth of the invasion:							
• T1	2	0	0.0	2	100.0	9.467	0.024*
• T2	4	2	50.0	2	50.0		
• T3	26	20	76.9	6	23.1		
• T4	18	16	88.9	2	11.1		
The lymph node status:							
• N0	20	11	55.0	9	45.0	9.498	0.009*
• N1	16	13	81.2	3	18.8		
• N2	14	14	100.0	0	0.0		
Distant metastasis:							
• M0	39	27	69.2	12	30.8	4.453	0.035*
• M1	11	11	100.0	0	0.0		
Tumor stage:							
• Stage I	6	2	33.3	4	66.7	11.217	0.001 *
• Stage II	14	9	64.3	5	35.7		
• Stage III	19	16	84.2	3	15.8		
• Stage IV	11	11	100.0	0	0.0		
The vascular invasion:							
• Present	12	8	66.7	4	33.3	0.754	0.385
• Abscent	38	30	78.9	8	21.1		
The perineural invasion:							
• Present	8	5	62.5	3	37.5	0.952	0.329
• Absent	42	33	78.6	9	21.4		

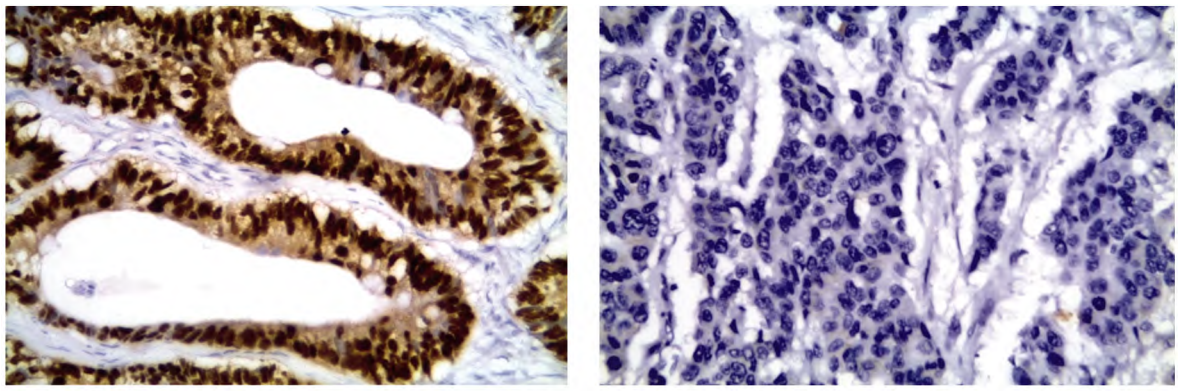
Table (3): Correlation between CDX2 immunohistochemical staining and different clinicopathological parameters.

Variables	n.	CDX2 immunohistochemical staining				χ^2	MC_P
		Positive		Negative			
		n.	%	n.	%		
Type:							
• Conventional adenocarcinoma	30	26	86.7	4	13.3	13.450	0.097
• Mucinous carcinoma	10	7	70.0	3	30.0		
• Signet ring carcinoma	3	2	66.7	1	33.3		
• Conventional with neuroendocrine differentiation	2	2	100.0	0	00.0		
• Medullary carcinoma	1	0	00.0	1	100.0		
• Adenosquamous carcinoma	1	0	00.0	1	100.0		
• Small cell carcinoma	1	1	100.0	0	00.0		
• Large cell carcinoma	1	1	100.0	0	00.0		
• Papillary carcinoma	1	0	00.0	1	100.0		
Grade:							
• Grade I	5	5	100.0	0	0.0	10.431	0.005*
• Grade II	25	23	92.0	2	8.0		
• Grade III	20	11	55.0	9	45.0		
The depth of the invasion:							
• T1	2	2	100.0	0	0.0	13.018	0.001 *
• T2	4	4	100.0	0	0.0		
• T3	26	24	92.3	2	7.7		
• T4	18	9	50.0	9	50.0		
The lymph node status:							
• N0	20	19	95.0	1	5.0	14.286	0.001 *
• N1	16	14	87.5	2	12.5		
• N2	14	6	42.9	8	57.1		
Distant metastasis:							
• M0	39	35	89.7	4	10.3	14.247	0.001 *
• M1	11	4	36.4	7	63.6		
Tumor stage:							
• Stage I	6	6	100.0	0	0.0	15.033	0.002*
• Stage II	14	13	92.9	1	7.1		
• Stage III	19	16	84.2	3	15.8		
• Stage IV	11	4	36.4	7	63.6		
The vascular invasion:							
• Present	12	4	33.3	8	66.7	18.358	0.001 *
• Abscent	38	35	92.1	3	7.9		
The perineural invasion:							
• Present	8	5	62.5	3	37.5	1.333	0.248
• Absent	42	34	81.0	8	19.0		



(A) (B)

Fig. (1): (1A) Conventional adenocarcinoma (grade I) showing weak cytoplasmic Cox2 expression, negative score (3) (X400). (1B) Conventional adenocarcinoma (grade III) showing strong cytoplasmic Cox2 expression, positive score (9) (X400).



(A) (B)

Fig. (2): (2A) Conventional adenocarcinoma (grade I) showing positive nuclear CDX2 staining (X400). (2B) Conventional adenocarcinoma (grade III) showing negative nuclear CDX2 staining (X400).

Discussion

Cox2 is a rate-limiting synthase which catalyzes the metabolism of Arachidonic Acid (AA) to PGs. Cox2 is an inducible enzyme and is associated with inflammatory diseases and carcinogenesis **[15]**. It is encoded by the gene located on chromosome 1 at q31.1 **[16]**. Overexpression of Cox2 plays a central role in intestinal tumorigenesis. In fact, the elevated level of Cox2-derived PGE2 is associated with resistance to apoptosis **[17]**; stimulation of cell proliferation; simulation of cell migration and angiogenesis **[18]**.

Cox2 expression was associated with increased depth of tumor invasion, increased lymph node metastasis, distant metastasis and increased tumor stage. From that, Cox2 expression was associated with poor prognosis of colorectal carcinoma which was in agreement with other studies who reported that Cox2 expression is a useful poor prognostic marker in CRC **[34,35,37-40]**. In contrast, Fux et al., **[41]** and Lim et al., **[42]** demonstrated that Cox2 overexpression has little prognostic impact in CRC. Besides, Wu et al., **[43]** and Yamac et al., **[44]** failed to prove a prognostic relevance of Cox2 expression in CRC.

Cox2 expression was observed to increase with increased depth of the tumor invasion and the relation between Cox2 score and depth of invasion (T) was statistically significant. Similarly, Lim et al., **[14]** reported that Cox2 expression was significantly associated with infiltration depth. In contrast, Lim et al., **[42]** and Shin et al., **[46]** found no significant correlation between Cox2 expression and depth of invasion. Cox2 expression was observed to increase with increased lymph node metastasis and the relation between Cox2 score and lymph node status (N) was statistically significant. Similarly, Xiong et al., **[45]** and Shin et al., **[46]** reported that Cox2 expression was significantly associated with lymph node metastasis. In contrast, Elzagheid et al., **[34]** and Mahmoud et al., **[47]** detected no association between Cox2 expression and lymph node metastasis. Cox2 expression was observed to increase in cases with distant metastasis than those with no documented distant metastasis

and the relation between Cox2 score and distant metastasis (M) was statistically significant. Similarly, Wan et al., [48] and Al-Maghrabi et al., [40] detected significant correlation between Cox2 expression and distant metastasis. In contrast, Okudur et al., [39] failed to demonstrate a statistically significant correlation between Cox2 and the presence of metastases. Yamauchi et al., [37] and Xiong et al., [45] reported that Cox2 expression was correlated with hepatic metastasis in contrast with Shin et al., [46] who found no relation between Cox2 expression and hepatic metastasis. Cox2 immunohistochemical score was observed to increase with increased stage of the tumor and the relation between Cox2 score and tumor stage in the studied colorectal carcinoma cases was statistically significant. Similarly, Al-Maghrabi et al., [40] and Elzagheid et al., [34] reported statistically significant correlation between Cox2 expression and tumor stage. In contrast, Lim et al., [42] and Mahmoud et al., [47] detected no significant association between Cox2 expression and tumor stage.

Caudal-related homeobox transcription factor 2 (CDX2) is an intestine-specific transcription factor essential for intestinal development and differentiation [19,20]. It is encoded by CDX2 gene which is a member of the caudal-related homeobox gene family [21] that maps to the ParaHox gene cluster [22] in chromosome 13q12 [23].

The role of CDX2 protein during CRC development remains controversial, as different studies suggest both negative and positive modulation of tumourigenesis [23].

CDX2 expression in the current study showed statistically significant inverse correlation with histopathological grade, depth of tumor invasion, lymph node status, distant metastasis, TNM stage and vascular invasion. From that, loss of CDX2 expression was associated with poor prognosis of colorectal carcinoma which was in agreement with other studies as Dalerba et al., [49] and Bonetti et al., [36] who suggested that loss of CDX2 expression may be useful as a prognostic marker for advanced CRCs. Besides, Kim et al., [50] demonstrated that the CDX2 negative phenotype was an independent adverse prognostic factor for MSI-H CRC. There was statistically significant inverse relation between CDX2 immunohistochemical staining and the histopathological grade. Loss of CDX2 immunohistochemical staining increased with increased tumor histopathological grade. Similarly, Oslen et al., [53] and Bonetti et al., [36] reported significant correlation between CDX2 loss and poor differentiation grade. Besides, Kim et al., [50] found that CDX2 loss was significantly associated with poor differentiation in MSI-H CRC tissues and Lugli et al., [54] found that the loss of CDX2 expression is associated with a higher tumor grade in mismatch repair-proficient (MSS or MSI-low) CRCs. There was statistically significant inverse relation between CDX2 immunohistochemical staining and the depth of tumor invasion (T). Loss of CDX2 immunohistochemical staining increased with increased depth of tumor invasion (T). Similarly, Bae et al., [24] reported that loss of CDX2 expression was significantly associated with depth of tumor invasion (T). Besides, Lugli et al., [54] found that loss of CDX2 expression is associated with a higher T stage in mismatch repair-proficient (MSS or MSI-low) CRCs. There was statistically significant inverse relation between CDX2 immunohistochemical staining and lymph node status (N). Loss of CDX2 immunohistochemical staining increased with increased lymph nodes metastasis (N). Similarly, Choi et al., [51] and Bae et al., [24] reported that loss of CDX2 expression was significantly associated with lymph node status (N). Besides, Kim et al., [50] found that CDX2 loss was significantly associated with lymph node metastasis in MSI-H CRC tissues and Lugli et al., [54] found that the loss of CDX2 expression is associated with a higher N stage in mismatch repair-proficient (MSS or MSI-low) CRCs. There was statistically significant inverse relation between CDX2 immunohistochemical staining and distant metastasis (M). Loss of CDX2 immunohisto-chemical staining is more common in cases with distant metastasis than those with no distant metastasis. Similarly, Bae et al., [24] reported that loss of CDX2 expression was significantly associated with distant metastasis (M). There was statistically significant inverse relation between CDX2 immunohistochemical staining and the tumor stage. Loss of CDX2 immunohistochemical staining increased with increased stage of the tumor. Similarly, Oslen et al., [23] and Bae et al., [24] reported that loss of CDX2 expression was significantly associated with tumor stage. In contrast, Oslen et al., [53] reported that cancer stage was not significantly associated with CDX2 protein level. There was statistically significant inverse relation between CDX2 immunohistochemical staining and vascular invasion. Loss of CDX2 immunohistochemical staining is more common in cases with vascular invasion than those with no vascular invasion. Similarly, Knösel et al., [52] reported that loss of CDX2 was significantly correlated with vascular invasion. Besides, Lugli et al., [54] found that loss of CDX2 expression is associated with more frequent vascular invasion in mismatch repair-proficient (MSS or MSI-low) CRCs.

The relation between Cox2 immunohistochemical score and CDX2 immunohistochemical staining in the studied colorectal carcinoma cases was statistically significant.

Therefore, we conclude that combined expression of Cox2 with loss of CDX2 suggests poor prognosis and high risk of metastasis in patients with colorectal cancer. Therefore, this combination could be used for evaluating the prognosis and screening for patients with high risk of metastasis.

Conflict of interest:

None declared.

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التعبير الهيستوكيميائى المناعى لكوكس ٢ وسى دى اكس ٢ وعلاقته بتطور المرض فى سرطان القولون والمستقيم

يعد سرطان القولون والمستقيم ثالث أكثر الأورام الخبيثة تشخيصا فى الذكور بعد سرطان الرئة وسرطان البروستاتا والثانى فى الإناث بعد سرطان الثدى ويعد هو ثانى أكثر الأسباب شيوعا للوفاة بسبب السرطان. يعد سرطان القولون والمستقيم فى مصر هو سابع السرطانات الأكثر شيوعا ممثلا ٣.٤٧٪ من سرطانات الذكور و٣٪ من سرطانات الإناث.

يعد إنزيم الأكسدة الحلقى ٢ (الكوكس ٢) إنزيم تصنيع هام جدا والذى يحفز تحويل حمض الأراكيدونيك إلى البروستاجلاندين. الكوكس ٢ هو إنزيم يرتبط تحفيز تصنيعه بالأمراض الإلتهابية والتسرطن. زيادة التعبير عن الكوكس ٢ يلعب دورا مركزيا فى تكون الأورام المعوية حيث ترتبط المستويات المرتفعة من الكوكس ٢ والبروستاجلاندين إى ٢ المشتقه منه مع (١) مقاومة موت الخلايا المبرمج، (٢) تحفيز تكاثر الخلايا، (٣) تحفيز هجرة الخلايا و (٤) تولد الأوعية الدموية.

يعد السى دى إكس ٢ عامل نسخ خاص بالأمعاء وهو ضرورى لتطور وتمايز الأمعاء ويتم تصنيعه بواسطة جين السى دى إكس ٢ الذى ينتمى إلى مجموعة جينات الباراهوكس. لا يزال دور بروتين السى دى إكس ٢ فى تطور سرطان القولون والمستقيم مثيرا للجدل، حيث تشير دراسات مختلفة إلى كل من التأثير السلبى والإيجابى لعملية تكون الورم.

كان الهدف من العمل الحالى هو دراسة التعبير الهستوكيميائى المناعى للكوكس ٢ والسى دى إكس ٢ فى الحالات المتاحة من سرطان القولون والمستقيم ومقارنة التعبير الهستوكيميائى المناعى لكل من الكوكس ٢ والسى دى إكس ٢ بالعوامل الإكلينيكية والباثولوجية المتاحة لتقييم دورهما التنبؤى بسرطان القولون والمستقيم.

تم تنفيذ العمل الحالى على ٥٠ حالة من حالات سرطان القولون والمستقيم والتى تم تجميعها بأثر رجعى من أرشيفات قسم الباثولوجى بطنطا والمعامل الخاصة خلال الفترة من فبراير ٢٠١٦ إلى ديسمبر ٢٠١٧. تعرضت جميع الحالات المدرجة فى هذا البحث إلى صبغة الهيماتوكسيلين والآيوسين الهستوباثولوجية والصبغة الهستوكيميائية المناعية لكل من بروتينات الكوكس ٢ والسى دى إكس ٢.

النتائج التى تم الحصول عليها:

كانت (٧٦٪) من الحالات إيجابية للكوكس ٢ وكانت ٢٤٪ من الحالات سلبية للكوكس ٢ وأظهرت النتائج علاقة ذات دلالة إحصائية مع عمق غزو الورم، ووضع العقد الليمفاوية ، والإنبثاث البعيد، ومرحلة الورم، ولكن لم تظهر علاقة ذات دلالة إحصائية مع النوع والدرجة الهيستوبوباثولوجية وغزو الأوعية الدموية والغزو العصبى.

كانت (٧٨٪) من الحالات إيجابية للسى دى إكس ٢ وكانت ٢٢٪ من الحالات سلبية للسى دى إكس ٢ وأظهرت النتائج علاقة ذات دلالة إحصائية عكسية مع الدرجة الهستوباثولوجية، عمق غزو الورم، وضع العقد الليمفاوية، الإنبثاث البعيد، مرحلة الورم، وغزو الأوعية الدموية ولكن لم تظهر علاقة ذات دلالة إحصائية مع النوع الهستوباثولوجى والغزو العصبى.

كانت العلاقة بين الناتج الهستوكيميائى المناعى للكوكس ٢ والصبغة الهستوكيميائية للسى دى إكس ٢ فى الحالات المدروسة من سرطان القولون والمستقيم ذات دلالة إحصائية.

من هذه الدراسة نستنتج أن:

- يعد الكوكس ٢ والسى دى إكس ٢ دلالات ورمية هامة والتى تشارك فى عملية تكون سرطان القولون والمستقيم وتشارك أيضا فى التنبؤ بسرطان القولون والمستقيم.
- يشير تعبير الكوكس ٢ بالإضافة إلى فقدان السى دى إكس ٢ إلى سوء التنبؤ بسرطان القولون والمستقيم وزيادة خطر الإنبثاث. لذلك، فإن الكشف عن كوكس ٢ وفقدان السى دى إكس ٢ فى أنسجة سرطان القولون والمستقيم يمكن أن يستخدم لتقييم التنبؤ بالمرض وتحرى المرضى الذين يعانون من إرتفاع خطر الإنبثاث.