Original Article

Immunohistochemical Expression of Estrogen and Progesterone Receptors in Human colorectal Carcinoma (Clinicopathological study)

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Summary:

Background: Colorectal adenocarcinoma is the most common type of gastrointestinal cancer, with about 150,000 cases each year in the United States and about 56,730 deaths from colorectal cancer risk. In Iraq and according to the Iraqi cancer registry (ICR) reports, the incidence of colorectal carcinoma was 4.55% of whole body malignancy, & it is the seventh cause of death from cancer (ICR 2005). In males, it's the 7th common cancer while in females it's the 4th most common cancer. The estrogen and progesterone receptors belong to a super- family of nuclear hormone receptors. These receptor proteins function as transcription factors when they are bound to their respective ligands, these receptors shares a common structural and functional organization

Objectives: to evaluate the immunohistochemical expression of estrogen (ER) and progesterone (PR) in colorectal adenocarcinoma and to correlate this expression with different clinical and pathological parameters.

Material and method: Twenty five cases of colorectal adenocarcinoma diagnosed in private laboratories in Baghdad/Iraq from November 2011 to march 2013, were respectively evaluated in term of age, gender, pathological diagnosis, including the tumor site, size, lymph nodes status, grade and stage of tumor. Using infiltrative ductal carcinoma of the breast as control for both estrogen and progesterone receptors expression were investigated immunohistochemically, nuclear and cytoplasmic staining of tumor cells were accepted positive.

Results: Fourteen (56%) of the cases were male, 11 (44%) case were female, with age distribution ranging from (24-84) years, with a mean age of 56.5 year. Tumor size ranges between 2.5-10 cm, mean of 6.25 cm. Seven cases (28%) cases were from the caecum, 5(20%) from each rectum, sigmoid and left colon respectively and 3(12%) cases were from more than one segment of the colon. Histologically the tumor grade ranges from moderately differentiated in 23(92%) cases and poorly differentiated in 2(8%) cases. Regarding pathological staging (TNM system), 5(20%) cases were stage T2, 17 (68%) cases were stage T3 and 3(12%) cases were T4, lymph node involvement found in 10(40%) cases and distant metastasis were found in 2 (12%) cases. Estrogen receptors expression was positive in 2(8%) cases, while progesterone receptor was positive in 5(20%) cases; both ER positive cases were PR positive. Both ER positive cases were female; one of the PR positive cases was male. All of the ER and PR positive cases were moderately differentiated, one case of ER positive tumor showed nodal involvement while three cases of PR positive showed nodal involvement.

Conclusion: - Estrogen and progesterone receptors in colorectal adenocarcinoma had same activity. The level of ER and PR expression in tumor tissue could not predict malignant biological behavior of the colorectal adenocarcinoma. No significant statistical correlation was observed between ER, PR expression and any of the studied clincopathological parameters.

Keywords: Colorectal adenocarcinoma, ER, PR.

Introduction:

Colorectal adenocarcinoma is the fourth most frequently diagnosed visceral cancer, and the second cause of cancer mortality in both genders worldwide (1). The estrogen and progesterone receptors belong to a super- family of nuclear hormone receptors. These receptor proteins function as transcription factors when they are bound to their respective ligands; these receptors share a common structural and functional organization (2). Colorectal cancer incidence has been reported to be 35% lower in women than in men (3). The correlation in mortality rate between breast cancer and colonic cancer in individual women with breast cancer suggest common factors in their etiology (4, 5). Estrogen and progesterone receptors have been found in normal and malignant colonic tissue (6).

The protective effect of increasing parity from colonic cancers is similar to breast cancer and the relatively better prognosis of colonic cancers in women, may also imply a common role for sex steroid hormones (7).

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ER & PR levels in colonic cancers are usually lower than those in mammary cancers and it may be difficult to detect immunohistochemical expression in gastrointestinal cancer with lower levels (8).

The aim of this study is to evaluate the immunohistochemical expression of ER & PR in colorectal adenocarcinoma and to correlate this expression with different clinicopathological parameters.

Material and methods

This study is retrospectively designed, a total of 25 cases of colorectal adenocarcinoma diagnosed in private pathology laboratories in Baghdad/ Iraq, in the period from November 2011 to march 2013, were evaluated in terms of age, gender, and pathological parameters including tumor size, location, grade and lymph nodes status (all specimens were colectomy).

Three sections of 5 microns thickness were taken from paraffin blocks of the tumor, one section was stained with hematoxylin and eosin (H&E) and the other two sections were stained immunohistochemically for ER and PR, using three steps; indirect streptavidin method for monoclonal mouse anti-human estrogen receptors (ER), clone 1D5, manufactured by DAKO, Denmark, and monoclonal mouse anti-human progesterone receptor (PR) clone PgR 636,DAKO, Denmark, using infiltrative ductal carcinoma of the breast as positive control for estrogen and progesterone receptors.

Expression was investigated, brown cytoplasmic and nuclear ER & PR staining was considered as positive reaction in colorectal tissue. Statistical analysis of all results were performed with the help of SPSS software statistical package, P value at level of less than 0.05 is significant.

Results

Fourteen (56%) cases were males and 11 (44%) cases were females, with an age distribution ranging from 24-89 years with a mean of 56.5 years. Only one case was younger than 40 years, the majority of cases were above 50 years. Cases were divided into two age groups: below and equal to 50 years, and above 50 years. Eight (32%) cases were equal or below 50 years, and 17(68%) cases were above 50 years.

Table 1 & 2 shows the gender & age distribution of the cases.

Tumor size ranges from 2.5-10 cm with a mean of 6.25 cm. regarding the site of tumor: seven (28%) cases were from the caecum, there were 15 cases from left colon, sigmoid and rectum: 5 (20%) cases each, and 3 (12%) cases were from more than one segment of the colon, as shown in table (3). Histologically the tumor grades range from a moderately differentiated in 23 (92%) cases and poorly differentiated in 2 (8%) cases as shown in table (4).

Regarding pathological staging the TNM staging system of AJCC 2010 was applied to all the tumors, 5 (20%) cases were T2, 17(68%) cases were T3 and 3 (12%) cases were T4. Lymph node involvement found in 10 (40%) cases & distant metastasis to liver was found in 2 (8%) cases as shown in table (5). Estrogen receptor expression was positive in 2 (8%) cases, progesterone receptors were positive in 5 (20%) cases. Both ER positive cases were also PR positive. Table (6) shows the distribution of cases according to expression of ER and PR.

Figure(1)showsexpressionofER&PRimmunohistochemically. Both ER positive cases were female, one of the PR positive cases was male, all of the ER and PR positive cases were moderately differentiated. Only one case of ER positive tumors showed nodal metastasis, whereas three cases of PR positive tumors showed nodal involvement. Table (7) showed ER, PR expression in relation to the clinicopathological parameters, No significant statistical correlation was detected between ER and PR expression by the tumor cells, and any of the studied clinicopathological parameters, including gender, size, site, and grade, stage of the tumor and lymph node involvement, the P values were > 0.05, which is statistically insignificant.

Table 1: Age distribution of colorectal adenocarcinoma

Age group	Number of cases	Percentage %
≤ 50 years	8	32%
>50 years	17	68%
Total	25	100%

Table 2: Gender distribution of colorectal adenocarcinoma

Sex	Number of cases	Percentage
Male	14	56
Female	11	44
Total	25	100%

Table 3: Site distribution of colorectal adenocarcinoma.

Site	Number	Percentage %
Caecum	7	28%
Rectum	5	20%
Sigmoid	5	20%
Left colon	5	20%
More than one segment	3	12%
Total	25	100%

Table 4: Grade distribution of the colorectal adenocarcinoma

grading	No	Percentage %
Well differentiated	0	0
Moderately differentiated	23	92 %
Poorly differentiated	2	8%
TOTAL	25	100%

Table 5: Stage distribution of the colorectal adenocarcinoma (TNM staging)

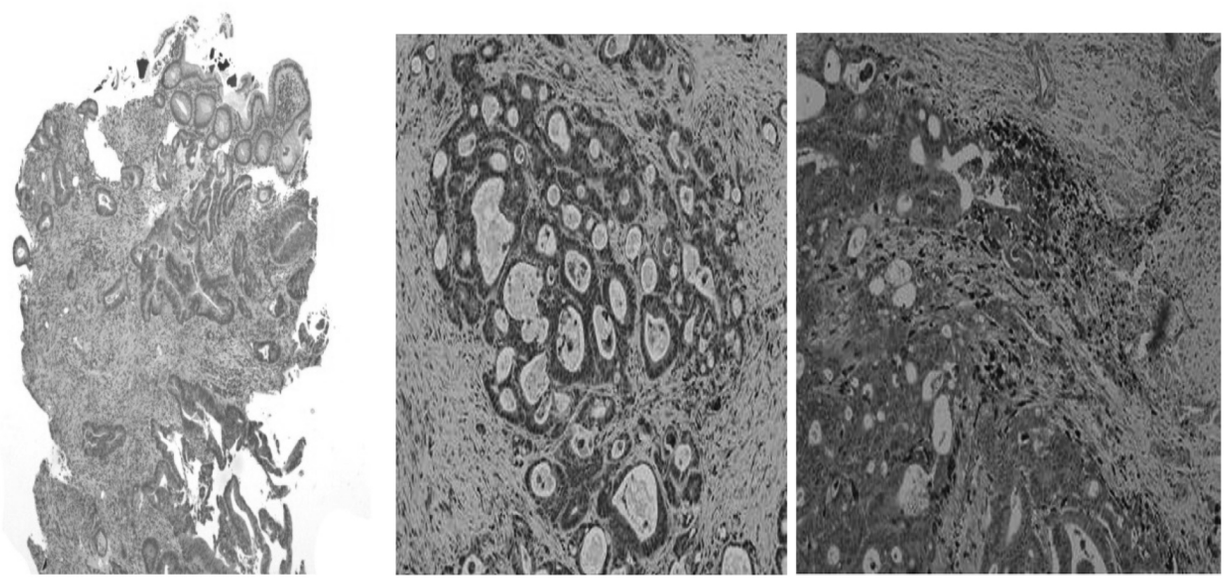
Parameter		No	Percentage %
Tumor T			
	T1	0	0%
	T2	5	20%
	T3	17	68%
	T4	3	12%
Lymph nodes			
	N0	15	60%
	N1	4	16%
	N2	6	24%
Metastasis M			
	M1	2	8%
	Mx	23	92%

Table 6: Expression of estrogen and progesterone receptors

Marker expression	Expression	No	%	P value
ER	Positive	2	8	> 0.05
	Negative	23	92	
	Total	25	100	
PR	Positive	5	20	> 0.05
	Negative	20	80	
	Total	25	100	

Table 7: Expression of estrogen and progesterone receptors in relation to clinincopathological parameters

Marker expression	Expression	Parameter (grade)		P value
		Moderately	Poorly	
ER	Positive	2 (8%)	0 (0%)	> 0.05 0.005
	Negative	23 (92%)	0 (0%)	
PR	Positive	5 (20%)	0 (0%)	> 0.05
	Negative	20 (80%)	0 (0%)	
		Gender Gender male		
		Male	Female	P value
ER	Positive	0 (0%)	2(8%)	> 0.05
	Negative	25 (100%)	23 (92%)	
PR	Positive	1 (4%)	4 (16%)	> 0.05
	Negative	24 (96%)	21 (84%)	
		Lymph nodes		
		Positive	Negative	
ER	Positive	1(4%)	1(4%)	> 0.05
	Negative	9(36%)	14(56%)	
PR	Positive	3(12%)	2(8%)	> 0.05
	Negative	7(28%)	13(52%)	



A B C

Figure 1: showed caecal adenocarcinoma, moderately differentiated: A stained by, H&E (X40), B and C: ER & PR expression (X100)

Discussion:

Colorectal adenocarcinoma primarily affects elderly people, with the sixth decade being the average age of incidence. It is exceptionally rare under 40 years (9, 10). This study showed similar findings almost akin to the given data. Proximal tumors seems to be increased during the last few decades as is also noted in this study, however a approximately 50% of the carcinoma occurs in the recto sigmoid area (11).

Comparable studies, either biochemically or immunohistochemically showed that both normal and malignant colonic mucosal cells may express ER & /or PR (12). By biochemical methods ER exhibited a wide range that varies between 20% to 54%, while PR expression was about 42% (13), as compared to our study where ER expression was 8% & PR expression was 20%, In part this may be attributed to low receptor level. It may also be associated with other causes such as characteristics affect by tissue processing, immunohistochemical methods, and perhaps clonality of antibodies (14). ER & PR levels in colonic cancers are usually lower than in mammary cancers and thus it may be difficult to be detected immunohistochemically (8). ER & PR reaction were consecutively found to be 32% and 23% by Kaklamanos et al (15). In terms of immunohistochemical staining pattern nuclear staining of more than 5 % of the tumor cells are generally accepted positive, while cytoplasmic reaction is considered nonspecific. However some reports proposed that cytoplasmic ER & PR staining should considered as in our study (16). In comparing the clinicopathological relevance of both receptors, ER expression in tumor cells was independent of sex and age of the patient, size, site, duke's staging of the tumor (17).

Some studies showed that there was no correlation between tumor tissue ER, PR expression and sex, invasion depth and lymph node metastasis (18). In contrast some other studies recorded that PR expression was significantly correlated with tumor size and stage and that it was correlated with venous invasion in females rather than males (19, 20, 21, 22). This study showed no significant correlation between these receptors expression and the studied parameters.

Conclusion

Estrogen and progesterone receptors in colorectal adenocarcinoma had same activity. The level of ER and PR expression in tumor tissue could not predict malignant biological behavior of the colorectal adenocarcinoma. No significant statistical correlation was observed between ER, PR expression and any of the studied clincopathological parameters.

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