Peripheral Blood CD3,CD4,CD8 & CD19 Lymphocytes Percentage in Patients with Colorectal Cancer

*** Batool H Al-Ghurabi**

Abstract:

Background and Aims:

Solid tumor is frequently accompanied by a depressed cellular and humoral immunity. This study analyzed changes of some these factors in colorectal cancer patients.

Methods:

Preoperative immune function was assessed by measuring the lymphocyte percentage, the CD3, the CD4, the CD8, the CD4/CD8 ratio, the CD19 in (40) patients with colorectal cancer compared to (35) healthy controls.

Results:

Lymphocytes where were in the normal range in patients and controls. However, tumor patients showed non-significant lymphopenia in comparison to controls.

There were no significant differences in CD3 T-cells and CD19 B-cells between patients and controls. Whereas there were significant decrease in CD4 T-cells and CD4/CD8 ratio ($P<0.001$), on the other hand CD8 T-cells was significantly increase ($P<0.001$).

Conclusion:

These finding suggest that colorectal tumor establishment and progression results in a malfunction of the immune system, and underline the importance of elucidating in details the mechanisms of immune modulation in cancer patients.

Keywords:

Colorectal cancer, Immune suppression.

Introduction:

The interactions between host immune system and malignant tumors are very complex, and it has been reported that malignant diseases are associated with decrease immune competence. Furthermore, changes in the immune system have also been demonstrated to influence the prognosis of the patients (1).

Lymphocytopenia in patients with neoplastic diseases has been associated with poor prognosis (2). Decrease in peripheral lymphocyte counts in patients with breast cancer had been previously attributed to the effects of radiotherapy on T-cells, similarly, lymphocytopenia primarily found in advanced carcinomatosis, had been attributed to the lymphocytotoxic effects of chemotherapy and/or radiotherapy (1).

Recently, evidence has been presented indicating that decrease in lymphocyte counts in patients with colon and breast cancer are independent of treatment and that there is an inverse correlation between tumor stage and levels of pretreatment peripheral lymphocyte counts (3&4).

Patients with malignant diseases and additional immune suppression **may** have an increase risk for the develop**ment** of postoperative complications, particularly infections. Therefore, adequate preoperative monitoring of essential immune parameters might identify patients with suppressed immune function and help to select patients with a high risk of postoperative complications. Furthermore, immune-modulating therapeutic strategies might lead to an improvement in the prognosis of these patients.

Patients and Methods:

Patients:

The present study included 40 Iraqi colorectal cancer (CRC) patients (18 females and 22 males; mean age 51 years, ranged between 21-81), they were attending the Gastroenterology and hepatology teaching hospital. Pathological stages are presented in table-1, compared with 35 healthy ages and sexes were matched control group.

Methods:

Direct Immunofluorescence Assay (DIF) Leuk--ocyte surfac molecules (CD-antigens) were

* H, PhD, Immunology, College of Dentistry/ University of Baghdad.

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identified by DIF technique using specific fluorescein labeled monoclonal antibodies including mouse anti-human (CD3, CD4, CD8) T-cells and CD19 B-cell.

The criterion for immunofluorescence was the presence of numerous fluorescent spots arranged over the surface of the cell, fluorescent caps were also seen (5).

Statistical analysis:

It was assessed using paired (T-test), for exploration of the statistical significance of difference in mean between two groups.

Table-1: Stage classification (Duke's A-D) of tumor.

Stage	NO	Female	male
Duke's A	3	2	1
Duke's B	18	10	8
Duke's C	14	5	9
Duke's D	5	1	4
NO	40	18	22

Results:

Peripheral lymphocyte counts were evaluated in 40 patients with CRC compared with 35 healthy control group,age and sex were matched. There was a slight, but not significant decrease in the percentage of lymphocyte in CRC patients [2021.7±960.66] as compared to control group [2289.8±879.12], table-2.

Table (3) pointed out to non significant differences in the means of CD3 T-cell and CD19 B-cells between CRC patients [60±11.3 & 18.3±1.85 respectively]and healthy control [68.6±12.5 & 17.6±1.79 respectively]. While the mean peripheral blood of CD4 showed significant decrease in CRC patients [19.9±4.1] in comparison with healthy subjects [40.9±4.1]. On the other hand the mean of CD8 revealed significant increase among patients with CRC [34.7±4.2] when compared with control group [20.0±1.9], $P<0.001$.

Regarding the mean of CD4/CD8 ratio in patients and controls, the present study showed significant decrease in CD4/CD8 ratio among CRC patients when compared to healthy control ($P<0.001$).

Table-2: The differences in mean percentage of lymphocytes count (cell/cu.mm) between the patients with CRC and healthy group.

	Colorectal cancer cases	Healthy control	P (T-test)
Lymphocyte count			
Minimum	230	980	
Maximum	5100	5772	
Mean	2021.7	2289.8	NS
SD	960.66	879.12	
NO.	40	35	

Table-3: The differences in mean of CD3, CD4, CD8 &CD19 (ceel/cu.mm) between patients with CRC and healthy group.

	Colorectal cancer cases	Healthy control	P (T-test)
CD3 T-cell			
Minimum	57	59	
Maximum	65	72	
Mean	61.2	68.6	NS
SD	11.3	12.5	
NO.	40	35	
CD4 T-cell			
Minimum	14	38	
Maximum	28	47	
Mean	19.9	40.9	P<0.001
SD	4.1	4.1	
NO.	40	35	
CD8 T-cell			
Minimum	30	18	
Maximum	45	23	
Mean	34.7	20.0	P<0.001
SD	4.2	1.9	
NO.	40	35	
CD19 B-cell			
Minimum	15	12	
Maximum	22	19	
Mean	18.3	17.6	NS
SD	1.85	1.79	
NO.	40	35	

Table-4: Comparing the CD4/ CD8 ratio in the two study groups.

Study Groups	CD4 Mean	CD8 Mean	CD4 / CD8 Ratio	P (T-test)
Colorectal cancer (40)	19.9	34.7	0.5	P<0.001
Healthy control (35)	4.09	20.0	2.0	

Discussion:

The measurement of T and B-cells lymphocyte subpopulations has been reported to be useful indicators of immune modulation reflecting the stage of malignant colorectal disease.

The present study found that patients with colorectal cancer have a slight, but not significant decrease in the percentage of lymphocytes compared to healthy control. This finding corresponds to that of other reports (6&7).

In agreement with previous studies (6,7&8), the present data demonstrate the presence of an immune dysfunction in patients with CRC manifesting by non significant decrease in CD3T-cells, significant decrease in CD4 T-cells and CD4/CD8 ratio, significant increase in CD8 T-cells, as well as no differences in CD19 B-cells.

Melichar and co-workers pointed out to the significant reduction in CD3, CD4, and CD4/CD8 ratio in CRC than in healthy control (9). However, it was noticed in addition to the above finding that the median number of CD4 T-cells in CRC patients with recurrences were significantly lower in comparison to patients without recurrences and healthy control, they concluded that that the reduction in CD4 T-cells occurs before detectable recurrence in CRC and therefore might be an important parameter in the early detection of tumor recurrence in CRC.

These result support hypothesis that tumor growth may cause the destruction of T-cells by a variety of different mechanisms including Fas-counterattack or activation-induced cell death(7). Similarly to human immunodeficiency virus (HIV) infection, systemic immune activation may be associated with activation-induced death of peripheral blood lymphocytes leading to CD4 T-cells lymphocytopenia (8).

Fuchs and colleagues (9) demonstrated that, similarly to patients with HIV infections, an inverse relation exists in cancer patients between peripheral blood CD4 T-cell counts and urinary concentrations of neopterin, which is a marker of systemic immune activation. On the other hand Wachter et al., (10), illustrated that the control of tumor growth by chemotherapy may also inhibit the direct or indirect destruction of T-cells. However, some T-cells may be destroyed by chemotherapy and this effect may be more visible in patients with normal CD4 T-cell number. It is likely that in patients with normal initial CD4 T-cell counts little or no tumor-induced T-cell destruction is taking place, therefore the reduction of T-cell number by chemotherapy may prevail.

In conclusion these finding suggest that colorectal tumor establishment and progression result in a malfunction of the immune system, and underline the importance of elucidating in detail the mechanisms of immune modulation in cancer patients.

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