Immune response in patient with Colorectal cancer

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ABSTRACT

Purpose: The immune response within colorectal cancer is widely studied and evaluated. The presence of lymphocytic infiltration in the main mass of the tumor and its front indicates a different clinical course of the disease. The aim of the study was to presence of CD3+ T lymphocyte infiltration in the tumor and its front in correlation with clinicopathological parameters.

Materials and Methods: The study included a group of patients operated on due to colorectal cancer. The histopathological results of the patients were analyzed, including the assessment of the expression of CD3 lymphocytes in the main mass of the tumor and its front, and an analysis of correlation with the patient's age, sex, histological malignancy stage, presence of metastases to lymph nodes and distant metastases was performed.

Results: We found the correlation between the differential infiltration from CD3+ T lymphocytes in the front of the invasion and the depth of tumor infiltration (p=0.008). But we do not found the correlation between the expression of CD3 in the main tumor mass and expression CD3 of the invasion front and patient's age, sex, tumor location, histological type of the tumor, histological grade, the presence of metastases to lymph nodes and the presence of distant metastases.

Conclusions: The obtained results suggest a relationship between the intensity of the CD3+ T lymphocyte infiltration in the front and the depth of the colorectal cancer infiltration.

Keywords: CD3, Lymphocytic infiltration, Colorectal cancer

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INTRODUCTION

Colorectal cancer (CRC) is one of the most common cancers in the modern world [1] - currently it is the third cause of cancer-related deaths after lung and prostate cancer in men and the second after breast cancer in women [2,3]. The prognostic parameters of CRC include the depth of tissue infiltration and the presence of lymph node metastases [4,5]. Within the tumor, the immune response is activated, which is associated with the appearance of, among others, T lymphocytes within the tumor [5,6]. T lymphocytes are essential for the development of inflammation, the process of carcinogenesis and its progression, and at the same time also for the stimulation of anti-cancer immunity [6]. CD3+ T cells are characterized by the presence of the CD3 surface marker. CD3+ lymphocytes are often aggregated into complex cell clusters [7]. The presence of CD3+, CD8+ and CD45RO+ T cell infiltration has been implicated in the antitumor immune response and has been shown to have prognostic value [6,7]. Therefore, the aim of our study was to analyze the assessment of the presence of CD3 lymphocytes in colorectal cancer in correlation with selected anatomically parameters.

MATERIALS AND METHODS

The study group consisted of 62 patients operated on due to CRC in the 2nd Department of General and Gastroenterological Surgery of the University Clinical Hospital in Bialystok. The research on which this paper focuses was based on the analysis of histopathological results carried out in patients, together with the immunohistochemical assessment of CD3+ T lymphocyte expression in histopathological preparations used in routine diagnostics. Consent of the Bioethics Committee (No. R-I-002/130/2018) to conduct this research.

Immunohistochemistry of T CD3 + lymphocyte

The following antibodies were used for immunohistochemical staining of CD3+ T cells: 2GV6 anti-CD3 using an automated technique according to the XT ultraView DAB v3 procedure. Diaminobenzidine (DAB) was used as the chromogen. The assessment was made by diagnosing pathologists using an Olympus CX41 light microscope at 400x magnification. The results of the counts were summed up and compiled for evaluation in the form of the true value of the number of lymphocytes in the inflammatory neoplastic infiltration in 5 fields of view. The results were statistically analyzed using Statistica 13.3 PL (StatSoft Polska). The age and sex of the patients, the location of the neoplastic lesion and its histological type, the degree of histological malignancy, the depth of tissue infiltration, as well as the presence of metastases to lymph nodes and metastases to distant organs were correlated. The significance level of $p < 0.05$ was considered statistically significant.

RESULTS

Characteristics of the study group: The group of selected patients consisted of 62 patients. Of which 17 < 60 yrs, 45 >60 yrs. In 24 cases they were women, in 38 men. The location of the primary tumor in 38 was the sigmoid colon and in 24 the rectum. In 54 cases, the tumors had no mucinous component and in 8 cases a mucinous component was observed. Low grade tumors were 60 patients, High Grade tumors were 2 patients. Stage pT1- was 1 patient, pT2- 1 patient, pT3-55 patients, pT4-5 patients. Lymph node metastases pN0-35 patients, pN1-27 patients. Distant metastases were found in 13 patients.

The analyzed data in individual groups presented the following results.

The tumor CD3+ T cell infiltration was not statistically significant in relation to the age of the patients. Statistical significance of CD3+ T lymphocyte infiltration in the tumor was demonstrated in relation to the sex of the patients ($p = 0.048$). The CD3+ T lymphocyte infiltration in the tumor invasion front was not statistically significant in relation to the sex of the patients. CD3+ T lymphocyte infiltration in the tumor was not statistically significant in relation to tumor location. The infiltration of TCD3+ lymphocytes in the invasion front was not statistically significant in relation to the location of the tumor. Statistical significance of TCD3+ lymphocyte infiltration in the tumor in relation to the histological type of the tumor was not demonstrated. There was no statistical significance for the correlation of differentiation of TCD3+ infiltration in the invasion front in relation to the histological type of the tumor. There was no statistical significance for the correlation between the differentiation of TCD3+ infiltration in the tumor and the histological malignancy of the tumor. There was no statistical significance between the infiltration of CD3+ T lymphocytes in the invasion front and the histological grade of the tumor. CD3+ T lymphocyte infiltration in the tumor with the depth of tumor invasion was not statistically significant.

Statistical significance of TCD3+ infiltration in the invasion front was demonstrated in relation to the depth of tumor infiltration ($p = 0.008$). There was no statistical significance between CD3+ T lymphocyte infiltration in the tumor and metastases to lymph nodes and distant metastases.

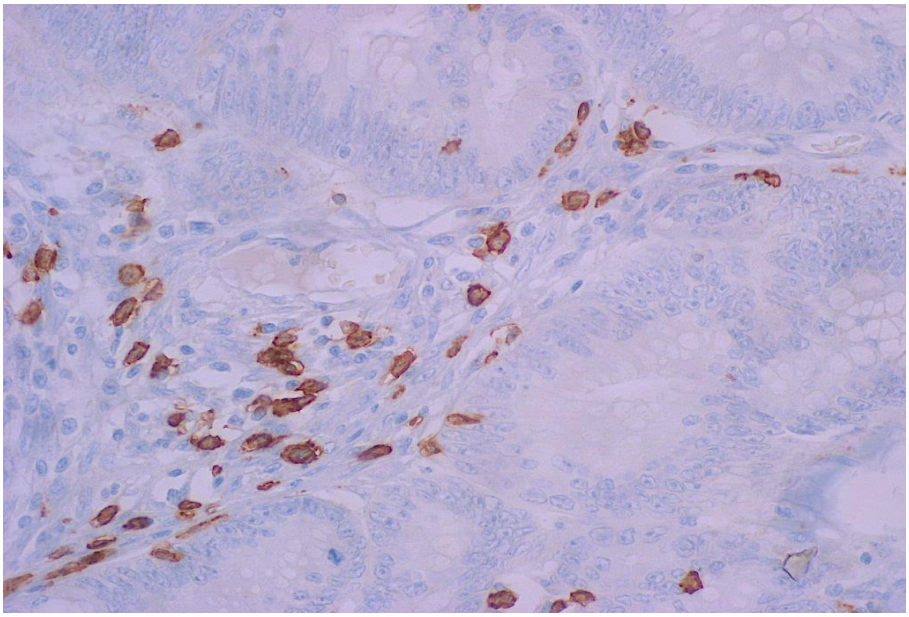

Figure 1 Expression of lymphocyte T CD3 + (400x)

DISCUSSION

The development of a malignant tumor is a multi-stage process. The response of the immune system plays an important role in it. These mechanisms affect the structure and development of the tumor microenvironment, composition and population of inflammatory cells [4,5]. Inflammatory infiltration has been shown to influence the formation and progression of colon cancer, particularly when T-cell-associated, and may vary between different types of cancer and among individual patients [5].

It should be emphasized that the front of the invasion is a key defensive area against cancer metastases. This is important in the appearance of metastatic foci in blood vessels as well as perineural infiltrates [6,7]. Perez et al. found a correlation between the degree of lymphocytic infiltration in rectal cancer and the presence of vascular occlusions as well as invasion into the lymphatic system. The number and activity of lymphocytes infiltrating the stromal layer in the invasive tumor front have been shown to be related to the ability to recognize tumor-specific antigens [7,8]. Also, Galon et al., examining the type, density and location (tumor / invasion front) of lymphocytic infiltration, including CD3+ and CD8+ T cells, showed a relationship between the presence of these T cells and recurrence and survival of patients [9]. Some scientists prove that the dense infiltration of CD3+ and CD8+ T lymphocytes observed in the biopsy material correlated with the reduction of tumor size after preoperative chemotherapy [8]. In 2013, a study was published showing a link between the abundance of CD3+ and CD8+ T cell infiltration, which strongly suggests that the number of CD3+ T cells in the front as well as in the invasive center gives a favorable prognosis for the patient [8]. Our studies concerning only the analysis of histopathological diagnoses indicate the usefulness of assessing the presence of CD3+ T lymphocyte expression in histopathological diagnostics in correlation with the stage of advancement.

CONCLUSION

The immune response within the tumor seems to be increasingly crucial and associated with new potential treatment options for patients with CRC. Retrospective analysis of diagnoses allows to discover significant correlations for possible prospective analyses.

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