Analysis of the PD-L1 Expression and Relevant Clinical Factors in Advanced Colorectal Cancer

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Abstract: This study aims to investigate the relation among PD-L1 expression and clinical, pathological and labo\expression, therapeutic effect and OS after chemotherapy with first-line chemotherapy. To reach that goal, 96 patients with advanced colorectal cancer were collected and analyzed retrospectively during the period from January 2016 to December 2016.

Keywords: PD-L1; Pathological; Cancer

1. Introduction

Colorectal cancer is a common , the rates of new colorectal cancer is the 4th highest among all diseases. The majority of the patients (normally at the age of 55-65) with colorectal cancer have missed the best chance of operation when they were diagnosed. At present, the majority of the patients with colorectal cancer were treated with chemotherapy, which is defective in the high risk of drug-resistance. Recently, the immunotherapy is getting more attention due to its advantages. By means of immunotherapy, the PD-L1 expression can be testified and helps with targeted therapy. However, there are limited studies about colorectal cancer to focus on the PD-L1 expression and its influence on cancer treatment. That is why the PD-L1 expression and relevant clinical factors in colorectal cancer was chosen as the major concern in this study.

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2. Materials and Methods

This study is a retrospective study to collect the data about 96 hospitalized patients of advanced colorectal cancer Yunnan Cancer Hospital from January to December, 2016. There was a follow-up in December, 2020. The following standards were observed in the selection of research subjects.

1 diagnosing criteria: histopathological analysis to show obvious symptom of colorectal cancer.

2 staging criteria: the patients' pathology reports and CT's were examined to stage their cancer in accordance with the eighth TNM staging plan.

3 sampling criteria: the research subjects should be the colorectal cancer patients whose samples were obtained in colonoscopy and whose chemotherapy has lasted for at least four cycles in accordance with the FOLFIRI or FOLFOX plans. If the samples are metastatic tissues, there should be other pathology reports to diagnose colorectal cancer such as CT, MRI and PET-CT. There should be no infection and other general systemic diseases observed in the patients, who should be diagnosed as colorectal cancer for the first time.

The major methods adopted in this experiment is the detection of PD-L1 in the samples obtained by the pathology department of the NO. 3 Affiliated Hospital of Kunming Medical University. The pathological sections consistent with the sampling criteria were chosen to be processed with IHC staining to testify the PD-L1 expression. The PD-L1 expression is testified to examine the treatment of colorectal cancer at the Stage I in accordance with the FOLFIRI or FOLFOX plans. All the research subjects have gone through four cycles of chemotherapy.

After the statistics about the PD-L1 expression and other data about the colorectal cancer patients were analyzed by means of statistical treatment and the tool employed in such statistical treatment is SPSS 25.0 and the statistical chard is drawn by means of GraphPad Prism 8.0. When the qualified materials appear to be normal distribution, the continuous variable of the normal distribution should be presented as the mean ± standard deviation. Besides, those statistics were analyzed by means of T Test of independent samples. In case of skewed distribution of qualified materials, rank sum test was employed to testify the two samples. The count data was testified by means of chi-square test. Kaplan-Meier Method was employed to

generate the survival curve. The difference is of statistical significance when P<0.05.

3. Result Analysis

The detection of PD-L1 in the samples of colorectal cancer patients was shown in the following table.

Table 1. PD-L1 Expression

PD-L1 Expression	Expression	Frequency (n)	Percentage
	Positive	25	26.0%
	Negative	71	74.0%

The positive expression of PD-L1in cancer cell of 5% is shown in the following figure

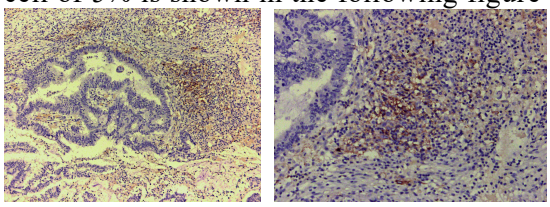

Figure 1. Positive Expression of PD-L1 in cancer cell (X100/X400)

In accordance with the PD-L1 Evaluation Standards in IHC, the 96 patients of colorectal cancers were divided into PD-L1 Positive Group and PD-L1 Negative Group in accordance with their PD-L1 expression. The statistics about the two groups were analyzed from the following perspectives.

3.1 Tumor Location

The left and right coletomy are both taken into the consideration in this study. The χ 2test shows that there are 15 samples (60%) of colorectal cancer in the right coletomy in the PD-L1Positive Group, 8 samples (32%) of colorectal cancer in the left coletomy and 2(8%) colorectal cancer in the rectum. In the PD-L1 Negative Group, there are 13 samples (18%) of colorectal cancer in the right coletomy, 26 samples (36%) of colorectal cancer in the left coletomy and 32(45%) colorectal cancer in the rectum. The χ 2test shows that there are differences in the tomor location ($\chi 2=18.304$, $P < 0.001$) and more colorectal cancer is detected in the right coletomy in the PD-L1 Positive Group.

3.2 Tumor Diameter

The tumor diameter in the preliminary diagnosis was analyzed in this study. In the PD-L1 Negative Group, their tumor diameter is within the scope of 5.30-12.88c, the median diameter is 9.09cm; In the PD-L1 Positive Group, their tumor diameter is within the scope of 3.10-5.12cm, the median diameter is 9.09cm. The rank sum test of the two samples shows that there are differences between the tumor diameter in the PD--L1 expression in tumor cells ($\chi 2=4.079$, $P < 0.001$), whicih means that the tumor diameter is lower in the PD-L1 Positive Group.

3.3 T Staging (Invasive Depth)

The statistics about the patients at T Stage (invasive depth) is analyzed as follows. In the PD-L1 Negative group, there are 10 samples at T2 Stage (14%), 35 samples at T3 Stage (49%), 26 samples at T4 Stage (36%). In the PD-L1 Positive group, there are 2 samples at T2 Stage (8%), 6 samples at T3 Stage (24%), and 17 samples at T4 Stage (68%). It is obvious that the percentage of samples at T4 Stage accounts for 68% in the PD-L1 Positive Group, which is of statistic significance ($\chi 2=7.383$, $P=0.025$). It is proved that the invasive depth of the tumor is higher in the PD-L1 Positive Group.

3.4 M Staging (Distant Metastases)

The statistic about the samples at M Stage (distant metastases) is analyzed as follows. In the PD-L1 Positive Group, there are 25 samples at the stage of M1a (40%), 7 samples at the stage of M1b 7 (28%), 8 samples at the stage of M1c (32%). the percentage of the samples at the stage of M1a is the highest. In the PD-L1 Negative Group, there are 33 samples at the stage of M1a (46%), 31 samples at the stage of M1b 7 (43%), 7 samples at the stage of M1c (9.8%). The differences between the two groups are of statistical significance ($\chi 2=7.120$, $P<0.05$). The patients in the PD-L1 Positive Group show more tendency for metastatic toward one or more organs.

3.5 Comparison Between Tumor Markers in the Two Groups

The t test of the independent samples shows that the CEA scope of the PD-L1 Negative Group is 167.90-723.60 10ng/ml and the median is 267.10. The CEA scope of the PD-L1Positive Group is 90.30-340.10ng/ml and the median is 345.60ng/ml. The CEA scope in the PD-L1 Positive Group is higher than the PD-L1 Negative Group, and the difference is of statistical significance ($P < 0.05$). The CA199

scope of PD-L1 Negative Group is 17.80-134.80U/mL and the median is 78.00U/mL. The CA199 scope of PD-L1 Positive Group is 34.50-335.60U/mL and the median is 125.00U/mL. The CEA and CA199 scope in the PD-L1 Positive Group is obviously higher than the scope in the PD-L1 Negative Group and the difference is of great statistical significance ($P < 0.05$). It is proved that the tumor markers increases rapidly and the tumor load is higher in case of positive PD-L1. There is no obvious differences between the tumor marks between the two groups ($P > 0.05$).

4. PD-L1 Expression and Chemotherapy Effect Analysis

The effect of the cancer chemotherapy of the 96 patients investigated in this study were evaluated in accordance with the RECIST1.1. The effect is evaluated by means of examining the target lesion. In accordance with the result of CT, MRI and other inspections, the patients were divided into PD Group, SD Group and PR Group, whose disease control rate was calculated in accordance with the formula of SD+PR+CR. Besides, since the samples analyzed in this study were all CR patients of advanced colorectal cancers, the disease control rate is calculated in accordance with the formula of SD+PR.

The $\chi 2$ test shows that the disease control rate (SD+PR) of the PD-L1 Negative Group is 91.5%. The disease control rate (SD+PR) of the PD-L1 Positive Group is 60%. The difference between the two groups is of great statistical significance ($\chi 2=13.251$ $P < 0.05$). It is proved that the disease control rate after chemotherapy of the PD-L1 Positive Group is lower than the rate of the PD-L1 Negative Group. It is obvious that the patients with positive expression of PD-L1 was under less positive influence of the chemotherapy.

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