Analysis of the levels of *in vivo* immunological indicators in patients with different types of malignanat lymphoma

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ABSTRACT

Objective: To analyze the levels of in vivo immunological indicators in patients with different types of malignanat lymphoma. **Methods:** A total of 69 patients with different types of malignanat lymphoma who were admitted in our hospital were included in the study, among which 31 had primary extranodular malignant lymphoma (extranodular group), and 38 had primary nodular malignant lymphoma (nodular group). Moreover, 34 patients with pure lymphnoditis were served as the control group. FCM and full-automatic speed scattering turbidimetry were used to detect T lymphocyte subsets proportion, IgG, IgA, IgM, C3, and C4 in the three groups. **Results:** The comparison of $CD3^+$, $CD4^+$, $CD8^+$, NK cell proportion, and $CD4^+/CD8^+$ among the three groups was significantly different. When compared with the control group, $CD3^+$, $CD4^+$, $CD8^+$, NK cell proportion, and $CD4^+/CD8^+$ in the extranodular group and nodular group were significantly reduced; moreover, $CD3^+$, $CD4^+$, $CD8^+$, and $CD4^+/CD8^+$ in the extranodular group were significantly lower than those in the nodular group, while NK cell in the extranodular group was significantly higher than that in the nodular group. The comparison of IgG, IgA, and C3 levels among the three groups was statistically significant. When compared with the control group, IgG and IgA levels in the extranodular group and nodular group were significantly elevated, while C3 level was significantly reduced, and the comparison between the extranodular group and nodular group between the two groups was statistically significant. IgM level in the extranodular group and nodular group was elevated, C4 level was reduced, but the comparison with the control group was not statistically significant. Spearman correlation analysis showed that $CD3^+$ and $CD4^+$ were significantly correlated with IgA, IgG, and C3. **Conclusions:** With the increasing of severity degree of lymphoma, the immunological level is reduced, while $CD3^+$ and $CD4^+$ are significantly correlated with IgA, IgG, and C3, indicating that detection of $CD3^+$ and $CD4^+$ proportion or IgA, IgG, and C3 contents in combined with pathological characteristics can evaluate the severity degree of malignant lymphoma in order to provide guidance for the clinical diagnosis and treatment.

1. Introduction

Malignant lymphoma is a kind of nodular or extranodular tumor caused by lymphocyte or lymphatic tissue canceration, and is one of the most common malignant tumors in the clinic, with manifestations of abnormal immunological function[1]. The cellular immunity, humoral immunity, and complement system can monitor the immunological function, play an important role in preventing the occurrence of tumor and the invasion of infection, and are the important immune defense system[2]. The study is aimed to analyze the levels of immunological indicators in patients with different types of malignant lymphoma in order to provide the immunological indicators for the disease progression.

2. Materials and methods

2.1. General materials

A total of 69 patients with different types of malignant lymphoma confirmed by the pathological examination who were admitted in

Table 1.

Comparison of T lymphocyte subets proportion and NK cell distribution among the three groups.

Groups	CD3$^+$	CD4$^+$	CD8$^+$	CD4$^+$/CD8$^+$	NK
Extranodular group (n=31)	30.75±4.65[**]	11.56±2.88[**]	12.34±1.97[**]	0.79±0.40[*]	18.39±2.74[**]
Nodular group (n=38)	40.62±5.17	20.64±3.47	19.71±2.36	1.02±0.51	7.58±1.32
Control group (n=34)	69.83±7.21	41.37±4.82	28.38±2.72	1.46±0.93	26.37±2.81
F	17.241	16.821	14.375	7.896	15.952
P	0.000	0.000	0.000	0.025	0.000[a]

[*]P<0.05, [**]P<0.01, when compared with the nodular group.

Table 2.

Comparison of Ig and complement levels among the three groups.

Groups	IgG	IgA	IgM	C3	C4
Extranodular group (n=31)	20.72±3.57[*]	5.25±1.09[*]	3.39±1.42	0.64±0.48[*]	0.88±0.71
Nodular group (n=38)	18.68±2.96	4.61±1.12	3.11±1.36	0.98±0.67	1.08±0.58
Control group (n=34)	16.98±2.59	3.95±1.08	2.87±1.25	1.49±1.01	1.25±0.67
F	9.751	8.963	6.427	10.752	5.438
P	0.022	0.024	0.161	0.018	0.275

[*]P<0.05, when compared with the nodular group.

our hospital from June, 2014 to November, 2016 were included in the study, among which 31 had primary extranodular malignant lymphoma (extranodular group), 16 were male, and 15 were female; aged from 23 to 65 years old, with an average age of (39.8±1.5) years old; primary sites: 2 in the skin, 2 in the nasopharynx, 17 in the gastrointestinal tract, and 10 in the breast; pathological types: 25 had diffuse large B cell lymphoma, and 6 had T cell lymphoma; 38 had primary nodular lymphoma (nodular group), 20 were male, and 18 were female; aged from 24 to 66 years old, with an average age of (41.2±1.7) years old. Moreover, 34 patients with pure lymphnoditis were served as the control group, among which 21 were male, and 13 were female; aged from 23 to 67 years old, with an average age of (40.5±1.9) years old. The comparison of the general materials among the three groups was not statistically significant (P>0.05), but it was comparable.

2.2. Methods

A volume of 6 mL fasting venous blood in the three groups was collected, among which 2 mL was used to detect the peripheral blood CD3$^+$, CD4$^+$, CD8$^+$, and NK cell proportion by FCM after anticoagulation processing. CD4$^+$/CD8$^+$ was calculated. Moreover, 4 mL venous blood was used for centrifugation to obtain the serum. The full-automatic speed scattering turbidimetry was used to detect the serum IgG, IgA, IgM, C3, and C4.

2.3. Statistical analysis

SPSS 18.0 software was used for the statistical analysis. The measurement data were expressed as mean ± SD, and t test was used. ANOVA was used for the comparison among groups. P<0.05 was regarded as statistically significant. Spearman correlation analysis was used to analyze the correlation of different types of malignant tumors with immunological indicators.

3. Results

3.1. Comparison of T lymphocyte subets proportion and NK cell distribution among the three groups

The comparison of CD3$^+$, CD4$^+$, CD8$^+$, NK cell proportion, and CD4+/CD8+ among the three groups was significantly different (P<0.05 or P<0.01). When compared with the control group, CD3$^+$, CD4$^+$, CD8$^+$, NK cell proportion, and CD4$^+$/CD8$^+$ in the extranodular group and nodular group were significantly reduced (P<0.05 or P<0.01); moreover, CD3$^+$, CD4$^+$, CD8$^+$, and CD4$^+$/CD8$^+$ in the extranodular group were significantly lower than those in the nodular group (P<0.05 or P<0.01), while NK cell in the extranodular group was significantly higher than that in the nodular group (P<0.01).

3.2. Comparison of Ig and complement levels among the three groups

The comparison of IgG, IgA, and C3 levels among the three groups was statistically significant (P<0.05). When compared with the control group, IgG and IgA levels in the extranodular group and nodular group were significantly elevated, while C3 level was significantly reduced (P<0.05), and the comparison between the extranodular group and nodular group between the two groups was statistically significant (P<0.05). IgM level in the extranodular group and nodular group was elevated, C4 level was reduced, but the comparison with the control group was not statistically significant (P>0.05).

3.3. Correlation of T lymphocyte subsets with Ig and complements

Spearman correlation analysis showed that in the control group, T lymphocyte subsets had no correlation with Ig and complements

(P>0.05); CD3^{+}, CD4^{+}, CD8^{+} proportion in the extranodular group had significant correlation with CD3^{+}, CD4^{+}, NK, CD4^{+}/CD8^{+}, IgA, IgG, and C3 in the nodular group (P<0.01), i.e. The serum CD3^{+} and CD4^{+} proportions in patients with malignant lymphoma were significantly correlated with IgA, IgG, and C3 (P<0.01).

4. Discussion

The initial diagnostic criteria for primary extranodular lymphoma are listed in the following: (1) the primary site for lymphoma is the extranodular tissue and organ; (2) the pathological symptoms are manifestated in the extranodular tissue and organ; (3) after 6-month onset, lymphoma occurs in other sites[3]. This diagnostic criteria have promoted the deep study of scholars to the primary extranodular lymphoma. With the wide application of chemoradiotherapy, the inhibition of immunological function, and infections by herpes virus, HIV, linear double-stranded DNA virus, and HP cause the gradual elevation of the morbidity of primary extranodular lymphoma, among which the linear double-stranded DNA virus is the main pathogenic factor for developing extranodular B cell lymphoma[4,5]. With the improvement of diagnostic technology and continuous deep recognition on the primary extranodular lymphoma, it is argued by the new diagnostic criteria for primary extranodular lymphoma that those whose lesions are mainly in the extranodular tissue and organ, accompanied by mild lymph node lesions are diagnosed as primary extranodular lymphoma[6].

The lymph node is an important immune organ. When there are lesions in the lymph nodes or extranodular tissues and organs, the immunological function will also be abnormal[7]. Some researches demonstrate that[8,9] Peyer patch consists of CD4^{+}, CD8^{+}, antigen presenting cells, and various immunocompetent cells, which are involved in the antigen processing and presenting, and play an important role in the immune system of malignant lymphoma. T lymphocyte subsets and NK cell have an important role in the antitumor immunity. Detection of T lymphocyte subsets and NK cell proportion can evaluate the cellular immunity level[10]. The activated NK cell can directly kill the tumor cells. Among T lymphocyte subsets, CD8^{+} can regulate the activity of T lymphocyte and plays an anti-tumor effect, while CD4^{+}/CD8^{+} can reflect the immunoregulation ability[11]. When there are nodular or extranodular tissue lesions, T lymphocyte subsets and NK cell number will change, resulting in cellular immune dysfunction, and weakening the anti-tumor ability[12]. The results in the study showed that the comparison of CD3^{+}, CD4^{+}, CD8^{+}, NK cell proportion, and CD4^{+}/CD8^{+} among the three groups was significantly different (P<0.05 or P<0.01); when compared with the control group, CD3^{+}, CD4^{+}, CD8+, NK cell proportion, and CD4^{+}/CD8^{+} in the extranodular

group and nodular group were significantly reduced (P<0.05 or P<0.01); moreover, CD3^{+}, CD4^{+}, CD8^{+}, and CD4^{+}/CD8^{+} in the extranodular group were significantly lower than those in the nodular group (P<0.05 or P<0.01), while NK cell in the extranodular group was significantly higher than that in the nodular group (P<0.01), indicating that with the increasing of the severity degree of diseases, the cellular immune level is reduced.

Ig is a kind of globulin with antibody activity, while complement is a kind of seroglobulin with enzymatic activity, the contents of which are relatively stable, are involved the humoral immunity, and the contents will fluctuate only when suffering from some diseases[13,14]. Some researches demonstrate that[15,16] in most malignant tumor patients, the complement content will be reduced, while Ig content will be elevated. The results in the study showed that when compared with the control group, IgG and IgA levels in the extranodular group and nodular group were significantly elevated, while C3 level was significantly reduced (P<0.05), and the comparison between the extranodular group and nodular group between the two groups was statistically significant (P<0.05); IgM level in the extranodular group and nodular group was elevated, C4 level was reduced, but the comparison with the control group was not statistically significant (P>0.05), suggesting that with the increasing of the severity degree of diseases, the humoral immune level is reduced, probably in that the effect of T lymphocyte subsets proportion disorder in patients with lymphoma on B cell maturity and the involvement of complement bypass in the anti-tumor immunity increase the consumption of C, while C4 is not involved in the complement bypass system; therefore, C4 level is not significantly changed. Moreover, Spearman correlation analysis showed that CD3^{+} and CD4^{+} were significantly correlated with IgA, IgG, and C3, indicating that CD3^{+} and CD4^{+} proportion or IgA, IgG, and C3 contents can evaluate the severity degree of malignant lymphoma.

In conclusion, with the increasing of severity degree of lymphoma, the immunological level is reduced, while CD3^{+} and CD4^{+} are significantly correlated with IgA, IgG, and C3, indicating that detection of CD3^{+} and CD4^{+} proportion or IgA, IgG, and C3 contents in combined with pathological characteristics can evaluate the severity degree of malignant lymphoma in order to provide guidance for the clinical diagnosis and treatment.

References

[1] Lina C, Qingzhi S, Jianyuan H. Research progress of malignant lymphoma secondary tumor. *Chem Life* 2015; **35**(6): 773-777.

[2] Qian W, Wenhua X. Role of tumor-source exosome in the immunological system and tumor microenvironment and its clinical application prospect. *Acad J Pla Postgrad Med School* 2017; **6**(1): 71-74.

[3] Sammassimo S, Pruneri G, Andreola G. A retrospective international study on primary extranodal marginal zone lymphoma of the lung (BALT lymphoma) on behalf of international extranodal lymphoma study group (IELSG). *Hematological Oncol* 2015; **11**(1): 116-117.

[4] Xige Y, Xigui Y, Liang M. Clinical pathological analysis of 304 cases with primary extranodular lymphoma. *J Clin Hematol* 2016; **29**(11): 894-897.

[5] Xunwu Z. Ultrasonic diagnostic manifestation of extranodular lymphoma. *Chin J Med Device* 2016; **29**(24): 111-112.

[6] Weiping L, Wenyan Z, Sha Z. Concept and pathological diagnosis of extranodular lymphoma. *Med J West China* 2016; **28**(11): 1485-1488.

[7] Yuhui C, Zhifeng Z, Yanyun C. Correlation of CT and immunohistochemical characteristics of primary extranodal non-hodgkin"s lymphoma in otolaryngol head and neck. *China Modern Doc* 2016; **54**(3): 17-19.

[8] Kim SH, Jeung W, Choi ID. Lactic acid bacteria improves Peyer's patch cell-mediated immunoglobulin A and tight-junction expression in a destructed gut microbial environment. *J Microbiol Biotechnol* 2016; **26**(6): 1035-1045.

[9] Hao W, Ling L, Qinghua T. Biological roles of somatostatin in intestinal macaque Peyer's patch B cells. *Nat Med J China* 2015; **95**(8): 606-610.

[10] Meiling L. Detection of peripheral blood T lymphocyte subsetsin patients with B cell lymphoma and its correlation with Ki67. *Proceed Clin Med* 2015; **10**(11): 831-833.

[11] Yuzhu Z, Yanliang B, Yuqing C. Observation on the efficacy of IL-2 in combined with autologous CIK cell in the treatment of malignant lymphoma. *J Clin Med Pract* 2015; **19**(21): 13-16.

[12] Weichao L, Xiaomin N, Huiqing H. Effect of autologous peripheral blood hematopoietic stem cell transplantation on T lymphocyte subsets in patients with malignant lymphoma. *Med J Liaoning* 2015; **11**(1): 9-10.

[13] Hong J, Yuan T, Yanmei H. Correlation of immunoglobulin variable heavy chain gene mutation status with prognosis in patients with mantle cell lymphoma. *Chin J Pathol* 2015; **44**(2): 90-94.

[14] Hussien AE, Furth C, Schonberger S. FDG-PET response prediction in pediatric hodgkin's lymphoma: impact of metabolically defined tumor volumes and individualized suv measurements on the positive predictive value. *Cancers* 2015; **7**(1): 287.

[15] Zeng J, Liu R, Wang J. A bispecific antibody directly induces lymphoma cell death by simultaneously targeting CD20 and HLA-DR. *J Cancer Res Clin Oncol* 2015; **141**(11): 1899-1907.

[16] Wu X, Qi D, Shen X. The molecular pathology detection analysis of Ig/TCR gene rearrangement in malignant lymphoma diagnosis. *Guizhou Med J* 2016; **1**(9): 908-910.