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RAPID COMMUNICATION

Investigation on correlation between expression of CD58 molecule and severity of hepatitis B

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Abstract

AIM: To investigate the correlation between expression of CD58 and severity of hepatitis B.

METHODS: The level of soluble CD58 (sCD58) in serum of patients with hepatitis B was detected by enzyme-linked immunosorbent assay. The level of expression of membrane CD58 molecule in PBMC was detected by direct immunofluorescence. The levels of serumal TBIL, DBIL, IBIL, ALT and AST were detected by the automated biochemistry analyzer as well.

RESULTS: The levels of sCD58 in serum and membrane CD58 molecule in PBMC of patients with hepatitis B were significantly higher than that in normal controls ($P < 0.05$). Level of CD58 was related to the levels of serumal TBIL, DBIL, IBIL, ALT and AST.

CONCLUSION: The level of CD58 molecule (in both serum and PBMC form) of patients with hepatitis B is related to the degree of liver damage.

Key words: Hepatitis B; CD58; Liver damage

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INTRODUCTION

Hepatitis B is caused by Hepatitis B virus (HBV), but the pathogenesis of hepatitis B is not well understood. HBV infects human liver cells but has no direct cytopathic effect on these cells. Therefore, it is unlikely that direct viral cytotoxicity is the primary cause of pathology in vivo. Several studies have suggested that hepatitis B may be mediated in part by immunopathologic mechanisms. As one of the intercellular adhesion molecules, CD58 provided co-stimulatory signals for the activation of T lymphocyte, it plays an important role in promoting the adhesion of T cells to targeted cells[1-3]. In this study, we used double antibody sandwich ELISA and direct immunofluorescece to analyze the levels of sCD58 in serum and the expression of CD58 on the surface of PBMC of patients with hepatitis B, and compared with those levels of healthy controls to evaluate the role of CD58 in the pathogenesis of hepatitis B.

MATERIALS AND METHODS

Sample collection and processing

Forty-three patients with hepatitis B are selected from outpatients and inpatients of the Department of Infectious Diseases of First Hospital of Xi'an Jiaotong University and Second Hospital of Xi'an Jiaotong University. The patients were divided into four groups, namely mild chronic hepatitis B group ($n = 12$), moderate chronic hepatitis B group ($n = 11$), severe chronic hepatitis B group ($n = 10$) and severe hepatitis B group ($n = 10$). Eleven healthy persons were taken as normal control group. The diagnostic code for Hepatitis B which edited by 5th Chinese Academic committee of Infection Disease and Parasite in 2000 was used as the classification criteria.

Detection of the sCD58 in serum

The serum samples were diluted 1:50 with assay buffer (5 μL sample + 245 μL assay buffer), and then the levels of sCD58 in the diluted samples were detected by use of double antibody sandwich ELISA following the kit instructions (Australia Science Laboratory company). The standard wells were designated by the instruction as well. The OD value of each well of the samples and the sCD58 standards was read out on an EL311 autoplate reader (BIO-TEK Instruments, American) with a test wavelength of 450 nm and a reference wavelength of 620 nm; hence the optimal concentration of sCD58 could be determined. Blank wells were used as background control.

Detection of membrane CD58 in PBMC

One ml of PBMC sample was mixed with 10 μL of

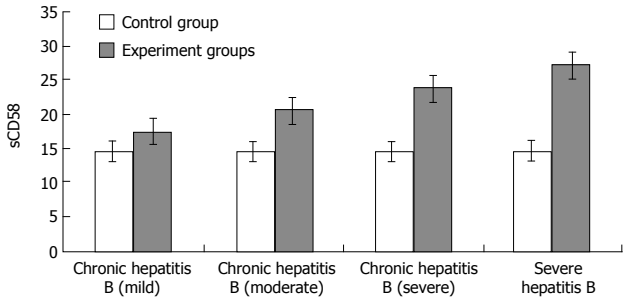

Figure 1 Content of CD58 in serum.

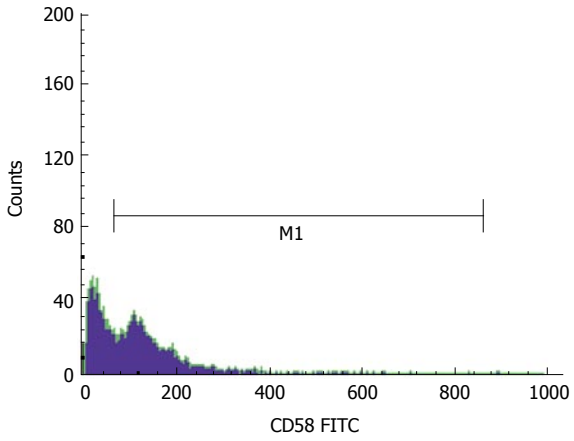

Figure 2 Content of membrane CD58 molecule in mild chronic hepatitis B.

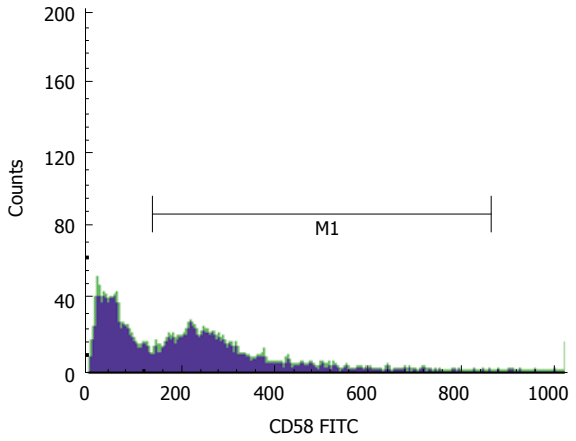

Figure 3 Content of membrane CD58 molecule in moderate chronic hepatitis B.

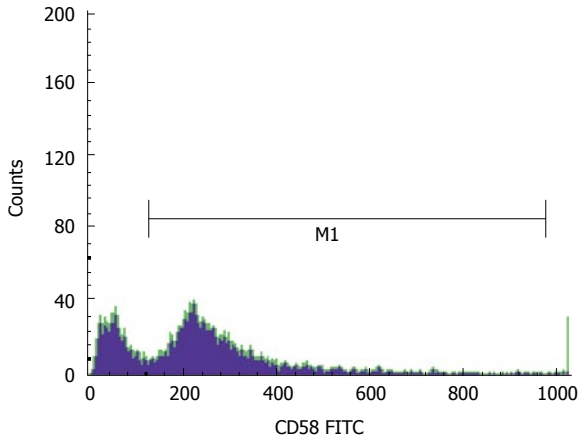

Figure 4 Content of membrane CD58 molecule in severe chronic hepatitis B.

mouse anti-human CD58 antibody marked by fluorescence FITC (American Southern Biotech), incubated in the dark at room temperature, washed twice with PBS, and centrifuged at 2500 r/min before abandoning supernatant. One ml of PBS-formaldehyde was added to fix cells, and CD58 positive cells were dectected by using FACS Calibur flow cytometer.

Detection of the liver function

One mL serum sample was used to test the levels of TBIL, DBIL, IBIL, ALT and AST by the CHEMIX-180 automated biochemistry analyzer (Japanese SYSMEX Corporation).

Statistical Analysis

The significance among different groups was examined by one-way analysis of variance followed by tow-sample Student's *t*-test. Differences between groups were considered significant if probability value of $P < 0.05$ were obtained. The data were presented by means ± SD.

RESULTS

Content of sCD58 in serum

The levels of sCD58 of patient with HBV infection were significantly higher than that of normal control ($P < 0.05$); and the difference among the groups were significant ($P < 0.05$) (Figure 1).

Content of membrane CD58 molecule

The results showed that the level of membrane CD58 molecule in PBMC of patients with HBV infection was significantly higher than that of the normal group and the differences among the groups were significant ($P < 0.05$). The levels of membrane CD58 molecule increased significantly in an order from light chronic hepatitis B, medium group, severe group and severe hepatitis B. The membrane CD58 molecule in PBMC might relate to the severity of the disease (Figures 2-5, Table 1).

DISCUSSION

CD58 is also called lymphocyte function associated antigen-3 (LFA-3)[4-6], which belongs to the CD2 family. As an important co-stimulating molecule, CD58 plays an important role in promoting the adhesion of T cells to targeted cells, and enhancing the recognition and sensitivity of T lymphocyte to the superantigen[7-9]. CD58 promotes hyperplasia and activation of T cell[1,2], promotes T cells soak inflammatory parts and takes part in signal transmission of T cells. Combined with CD2 molecules on the surface of NK cells, CD58 increases the adhesion between NK cells and target cells, activates NK cells[10,11], and increases the toxin of the cells[12,13]. After integrating

Table1 The liver function

Group	*n*	TBIL (μmol/L)	DBIL (μmol/L)	IBIL (μmol/L)	ALT (IU/L)	AST (IU/L)
Normal control	11	11.25 ± 2.14	3.12 ± 1.54	6.41 ± 1.85	25.19 ± 2.58	19.57 ± 3.06
Chronic hepatitis B (mild)	12	15.14 ± 3.26[a]	15.92 ± 2.05[a]	10.39 ± 2.63[a]	63.33 ± 3.68[a]	46.67 ± 9.81[a]
Chronic hepatitis B (moderate)	11	39.21 ± 8.73[a]	25.21 ± 7.11[a]	23.74 ± 3.87[a]	98.21 ± 18.90[a]	114.43 ± 12.80[a]
Chronic hepatitis B (severe)	10	105.33 ± 17.67[a]	49.88 ± 8.62[a]	50.86 ± 16.05[a]	221.61 ± 18.19[a]	157.01 ± 22.54[a]
Severe hepatitis B	10	143.57 ± 23.15[a]	75.26 ± 6.56[a]	117.35 ± 15.27[a]	116.73 ± 28.57	94.82 ± 41.49

[a]$P < 0.05$, compared with control group.

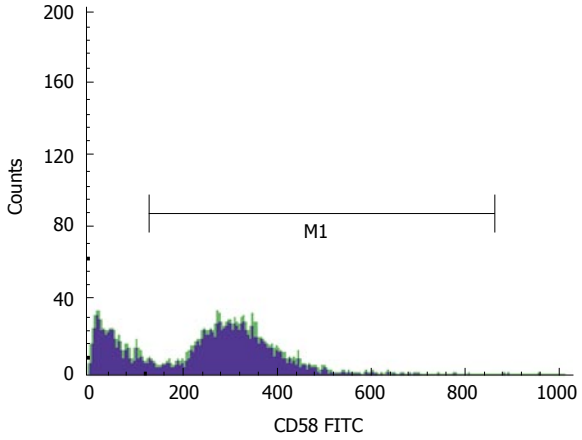

Figure 5 Content of membrane CD58 molecule in severe hepatitis B.

with activated T cells, CD58 and CD2 facilitate interferon γ and IL-2 mRNA record and translate, differentiate $CD4^+$T to Th1 and further initiate the immune response of the cell[3,14]. Some researchers proved that integrated with matching cells, CD58 may boost the ability of activated T cells and NK cells[15,16].

Our experiment showed that the levels of sCD58 in serum and membrane CD58 molecule in PBMC of patients with HBV infection were significantly higher than that of the normal group. The levels of CD58 varied from different groups of patients with hepatitis B, correlated to the severity of the disease. The results also showed that the percentage of $CD58^+$ cell of patients with hepatitis B might be related with TBIL, DBIL, IBIL, ALT and AST, which prove the expression of CD58 is closely correlated with the liver damage. According to the results of the research, the increased levels of sCD58 molecule in serum and membrane CD58 molecule in PBMC of patients with hepatitis B could enhance the adhesion of APC and T cells to identify antigen[17,18]. This study proved that the combination of CD58 and CD2 activated T cells was similar to the way of TCR/CD3. This might lead to a series of responses in the cells, including the increase of the concentration of $Ca2^+$, the activation of PKC, several limpid genes in the resting cells such as IL-2 and IFN-γ being recorded and the transformation of T cells from G0 stage to S stage. The T cells activated by integration of CD58 and CD2 would increase the record and translate of IL-2 and IFN-γ mRNA, and then differentiate into Th1 which would enhance the cell immune response. Combined with CD2 molecules on the surface of NK cells, CD58 could activate NK cells and increase the cytotoxic effect[19]. And this would contribute to the organisms to eliminate HBV. The cytotoxic effect of the immune cells might be implemented by releasing PF or inducing apoptosis of CD95 cells[20].

In summary, this study showed that the sCD58 in serum and membrane CD58 molecule in PBMC of the patients with hepatitis B is related to the severity of the disease and the liver damage. CD58 might enhance the elimination of viruses through activating T and NK cells and promoting cell immune response. However, this would also lead to the damage of liver cells.

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