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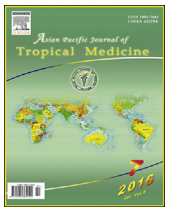

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Effect of partial splenic embolization on the immune function of cirrhosis patients with hypersplenism

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ABSTRACT

Objective: To discover the effect of partial splenic embolization on the immune function of cirrhotic patients with hypersplenism.

Methods: Patients involved in the study were enrolled and divided into three groups, including control group, experimental group, and complication group. Numbers of $CD3^+$, $CD4^+$ and $CD8^+$ T cells and $CD4^+CD25^+CDl27^{low/-}$ Treg cells in the peripheral blood of patients before surgery, 1 month, 6 months, 1 year, and 2 years after surgery were analyzed by fluorescence active cell sorting (FACS). Contents of immunoglobulins (IgA, IgG and IgM) were analyzed by auto immunoassay analyzer.

Results: In the peripheral blood of patients from experimental group, numbers of $CD3^+$, $CD4^+$ and $CD8^+$ T cells initially declined, but afterwards increased to normal level; in the peripheral blood of patients from complication group, $CD3^+$ and $CD8^+$ T cells showed the same trend, but the number of $CD4^+$ T cells was below normal level at all detection times. Furthermore, $CD3^+$, $CD4^+$ and $CD8^+$ T cells in the peripheral blood of patients from complication group were initially less than those in experimental group, and afterwards were comparable between two groups. In patients from both experimental group and complication group, the number of $CD4^+$ $CD25^+$ $CDl27^{low/-}$Treg cells increased 1 month and 6 months after surgery, and gradually restored to normal level. $CD4^+CD25^+CDl27^{low/-}$ Treg cell counts in patients from complication group were initially more than those in patients from experimental group 1 month and 6 months after surgery, but then they were comparable. Furthermore, contents of immunoglobulins (IgA, IgG and IgM) were comparable in three groups at all detection times.

Conclusion: Partial splenic embolization influenced the immune function of cirrhotic patients with hypersplenism in the short term but the immune function could afterwards gradually restore to normal. Our results implicated that measures that prevent infection and improve immune function were necessary in early stage after undergoing PSE in order to reduce complications.

1. Introduction

Chronic viral hepatitis B is a common disease in China, the morbidity of which is 8%–10%. Patients with hepatitis B usually develop hypersplenism in the period of liver cirrhosis decompensation. Hypersplenism is clinically characterized as decline of hemocytoes, such as white blood cells, red blood cells, and platelet, which can result in gastrointestinal bleeding, anemia, and infection. As the development of interventional techniques, partial splenic embolization (PSE) with advantages of smaller trauma and partial spleen-conserving has been widely applied in clinic to replace splenectomy.

PSE, however, has been proved to cause some complications, such as peritoneal cavity infection, intractable abdominal cavity effusion, intestine flatulence, splenic abscess, and also portal vein and mesenteric arterial thrombosis, which can even lead to death [1–3]. Additionally, the effect of PSE on the immune function of patients has been a hot topic of academic research. However, there is still no unified evaluation criterion of spleen

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swelling and immune function in patients with PSE, and the mechanism of which has not been fully elucidated.

Here, to uncover the relevance between PSE, postoperative complications and immune function, $CD3^+$, $CD4^+$ and $CD8^+$ T cells, $CD4^+CD25^+CDl27^{low/-}$ Treg cells (regulatory T cell, Treg), and contents of immunoglobulins (including IgA, IgG and IgM) in the peripheral blood of cirrhotic patients with hypersplenism were analyzed.

2. Materials and methods

2.1. Patients

The study was approved by the Ethics Committee of the authors' affiliation prior to initiation. Patients have been informed and signed the informed consent before blood drawing. Patients involved in this study were enrolled and divided into three groups: control group (healthy population), experimental group (patients without complications after PSE), and complication group (patients with complications after PSE). Symptoms of hepatitis B cirrhotic and hypersplenism were diagnosed according to clinic history, virus immunology examination, liver tests, peripheral hemogram test, and imageological examination. A total of 50 persons, including 33 males and 17 females, who were physically healthy, were enrolled as the control group (age range: 45–68 years, mean age: 56.2 years). The experimental group was consists of 57 cases, including 38 males and 19 females (age range: 41–64 years, mean age: 52.6 years). The complication group had 51 cases, including 37 males and 14 females (age range: 50–68 years, mean age: 57.3 years).

2.2. Partial splenic embolization

Partial splenic embolization (PSE) was operated as follows. The participants were asked to fast for 12 h and not to drink for 6 h before undergoing the surgery. Seldinger puncture, combined with digital subtracting X-ray system, were applied to right arteriopuncture to reach carotid sheath. Catheter (Yashiro) was guided by guide wire to spleen artery to monitor splenomegalia. We also measured the size of spleen during operation. Area of embolism was subsequently calculated according to projected area and preoperative hemogram indexes. The area of embolism was accounted for about 1/3 to 1/2 of total spleen area. Spleen was perfused with gentamicin (1.6×10^5 units) and embolized using gelatin sponge particles (diameter: 150–350 μm) to retard bloodstream. Spleen artery radiography was operated to monitor range and degree of embolism. If necessary, re-embolism was conducted in case of insufficient embolism or excessive embolism.

2.3. Fluorescence active cell sorting (FACS) analysis

Draw peripheral blood from patients was conducted 1 day before PSE, 6 months, 1 year, and 2 year after PSE, respectively. $CD3^+$, $CD4^+$ and $CD8^+$ T cells and $CD4^+$ $CD25^+CDl27^{low/-}$ Treg cells in patients' peripheral blood were analyzed by FACS. Three repeats of each peripheral blood sample were labeled with anti-CD4-PE, anti-CD4-PE/anti-CD25 FITC, anti-CDl27, and anti-CD3-PE/anti-CD8-FITC antibodies, respectively. Add 100 μL anticoagulant whole blood and incubate in dark for 25 min. Then, 2 mL lysis buffer was added in each samples and incubated in dark for 15 min. After red blood cells hemolysis, samples were centrifuged at a speed of 200 g for 5 min and washed with PBS three times in the same way. Pallets were resuspended in 200 μL 1% paraformaldehyde (PFA) and analyzed by FACS.

2.4. Analysis of immunoglobulins

Immunoglobulins (IgA, IgM and IgG) in patients' peripheral blood, drawn 1 day before PSE, 6 months, 1 year and 2 years after PSE, were analyzed by auto immunoassay analyzer, respectively.

2.5. Statistical analysis

All statistical analyses were performed using SPSS 16.0 software. Data were presented as Mean ± SD. For each group, data from different detection times were tested by repetitive measurement ANOVA. For the same detection times, data from different groups were tested by one-way ANOVA. Dunnett-*t* test was used for analyzing variation between two groups. $P < 0.05$ was considered statistically significant.

3. Results

3.1. FACS analysis

3.1.1. $CD3^+$ T cells in peripheral blood

$CD3^+$ T cells in the peripheral blood of patients from complication group were less than those in control group form pre-PSE to post-PSE ($P < 0.05$). Numbers between two groups were comparable 2 years after PSE ($P > 0.05$). 1 year and 2 years after PSE, numbers of $CD3^+$ T cells in patients from complication group were not significantly different from those before PSE ($P > 0.05$).

$CD3^+$ T cells in the peripheral blood of patients from experimental group were less than that in control group from pre-PSE to 6 months after PSE ($P < 0.05$). The numbers between two groups were comparable one year later ($P > 0.05$). 1 month after PSE, the number of $CD3^+$ T cells dramatically declined ($P < 0.05$). However, 6 months after PSE, it increased to normal level and maintained to 2 years after PSE.

1 month, 6 months and 1 year after PSE, $CD3^+$ T cells in complication group were less than those in experimental group ($P < 0.05$). Then, they increased to the level of experimental group 2 years after PSE ($P > 0.05$) (Table 1).

3.1.2. $CD4^+$ T cells in peripheral blood

$CD4^+$ T cells in the peripheral blood of patients from both complication group and experimental group were less than those in control group ($P < 0.05$). 1 month, 6 months and 1 year after PSE, $CD3^+$ T cells of complication group and experimental group were less than those pre-PSE ($P < 0.05$). The significant difference disappeared until 2 years after PSE. 1 month after PSE, the number of $CD4^+$ T cells in the peripheral blood of patients from experimental group was lower than preoperative level ($P < 0.05$). However, it increased to the preoperative level 6 months after PSE, and maintained to 2 years after PSE. 6 months after PSE, $CD4^+$ T cells in the peripheral blood of patients from complication group were less than those in