

Study of the Clinical Effects of Concomitant Splenectomy in Patients with Hepatocellular Carcinoma Accompanied with Cirrhosis and Hypersplenism

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OBJECTIVE To discuss the clinical effects of concomitant splenectomy in hepatocellular carcinoma patients accompanied with cirrhosis and hypersplenism

METHODS Sixty-seven patients who had hepatocellular carcinoma (HCC) accompanied with hypersplenism from December 1999 to March 2002 were reviewed retrospectively. Thirty-eight patients underwent liver and spleen united resection (splenectomy group) and 29 patients received a hepatectomy (non-splenectomy group). One day before operation and 7 days after operation, the concentration of vascular endothelium growth factor (VEGF) in peripheral blood and splenic venous blood were compared between the two groups.

RESULTS The increase of PLT and WBC was significantly higher in patients who underwent concomitant splenectomy compared to patients who did not receive a splenectomy ($P < 0.05$). The occurrence of complications was 28.9% (11/38) in the splenectomy group and 20.6% (6/29) in the non-splenectomy group, and the recurrence rate one year later was 21.1% (8/38) in the splenectomy group and 20.6% (6/29) in the non-splenectomy group. There was no significant difference in occurrence of complications and recurrence rates between the two groups. The concentration of VEGF was not significantly different between peripheral blood versus splenic venous blood. Twenty-nine patients in the splenectomy group received hepatic arterial chemoembolization 1-3 times successfully after operation, but in the non-splenectomy group there were 7 patients who had to stop receiving the successive treatment because the PLT and WBC were too low.

CONCLUSION Combined splenectomy is helpful to raise the PLT and WBC count and enable patients to receive subsequent chemoembolization. Early recurrence and metastases are not significantly different between patients with and without splenectomy.

KEYWORDS: hepatocellular carcinoma, cirrhosis, hypersplenism, concomitant splenectomy, metastasis, recurrence.

At this time in clinical surgery, it has been of major concern to know what effect concomitant splenectomy compared to non-splenectomy will have on patients who suffer from primary carcinoma of liver (here called hepatocellular carcinoma) accompanied

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with cirrhosis and hypersplenism. Information on this problem can serve as a basis for how patients should be treated. To study the clinical effect of splenectomy and non-splenectomy in treatment of hepatocellular carcinoma, we analyzed the operation files of 67 patients who had hepatocellular carcinoma accompanied with cirrhosis and hypersplenism. The cases were reviewed retrospectively from December 1999 to March 2002.

MATERIALS AND METHODS

Clinical data

From December 1999 to March 2002, totally 67 patients who had hepatocellular carcinoma accompanied with cirrhosis and hypersplenism were shown to have hepatic pathology by medical imaging. Ultrasonography showed a spleen thickness > 4 cm, and $PLT < 100 \times 10^9/L$ or $WBC < 4.0 \times 10^9/L$. Thirty-eight patients (27 male, 11 female) underwent liver and spleen united resection (splenectomy group, S-G), the other 29 patients (21 male, 8 female) received only hepatectomy (non-splenectomy group, N-S-G). The average age of patients was 54.9 in the splenectomy group, and 50.4 in the non-splenectomy group.

Child grade

The S-G had 32 Class A patients and 6 Class B patients; the N-S-G had 25 Class A, 4 class B patients.

Operation mode

Seven patients underwent regular hepatectomy in the S-G and 6 in the N-S-G; 31 patients underwent irregular hepatectomy in the S-G and 23 the in N-S-G.

The average amount of intraoperative bleeding was 752 ml (100~2350 ml) in S-G, and 650 ml (200~1790 ml) in N-S-G. After the operations, the pathological examination results proved that all 67 patients had a hepatocellular carcinoma accompanied with cirrhosis at different levels. In the splenectomy group, 2 patients displayed an increasing PLT count after operation, until it reached $10 \times 10^9/L$. By taking aspirin and Fufangdanshen orally, the platlet count gradually came back to a normal level after 3 months.

Method

One day before and 7 days after the operation, 5 ml of peripheral blood was drawn from each of the 67 patients. Seven days after operation, the general condition of the patients with hepatocellular carcinoma improved nicely, tissue rehab at the operation wound was almost completed. The state of health had a slight influence on the level of vascular endothelial growth factor in serum. The splenic vein had been dissected at the beginning of the operation, we ligated and blocked the splenic vein after 5 ml blood had been taken from it in the splenectomy group. In the patients of the non-splenectomy group, "8" shape stitching had been done with a 5-0 blood vessel suture line on the splenic venous wall before 5 ml of splenic venous blood was drawn, then the splenic vein was ligated and bleeding ceased.

After the serum was centrifuged from the peripheral and splenic venous blood, an ELISA method was used to measure the VEGF level, an indictor related to recurrence and metastasis of hepatocellular carcinoma. The general background of the patients medical history, the results of occurrence, recurrence and metastasis of the complications in the two groups were compared. The data were statistically analyzed using SPSS 11.5 software and the statistical method was based on the *t* and chi-square tests.

RESULTS

The following data were not found significantly different between the two groups: average age, sex ratio, liver function gradation before operation, hepatectomy method, level of hepatic cirrhosis, tumor diameter, and mean of platelet and WBC counts (before operation). Although the intraoperative bleeding amount in the splenectomy group was more than the non-splenectomy group, there was no significant difference.

After the operations, no severe complications were found in the two groups, e.g. respiratory system infection, hydrothorax and ascites, hemorrhage of the digestive tract, intraperitoneal infection, wound surface bleeding, wound fat colliquation, etc. There were

complications in 28.9% (11/38) of the patients in the S-G and 20.6% (6/29) of the patients in the N-S-G, but no there was significant difference, $P>0.05$ (Table 1). After operation, the PLT and WBC counts were $224.3 \times 10^9/L$ and $11.5 \times 10^9/L$ for the S-G, and $78.6 \times 10^9/L$ and $4.3 \times 10^9/L$ for the N-S-G. The splenectomy group's levels were significantly higher than the non-splenectomy group's levels (Table 2).

The follow-up for the 67 patients was 5~32 months with an average of 18.5 months. Within the follow-up, no severe infections or venous thromboses occurred. After their operations, 29 patients in the splenectomy group received hepatic arterial chemoembolization 1~3 times. No one stopped treatment because of changes in their hemogram. But in the non-splenectomy group, 7 patients out 22 had to stop the successive treatment because the PLT and WBC counts were too low.

In the splenectomy group, 8 patients experienced a recurrence and metastasis 4~12 months after their operation, 7 with a remnant hepatic recurrence, and 1 with metastasis in the left adrenal. In the non-splenectomy group, 6 patients experienced a recurrence and metastasis 3~12 months after their operation, 4 with a remnant hepatic recurrence, and 2 with metastases in lung and bone. The recurrence rate one year later was 21.1% (8/38) in S-G, and 20.7% (6/29) in N-S-G. There was no significant difference between the two groups ($P>0.05$). Before and after operation, the concentration of VEGF was not significantly different between the peripheral blood and the splenic venous blood (Table 2).

DISCUSSION

Up to now, surgery is still the most effective method for

treating primary carcinoma of the liver. Since the technology has improved, the operation risk has been greatly decreased.

Table 1. Comparison of occurrence of complications (patient number)

Complication	S-G (n=38)	N-S-G (n=29)
Respiratory system infection	2	1
Hydrothorax and ascites	4	1
Hemorrhage of digestive tract	1	2
Abdominal cavity infection	2	1
Wound surface bleeding	1	0
Wound fat colliquation	1	1

About 75~90% patients, who have hepatocellular carcinoma accompanied with cirrhosis, especially together with splenomegaly and hypersplenism, have a damaged blood coagulation system because of the decrease of their PLT and WBC. Therefore there is increased risk of an operation for hepatocellular carcinoma patients, and hepatic cirrhosis and hypersplenism introduce a major problem in their treatment.

For years, many researchers have studied the clinical outcome in treating hepatocellular carcinoma accompanied with cirrhosis and hypersplenism.^[1] Some maintain that concomitant splenectomy can quickly increase the PLT and WBC counts, with early improvement of hepatic function, and consequently believe that concomitant splenectomy is beneficial.^[2-6] On the another hand, some believe that removal of the spleen can damage the body's immune function, and thereby increase the risk of the operation. Also the rapid rise of the PLT count might increase the risk of portal vein emboli. Therefore they are against the concomitant

Table 2. Comparison of test results

Item tested	S G (n=38)	N-S-G (n=29)	P
PLT ($\times 10^9/L$) before operation	65.3	85.2	> 0.05
WBC ($\times 10^9/L$) before operation	4.1	4.4	> 0.05
PLT ($\times 10^9/L$) after operation	224.3	85.2	< 0.05
WBC ($\times 10^9/L$) after operation	11.5	4.3	< 0.05
Peripheral blood VEGF (pg/ml) before operation	244.23	262.34	> 0.05
Peripheral blood VEGF (pg/ml) after operation	900.25	842.17	> 0.05
Intraoperative splenic venous blood VEGF (pg/ml)	301.36	326.96	> 0.05

splenectomy.^[7]

Our result showed that splenectomy resulted in an increase on PLT and WBC that was significantly better than the non-splenectomy group. With regard to the amount of intraoperative bleeding and occurrence of complications, there was no significant difference. Follow-up of the splenectomy group showed no development of thrombi. So we believe that, by ensuring a careful dissection and well-executed operation, closely supervising the changes in the hemogram, and using an anticoagulant in time once the PLT count is too high, the complications of splenectomy can be prevented.

In addition, 29 patients in the splenectomy group received hepatic arterial chemoembolization 1~3 times successfully, and no patients discontinued treatment because of changes in the PLT and WBC count. But in the non-splenectomy group, 7 patients had to stop a successive treatments because the PLT and WBC fell too low. This result shows that combined splenectomy will enable patients who have hepatocellular carcinoma accompanied with cirrhosis and hypersplenism to receive subsequent chemoembolization.

Since the spleen is the biggest immune organ in the body, surgeons have to face the problem of deciding whether splenectomy will decrease the body's immune ability, and cause severe infection, especially increase the recurrence of metastasis of the hepatocellular carcinoma.

Some studies have shown,^[8,9] that in patients with hepatocellular carcinoma accompanied with cirrhosis and hypersplenism, splenic positive immunocompetence was highly damaged, and at the same time the hepatocellular carcinoma released immunosuppressive factors which caused splenic negative immunocompetence.

The studies of Cao and others^[10-12] showed that, the concomitant splenectomy in patients of hepatocellular carcinoma accompanied with cirrhosis and hypersplenism, not only did no damage to a T-cell subgroup and the Th-cell balance, but also improved the body's anti-cancer immune ability.

Although we didn't undertake a study of the immune system, the comparison of the recurrence rates one-year

later showed no significant difference in the two groups, and in the splenectomy group, no severe infections occurred. It suggests, from another angle, that splenectomy for patients who have hepatocellular carcinoma accompanied with cirrhosis and hypersplenism, does not cause a major change in their immune ability.

The results of previous studies have indicated that the concentration of VEGF in the peripheral blood related to recurrence and metastasis of hepatocellular carcinoma.^[13-15] The higher the concentration of VEGF, the more recurrence and metastasis will occur. So, the examination of VEGF's concentration will be helpful to foretell the recurrence and metastasis of hepatocellular carcinoma.^[16]

To further study whether splenectomy might increase the rates of recurrence and metastasis of hepatocellular carcinoma, we examined the VEGF's concentration in both splenic venous and peripheral blood. Our purpose was to identify whether the concentration of VEGF will be changed in the splenic venous. The results showed that there was no significant difference between the concentration of VEGF in the two groups, whether in the peripheral blood before or after the operation, or in the intraoperative splenic venous blood.

Our results show that there is no significant influence of splenectomy on the early recurrence and metastasis after an operation for hepatocellular carcinoma.

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