Yunfu et al., J Hypertens (Los Angel) 2018, 7:1
DOI: 10.4172/2167-1095.1000249

Journal of Hypertension: Open Access

Research Article Open Access

Peripheral Blood Cells Changes After Two Groups of Splenectomy and Prevention and Treatment of Postoperative Complication

Yunfu Lv[1*], Xiaoguang Gong[1], XiaoYu Han[1], Jie Deng[1] and Yejuan Li[2]

[1]*Department of General Surgery, Hainan Provincial People's Hospital, Haikou, China*

[2]*Department of Reproductive, Maternal and Child Care of Hainan Province, Haikou, China*

[*]**Corresponding author:** Yunfu Lv, Department of General Surgery, Hainan Provincial People's Hospital, Haikou 570311, China, Tel: 86-898-66528115; E-mail: yunfu_lv@126.com

Received Date: January 31, 2018; **Accepted Date:** March 12, 2018; **Published Date:** March 15, 2018

Abstract

Objective: This study aimed to investigate the changes in peripheral blood cells after two groups of splenectomy in patients with traumatic rupture of the spleen and portal hypertension group, as well as causes and prevention and treatment of splenectomy related portal vein thrombosis.

Methods: Clinical data from 109 patients with traumatic rupture of the spleen who underwent splenectomy in our hospital from January 2001 to August 2015 were retrospectively analyzed, and compared with those from 240 patients with splenomegaly due to cirrhotic portal hypertension who underwent splenectomy over the same period.

Results: After splenectomy, peripheral platelet (PLT) count was significantly increased in both groups ($P<0.01$), and the increase was significantly greater in the traumatic rupture group than in the portal hypertension group ($P<0.05$). The red blood cell (RBC) count remained unchanged ($P>0.05$), while the white blood cell (WBC) count was significantly decreased ($P<0.05$) in the traumatic rupture group. Both WBC and RBC counts were increased significantly ($P<0.05$) in the portal hypertension group. Both groups received routine anticoagulant therapy after splenectomy. The incidence of portal vein thrombosis was 8.26% and 6.67% in the traumatic rupture and portal hypertension groups ($P>0.05$), respectively, which was alleviated with urokinase.

Conclusion: The significant increase of peripheral PLT count in both groups after splenectomy might be caused by the removal of the site that stored blood cells. The more significant increase of PLT in the traumatic rupture group might be related to a constant production and release of thrombopoietin by the normal liver into blood circulation. The lack of increase of RBC count in the traumatic rupture group indicated no storage of RBCs in the spleen, and the significant increase of WBC count was related to the control of inflammation. The significant increase of WBC and RBC counts in the portal hypertension group was related not only to the elimination of spleen storage, but also to the elimination of hypersplenism. Postoperative routine anticoagulant and thrombolytic therapy could prevent and treat portal vein thrombosis.

Keywords: Changes in blood cells; Traumatic rupture of the spleen; Cirrhotic portal hypertension; Two splenectomy; Prevention; Treatment

Introduction

It was previously believed that the common development of mono-lineage or multi-lineage peripheral cytopenias as complications of splenomegaly due to cirrhotic portal hypertension was caused by retention of blood cells in the spleen and hypersplenism [1]. Moreover, the retention of blood cells in the spleen contributes to the destruction of blood cells by spleen macrophages, thus enhancing hypersplenism; the decreased peripheral blood cells are generally increased to normal levels after splenectomy [2-4]. Recently, we found that peripheral platelet (PLT) count was also significantly increased after splenectomy in patients with traumatic rupture of the spleen, but not cirrhotic portal hypertension or hypersplenism, and this increase was higher than that in patients with cirrhotic portal hypertension. What is the cause of this increase? To answer this question, clinical data from 109 patients with traumatic rupture of the spleen who underwent splenectomy in our hospital from January 2000 to August 2015 (44.1% of all patients admitted for traumatic rupture of the spleen over the same period [109/247]) were retrospectively analyzed and compared 240 patients who underwent splenectomy for splenomegaly due to cirrhotic portal hypertension over the same period.

Materials and Methods

The 109 patients with traumatic rupture of the spleen included 81 males and 28 females (male-to-female ratio 2:1) aged 15 years to 75 years (median age 31 years). The rupture was caused by falling in 43 patients, a traffic accident in 39 patients, striking in 23 patients, bumping in two patients, and a falling object in two patients. All 109 patients had hemorrhagic shock and acute generalized peritonitis. The average spleen size was measured to be 100 mm × 71 mm × 35 mm by B ultrasound or CT. Twenty seven patients had 500 to 800 ml of bloody ascites, 46 had 900 to 1900 ml, and 36 had more than 2000 ml, with an average of 1524 ml. The volume of blood transfusion ranged from 400 to 3350 ml. All patients underwent open total splenectomy. All patients had a soft liver with a normal color, except one patient who had

nodular cirrhosis. Thirty six patients had left lower rib fractures, nine had diaphragmatic hernia due to diaphragmatic rupture, five had pancreatic rupture, and three had gastric wall injury. All these injuries were treated during surgery. All patients recovered, except one who died of serious combined injuries after surgery.

The 240 patients with splenomegaly due to cirrhotic portal hypertension included 199 males and 41 females (male-to-female ratio 4.9:1) aged 15 years to 69 years (mean 45 years). In total, 203 patients (84.6%) had post-hepatitis B cirrhosis, 27 (11.2%) had post-hepatitis C cirrhosis, and 10 (4.2%) had other types of cirrhosis. The average spleen size was measured to be 230 mm × 164 mm × 95 mm by B ultrasound or CT. All patients underwent open total splenectomy and porta-azygous devascularization, and 36 patients underwent additional splenorenal shunt. Overall, 180 patients (75.0%) underwent surgery for upper gastrointestinal bleeding, 43 (17.9%) for moderate to severe thrombocytopenia (PLT <50 × 10^9/L), and 17 (7.1%) for the influence on daily activities/work from splenomegaly. Intraoperative found obvious atrophy, liver surface shows nodular changes. Regarding ascites, 112 patients (46.7%) had a small amount (≤ 200 ml), 15 patients (6.2%) had a medium amount (200-500 ml), and the rest had none. All but five patients were successfully discharged (one died of encephalopathy, two patients died of coagulation disorders, and two died of liver failure).

Both groups of patients received 500 ml of intravenous dextran, qd, 7-14 days after surgery, and 4250-4500 U of subcutaneous low-molecular-weight heparin, q12h, for one week 24h after surgery. Patients with portal vein thrombosis (PVT), as revealed by color B ultrasound and CT examination, were treated with 500,000 to 1,000,000 U of urokinase + 250 ml of 0.9% sodium chloride by intravenous infusion, qd, for 7-10 days until complete resolution of PVT.

Statistical Analysis

Statistical analysis was performed using SPSS 19.0. Measurement data are presented as mean ± standard deviation ($\bar{x} \pm s$). Changes in blood cells before and after surgery in the same group were examined using the Wilcoxon signed rank test.

Postoperative differences in blood cells between the two groups were examined using the Mann-Whitney U test. P<0.05 was considered statistically significant.

Results

Changes in blood cells before and after surgery

A white blood cell (WBC) count of <4.0 × 10^9/L, a red blood cell (RBC) count of <3.5 × 10^{12}/L, or a PLT count of <100 × 10^9/L in the peripheral blood are the criteria for peripheral cytopenia. Changes in peripheral blood cells before and after surgery in the two groups are summarized in Table 1.

Preoperative blood counts in Table 1 were defined by the first measurement after admission, and postoperative blood counts were defined by the last measurement before admission.

Group	n	Blood cells	Preoperative	Postoperative	Z value	P value
Traumatic spleen rupture	109	WBC☆	16.01 ± 6.65	12.59 ± 5.26	4.051	0
		RBCΔ	3.58 ± 0.82	3.53 ± 0.58	0.801	0.423
		PLT□	187.73 ± 92.98	325.38 ± 222.86	-4.656	0
		HB◇	104.23 ± 24.79	103.45 ± 16.78	0.689	0.491
Portal hypertension	240	WBC☆	4.68 ± 2.86	12.41 ± 7.37	-9.107	0
		RBCΔ	3.54 ± 1.19	3.82 ± 1.03	-3.161	0.002
		PLT□	99.28 ± 80.63	201.19 ± 148.35	-6.367	0
		HB◇	89.98 ± 28.18	105.31 ± 28.80	-4.725	0

Note: A significant difference in preoperative WBC count between the groups (P<0.05). ☆☆No significant difference in postoperative WBC count between the two groups (P>0.05). ΔNo significant difference in preoperative RBC count between the two groups (P>0.05). ΔΔNo significant difference in postoperative RBC count between the two groups (P>0.05). □A significant difference in preoperative PLT count between the groups (P<0.05). □□A significant difference in postoperative PLT count between the groups (P<0.05). ◇No significant difference in preoperative hemoglobin (Hb) level between the two groups (P>0.05). ◇◇No significant difference in postoperative Hb level between the two groups (P>0.05)

Table 1: Changes in peripheral blood cells before and after surgery in the two groups ($\bar{x} \pm s$).

Postoperative PVT

During hospitalization, superior mesenteric vein thrombosis was observed in two patients in the traumatic rupture group and in five patients in the portal hypertension group (P>0.05).

Group	Count (×10^9/L)	n	%	PVT (Grade)				
				I	II	III	IV	Total
Traumatic spleen rupture (n=109)	<400	76	69.7	1	0	0	0	1
	400-600	21	19.3	1	2	0	0	3
	>600	12	11	1	2	1	1	5
Portal hypertension (n=240)	<400	222	92.5	2	1	0	0	3
	400-600	13	5.4	2	3	3	0	8
	>600	5	2.1	1	1	2	1	5

Note: A PLT count of >400 × 10^9/L was measured in 33 patients with traumatic rupture, and in 18 patients with portal hypertension, with a significant difference between the two groups (P<0.01, X2=31.160). PVT occurred at an incidence of 8.26% in patients with traumatic rupture and 6.67% in those with portal hypertension, with no significant difference between the two groups (P>0.05, X2 = 0.285)

Table 2: Postoperative changes in PLT count and their relationship with PVT.

Related results are shown in Table 2. The postoperative PLT count in Table 2 was the highest PLT count prior to PVT. PVT was graded according to the grading standard developed by Yerdel et al. [5]. PVT was alleviated by urokinase.

Discussion and Conclusion

If the pulse, blood pressure, temperature, breathing rate, and other vital signs are normal and stable, and no other organ injury is observed, non-surgical treatment (55.9%) is often chosen for traumatic rupture. In this study, the 109 patients (44.1%) underwent open total splenectomy because of extremely unstable vital signs or injury of the diaphragm, pancreas, stomach, or other organs. Of course, selective partial splenectomy might be a better option, but it is difficult to perform such a surgery in an emergency.

Changes in blood cells and the causes

After splenectomy, peripheral PLT counts were significantly increased in both groups, perhaps because the site that retained blood cells was removed after splenectomy. Generally, 200 ml of blood is stored in a normal spleen. As the spleen is significantly enlarged in patients with cirrhotic portal hypertension, a large number of blood cells are retained in the spleen, leading to storage of more than a thousand milliliters of blood [6], which is 10-20 times greater than the normal splenic blood reservoir. As a result, peripheral blood cell counts are decreased. Using 51Cr-labeled PLT, Aster [7] found that, under normal circumstances, one-third of PLTs were stored in the spleen and the remaining two-thirds in the blood circulation; however, in patients with splenomegaly due to cirrhotic portal hypertension, 50-90% of the PLTs were stored in the enlarged spleen, leading to a reduction in circulating PLTs. Because of the retention of PLTs by the spleen, PLT count would be significantly increased after splenectomy in patients with traumatic rupture of the spleen and in those with splenomegaly due to cirrhotic portal hypertension. In our study, the PLT count was significantly increased by an average of 138×10^9/L in the traumatic rupture group ($P<0.05$) and by 102×10^9/L in the portal hypertension group ($P<0.05$), with the former being significantly higher than the latter ($P<0.05$). Moreover, a postoperative PLT count of $>400 \times 10^9$/L was measured in 33 patients (33.3%) with traumatic rupture and 18 patients (7.5%) with portal hypertension, with a significant difference between the two groups ($P<0.01$). The reason for the significantly higher PLT count in the traumatic rupture group compared with the portal hypertension group is not clear. It could be associated with the younger age and consequent morphologically and functionally intact liver of the traumatic rupture group (mean 31 years). Thrombopoietin (TPO) produced by the healthy liver is released at a constant rate into the blood circulation [8] to continually promote PLT generation. In the portal hypertension group, liver production of TPO was reduced due to liver atrophy and cell dysfunction [9], thus resulting in reduced PLT generation.

The significant increase of WBC and RBC counts in the portal hypertension group is related not only to the elimination of spleen retention, but also to the elimination of hypersplenism [10-12]. In patients with portal hypertension, the increased number of macrophages in the enlarged spleen leads to enhanced phagocytosis and destruction of blood cells [13,14]. After splenectomy, peripheral WBC and RBC counts are significantly increased with the resolution of hypersplenism [15]. Storage of blood cells in the spleen and hypersplenism are the major causes of peripheral cytopenia in patients with splenomegaly due to cirrhotic portal hypertension. Blood cells in the spleen in storage and retention are two different concepts, storage of blood cells is spleen physiological phenomenon, and resistance to keep blood cells is a pathological phenomenon. The blood cells in the blood is mainly through the basement membrane between the splenic cords-blood sinus holes can enter blood sinus, reach the spleen vein. The basement membrane pores straight after only 2-3 μm, and direct the WBC and RBC of 7-12 μm, blood cells must be extremely deformation to pass, and deformation performance of blood cells of patients with liver cirrhosis is very poor, often cannot pass, long-term resistance in splenic cord and damaged by macrophages [16], therefore, retention belong to the category of hypersplenism. Based on the findings of increased peripheral blood cells in the two groups in this study, the storage of blood cells in the spleen may be a more important cause. This can explain not only the increase of peripheral blood cells in patients with splenomegaly due to cirrhotic portal hypertension after splenectomy, but also the increase of peripheral PLT count in patients with traumatic rupture of the spleen. In patients with traumatic rupture, there was no significant change in the peripheral RBC count ($P>0.05$) after splenectomy, which indicated that RBCs were neither stored or retained nor generated in the spleen, i.e., splenectomy had no significant effect on the RBC count. The preoperative increase of WBC is caused by the inflammatory reaction because of the rupture of the spleen. As inflammation is controlled by splenectomy, removal of splenic lesions and intraperitoneal blood shed from the spleen, and postoperative heavy use of antibiotics, in our study, WBCs decreased significantly after surgery and gradually returned to normal levels.

PVT and its prevention

PVT is the most important and potentially fatal complication after splenectomy [17,18]. It occurs in patients with splenomegaly due to cirrhotic portal hypertension and those with traumatic rupture of the spleen, and its incidence is significantly higher in patients with versus without surgery [19]. No obvious symptoms are observed in most patients with grade II and lower-grade PVT, while loss of appetite, increased ascites, impaired liver function, and secondary gastrointestinal bleeding or life-threatening intestinal necrosis can occur in most patients with grade III and higher-grade PVT [5,20]. PVT that occurs in patients with traumatic rupture of the spleen after splenectomy is generally grade II and lower, usually transient [21], and not easily detected due to lack of obvious symptoms. PVT that occurs in patients with splenomegaly due to cirrhotic portal hypertension is generally at grade III and higher, and is easily detected due to the presence of clinical symptoms. Moreover, the incidence of PVT is even higher with additional shunt placement, and the symptoms are even more severe. All six patients with grade III and higher-grade PVT in the portal hypertension group underwent an additional splenorenal shunt. Although PVT can be induced by many factors, such as vascular intimal injury, increased blood viscosity, slow blood flow, increased portal vein diameter [22], splenomegaly [23], and increased spleen weight [24], significantly increased PLT count after splenectomy is an important factor in inducing vascular embolic disease [25,26]. Matsuura et al. [27] suggested that a high postoperative PLT count was a risk factor that should be stressed. Therefore, patients should be closely monitored after surgery [28,29], and should be promptly treated once a high PLT count is measured. Although the postoperative PLT count was significantly higher in patients with traumatic rupture of the spleen than in those with splenomegaly due to cirrhotic portal hypertension, there was no significant difference in the incidence of PVT (8.26% in the traumatic rupture group and 6.67% in the portal

hypertension group; P>0.05), and no adverse outcomes were observed. Moreover, the incidence was significantly lower than the 41.49-47.83% reported in previous studies [30,31], which might be related to the early prevention with low-molecular-weight dextran and low-molecular-weight heparin. The postoperative routine use of low-molecular-weight dextran could not only expand blood volume, but also prevent the accumulation of RBCs, reduce blood viscosity, and improve microcirculation. When the PLT count is increased to >450 × 10^9/L, oral enteric-coated aspirin can be used to inhibit platelet aggregation, and may reduce the incidence of PVT when combined with low-molecular-weight heparin. Satisfactory thrombolysis results can be achieved by administrating urokinase as soon as grade II or higher PVT is detected. Lai et al. [32] suggested that early regular anticoagulation and timely and effective thrombolysis was a necessary, feasible, and effective treatment.

Financial Supports

Funded by the Special Fund for Scientific and Technological Cooperation of Hainan, China (Project No.: KJHZ2015-28). The work is supported by the Hainan provincial key scientific and technological research and development projects (ZDYF2016158).

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