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ORIGINAL ARTICLE

Laparoscopic splenectomy for immune thrombocytopenia (ITP) patients with platelet counts lower than 1 × 109/L

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Abstract Laparoscopic splenectomy (LS) has become the gold-standard surgical intervention for the treatment of immune thrombocytopenia (ITP) and the patients who experienced medical relapse to steroid. Fewer series are available regarding LS for patients with an extremely low platelet count. The aim of this study is to investigate the feasibility and safety of laparoscopic splenectomy in the treatment of patients with a preoperative platelet count of less than 1 × 109/L. From April 2006 to Jan 2011, 10 patients were managed by laparoscopic splenectomy for idiopathic thrombocytopenia with an extremely low preoperative platelet count. Preoperative, perioperative, and postoperative medical management has been reviewed. Before laparoscopic splenectomy, all of the 10 patients had a platelet count of less than 1 × 109/L but a normal level of coagulation function. Emergency laparoscopic splenectomy was performed. The mean operating time was 157 min; the mean intraoperative blood loss was 44 mL. During the operations, transfusion was provided in two patients. No intraoperative complications ensued. The patients were followed up for a mean of 28 months and showed good recovery without any postoperative complications. Laparoscopic splenectomy is a feasible technique in the treatment of ITP patients, characterized by severe mucocutaneous bleeding, extremely low platelet count, and normal prothrombin time (PT) and activated partial thromboplastin time (APTT).

Keywords Laparoscopy · Splenectomy · Idiopathic thrombocytopenia · Platelet count · Platelet transfusion

1 Introduction

Immune thrombocytopenia (ITP, also known as idiopathic thrombocytopenia) is an idiopathic autoimmune disease characterized by destruction of opsonized platelets in the reticuloendothelial system, especially in the spleen, leading to low platelet count. The first-line therapy is oral corticosteroids [1]. Generally, splenectomy is considered to be the second-line treatment in the following situations: (1) refractory symptomatic thrombocytopenia after 3–6 months of corticosteroids therapy, (2) contraindications to corticosteroid in the patient, and (3) relapse of thrombocytopenia after an initial response to medical therapy or intolerant doses of steroids are required to achieve remission [2]. Since Delaitre [3] reported the first adult laparoscopic splenectomy in 1991, this procedure has its remarkable benefits such as lower morbidity and mortality rates, less surgical trauma and postoperative pain, less blood loss, shorter postoperative hospital stay, and better cosmetic. LS has been considered as gold standard modalities for the patients suffering from ITP [4].

Low preoperative platelet count proved to be one factor which prohibits successful utilization of LS [5]. Low platelet count was proved to be less beneficial in LS with higher morbidity, transfusion requirements and conversion

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rates [6]. Therefore, a platelet count of at least 30–50 $\times$ 10^9/L is recommended by most physicians and surgeons [7]. However, no previous studies discussed the treatment of patients with severe platelet count who response poorly to, or who relapse immediately after medical therapy. We, therefore, investigated the feasibility and safety of laparoscopic splenectomy for treating patients with extremely low platelet count.

2 Materials and methods

From April 2006 to Jan 2011, 1229 patients transferred to our hospital were diagnosed with ITP. During the same period of time, 1196 patients underwent open or laparoscopic splenectomy, while 162 patients underwent splenectomy for ITP. Of these, 10 ITP patients underwent LS because of severe thrombocytopenia (platelet count lower than 1 $\times$ 10^9/L). Clinical manifestations, medical treatment, perioperative details of these patients were retrospectively reviewed. All 10 patients have been followed up to date; the median overall follow-up after splenectomy was 28 months. None was lost to long-term follow-up, and none has died.

2.1 Principles of surgical technique

The surgical technique we use for laparoscopic splenectomy has been detailed in a previously published paper [8]. The ligaments and attachments around the spleen were dissected with the ultrasonic dissector (Ethicon Endo-Surgery, LLC, USA) and en bloc transecting the splenic hilum using the linear laparoscopic vascular stapler (Echelon 60 Endopath stapler, Ethicon Endo-Surgery, LLC, USA).

2.2 Statistical analysis

Numerical data are expressed as mean $\pm$ standard deviation. Differences between variables were compared using the Student's *t* test, the Chi-square test, and Fisher's exact test. All statistical analyses were performed using SPSS 16.0, and *p* values <0.05 were considered statistically significant.

3 Results

3.1 Demographic data

The demographics and clinical features of these ten ITP patients are summarized in Table 1. The median age at diagnosis of ITP was 21.5 years (range 9–43 years), and 8 (80%) were women. At the time of diagnosis, the mean platelet count was 6.1 $\times$ 10^9/L. All the patients underwent a regular medical treatment for 6 months including at least one course of a high dose (steroid pulse) of prednisolone combined with intravenous immunoglobulin 20 g/day (400 mg/kg) for 5 days. All the patients were refractory to medical treatment or relapsing at the interruption of steroid therapy. All of the 10 patients had a normal level of normal coagulation function. Laparoscopic splenectomy was performed immediately.

3.2 Perioperative details (Table 2)

There was no conversion to open approach during the surgery. The average operating time was 157 min, and the average intraoperative bleeding was 44 mL. Patient 8 received an intraoperative transfusion of 2 U packed red

Table 1 Patients demographics characteristics [data represent mean $\pm$ standard deviation (SD)]

Patient	1	2	3	4	5	6	7	8	9	10	Mean $\pm$ SD
Gender	F	M	F	M	F	F	F	F	F	F	
Age at diagnosis of ITP (years)	24	20	15	43	21	25	13	9	32	13	21.5 $\pm$ 10.2
PLT at diagnosis ($\times$$10^9$/L)	15	5	9	10	2	3	6	4	2	5	6.1 $\pm$ 4.1
Age at LS (years)	26	24	23	62	40	27	25	29	55	15	32.6 $\pm$ 15.1
PLT at LS ($\times$$10^9$/L)	1	0	1	0	0	1	1	1	0	1	0.6 $\pm$ 0.5
Hgb at LS (g/L)	101	135	83	116	118	130	134	130	126	126	119.9 $\pm$ 16.5
WBC at LS ($\times$$10^9$/L)	9.23	19.98	12.31	10.28	5.78	11.19	9.71	6.30	11.08	3.19	9.9 $\pm$ 4.5
PT at LS (s)	16.7	11.8	12.0	11.8	12.5	13.4	14.5	10.1	9.4	12.8	12.5 $\pm$ 2.1
APTT at LS (s)	33.7	35.0	29.5	32.1	33.3	34.4	33.5	15.7	16.5	39.2	30.3 $\pm$ 7.9
TT at LS (s)	27.6	16.9	17.4	18.5	19.5	14.2	9.8	16.5	15.0	18.3	17.4 $\pm$ 4.5
FIB at LS	1.35	4.92	3.7	2.4	1.76	3.91	2.75	1.32	2.11	2.41	2.7 $\pm$ 1.2

F Female, *M* Male, *ITP* idiopathic thrombocytopenia, *PLT* platelet count, *LS* laparoscopic splenectomy, *WBC* white blood count, *PT* prothrombin time, *APTT* activated partial thromboplastin time, *TT* thrombin time, *FIB* fibrinogen

Table 2 Perioeperative details [data represent mean ± standard deviation (SD)]

Patient no.	1	2	3	4	5	6	7	8	9	10	Mean ± SD
Operative time (min)	130	240	130	180	140	175	215	130	140	90	157.0 ± 45.2
EBL (mL)	20	100	50	30	20	30	100	50	30	10	44.0 ± 32.0
Transfusion	(−)	(−)	(−)	(−)	(−)	(−)	(−)	(+)	(−)	(+)	/
Conversion	/	/	/	/	/	/	/	/	/	/	/
PHS (days)	8	4	7	7	8	7	4	7	9	7	6.8 ± 1.6
3 days after LS											
PLT ($\times 10^9$/L)	134	361	211	367	235	442	195	314	180	228	266.7 ± 98.8
Hgb (g/L)	145	112	111	135	112	139	98	100	128	145	122.5 ± 18.0
Last visit (months)	23	16	36	26	18	42	33	24	30	32	28.0 ± 8.1
PLT ($\times 10^9$/L)	126	284	232	257	230	305	219	245	154	213	226.5 ± 54.1
Hgb (g/L)	139	124	123	112	127	109	118	120	106	132	121 ± 10.3

EBL estimated blood loss, *PHS* postoperative hospital stay, *Transfusion* patients who received a blood cell or platelet transfusion, *PLT* platelet count, *LS* laparoscopic splenectomy

Table 3 Laboratory examinations before and after LS [all data represent mean ± standard deviation (SD)]

	Before LS	3 days after LS	Last visit	p^1 value	p^2 value
PLT	0.6 ± 0.5	266.7 ± 98.8	226.5 ± 54.1	0.000*	0.000
HGB	119.9 ± 16.5	122.5 ± 18.0	121.0 ± 10.3	0.740	0.860
WBC	9.9 ± 4.5	15.8 ± 5.3	7.0 ± 1.1	0.015*	0.066
PT	12.5 ± 2.1	12.5 ± 1.4	/	0.970	/
APTT	30.3 ± 7.9	29.8 ± 5.5	/	0.876	/
TT	17.4 ± 4.5	18.7 ± 4.0	/	0.493	/
Fib	2.7 ± 1.2	3.0 ± 1.1	/	0.496	/
INR	2.2 ± 3.7	1.1 ± 0.1	/	0.368	/

PLT platelet count, *HGB* hemoglobin, *WBC* white blood count, *PT* prothrombin time, *APTT* activated partial thromboplastin time, *TT* thrombin time, *FIB* fibrinogen, *INR* international normalized ratio

* $p < 0.05$ with a statistically difference

[1] Comparison before LS and 3 days after LS

[2] Comparison before LS and at the last visit

blood cells. Patient 10 received 3 U of platelets combined with 600 mL fresh frozen plasma during operation. The mean postoperative hospital stay was 6.8 days.

3.3 Efficacy of splenectomy

Hematological responses are shown in Table 3. After third postoperative day, the platelet count increased sharply to 226.7 × 10^9/L, as well as white blood count. No significant differences were found in hemoglobin and the coagulation function. These 10 ITP patients were followed up for an average time of 28 months. At the last visit, prednisolone use reduced gradually while the platelet count remained at normal level (median 226.5 × 10^9/L). No differences were found in white blood count and hemoglobin.

3.4 Manifestation of a typical case

A 14-year-old girl, presented at our department complaining of severe mucocutaneous bleeding, who was diagnosed as ITP 7 months ago. Previous medication therapy including the platelet count and the use of prednisolone were shown in Fig. 1. At the time of diagnosis, the platelet count was 5 × 10^9/L. Prednisolone was used as 60 mg/day for 3 days, and the platelet count increased to 20 × 10^9/L. The dose was kept for 1 month, with an unstable platelet count, ranging from 17 × 10^9 to 30 × 10^9/L. After a 2-day decrease of the prednisolone by 10 mg/day, the platelet was sharply followed down to 6 × 10^9/L. Even after 10 days, the platelet count fell to the bottom (below the measurable limit). The amount of prednisolone rose, with an increased platelet count. A large dose of prednisolone was carried out;

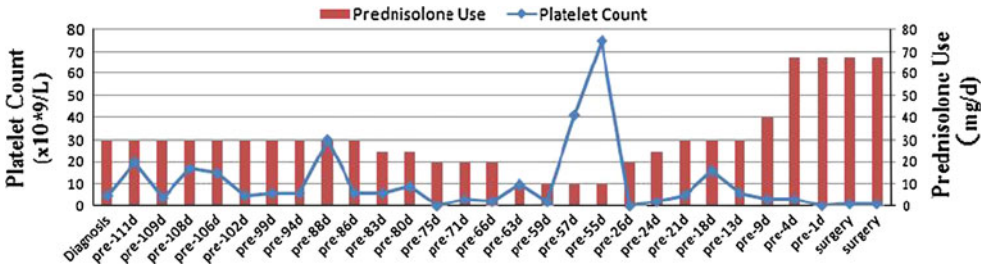

Fig. 1 Platelet count and the use of the prednisolone before surgery (patient 10)

with intravenous immunoglobulin 20 g/day (400 mg/kg) for 5 days but the response to the platelet elevation was not satisfactory. After regulated treatment for 3 months, the patient showed medical refractory, the platelet count was less than 20×10^9/L. After she was transferred to our department, widespread petechiae were shown, and no splenomegaly was marked by physical and imaging examinations as well. A complete blood count showed a platelet count of 3×10^9/L, hemoglobin level of 126 g/L and white blood cell count of 11.06×10^9/L. Prothrombin time was 12.8 s (normal 9.6–12.8 s) and activated partial thromboplastin time was 39.2 s (normal 20–40 s). The CT (computed tomography) revealed normal volume of spleen without any significant splenomegaly (Fig. 2). On arrival, the patient was treated with intravenous immunoglobulin 20 g/day and some hemostatics for 3 days, unfortunately, the platelet count decreased to 0×10^9/L (below the measurable limit). Three units platelet was immediately transfused but the platelet count poorly increased to 1×10^9/L, with the beginning of gross hematuria. In order to prevent the occurrence of intracranial hemorrhage, an emergency laparoscopic splenectomy was carried out. Laparoscopic splenectomy was performed. Three units platelet was provided during the splenectomy and 600 mL fresh frozen plasma (FFP) was transfused after the splenic artery had been clamped, in order to decrease the blood loss. The operation lasted for about 90 min and the estimated blood loss was 100 mL. Since we used laparoscopic, the vascular stapler (Echilon 60 Endopath stapler, Ethicon Endo-Surgery, LLC, USA) at splenic hilum, so there was not significant blood loss while dealing at the splenic hilum, which pay much attention toward the intraoperative complications. The platelet count increased to 39×10^9/L on the first postoperative day and 57×10^9/L on the third day. The patient was discharged on the sixth day, with a platelet count of 67×10^9/L. The patient was followed up for 2 year, during which there was no mucocutaneous bleeding again and the blood count showed a platelet count of 213×10^9/L, with a tapered dose prednisolone use for half a year. After 6 month of the surgery, the use of steroid was stopped. The follow-up of perioperative platelet count and corticosteroids use were shown in Fig. 3.

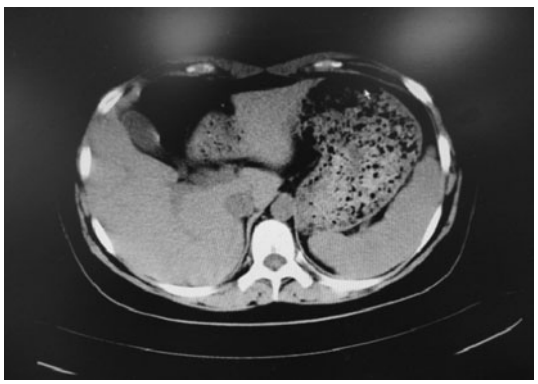

Fig. 2 CT scan of ITP patient showing normal spleen

4 Discussion

Idiopathic thrombocytopenia (ITP) is a disease with the increasing destruction of platelet count caused by the antiplatelet antibodies, leading to a clinical manifestation of thrombocytopenia [9]. Treatment was indicated in patients whose platelet count was lower than 30×10^9/L or in patients whose platelet count lower than 50×10^9/L but suffering mucous membrane bleeding (or risk factors for

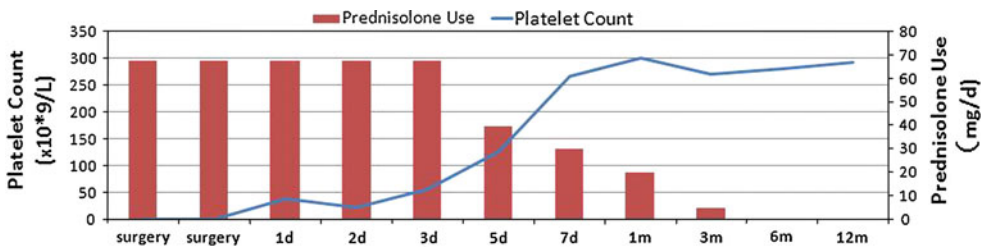

Fig. 3 Platlet count and the use of the prednisolone after surgery (patient 10)

bleeding, such as peptic ulcer disease, or a potential for substantial trauma to the body) [10]. The first-line therapy is corticosteroids and most of patients respond to corticosteroids initially, but only 20% of the patients get a durable remission [1]. Although splenectomy is the second-line therapy, it is the most effective treatment, superior to various medical therapies and produces a long-lasting response in most of patients [11]. If the patients have poor response to medical therapies, splenectomy is a proper intervention [12]. In our series, patients had a poor response to kinds of medical interventions mentioned above, or relapsed at the interruption of steroid therapy, with platelet count decreasing gradually. In this situation, splenectomy should be performed earlier, not until the platelet count decreased to a dangerous scope.

Since its introduction in 1992 [3], laparoscopic splenectomy has been accepted in several centers for removal of the spleen, especially for benign hematological disorders. Concerning the safety of the surgery, much literature supports the role of LS for ITP if the platelet count is higher than 30×10^9/L . Intraoperative hemorrhage at the splenic hilum, severe oozing of blood from the cut edge, is the biggest challenge for the laparoscopic splenectomy due to severe thrombocytopenia. After the splenic hilum was transected, platelet transfusion can increase the platelet count promptly and stop the oozing of blood. If the intraoperative bleeding is unstopped, continuous platelet monitoring should be considered. Yoneoka [13] reported a successful emergence laparoscopic splenectomy for a patient whose platelet count was below the measurable limit, with the help of continuous platelet transfusion at the rate of 2 U/h. However, Chen et al. [5] reported that perioperative platelet transfusion may be unnecessary for ITP patients with very low platelet count. No study has been published with regard to patients with extremely platelet count. In our series, all the patients had an extremely platelet count, but a normal level of prothrombin time (PT) and activated partial thromboplastin time (APTT). Only one patient received 2 U packed red blood cells, due to sudden fall of blood pressure intraoperatively, ranging 93/71 to 60/38 mmHg. Reason may be the sudden autonomic pull of nervous system at the point of ligation of the splenic hilum. All the patients underwent successful surgery, and recovered quickly. We can hold that LS can be a feasible and safe therapy in those selected patients.

Furthermore, accompanying the development of laparoscopic technology, such as ultrasonic dissector, LigaSure vessel sealing system and linear laparoscopic vascular stapler, the increase of completed cases, as well as the skilled surgical and anesthetic techniques, our surgical technique was improved and the procedure was more smooth and safer. The operation become much safer and the intraoperative blood loss decrease apparently [14].

It was reported that during the laparoscopic splenectomy, remission rates were 78–93% [15]. In our series, during the following 1 year, the patient received a gradual decrease of the corticosteroid and increase of the platelet count.

Intravenous immunoglobulin (IVIG) was considered as the first-line treatment options in adults with ITP and introduced as a means of transiently reversing the thrombocytopenia in patients with ITP, especially in those with extreme low platelet count [12]. It is often used in hospitalization and emergency therapy. It was reported up to 80% of patients respond initially and half of the patients achieve normal platelet count [16]. Furthermore, it is effective for ITP patients who failed to respond to the first IVIG therapy. In our series, all the patients were repeated before the surgery, and some of the patients were effective for IVIG therapy. However, they relapsed quickly after the steroid pulse. In that case, emergency laparoscopic splenectomy should be undertaken.

Despite there are just a few literatures are available mentioning the emergency splenectomy for severe thrombocytopenia [13, 17–19], especially for those patients who show a poor reaction to the intravenous pulse therapy of a large dose of corticosteroids and immunoglobulin. In spite of that, we believe that good surgical technique along with the use to sophisticated apparatus and continuous monitoring of platelet count in dangerous situation, such as severe mucocutaneous bleeding, extremely low platelet count and normal PT and APTT is mandatory for safety and efficacy of laparoscopic splenectomy.

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Conflict of interest Zhong Wu, Jin Zhou, Prasoon Pankaj and Bing Peng have no conflicts of interest or financial ties to disclose.

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