Results of Laparoscopic Splenectomy for Immune Thrombocytopenic Purpura

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Objective: *To study the safety and efficacy of Laparoscopic Splenectomy (LS) for Immune Thrombocytopenic Purpura (ITP).*
Material and Method: *Twenty-five consecutive adult patients with chronic ITP who did not achieve sustained remission or refractory to medical treatment underwent elective LS between March 1995 and July 2005. The perioperative course was documented and the follow up data were recorded.*
Results: *All 25 patients underwent successful LS by a single surgeon. Twenty patients were available to analyze with a median follow-up time of 739 days (range, 18-3,555). The mean age was 29.8 years (range, 15-44) and 17 patients were female. The median preoperative platetlet count was 16,500/ L (range, 2,000-180,000). Accessory Spleens (AS) were removed in three patients (15%). A female patient died 24 days after LS from fungal brain abscesses. Fifteen patients (75%) had platelet count >100,000/ L at initial response. Thirteen patients (65%) are in Complete Remission (CR) (platelet count >100,000/ L). The probability of staying in CR after LS was 60.2% by Kaplan-Meier analysis. All failures occurred within 218 days of the operation. The mean age of the patients with CR was 27.2 years (range, 15-43) while the mean age of the nonCR was 34.7 years (range, 21-44).*
Conclusion: *LS should be considered as a safe and effective therapy when elective splenectomy is indicated for chronic ITP patients.*

Keywords: *Immune thrombocytopenic purpura, Laparoscopic splenectomy, Accessory spleen, Complete remission*

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Immune Thrombocytopenic Purpura (ITP) is an acquired autoimmune disease characterized by accelerated platelet destruction caused by autoantibodies. Spleen is the primary site of both antiplatelets autoantibodies synthesis and antibody-sensitized platelet sequestration and destruction. Glucocorticosteroids are recommended as the initial treatment, resulting in a good response in 70-80% of cases[1]. Splenectomy is indicated in patients who are refractory to steroids (steroid resistant or relapse after steroid withdrawal). Laparoscopic Splenectomy (LS) was introduced in 1991 by Delaitre and Maignien[2] and has been shown in several retrospective series to be technically successful, effective and safe[3-6] The authors reviewed the past 10 years experience of LS at Rajavithi Hospital, Thailand.

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Material and Method

Study population

A personal case series of 25 consecutive adult patients with chronic ITP refractory to medical treatment underwent LS between March 1995 and July 2005 at Rajavithi Hospital in Bangkok, Thailand was analyzed. The indications for surgery were steroid dependence or resistance. Emergency cases with hemodynamic instability were excluded. The perioperative course and the follow-up data were recorded.

Surgical technique

The anterior approach technique was performed in the first 10 patients (1995-2000) and the lateral approach technique was performed in the last 15 patients. The operative techniques have been described in another paper[7,8]. The use of 3-4 trocars was appropriate in all cases, and 0 degree laparoscope was standard practice. Vessels were simply ligated by monopolar cautery or clips and in more recent years by a Harmonic scalpel. No endovascular staplers were used.

Definitions and outcome assessment

Initial response is typically defined as a rise in platelet count within several days of splenectomy[9]. The platelet count determining a remission was defined as the first count obtained after at least 2 weeks following LS, to avoid the influence of perioperative treatment for ITP. Complete Remission (CR) was defined as achievement and maintenance of a platelet count >100,000/ L[10-12] for all measurements 2 weeks or longer after LS with no additional treatment for ITP.

Follow-up

All patients were followed up in the surgical and hematological outpatient clinics. The outcome measures were platelet counts, medical treatment and complications.

Statistical analysis

All data were analyzed using SPSS 12.0 software (SPSS, Chicago, IL, USA). Descriptive statistics presented to describe the demographic characteristic and results and Kaplan-Meier curve was used to estimate the probability of complete remission (platelet count > 100,000/ L without medical treatment). A p-value of < 0.05 was considered significant.

Results

Twenty-five patients underwent LS for chronic ITP by a single surgeon with no conversions to laparotomy. Five patients in the early year were excluded due to loss of follow-up data. There was no perioperative complication among them. Twenty patients were available to analyze with a median follow-up time of 739 days (range,18-3,555). Fifteen patients (75%) were followed up longer than 12 months. Patient demographics are shown in Table1 and Results in Table 2.

A 19 year old female patient with preoperative high doses of intravenous glucocorticoids and immunosuppressive drugs died 24 days after LS from fungal brain abscesses. Fifteen patients (75%) had a platelet count >100,000/ L at initial response. Thirteen patients (65%) are in CR (platelet count >100,000/ L). The probability of staying in CR after LS was shown by Kaplan-Meier analysis in Fig. 1. 60.2% of the patients were still in CR postoperatively.

Four of seven patients (57.1%) who did not completely respond to LS, could reduce their daily dose of prednisolone. Finally, 17 patients (85%) earned benefit from LS. Six of seven failures (85.7%) occurred within 132 days of the operation and all occurred within 218 days. The mean age of the patients with CR was 27.2 years (range,15-43), 7.5 years younger than the mean age of the non CR (34.7 years) (range, 21-44).

Discussion

Several retrospective or case-controlled comparisons between laparoscopic and Open Splenectomy (OS) revealed that the laparoscopic approach typically results in longer operative time, similar blood loss, reduced postoperative pain and analgesic consumption, earlier resumption of diet and normal activity, shorter hospital stays mostly within 72 hours, lower morbidity and better cosmesis[5,7,9,11-14]. In 29 case series (1,301 patients) published since 1995-2004, there were only two LS-related deaths (0.15% mortality rate), one from intra-abdominal bleeding and the other from sepsis[11]. This review did not include a patient who died from

Table 1. Patient demographics

Number of patients	20
Sex (F/M)	17:3
Mean age (years) (range)	29.85 (15-44)
Indication for surgery- Steroid dependence:resistance	9:11
Median time from diagnosis to surgery (months) (range)	20 (1.5-276)
Median preoperative platelet counts (/ l) (range)	16,500 (2,000-180,000)

Table 2. Statistical results

Mean operative time (minutes) (range)	230 (100-320)
Accessory spleens	3 (15%)
Median postsurgical stay (days) (range)	3 (2-24)
Mortality	1 (5%)
Platelets count >100,000/ L at initial response (no. of patients)	15 (75%)
No. of patients in complete response	13 (65%)

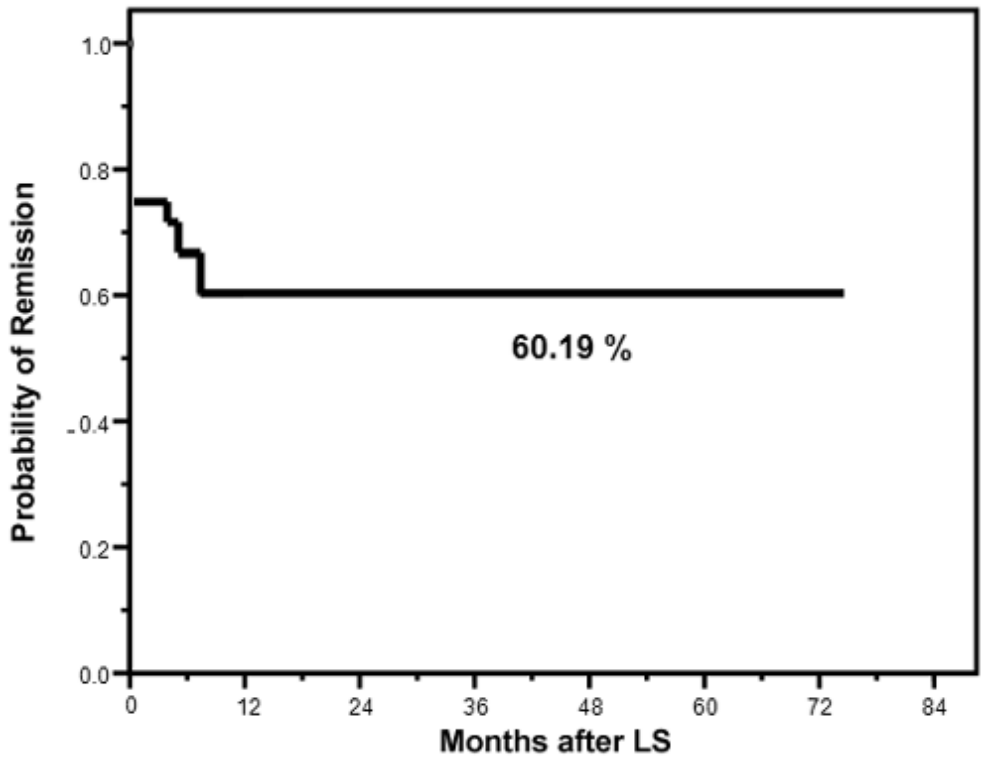

Fig. 1 Kaplan-Meier analysis of the probability of CR (maintaining a platelet count >100,000/ L without medical treatment) after LS for ITP in 20 patients

Legionella pneumonia and Staphylococcus sepsis[15]. A female patient who died in this study had severe fungal infection after cytotoxic treatment that was a high risk of serious morbidity and mortality[16].

In the present study the complete remission rate of 65% (the probability of staying in complete remission after LS 60.2% by Kaplan-Meier analysis) with a median follow-up time of 24.6 months is comparable to 66% CR (range,37-100) with a median follow-up time of 29 months (range,1-153) in the recent review article[11] of 47 case series (2623 adult patients) that were composed of both LS and OS. The response rate in the present study can not be attributed to a short follow-up period as the median follow-up time exceeded the time span that most recurrences are expected to occur (14 months)[12].

Although 65% of LS patients were in CR, 85% of them improved and either reduced or stop oral steroid. This improvement can not be explained by spontaneous remission after failure to splenectomy because the incidence is only 5%[12].

Several mechanisms can be responsible for the relapse or failure after splenectomy. Not only does splenectomy remove the potential site of destruction of damaged platelets, it also removes the most important site for platelet antibody production. However, antiplatelet antibody titers often do not decrease[17,18]. Furthermore, other reticuloendothelial organs such as the liver and bone morrow remain capable of destroying highly sensitized antibody-coated platelets, thus giving rise to relapse or failure.

Residual Accessory Spleens (AS) are believed to be an important mechanism of recurrence of disease after surgery. The 15% rate of AS which was discovered during LS in the present study is comparable to the rate of 10-23% from previous study[1,5,6,12,14,15,19,20]. LS allows a good exploration of the most common location for AS[6,15,21], included in the splenic hilum (two-thirds to three-fourths), tail of the pancreas (20%), omentum, splenic artery, splenocolic ligament, mesentery and gonad in descending order[22]. Another possible reason for surgical failure is splenic injury with subsequent splenic splenosis[23]. During surgery, the spleen should be handled with great care to avoid fragmentation and spillage of splenic tissue. Gigot et al[24] reported a 50% residual splenic tissue detected

on routine postoperative scintigraphy after LS. The patients who did not have CR in the present study did not have postoperative scintigraphy as most of them had partial response and could tolerate well with much lower doses of oral prednisolone after LS, some patients may have residual splenic tissue.

Many studies have attempted to identify prognostic factors for response to splenectomy in patients with ITP. Patient age has been found consistently to be the best prognostic variable for predicting response to splenectomy[11,25]. Some authors tried to explain the relationship between young age and response to splenectomy such as differentiating sites of platelet sequestration in the two groups. Using radionuclide platelet kinetic studies, Fenaux et al[26] showed that younger ITP patients have primarily splenic sequestration whereas hepatic sequestration, which responds poorly to splenectomy is more likely to occur in older patients. Najean et al[27] reported an exceptionally high splenectomy success rate of 91-96% for the patients with exclusively or predominately splenic sequestration, conversely when platelet destruction was hepatic or diffuse, failure or incomplete results were 92%. The average age of the responding patients in the present study was 27.2 years. This was 7.5 years younger than the nonCR group even though there was insignificant correlation ($p = 0.14$).

Conclusion

The 10 years surgical experience of elective LS for chronic ITP refractory to medical treatment at Rajavithi Hospital was reviewed. LS generally appears to be safe and effective with CR rate of 65% (the probability of staying in CR after LS 60.2%) with a median follow-up time of 24.6 months. This information will allow an informed decision about the risks and benefits of LS for chronic ITP patients.

References

1. George JN, Woolf SH, Raskob GE, Wasser JS, Aledort LM, Ballem PJ, et al. Idiopathic thrombocytopenic purpura: a practice guideline developed by explicit methods for the American Society of Hematology. Blood 1996; 88: 3-40.
2. Delaitre B, Magnien B. Splenectomy by the coelioscopic approach: report of a case [letter]. Press Med 1991; 26: 2263-4.
3. Poulin EC, Thibault C, Mamazza J. Laparoscopic splenectomy. Surg Endosc 1995; 9: 172-6.
4. Emmermann A, Zornig C, Peiper M, Weh HJ, Broelsch CE. Laparoscopic splenectomy. Technique and results in a series of 27 cases. Surg Endosc 1995; 9: 924-7.
5. Brunt LM, Langer JC, Quasebarth MA, Whitman ED. Comparative analysis of laparoscopic versus open splenectomy. Am J Surg 1996; 172: 596-9.
6. Watson DI, Coventry BJ, Chin T, Gill PG, Malycha P. Laparoscopic versus open splenectomy for immune thrombocytopenic purpura. Surgery 1997; 121: 18-22.
7. Mahatharadol V, Chantawibul S, Ratanachu-ek T. Laparoscopic splenectomy. J Rajavithi Hosp 1996; 7: 55-65.
8. Park A, Gagner M, Pomp A. The lateral approach to laparoscopic splenectomy. Am J Surg 1997; 173: 126-30.
9. Park AE, McKinlay R. Spleen. In: Brunicardi F, Andersen DK, Billiar TR, Dunn DL, Hunter JG, Pollock RE, editors. Schwartz's principles of surgery. 8th ed. New York: McGraw-Hill; 2005: 1297-315.
10. Levine SP. Thrombocytopenia caused by immunologic platelet destruction. In: Lee GR, editor. Wintrobe's clinical hematology. Vol. 2. 10th ed. Maryland: Williams & Wilkins; 1999: 1583-611.
11. Kojouri K, Vesely SK, Terrell DR, George JN. Splenectomy for adult patients with idiopathic thrombocytopenic purpura: a systematic review to assess long-term platelet count responses, prediction of response, and surgical complications. Blood 2004; 104: 2623-34.
12. Szold A, Kais H, Keidar A, Nadav L, Eldor A, Klausner JM. Chronic idiopathic thrombocytopenic purpura (ITP) is a surgical disease. Surg Endosc 2002; 16: 155-8.
13. Beauchamp RD, Holzman MD, Fabian TC. Spleen. In: Townsend CM, Beauchamp RD, Ever BM, Mattox KL, editors. Sabiston textbook of surgery: the biological basis of modern surgical practice. 17th ed. Philadelphia: Saunders; 2004: 1679-708.
14. Berends FJ, Schep N, Cuesta MA, Bonjer HJ, Kappers-Klunne MC, Huijgens P, et al. Hematological long-term results of laparoscopic splenectomy for patients with idiopathic thrombocytopenic purpura: a case control study. Surg Endosc 2004; 18: 766-70.
15. Rosen M, Brody F, Walsh RM, Tarnoff M, Malm J, Ponsky J. Outcome of laparoscopic splenectomy based on hematologic indication. Surg Endosc 2002; 16: 272-9.
16. Schattner E, Bussel J. Mortality in immune thrombocytopenic purpura: report of seven cases and

consideration of prognostic indicators. Am J Hematol 1994; 46: 120-6.
17. Cines DB, Schreiber AD. Immune thrombocytopenia. Use of a Coombs antiglobulin test to detect IgG and C3 on platelets. N Engl J Med 1979; 300: 106-11.
18. Karpatkin S. Autoimmune (idiopathic) thrombocytopenic purpura. Lancet 1997; 349: 1531-6.
19. Katkhouda N, Hurwitz MB, Rivera RT, Chandra M, Waldrep DJ, Gugenheim J, et al. Laparoscopic splenectomy: outcome and efficacy in 103 consecutive patients. Ann Surg 1998; 228: 568-78.
20. Katkhouda N, Grant SW, Mavor E, Friedlander MH, Lord RV, Achanta K, et al. Predictors of response after laparoscopic splenectomy for immune thrombocytopenic purpura. Surg Endosc 2001; 15: 484-8.
21. Pace DE, Chiasson PM, Schlachta CM, Mamazza J, Poulin EC. Laparoscopic splenectomy for idiopathic thrombocytopenic purpura (ITP). Surg Endosc 2003; 17: 95-8.
22. Skandalakis JE, Gray SW, Rowe JS. Spleen. In: Skandalakis JE, Gray SW, Rowe JS, editors. Anatomical complications in general surgery. New York: McGraw-Hill; 1983: 173-85.
23. Metwally N, Ravo B. Splenosis-a review. Contemp Surg 1991; 39: 33-6.
24. Gigot JF, Jamar F, Ferrant A, van Beers BE, Lengele B, Pauwels S, et al. Inadequate detection of accessory spleens and splenosis with laparoscopic splenectomy. A shortcoming of the laparoscopic approach in hematologic diseases. Surg Endosc 1998; 12: 101-6.
25. Duperier T, Brody F, Felsher J, Walsh RM, Rosen M, Ponsky J. Predictive factors for successful laparoscopic splenectomy in patients with immune thrombocytopenic purpura. Arch Surg 2004; 139: 61-6.
26. Fenaux P, Caulier MT, Hirschauer MC, Beuscart R, Goudemand J, Bauters F. Reevaluation of the prognostic factors for splenectomy in chronic idiopathic thrombocytopenic purpura (ITP): a report on 181 cases. Eur J Haematol 1989; 42: 259-64.
27. Najean Y, Rain JD, Billotey C. The site of destruction of autologous 111In-labelled platelets and the efficiency of splenectomy in children and adults with idiopathic thrombocytopenic purpura: a study of 578 patients with 268 splenectomies. Br J Haematol 1997; 97: 547-50.

ผลการตัดม้ามทางกล้องวีดิทัศน์ในโรค Immune thrombocytopenic purpura

วีรชัย มหธราดล, สมชาย มีศิริ

วัตถุประสงค์*: ผู้วิจัยได้ศึกษาผลการตัดม้ามทางกล้องวีดิทัศน์ในผู้ป่วยโรค Immune thrombocytopenic purpura ที่รักษาทางยาไม่ได้ผลของกลุ่มงานศัลยศาสตร์ โรงพยาบาลราชวิถี*

วัสดุและวิธีการ*: การศึกษาย้อนหลังตั้งแต่เดือนมีนาคม พ.ศ. 2538 ถึง เดือนกรกฎาคม พ.ศ. 2548*

ผลการศึกษา*: ผู้ป่วยได้รับการตัดม้ามทางกล้องวีดิทัศน์สำเร็จทุกคน 25 ราย โดยศัลยแพทย์คนเดียว สามารถติดตามผลได้ 20 ราย เป็นเพศหญิง 17 ราย ระยะเวลาติดตามผลเฉลี่ย 739 วัน (range, 18-3,555 วัน) อายุเฉลี่ย 29.8 ปี (range, 15-44) จำนวนเกล็ดเลือดก่อนการผ่าตัดเฉลี่ยเท่ากับ 16,500/ L (range, 2,000-180,000) พบ accessory spleen 3 ราย (15%) มีผู้ป่วยเสียชีวิตหลังผ่าตัด 1 ราย จากฝีในสมองเนื่องจากเชื้อรา ในระยะแรกผู้ป่วย 15 ราย (75%) มีเกล็ดเลือดมากกว่า 100,000/ L ผู้ป่วย 13 ราย (65%) อยู่ในภาวะ complete remission โดยมีโอกาสมี CR 60.2% ผู้ป่วยที่มี CR มีอายุเฉลี่ย 27.2 ปี (range, 15-43) ขณะที่ผู้ป่วยที่ไม่มี CR มีอายุเฉลี่ย 34.7 ปี (range, 21-44)*

สรุป*: ในภาวะที่ไม่ฉุกเฉิน การตัดม้ามในผู้ป่วยโรค ITP ที่รักษาทางยาไม่ได้ผลควรพิจารณาวิธีการผ่าตัด ทางกล้องวีดิทัศน์ด้วย เนื่องจากได้ผลดีและปลอดภัย*
