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The role of splenectomy before liver transplantation in biliary atresia patients☆,☆☆

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ABSTRACT

Background/Purpose: There is currently no unified view regarding whether liver transplantation or splenectomy should be performed for hypersplenism before liver transplantation in biliary atresia (BA) patients. We herein describe the efficacy of splenectomy before liver transplantation.
Methods: Splenectomy was performed in ten patients with hypersplenism associated with BA. We retrospectively reviewed their perioperative and postoperative courses, the number of leukocytes and thrombocytes, and the MELD score.
Results: The mean age was 17.5 ± 7.0 years (range 11–31 years), and the male-to-female ratio was 1:1. The platelet and leukocyte levels increased after splenectomy and returned to normal levels one month postoperatively. The mean MELD score after splenectomy was significantly decreased after splenectomy: 10 ± 2.1 vs 7.6 ± 1.8. In particular, PT-INR improved. Five patients underwent liver transplantation because of hepatopulmonary syndrome and repeated bouts of cholangitis, whereas the remaining five patients did not undergo liver transplantation because of improvements in the liver function (the mean follow-up period was 56 months). The postoperative complications included portal vein thrombosis and intestinal perforation, but the patient survival rates remained at 100%.
Conclusion: After splenectomy, both pancytopenia and the liver function clearly improved. Splenectomy should therefore be a treatment option for patients with hypersplenism before liver transplantation.
Level of Evidence: Retrospective Comparative Study – Level III.

Hypersplenism is a late and severe complication in biliary atresia (BA). These patients often have clinical hypersplenism with thrombocytopenia and variceal bleeding. Severe thrombocytopenia resulting in bleeding complications during the postoperative period may lead to increased mortality.

We occasionally experience cases with hypersplenism with almost normal liver function. In such cases, we cannot decide whether we should perform splenectomy or early liver transplantation (LT). Although the splenic size generally decreased after LT and thrombocytopenia could be resolved, our previous study showed that 6 of 38 patients who underwent LT in Kyushu University Hospital experienced persistent thrombocytopenia and splenomegaly even several years after LT [1]. We have performed splenectomy before LT in selected cases with normal liver function. However, there is currently no unified view about the treatment. We herein describe the efficacy of splenectomy before LT.

1. Patients and methods

Splenectomy before LT is typically performed for patients with bleeding tendency because of thrombocytopenia (platelet count lower than $50 \times 10^3/\mu l$), sclerotherapy-resistant esophagogastric varices, or relatively preserved liver function. Abdominal ultrasound should be performed to assess the portal blood flow, and patients with a decreased portal blood flow should not undergo splenectomy. Patients with a MELD score >15 should undergo LT with or without splenectomy.

A retrospective study was carried out for BA patients who underwent splenectomy before LT at Kyushu University Hospital. Blood samples were taken before splenectomy and at 1, 6, and 12 months after splenectomy. Pancytopenia, especially neutropenia and thrombocytopenia, was followed up after splenectomy. The liver function was evaluated by measuring serum direct bilirubin (DB), albumin (ALB), aspartate aminotransferase (AST), alanine aminotransferase (ALT) and international normalized ratio of prothrombin time (PT-INR). The severity of hepatic cirrhosis was graded according to the Model for End-Stage Liver Disease scores (MELD scores).

All the data are expressed as the mean ± standard deviation. A single-factor analysis of the variance was used for comparisons among

☆ This retrospective study was performed according to the Ethical Guidelines for Clinical Research published by the Ministry of Health, Labor and Welfare of Japan on July 30, 2003 (revised 2008) and complies with the Helsinki Declaration of 1964 (revised 2008). All parents or guardians of infants in this study gave informed consent prior to their inclusion in this study.

☆☆ Conflict of interest: None of the authors have any conflict of interest to declare concerning the present manuscript.

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the groups using Student's *t*-test and Fischer's exact test. A *p*-value of <0.05 was considered to be significant.

This retrospective study was performed according to the Ethical Guidelines for Clinical Research published by the Ministry of Health, Labor and Welfare of Japan on July 30, 2003 (revised 2008) and complies with the Helsinki Declaration of 1964 (revised 2008). All parents or guardians of infants in this study gave informed consent prior to their inclusion in this study.

2. Results

Ten BA patients underwent splenectomy before LT. The male-to-female ratio was 1:1 and the mean age was 17.5 ± 7.0 (range 11–31) years. All patients had pancytopenia, especially neutropenia (the mean number was 1965 ± 939/μl) and thrombocytopenia (the mean number was $3.1 \pm 1.3 \times 10^4$/μl), thus they were regarded to be indicated for surgical treatment. The mean number of leucocytes increased significantly after splenectomy from 1965 ± 939/μl to 5459 ± 1533/μl ($p < 0.05$). The levels normalized 10.8 ± 4.8 days after splenectomy, and remained stable thereafter. The mean number of platelets increased significantly as well from $3.1 \pm 1.3 \times 10^4$/μl to $21.9 \pm 4.6 \times 10^4$/μl ($p < 0.05$). They peaked at 12.4 ± 2.9 days after splenectomy, normalized at 25.9 ± 8.8 days and stabilized thereafter.

Changes in the laboratory data associated with the liver function and MELD score before and after splenectomy are shown in Fig. 1. The preoperative values of DB, Alb, AST, ALT and PT-INR were 0.3 ± 0.2 mg/dl, 4.2 ± 0.3 g/ml, 76 ± 48 U/L, 79 ± 67 U/L and 1.27 ± 0.11, respectively. These results indicated that the liver function was well controlled. The mean MELD score was 10.0 ± 2.1. The postoperative values of DB, ALB, AST and ALT did not improve significantly. However, PT-INR significantly improved from 1.27 ± 0.11 to 1.09 ± 0.08 (6 months after splenectomy, $p = 0.001$) and 1.08 ± 0.08 (12 months, $p < 0.05$). As a result, the MELD score significantly improved 12 months after splenectomy from 10 ± 2.1 to 7.6 ± 1.8 ($p = 0.01$).

Postoperative complications occurred in 2 patients (20%), including portal vein thrombosis (PVT) (n = 1) and intestinal perforation (n = 1). PVT was detected by follow-up CT at 1 week after splenectomy. Anticoagulation therapy was immediately initiated after the detection of PVT for 2 months, with the administration of warfarin with heparin, adjusted to achieve PT-INR approximately 2.0. Three weeks later after anticoagulation therapy, follow-up CT revealed complete resolution of the thrombus. Thereafter, there was no episode of PVT recurrence, and oral administration of warfarin was discontinued. The case of intestinal perforation occurred in a 16-year-old girl. During splenectomy, the transverse colon strongly adhered to the abdominal wall and we peeled off these adhesions. Six days after splenectomy, intestinal fluids were discharged from the wound, and we performed an emergency operation. The transverse colon was perforated, so we performed washing drainage in the abdominal cavity and temporary colostomy. The patient improved gradually by intensive care after re-operation and the closure of colostomy underwent two months after re-operation.

The characteristics of all patients were shown in Table 1. Five cases finally underwent LT. The MELD score of these patients significantly improved before LT, however, they underwent LT because of intractable cholangitis (n = 4) and hepatopulmonary syndrome (n = 1).

The other five cases did not undergo LT because of an improvement in the liver function. The follow-up period after splenectomy ranged from 14 to 105 months (mean 57.4 ± 40.9 months). The longest follow-up period was more than 8 years without LT.

3. Discussion

Postoperative hypersplenism is a well-known complication in BA. Thrombocytopenia and variceal bleeding occasionally occur. Some BA patients with hypersplenism whose liver function are relatively preserved undergo both LT and splenectomy simultaneously. There is currently no unified view about treatment for hypersplenism before LT in BA patients. Our previous study showed that 15.8% of patients who underwent LT suffered from persistent thrombocytopenia and splenomegaly for several

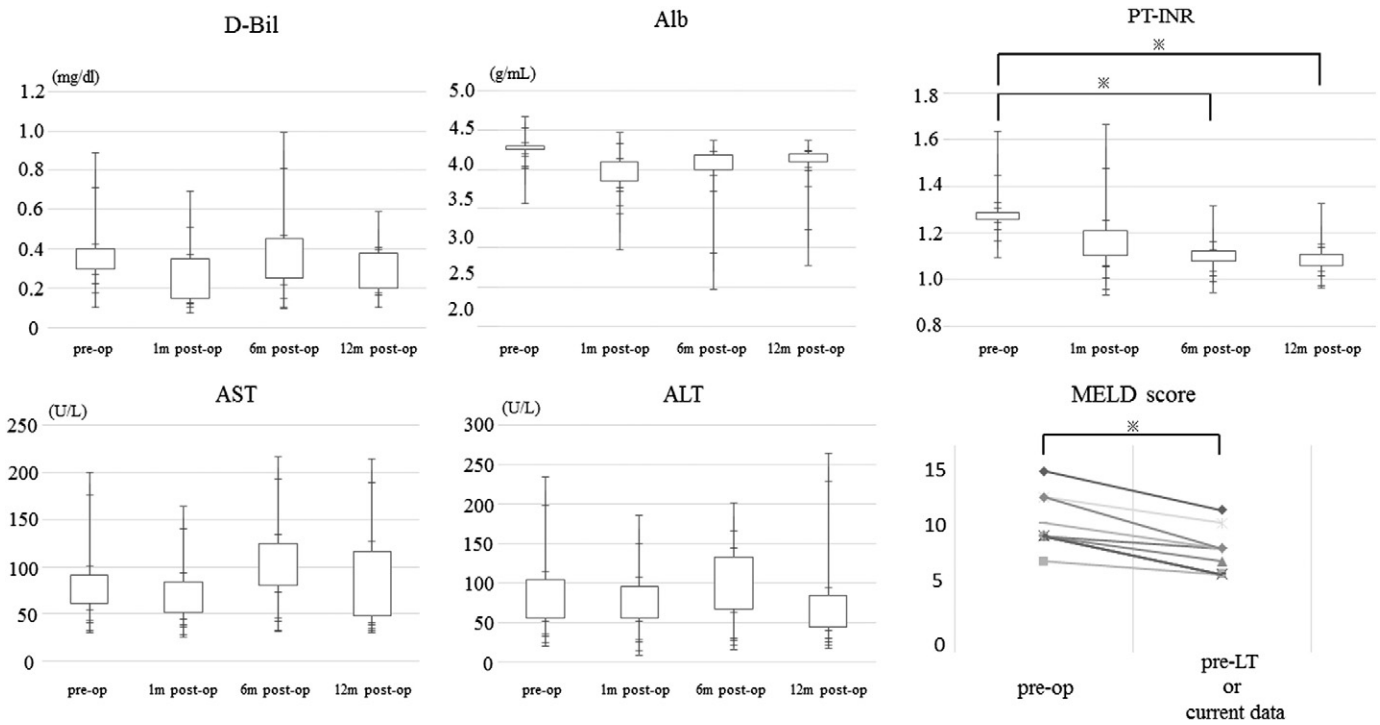

Fig. 1. Changes in serum direct-bilirubin, Albumin, AST, ALT, PT-INR and MELD score before and after splenectomy. (T-Bil: total bilirubin, D-Bil: direct bilirubin, ALB: albumin, AST: asparate aminotransferase, ALT: alanine aminotransferase, PT-INR: prothrombin time-international normalized ratio, MELD score: Model for End-Stage Liver Disease score). Postoperative DB, ALB, AST and ALT did not improve significantly. PT-INR improved significantly from 1.27 ± 0.11 to 1.09 ± 0.08 (6 months after splenectomy, $p = 0.001$) and 1.08 ± 0.08 (12 months, $p < 0.05$). MELD score improved significantly after splenectomy from 10 ± 2.1 to 7.6 ± 1.8 ($p = 0.01$). ※ There is significant difference.