Gut perforation after orthotopic liver transplantation in adults

Jun Xiong, Shen You, Xiao-Shun He

AIM: To describe cases of gut perforation after orthotopic liver transplantation.

METHODS: Data were collected from our center database and medical records. Six of 187 patients (3.2%) who underwent orthotopic liver transplantation from January to December 2005 developed gut perforation. All patients were male with an average age of 46 years. Modified piggyback liver transplantation was performed at the Organ Transplantation Center, First Affiliated Hospital, Sun Yat-Sen University.

RESULTS: Previous operation, steroid therapy, and prolonged portal venous cross clamp time, poor nutritional status and iatrogenic injury were found to be its ecological factors. The patients with gut perforation were found to have fever, increased leukocytes, mild abdominal pain and tenderness. The median portal venous clamp time was 63 min (range 45-72 min), median cold ischaemia time was 11.3 h (range 7-15 h). Median intraoperative blood loss was 500 mL (range 100-1200 mL) and median operation time was 8.8 h (range 6-12 h). None of the six patients developed acute cellular rejection. White cell count was above 18 × 10^9/L in five patients (neutrophilic leukocytes were above 90%) and 1.5 × 10^9/L in one patient. Bacterial culture in drainage liquid revealed enterococci in five patients. Of the 6 patients undergoing orthotopic liver transplantation, 3 survived and 3 died after modified piggyback liver transplantation.

CONCLUSION: Gut perforation occurs after orthotopic liver transplantation in adults. A careful and minimal dissection during OLT, longer retention of the stomach tube, and reducing the portal clamp time and steroid dose should be taken into consideration. If gut perforation is not prevented, then early diagnosis, preferably through detection of enterococci may ensure better survival.

Key words: Orthotopic liver transplantation; Gut perforation; Enterococcus faecalis

Xiong J, You S, He XS. Gut perforation after orthotopic liver transplantation in adults. World J Gastroenterol 2007; 13(14): 2125-2128

http://www.wjgnet.com/1007-9327/13/2125.asp

INTRODUCTION

Gut perforation is a rare complication that occurs after orthotopic liver transplantation (OLT). It is more common in children than in adults and causes surgical morbidity. Steroid administration can induce gut perforation after OLT. Steroid therapy often accompanies OLT because it decreases inflammation by suppressing macrophages, lymphocytes and other inflammatory factors. However, it also stimulates the secretion of gastric acid and pepsin, inhibits the secretion of gastric mucus, and reduces the resistance of gastric mucosal barrier which can induce ulcers and perforate vulnerable sites in the gut. Moreover, glucocorticosteroids reduce the utilization of glucose and enhance gluconeogenesis and proteolysis, thus delaying the repair of gastrointestinal injury which can cause microbes to perforate the gut.

Early diagnosis of gut perforation may be difficult, and if the diagnosis is delayed, the condition may be life-threatening. Etiological factors include previous operation, steroid therapy, and prolonged portal venous cross clamp time, poor nutritional status and iatrogenic injury. This study was to describe cases of gut perforation after OLT in adults encountered at our facility over a one-year period.

MATERIALS AND METHODS

Data were collected from our center database and medical records. Six of 187 patients (3.2%) who underwent OLT from January to December 2005 developed gut perforation. All patients were male with an average age of 46 years. Modified piggyback liver transplantation was performed at the Organ Transplantation Center, First Affiliated Hospital, Sun Yat-Sen University. Table 1 summarizes the operative history, liver dysfunction, and post-surgical outcome of the six patients. Of the four patients undergoing operation, two received OLT, one a hepatectomy, and one a splenectomy with extensive esophageal devascularization. Among the three patients with cirrhosis, stenosis of the bile duct was found in one after OLT, and hepatoma in two.
venous bypass was performed in one of the three patients. Immunosuppression was achieved with tacrolimus (maintaining blood drug concentration at 8-12 μg/mL) and steroid (diminishing from 1 g/d to 4 mg/d) in all patients.

RESULTS

Parameters of OLT
Of the six patients with gut perforation, four patients (67%) underwent a difficult dissection due to dense adhesions caused by a previous abdominal surgery. The median portal venous clamp time was 63 min (range 45-72 min), median cold ischaemia time was 11.3 h (range 7-15 h), median intraoperative blood loss was 500 mL (range 100-1200 mL) and median operation time was 8.8 h (range 6-12 h). None of the six patients developed acute cellular rejection. White cell count was above 18 × 10⁹/L in five patients (neutrophilic leukocytes were above 90% and 1.5 × 10⁹/L. Bacterial culture revealed enterococci in five patients. None of the six patients developed acute cellular rejection.

Symptoms and diagnosis of gut perforation
All patients with gut perforation after OLT complained of sudden subtle or moderate abdominal pain, abdominal tenderness without rebound tenderness. Their temperature ranged from 36.5℃ to 38℃ without chill. The diagnosis of gut perforation was established based on a stool-like substance discovered in the abdominal incision and a bile-like or unclean liquid from the drainage tube detected after cholangiography or peroral administration of methyleneum coeruleum 11-12 d after OLT.

Site of gut perforation and corrective surgery
The incidence rate of perforation in the jejunum, transverse colon, ileum and stomach was 33%, 33%, 17% and 17%, respectively. Patient 4 had stomach and jejunum perforation. To correct the perforated gut, two patients underwent simple oversew of the perforation and one colostomy. Patient 5 underwent oversew as well as gastrostomy and enterostomy for multiple perforations. Patient 2 received small bowel resection and enterostomy. None of the six patients had reperforation.

Surgical observations and post-surgical outcome
Three patients (50%) died of gut perforation 2-33 d after operation for gut perforation. Perforation of Michale diverticulum at the distal segment of ileum and seriously contaminated abdominal cavity were observed during surgery in patient 2. The patient died of multiple organ failure on d 9 after operation. Similarly, multiple perforations and seriously contaminated abdominal cavity were observed during surgery in patient 4. This patient died of multiple organ failure 2 d after operation. Perforation of the transverse colon and bulky stool in the abdominal cavity were observed during surgery in patient 6. The patient died of multiple organ failure 33 d after operation. The other patients (50%) recovered after surgery. All three survivors were characterized by mild contamination of the abdominal cavity.

DISCUSSION
The incidence rate of perforation after OLT in our study was 3.2%. Studies showed that the incidence rate of perforation after OLT is 1%-5.3%[1-3] in adults and 8.3%-14% in children[6,9]. The higher incidence in children than in adults is most likely due to tight adhesions during hepatectomy and portal venous clamp time and portal venous collateral circulation. Iatrogenic injury may be another important reason for gut perforation. In our study, two cases had gastric wall injuries when the adhesion was dissected. Other risk factors for gut perforation include postoperative immunosuppression causing difficulties in sealing microperforations, and some unidentified congenital diseases, such as diverticula. Portal venous clamp time and portal venous collateral circulation can also be important factors for gut perforation[6,9]. If portal venous clamp time is long, collateral circulation is incomplete leading to gut congestion. These factors may have contributed to gut perforation in our study in that four patients had long portal venous clamp time (above 65 min) and portal venous collateral circulation was insufficient. Liver dysfunction or rejection has not been
associated with perforation\cite{12,15,16}, and accordingly, in our group, none had acute rejection.

Many other factors, including early postoperative portal vein thrombosis\cite{16,18,19} and intra-abdominal bleeding\cite{5,13} after OLT requiring re-operation, have been suggested to increase the risk of gut perforation\cite{17} but were not encountered in the patients of this study.

Gut perforation following OLT can occur in all parts of the gastrointestinal tract\cite{6,10,15}. In our study, it was observed in the ileum, transverse colon, jejunum, stomach, or in both of jejunum and stomach. Initially, the surgical treatment was to oversew the perforation, particularly for the small bowel. To prevent re-perforation, resection should be performed for colonic lesions. More radical suggestions include planned re-exploration for high-risk cases between three and five days post-OLT. However, we think this is unnecessary because of the low-incidence of gut perforation after OLT. The incidence rate of re-perforation ranges 31%-40% and no re-perforation occurred in our study.

The mortality after OLT is higher in patients with gut perforation than in those without\cite{11,20-22}. In our study, the patients who died had more serious contamination of the abdominal cavity than the survivors, suggesting that the degree of abdominal infection is directly related to postoperative mortality. Therefore, early diagnosis and treatment are the most important factors for decreasing morbidity.

Clinical features of gut perforation include fever, presence of bowel content from a drain, increased white blood cell count, abdominal distension and tenderness\cite{4}. All these symptoms occurred in our patients. Abdominal pain alone should not be considered the most important index of perforation because patients with OLT are often given large doses of steroid and immunosuppressant which could make this feature atypical. However, when it is accompanied with a high white blood cell count and fever with unknown reason, abdominal pain may be a better indicator. Free gas seen on a plain abdominal X-ray has been reported in 30-70 cases, but does not seem to be an early predictor of gut perforation\cite{9}. If it was reported that abdominal ultrasound is helpful in localizing and aspirating intraperitoneal collections if perforation is suspected\cite{10}. However, in our study, although all cases received an ultrasound, the findings were not specific. In our study, the majority of patients showed enterococci in bacterial cultures, suggesting that a final diagnosis of gut perforation based on the presence of enterococci\cite{20}. This is why the presence of bowel contents and enterococci from a drain, increased white cell counts and abdominal discomfort are good indicators of gut perforation. Once gut perforation has been identified, exploration is an exclusive approach and steroid treatment should be stopped. In our study, all patients ceased steroid usage and none of them had acute cellular rejection.

In conclusion, gut perforation after OLT is a serious complication and frequently results in death. A careful and minimal dissection during OLT, longer retention of the stomach tube, and reducing the portal clamp time and steroid dose should be taken into consideration. If gut perforation is not prevented, then early diagnosis, preferably through detection of enterococci may ensure better survival.

REFERENCES

1. Koep LJ, Starzl TE, Weil R. Gastrointestinal complications of hepatic transplantation. Transplant Proc 1979; 11: 257-261
2. Lebeau G, Yanaga K, Marsh JW, Tzakis AG, Makowka L, Gordon RD, Todo S, Stieber AC, lwatsuki S, Starzl TE. Analysis of surgical complications after 397 hepatic transplantations. Surg Gynec Obstet 1990; 170: 317-322
3. Moncorge C, Baudin F, Vigouroux C, Ozier Y, Ortega D, Lecam B, Garnier JF, Houssin D, Chapuis Y, Conseiller C. Liver transplantation in adults: postoperative management and development during the first months. Ann Fr Anesth Reanim 1989; 8: 497-517
4. Vilca Melendez H, Vougas V, Muiresan P, Andreani P, Mieli-Vergani G, Rela M, Heaton ND. Bowel perforation after paediatric orthotopic liver transplantation. Transpl Int 1998; 11: 301-304
5. Soubrane O, el Meteoni M, Devictor D, Bernard O, Houssin D. Risk and prognostic factors of gut perforation after orthotopic liver transplantation for biliary atresia. Liver Transpl Surg 1995; 1: 2-9
6. Yamanaka J, Lynch SV, Ong TH, Baldersen GA, Strong RW. Posttransplant gastrointestinal perforation in pediatric liver transplantation. J Pediatr Surg 1994; 29: 635-638
7. Muiiesan P, Vorgani D, Mieli-Vergani G. Liver transplantation in children. J Hepatol 2007; 46: 340-348
8. Reves J, Bueno J, Kocosshis S, Green M, Abu-Elmagd K, Furukawa H, Barksdale EM, Strom S, Fung J, Todo S, Irish W, Starzl TE. Current status of intestinal transplantation in children. J Pediatr Surg 1998; 33: 243-254
9. Marujo WC, Stratta RJ, Langnas AN, Wood RP, Markin RS, Shaw BW. Syndrome of multiple bowel perforations in liver transplant recipients. Am J Surg 1991; 162: 594-598
10. Caraceni P, Fagioulis S, Wright HI, Nadir A, Van Thiel DH. Gastrointestinal complications of liver transplantation. Ital J Gastroenterol 1995; 27: 29-39
11. Casavilla A, Moysiuik Y, Stieber AC, Starzl TE. Esophageal complications in orthotopic liver transplant patients. Transplantation 1991; 52: 150-151
12. Kirby RM, McMaster P, Clements D, Hubscher SG, Angrisani L, Sealey M, Gunson BK, Salt PJ, Buckels JA, Adams DH. Orthotopic liver transplantation: postoperative complications and their management. Br J Surg 1987; 3: 71-11
13. Pungpapong S, Alvarez S, Hellinger WC, Kramer DJ, Willingham DL, Mendez JC, Nguyen JH, Hewitt WR, Aranda-Michel J, Harnois DM, Rossor BG, Hughes CB, Grewal HP, Satyanarayana R, Dickson RC, Steers JL, Keaveny AP. Peritonitis after liver transplantation: Incidence, risk factors, microbiology profiles, and outcome. Liver Transpl 2006; 12: 1244-1252
14. Lange R, Erhard J, Sander A, Kenniz J, Garkuwa DA, Egler FW. Animal experiment studies of arterialization of the portal vein in liver transplantation using the Göttingen minipig. Langenbecks Arch Chir 1997; 382: 277-283
15. Shaked A, Vargas J, Csete ME, Kiai K, Jurim O, Colquhoun S, McDiamid SV, Ament ME, Busuttil RW. Diagnosis and treatment of bowel perforation following pediatric orthotopic liver transplantation. Arch Surg 1993; 128: 994-998; discussion 998-999
16. Bonatti H, Muiiesan P, Connelly S, Baker A, Mieli-Vergani G, Gibbs P, Heaton N, Rela M. Hepatic transplantation in children under 3 months of age: a single centre's experience. J Pediatr Surg 1997; 32: 486-488
17. Peng T, Peng MH, Li LQ, Dong YL, Yang DH, Lu BY, Chen XG, Guo Y, Xiao KY, Chen B, Zhong Q, Wei MY. Intestinal perforation after combined liver-kidney transplantation for a case of congenital polycystic disease. World J Gastroenterol 2004; 10: 2769-2771
18. Yamanaka J, Lynch SV, Ong TH, Fawcett J, Robinson HE, Beale K, Baldersen GA, Strong RW. Surgical complications
and long-term outcome in pediatric liver transplantation. *Hepatogastroenterology* 2000; 47: 1371-1374

19 **Ferraz-Neto BH**, Sakabe D, Buttros DA, Resende MB, Afonso RC. Portal vein aneurysm as late complication of liver transplantation: a case report. *Transplant Proc* 2004; 36: 970-971

20 **Hasegawa T**, Nara K, Kimura T, Soh H, Sasaki T, Azuma T, Okada A. Oral administration of tacrolimus in the presence of jejunostomy after liver transplantation. *Pediatr Transplant* 2001; 5: 204-209

21 **Meijer S**, Hoitsma HF, Visser JJ, de Lange JJ. Long term survival following orthotopic liver transplantation in pigs; with special reference to gastric ulcer complications. *Neth J Surg* 1984; 36: 168-171

22 **Matthews DE**, West KW, Rescorla FJ, Vane DW, Grosfeld JL, Wappner RS, Bergstein J, Andreoli S. Peritoneal dialysis in the first 60 days of life. *J Pediatr Surg* 1990; 25: 110-115; discussion 116

23 **George DL**, Arnow PM, Fox AS, Baker AL, Thistlethwaite JR, Emond JC, Whittington PF, Broelsch CE. Bacterial infection as a complication of liver transplantation: epidemiology and risk factors. *Rev Infect Dis* 1991; 13: 387-396