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World J Gastroenterol 2007 April 14; 13(14): 2125-2128
World Journal of Gastroenterology ISSN 1007-9327

RAPID COMMUNICATION

Gut perforation after orthotopic liver transplantation in adults

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Received: 2007-02-03 Accepted: 2007-03-24

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

Abstract

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

METHODS: Data were colleted 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.

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 gut perforation. 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 colleted 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 esphagogastric devascularization. Among the three patients with cirrhosis, stenosis of the bile duct was found in one after OLT, and hepatoma in two. Portal

Table 1 Description of patients with gut perforation after OLT

Patient No.	Age (yr)	Sex	Operative history	Diagnosis	Localization	Treatment	Outcome
1	38	Male	None	Hepatoma	Ileum	Oversew	Survived
2	40	Male	None	Cirrhosis	Jejunum	Small bowel resection, enterostomy	Died
3	49	Male	Splenectomy, extensive esophagogastric devascularization	Cirrhosis	Stomach	Oversew, gastrostomy, enterostomy	Survived
4	49	Male	OLT	Stenosis of bile duct	Stomach, jejunum	Oversew, enterostomy	Died
5	59	Male	Hepatectomy	Cirrhosis	Transverse colon	Oversew	Survived
6	41	Male	OLT	Hepatoma	Transverse colon	Colostomy	Died

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 18×10^9/L in five patients (neutrophilic leukocytes were above 90% and 1.5×10^9/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 methylenum coeruleumin 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 3 underwent oversewn 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 peration 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[4-6]. The higher incidence in children than in adults is most likely due to tight adhesions between the liver and formation of intestinal loops during portoenterostomy before liver transplantation. These tight and diffuse adhesions complicate hepatectomy and necessitate extensive gut dissection, which increases the risk of gut perforation after transplantation. In support of this, the majority of adults with gut perforation after OLT in this study had dense adhesions complicating the OLT procedure due to previous operation[7,8].

The etiology of gut perforation is multifactorial[6,9-11]. As mentioned above, previous abdominal surgery and intraperitoneal adhesions[12] may result in difficult or extensive dissection and are likely the underlying cause of most gut perforations after OLT[13]. Iatrogenic injury[5,9] 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[5,14]. 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[12,15,16], and accordingly, in our group, none had acute rejection.

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

Gut perforation following OLT can occur in all parts of the gastrointestinal tract[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[13,20-22]. 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[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[4]. It was reported that abdominal ultrasound is helpful in localizing and aspirating intraperitoneal collections if perforation is suspected[5]. 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[23]. 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.

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