Management of Asymptomatic Gallstones in Renal Transplantation

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Background: In solid organ transplantation patients, complications of cholelithiasis may run a fulminant course, resulting in high morbidity and mortality under immunosuppression and may even result in rejection. Here, we reviewed medical records of 66 patients in order to determine the outcome of management approach for asymptomatic gallstones in renal transplantation patients.
Methods: We retrospectively reviewed clinical courses of 66 cases of renal transplantation performed between 2000 and 2012 at Kosin University Gospel Hospital.
Results: Among 66 cases, eight had gallstones before transplantation. Three of these cases had undergone previous cholecystectomy for symptomatic gallstones, one had a simultaneous laparoscopic cholecystectomy and renal transplantation, and four were observed by regular abdominal ultrasonography. One patient was found to have cholangitis, and endoscopic retrograde biliary drainage was performed, resulting in alleviation of symptoms. Among 58 cases without preoperative gallstones, three developed gallstones after transplantation. One patient had cholecystitis, and the symptoms subsided after conservative treatment.
Conclusions: For patients with asymptomatic gallstones who are awaiting renal transplantation, expectant management should be considered.

Key Words: Kidney transplantation, Prophylactic laparoscopic cholecystectomy, Gallstones
중심 단어: 신장이식, 예방적 담낭절제술, 담석

INTRODUCTION

Gallstones are common, with an approximate 10% incidence in the Western world and a 2.0% incidence in Korea(1-3). The incidence increases with age and is more common in women(4). In the general population, asymptomatic gallstones are often created unless specific surgical indications are met(5,6). However, following solid organ transplantation, patients taking immunosuppressants may be

predisposed to gallstone complications(7).

Asymptomatic gallstones that are followed with observation result in a 1.0% complication rate annually, including effects such as cholecystitis, cholangitis, and biliary pancreatitis(8). One study reports an approximately 18% 15-year risk for symptomatic disease following observation(9). In solid organ transplantation cases, there is a higher rate of gallstones leading to fulminant complications, and immunosuppressive medications could result in a higher mortality(7,10-13). Moreover, complications could result in rejection or failure of the transplanted organ(14).

A laparoscopic cholecystectomy is standard treatment for gallstone patients presenting with surgical indications(15-17). However, in solid organ transplantation patients, there is debate about performing prophylactic laparoscopic cholecystectomies for the same indications due to different complication courses(15-18). We reviewed renal transplantation

cases at Kosin University Gospel Hospital between 2000 and 2012 to assess the clinical course of gallstone cases.

MATERIALS AND METHODS

We performed chart review for 66 patients who underwent renal transplantations at Kosin University Gospel Hospital to obtain their demographic information and clinical data. In order to obtain details about biliary symptoms and other medical history, we used patients' initial medical examinations and surgical consultations. We additionally reviewed the results of follow-up examinations.

Among 66 patients, 64 patients underwent preoperative abdominal ultrasonography or abdominal computed tomography in an effort to detect other abdominal disease. After transplantation, regular ultrasonography of the transplanted kidney was performed, with abdominal survey including assessment of the liver, biliary system, and pancreas, as well as abdominal computed tomography.

We used SPSS ver. 18.0 (IBM Co., Armonk, NY, USA) to compare the mean and median values of each variable.

RESULTS

Between 2000 and 2012, 66 patients underwent renal transplantations in Kosin University Gospel Hospital. The mean age of patients at the time of transplantations was 47.6 years (range, 21~74). There were 37 male patients (56.1%) and 29 female patients (43.9%). We performed preoperative ultrasound in 64 cases. The mean period of follow-up from first preoperative abdominal ultrasound was 94.8 months (median, 95.5), and the mean period of follow-up from transplantation was 77.1 months (median, 63.6). The median period from first abdominal ultrasonography to transplantation was 1.7 months.

We observed acute rejection in six cases, chronic rejection in two cases, and graft failure in one case. Hospital death occurred in one case secondary to brain hemorrhage on postoperation day 48. The causes of dialysis included glomerulonephritis (n=35, 53%), diabetic nephritis (n=7, 10.6%), polycystic kidney disease (n=1, 1.5%), and systemic causes included hypertension (n=15, 22.7%) and other nephropathy (n=8, 12.1%). The immunosuppressant used

after transplantation was cyclosporine A in 35 cases (53%) and tacrolimus in 31 cases (47%). Aside from two cases, abdominal ultrasonography was performed for all patients. In all except the one case of hospital death, regular follow-up with ultrasonography was performed during 6~12 month periods (Table 1).

Among the 66 cases, preoperative abdominal ultrasonography and history taking revealed eight cases of gallstones (12.1%). Three cases were in patients with prior cholecystectomies for symptomatic gallstones. Because of multiple gallstones, one case had a simultaneous laparoscopic cholecystectomy with renal transplantation. And the remainder had no gallstone treatment.

Previous cholecystectomies were performed because of symptomatic gallstones, and one of those three cases was performed before a diagnosis of renal disease. In those cases, there were no biliary complications. The case of simultaneous laparoscopic cholecystectomy during transplantation was discharged from the hospital without surgical complications and continues without complications 7 months postoperatively. Among four cases without gallstone treatment, biliary complication occurred in one case. Cholangitis and sludge in the common bile duct were found, so endoscopic retrograde cholangiogram and papillotomy were performed. The patient was managed with endoscopic retrograde biliary drainage insertion and antibiotics. This episode occurred 136 months after renal transplantation.

Table 1. Clinical characteristics

Clinical characteristic	No. (%)
Total no. of patients	66
Male	37 (56.1)
Female	29 (43.9)
Mean age at transplantation (yr)	47.6
Cause of dialysis	
GN	35 (53)
DN	7 (10.6)
PCKD	1 (1.5)
Systemic disease include HTN[a]	15 (22.7)
Other nephropathy[b]	8 (12.1)

Abbreviations: GN, glomerulonephritis; DN, diabetic nephropathy; PCKD, polycystic kidney disease; HTN, hypertension.
[a]HTN, Autoimmune disease; [b]Obstructive nephropathy, membranous nephropathy.

Among 58 cases without evidence of gallstones during the first preoperative abdominal ultrasonography, three cases had newly developed gallstones postoperatively. They developed after 108, 144, and 110 months, respectively. All three cases used cyclosporine A as an immunosuppressant. One case resulted in cholecystitis as a biliary complication, but it resolved with conservative management without cholecystectomy (Fig. 1). Two cases did not have preoperative ultrasonography and did not have evidence of gallstones during the first postoperative ultrasonography.

There were no cases of graft failure due to biliary complications.

DISCUSSION

In a large study of autopsies, Lieber(19) reported that incidence of gallstones was 11.6% in 26,895 people representing a general Western population and 30.2% in patients with diabetes mellitus. In Korea, 2007 data reported the incidence as 2.0%(1). In our review, there were eight cases in 65 patients (12.1%) with end stage renal disease who were waiting for renal transplantations.

The management of asymptomatic gallstones in the general population is well established. If specific surgical indications, such as the size of gallstone, coexistence of tumors, and pancreatobiliary ductal system anomalies, are not met, the standard management is observation(20). However,

in the case of a solid organ transplantation, complications of gallstones could be more fulminant and even cause graft failure. Further, immunosuppression may mask signs of inflammation and delayed diagnosis of cholecystitis can occur(21). Concomitant diseases like diabetes mellitus may increase complication rate(22); therefore, there is some debate regarding prophylactic cholecystectomy in these cases(7,10-13). Moreover, after the introduction of laparoscopic cholecystectomy and establishment of its safety, there have been more persuasive suggestions for prophylactic laparoscopic cholecystectomy(23).

Some authors suggest that routine prophylactic cholecystectomy is not justified because only a small number of patients with asymptomatic gallstones develop symptoms after transplantation(16,24). There are some reports about the natural history of asymptomatic gallstones in transplant patients. The rate of developing symptoms in transplant population is not greater than the normal population(9,25). Melvin et al.(26) have evaluated cholecystectomy in kidney/pancreas transplant patines, concluded that renal transplant recipients are not at higher risk for biliary tract disease than the normal population. Kao et al.(27) suggested expectant management for asymptomatic cholelithiasis is favored in kidney/pancreas transplant patients, resulting in 2:1,000 deaths compared with 5:1,000 for prophylactic cholecystectomy.

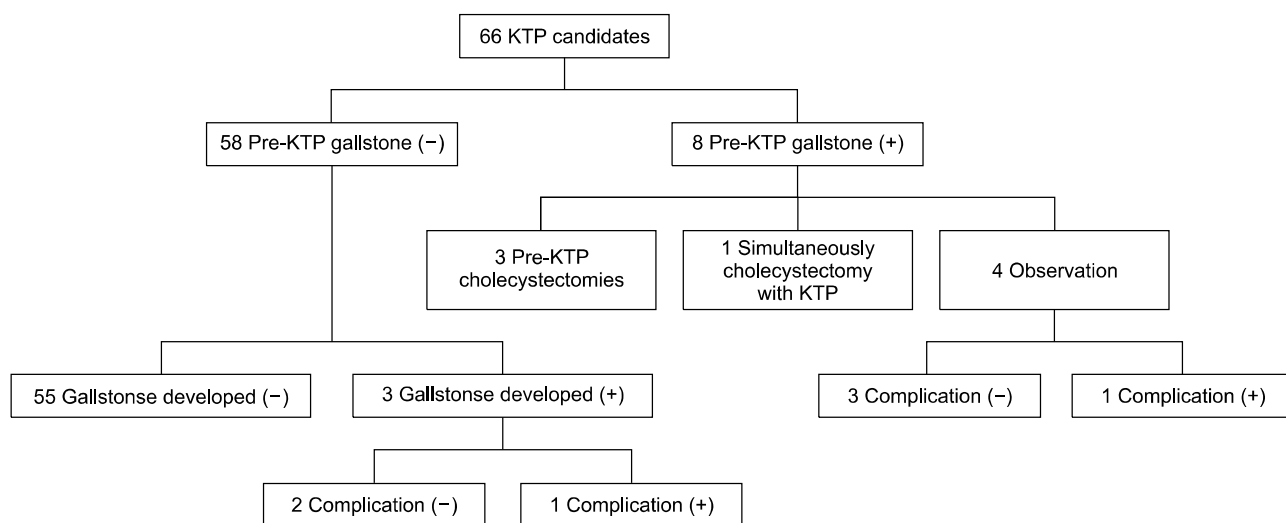We observed four cases of asymptomatic gallstones which

Fig. 1. Distribution of diagnosed gallstones in renal transplantation patients. Abbreviation: KTP, renal transplantation.

were diagnosed before transplantation, and one case developed sludge in the common bile duct, causing obstruction and cholangitis. Endoscopic retrograde cholangiogram, papillotomy, balloon swap to remove the sludge, and retrograde biliary drainage and antibiotics were used.

Risk factors for gallstone include age, gender, race, obesity, diabetes, hyperlipidemia, oral contraceptive use, pregnancy, rapid weight loss, and cyclosporine A after transplantation(12,28). Cyclosporine A could affect the biliary system by decreasing bile flow, leading to cholestasis(29,30). These mechanisms help in forming the nucleus of a gallstone(31). We report three of 58 cases (5.2%) without gallstones before renal transplantation where gallstones developed postoperatively at 108, 144, and 110 months, respectively, and all used cyclosporine A. However, we only began using tacrolimus after 2006, and the follow-up period is relatively short to compare the rate of gallstone development based on immunosuppressant. Maio et al.(21) suggested regular ultrasonographic screening in an immunocompromised patients even after transplantation to identify gallstones.

The standard surgical treatment of gallstones meeting general surgical indications is laparoscopic cholecystectomy. Outcomes include pain reduction, reduced bleeding, improved wound infection, and shorter hospital stay and early resumption to oral immunosuppression than after conventional cholecystectomy(23,32). Laparoscopic cholecystectomy can be performed safely with low morbidity in renal transplant patients who have symptomatic gallstone disease. The morbidity rate is comparable to nontransplant patients(16). Prompt surgical intervention is desirable for specific surgical indication both pretransplantation and posttransplantation.

There are some case reports supporting simultaneous laparoscopic cholecystectomy with renal transplantation as well as laparoscopic cholecystectomy before renal transplantation(33). In our hospital, there was one case of simultaneous laparoscopic cholecystectomy and renal transplantation. The patient was discharged without surgical complications and without adverse sequelae.

CONCLUSION

In our study complications of asymptomatic gallstones occurred in one of four cases. And the symptoms resolved without operation. Therefore, we suggest that expectant management is the preferred strategy for kidney transplant recipients with asymptomatic gallstones.

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