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Case Report

Acalculous Gallbladder Perforation and Coronary Artery Aneurysm after Kidney Transplantation

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Although gallbladder (GB) perforation due to acalculous cholecystitis after kidney transplantation is rarely observed, it can be life threatening and result in cholecystectomy. Coronary artery aneurysm (CAA) is also rare and may require invasive therapy depending on its diameter. We report herein the case of a 69-year-old female who developed GB perforation due to acalculous cholecystitis after kidney transplantation and underwent cholecystectomy. The patient was later invasively treated when CCA was detected by coronary angiography.

Key Words: Kidney transplantation, Acalculous cholecystitis, Coronary artery aneurysm
중심 단어: 신장이식, 비결석성 담낭염, 관상동맥류

Introduction

Cases of acalculous cholecystitis leading to the infarction or perforation of the gallbladder (GB) are extremely rare and are worth reporting because, while complications due to calculous cholecystitis (cholecystitis, cholangitis, and pancreatitis) after kidney transplantation are generally known to occur at the rate of 12～27%, only 6% of patients with acute GB inflammation are reported to have acalculous cholecystitis(1,2). The morbidity rate of GB perforation in patients with acalculous cholecystitis is at least 2-fold higher than that of cholecystitis resulting in perforation due to GB stones, and the reported mortality rate is also high; early diagnosis and prompt medical intervention are therefore required(2).

Coronary artery aneurysm (CAA) is a relatively rare disease defined as coronary dilation exceeding either the diameter of the normal adjacent segments or the diameter of the patient's largest coronary vessel 1.5-fold, and has an incidence rate of 1.5～5%(3). CAA occurs as a consequence of congenital or acquired malformation, primarily from atherosclerosis in adults and acute conditions resulting from Kawasaki disease in children. CAA is generally asymptomatic, but patients may present with myocardial infarction (MI) or cardiac tamponade. There is no consensus as of yet, however, on the optimal therapy for it(4).

Reported herein is the case of a patient who was treated surgically for GB perforation due to acalculous cholecystitis after kidney transplantation, readmitted due to chest pain, and who then underwent coil embolization for CAAs observed through coronary angiography. The results of a review of the existing literature are also reported.

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Case Report

A 69-year-old female patient complained of right upper abdominal pain on postkidney transplantation day 7. The patient was initially diagnosed with hypertension resulting in chronic kidney disease in 2008 and had been on hemodialysis since 2010 when she

progressed to chronic kidney disease stage V. She underwent kidney transplantation in April 2012 when her sister donated a kidney to her. Human leukocyte antigen (HLA) typing was performed, and HLA antigens were matched. The postoperative immunosuppressive therapy consisted of tacrolimus, prednisolone, mycophenolate mofetil, and basiliximab, and the patient's serum blood urea nitrogen (BUN) and creatinine (Cr) levels (14.0 and 0.97 mg/dL, respectively) had normalized on postoperative day 2, with 2,000～3,000 mL/day urine output maintained.

The patient complained of right upper abdominal pain on postoperative day 7 with 130/80 mmHg blood pressure, 148 beats per minute pulse rate, 28 breaths per minute respiratory rate, 37.4°C body temperature, and a positive Murphy's sign. The complete blood count revealed the following: 30,660/mm^3 white blood cell (WBC) count, 11.4 g/dL hemoglobin, and 245,000/mm^3 platelets. The laboratory parameters demonstrated an elevated C-reactive protein (CRP) 17.2 mg/dL, aspartate aminotransferase (AST) 29 IU/L, alanine aminotransferase (ALT) 47 IU/L, lactate dehydrogenase 413 IU/L, alkaline phosphatase 56 IU/L, γ-glutamyl transferase 91 IU/L, total bilirubin 1.5 mg/dL, and direct bilirubin 1 mg/dL. The BUN level was 10.9 mg/dL with Cr 0.69 mg/dL, Na 135 mEq/L, K 4.4 mEq/L, and Cl 102 mEq/L. Urinalysis showed pH 5.5, specific gravity 1.015, glucose (-), ketone (-), blood (1+), protein (1+), bilirubin (-), urobilinogen (trace), red blood cell 10～29/high power field (HPF), and WBC 5～9/HPF. The serum tacrolimus trough level was 6.3 ng/mL. A simple abdomen X-ray film showed general bowel distension and the abdomen and pelvis computed tomography (Fig. 1) revealed no stones in the GB or biliary tract and no biliary dilation or obstruction, but did display a distended GB with irregular GB mucosa and defects in the GB wall. The patient was treated with antibiotics with a suspicion of acute acalculous cholecystitis and GB perforation; cholecystectomy was performed on postoperative day 9.

The operative findings included a 0.5 cm perforation in the GB fundic mucosa, with multiple necrotic lesions in the GB walls and the collection of a large amount of fluid (Fig. 2). The macroscopic findings included no GB stones, no sludge nor polyps in the GB while the microscopic findings included diffusely necrotic lesions of the GB mucosa but no other findings

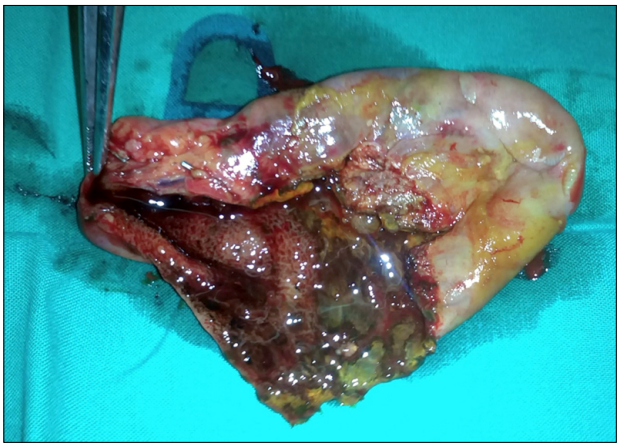

Fig. 2. This gallbladder (GB) specimen consists of a previously opened GB measuring 10 cm in length and 4.5 cm in diameter. The serosa is dull gray tan and the mucosa is diffusely necrotic in appearance. There is no tumorous appearance and no gallstones, GB sludge nor GB polyps in this specimen.

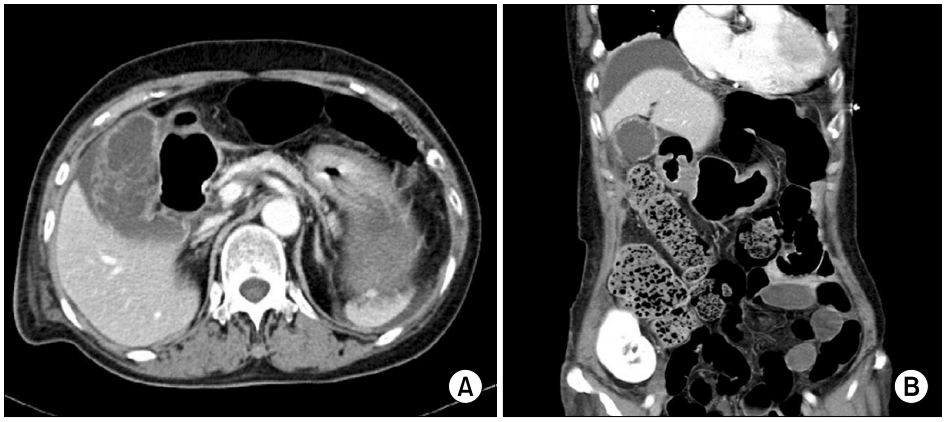

Fig. 1. Abdomen and pelvic computed tomography findings of the patient. (A) Cross section image revealing the irregular mucosa of gallbladder (GB) with suspicious wall defects and distended GB without definite radiopaque stone in GB. (B) Coronal section image showing a small amount of ascites in the perihepatic space and bowel ileus.

such as tumorous areas. Postoperatively, the right upper abdominal pain was resolved, and the laboratory parameters were normalized: WBC 4,620/mm^3, CRP 0.37 mg/dL, AST 20 IU/L, ALT 36 IU/L, and total bilirubin 0.8 mg/dL. The patient was discharged from the hospital on day 21 after the kidney transplantation with little change in BUN and Cr levels (9.0 and 0.70 mg/dL, respectively), maintaining about 1,500～2,500 mL/day urine output.

One week after discharge, the patient presented herself at the emergency room complaining of acute chest pain at rest, with onset 12 hours before visiting the hospital on postoperative day 28. After being previously discharged, the patient had taken tacrolimus, prednisolone, and mycophenolate mofetil and maintained a urine output of approximately 1,500 mL/day. The follow-up outpatient serum chemistry showed little change in BUN and Cr levels (10.6 and 0.88 mg/dL, respectively) compared to those when discharged, and the patient's postoperative course was uneventful. At the emergency room, her blood pressure was 145/76 mmHg, pulse rate was 98 beats per minute, respiratory rate was 18 breaths per minute, body temperature was 37.1°C, and the patient was alert. An echocardiogram showed a depressed ST segment in the inferior leads (II, III, and aVF) with sinus tachycardia. Serum Cr kinase-MB and troponin-I were 4.2 and 0.47 ng/mL, respectively and serum D-dimer was elevated to 2.40 mg/L. A chest X-ray film showed cardiomegaly with little change compared to that in the previous image and no signs of pulmonary edema. The echocardiographic finding indicated enlargement of the left atrium and left ventricle, 55% left ventricular ejection fraction, normal overall contraction of the left ventricle, no findings of abnormal regional wall motions and suggestive pulmonary thromboembolism. With a suspicion of non-ST-segment elevation MI (NSTEMI), the patient underwent anticoagulant therapy, after which the chest pain was relieved.

The coronary angiography performed on postoperative day 29 revealed no findings of stenosis in the right coronary artery nor the left anterior descending artery but demonstrated saccular aneurysmal change at the distal segments of the obtuse marginal branch in the left circumflex artery (Fig. 3). On postoperative day 33, coronary angiography was repeated for embolization of the coronary aneurysm. Tornado coils (3.0 mm×2.0 cm) were placed into the aneurysmal sac, after which the distal blood flows under the aneurysms disappeared. After the embolization, the patient was discharged from the hospital without any chest pain episodes. At present, 6 months after kidney transplantation, the patient's serum BUN is 8.7 g/dL and Cr is 0.88 mg/dL.

Discussion

GB perforation due to acalculous cholecystitis after kidney transplantation is very rarely reported. According to a case report in a foreign country, GB perforation

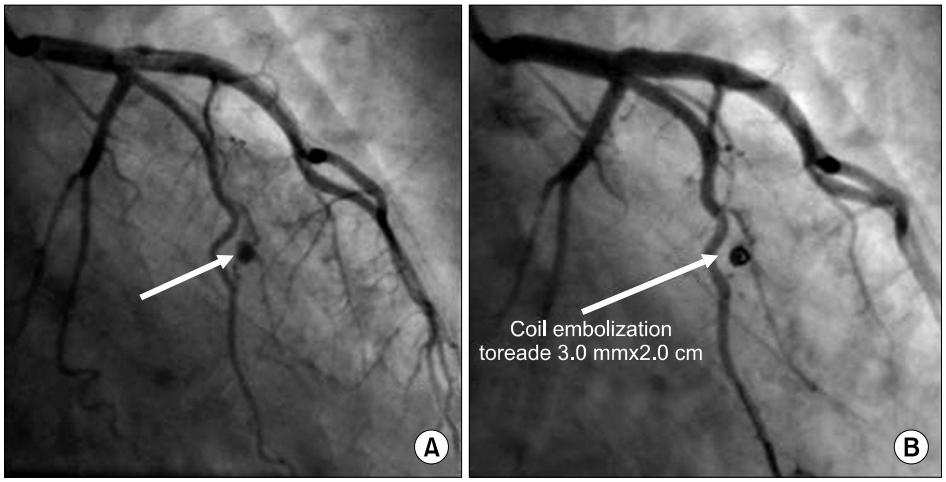

Fig. 3. Coronary angiographic findings of the patient. (A) The short arrow indicates saccular aneurysmal change in the distal part of the obtuse marginal branch of the left circumflex artery. (B) The long arrow indicates the 3.0 mm×2.0 cm-sized tornado coil located in the aneurysmal sac. After this embolization, no more contrast agent filling the aneurysmal sac was observed and distal flow below aneurysmal sac disappeared.

was observed in only two patients who received cadaveric transplants at a center where more than 1,000 cases of kidney transplantation had been performed(2). One patient, a 49-year-old male, whose case was uneventful while receiving immunosuppressant drugs (prednisolone and azathioprine) after kidney transplantation, developed GB perforation on postoperative day 14. The same occurred in another patient, a 64-year-old male, immediately after kidney biopsy was conducted to identify the cause of a renal graft dysfunction that developed from postoperative day 7(2). This is a case in which GB perforation occurred 7 days after kidney transplantation in a 69-year-old female patient. Compared to the other reported cases, the patient was relatively old. However, the interval between the kidney transplantation and the occurrence of GB perforation was similarly 7～14 days. Although it is difficult to come to a general conclusion with such a small number of reported cases, it appears that kidney transplantation patients over 60 may have an increased risk of GB perforation due to acalculous cholecystitis within 1～2 weeks of surgery.

Although the pathogenesis of GB perforation due to acalculous cholecystitis is unclear, it is widely known to occur due to infarction of the muscular mucosa and the serosa following acute inflammatory reactions, and its predisposing risk factors include a change in coagulation factor XII(5), previous operation/trauma, total parenteral nutrition or prolonged fasting(6).

Of the multiple immunosuppressive drugs used for kidney transplant recipients, cyclosporine A is metabolized principally in the liver, and the formation of GB stones is increased by decreasing bile flow, resulting in cholestasis(7). There is no evidence, however, that specific immunosuppressives are toxic to the GB or cause GB diseases. Kidney transplant recipients who are prescribed multiple immunosuppressives become more susceptible to inflammation, and presumably have a higher risk of developing acalculous cholecystitis(2). In this case, the immunosuppressive medications of the kidney transplant recipient consisted of tacrolimus, prednisolone, mycophenolate mofetil, and basiliximab; no drug with a known association with GB disease was prescribed. In older kidney transplant recipients, scarcity of oral feeding due to postoperative pain, overall weakness, and prolonged postoperative bed rest are thought to be risk factors for GB perforation due to acalculous cholecystitis.

CAA is rare, occurring more commonly in males and most often in the right coronary artery, followed by the left anterior descending artery, and rarely occurring in the left main artery(3). The causes of CAA depend on age; in adults, the most common cause is atherosclerosis followed by connective-tissue diseases, cocaine abuse, and trauma(4,8). In most cases, CAA is asymptomatic and is encountered incidentally in coronary angiography. In some cases, MI may occur when blood clots obstruct the blood vessels due to slow blood flow in aneurysms, or other rare presentations may follow due to hemopericardium, tamponade, and the compression of the adjacent cardiac chamber(9). Although the appropriate therapy criteria remain uncertain and controversial, even asymptomatic patients are required to undergo invasive therapy if the diameter of the aneurysm is 3- or 4-fold bigger than the normal diameter, or if the adjacent coronary artery stenosis is severe. As the saccular aneurysm, although minor, has an increased risk of forming blood clots and of causing rupture, invasive treatment should be applied. Medications may include anticoagulants for inhibiting blood clotting in aneurysms, or rarely, nitrates or calcium channel blockers for the prevention of vasospasm. The prognosis is known to differ depending on the location or degree of obstruction of the coronary artery, but further studies on this topic are needed(10). Coronary angiography of the patient herein showed no aberrant findings of obstruction or stenosis of the blood vessels, but did indicate aneurysms in the obtuse marginal branch of the left circumflex artery. The NSTEMI symptom was thus thought to be caused by vascular occlusion due to blood clots in the aneurysms.

Reported herein is the case of a patient who developed GB perforation due to acalculous cholecystitis after kidney transplantation, who underwent cholecystectomy, and who was later invasively treated when CCA was detected through coronary angiography, which was performed due to NSTEMI occurrence. We

hypothesize that age is the root cause of these two rare complications and, therefore, special attention may be required in kidney transplantation in elderly patients. Both GB perforation due to acalculous cholecystitis after kidney transplantation and CAA occur very rarely. This is the first reported case of the diagnosis and treatment of both anomalies in the same patient, and it is accompanied herein by a review of pertinent literature.

In conclusion, GB perforation due to acalculous cholecystitis and CAA are rarely observed in postoperative kidney transplantation patients; however, these complications can be life threatening and therefore good outcomes are contingent upon early diagnosis and prompt treatment. We report herein a case of the diagnosis and treatment of both complications in an elderly patient after kidney transplantation.

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