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Anesthetic management for coronary artery bypass grafting surgery in a post-kidney-transplant patient

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Introduction

Following recent improvements in the results of kidney transplantation, anesthesiologists have increasingly been encountering post-kidney-transplant patients requiring anesthesia and surgery. Anesthetic management of these patients presents many difficulties associated with protection of transplant organ functions and the adverse effects of immunosuppressive therapy, such as susceptibility to infections and reduced adrenal function. However, the reports of perioperative management of post-kidney-transplant patients receiving open heart surgery with extracorporeal circulation are particularly rare [1–4].

We report a case of perioperative management of coronary artery bypass grafting (CABG) surgery on a patient with a cadaver kidney transplant. In this case, we examined whole blood cyclosporin (CYA) levels and renal function during the perioperative period.

Case report

The patient was a 46-year-old woman with a weight of 51 kg and height of 151 cm. At 25 years of age, she was diagnosed as having renal failure due to chronic glomerulonephritis. At that time, she began receiving hemodialysis three times a week. In 1978, she received a cadaver kidney transplant at our hospital and was weaned from hemodialysis. After kidney transplantation, she received immunosuppressive therapy using three drugs: CYA 125 mg/day, mizoribine 150 mg/day, and methylprednisolone 4 mg/day. In April 1991, the patient noticed effort-induced chest pain. In October of the same year, chest pain was felt even at rest. On December 9, chest pain continued throughout the night. For these reasons, she visited the Department of Cardiovascular Medicine of our hospital. Upon admission, electrocardiography (ECG) revealed ST elevation in leads II, III, aVF, QS pattern in lead III, and ST depression in leads V_{3-6}. Based on these findings, the patient was diagnosed with acute inferior myocardial infarction and angina at rest. Coronary arteriography revealed 100% stenosis of the right coronary artery (segment 1), 90% and 100% stenosis of the left coronary artery (segment 9 and segment 11). The patient was referred to the Department of Thoracic Cardiovascular Surgery in February, 1992, to receive CABG surpery.

Preoperative plasma blood urea nitrogen (BUN) and creatinine values were 18.2 mg/ml and 1.57 mg/ml, respectively, and the trough blood level of CYA was 131 ng/ml (normal range; 100–250 mg/ml). The patient's response to the early morning rapid adrenocorticotropic hormone (ACTH) test was low (basal blood cortisol level; 1.34 μg/dl, 5.6 μg/dl at 30 min, 11.5 μg/dl at 60 min after synthetic ACTH cortorosin 0.25 mg i.v.). Hypertension (160–170/90–100 mmHg) had been detected together with chronic glomerulonephritis. After kidney transplantation, steroidal diabetes was detected. For this reason, the patient temporarily received insulin therapy. Before CABG operation, the patient was orally treated with isosorbide sulfate 60 mg/day, diltiazem 180 mg/day, disopyramide 300 mg/day, mexiletine 300 mg/day, CYA 125 mg/day, mizoribine 150 mg/day, and methylprednisolone 4 mg. Furthermore, two nitroglycerin tapes 50 mg/day were applied to the skin before CABG.

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Anesthetic procedure

Sixty min before surgery, atropine sulfate 0.5 mg and morphine hydrochloride 5 mg were injected intramuscularly for premedication. In the operating room, the patient's right radial artery was cannulated under local anesthesia, followed by insertion of a 7.5-gauge Fr flow-directed pulmonary artery catheter via the right internal jugular vein for continuous pressure monitoring. Anesthesia was induced with thiamylal 150 mg, fentanyl 3.0 mg, and vecuronium 12 mg. At the same time, hydrocortisone 100 mg was injected intravenously as supplemental therapy. Immediately after induction of anesthesia, continuous infusions of nitroglycerin (1 μg/kg/min), dopamine (2 μg/kg/min) and CYA 1.7 mg/h were started. Infusion of antibiotics (piperacillin 1 g and fosfomycin 2 g) was also begun. Simultaneously with the start of surgery, the administration of 20% mannitol (100 ml) was started for diuresis. Anesthesia was maintained with high-dose fentanyl, oxygen, and vecuronium, without nitrous oxide. The total dose was 5.7 mg (112 μg/kg) of fentanyl and 56 mg (0.1 μg/kg/min) for vecuronium. Until the start of extracorporeal circulation, blood pressure (110/60–70 mmHg) and heart rate (50–70 beats/min) were stable. During extracorporeal circulation (ECC), mild hypothermia (rectal temperature; 28°C) was induced, and the perfusion index and pressure were set at 2.4–2.8 l/min/m^2 and 70–90 mmHg, respectively. For immunosuppressive therapy, CYA (1.7 mg/h) was infused during ECC. Immediately before weaning from ECC, dopamine and nitroglycerin were increased up to 5 μg/kg/min and 1 μg/kg/min, respectively, and continuous infusion of lidocaine 50 mg/h was started. The weaning from ECC went on smoothly. Immediately after weaning from ECC, administration of furosemide 20 mg and 20% mannitol (100 ml) was started. After ECC, blood pressure (130–180/70–90 mmHg), heart rate (70–90 beats/min), and cardiac index (2.5–4.0 l/min/m^2) were stable. During surgery, 5350 ml of urine output was observed.

The endotracheal tube was extubated at about 40 h after admission to the ICU. The functions of the transplanted kidney and whole blood CYA concentrations are listed in Table 1. Upon admission to the ICU, BUN was 13.1 mg/dl, and creatinine was 1.08 mg/dl. From the day after surgery, BUN remained between 10.0 and 18.0 mg/dl, and creatinine 1.15 and 1.80 mg/dl. Urine output was 60–150 ml/h with furosemide. Creatinine clearance was 30–65 ml/min. She stayed in the ICU until on the 7th postoperative day. The subsequent course was uneventful, and the patient was discharged on the 40th hospital day. Hemodialysis after surgery was not required on this patient.

Discussion

According to the literature search, only a few reports of perioperative anesthetic management for open heart surgery on post-kidney-transplant patients have been published [1–4]. As the survival rate after renal graft increases, the number of such patients who require anesthetic management will increase. Anesthetic management of post-kidney-transplant patients involves many problems. The protection and maintenance of renal

Table 1. Changes in plasma creatinine (Cr), blood urea nitrogen (BUN), whole blood cyclosporin A (CYA), and urine volume.

	Plasma Cr (mg/dl)	BUN (mg/dl)	Blood CYA (ng/ml)	Urine volume (ml/day)
Pre. OP.	1.57	18.2	136	1200
Anes. Ind.	1.6	15.3	132	
OP. 30 min	1.3	17.4	128	
150 min	1.3	12.3	191	1700 ml/150 min
ECC 10 min	1.1	10.9	222	
30 min	1.2	9.5	146	
60 min	1.1	11.2	136	
150 min	1.2	10.4	173	2050 ml/150 min
Post-ECC 10 min	1.4	10.0	265	
30 min	1.4	11.5	213	
60 min	1.4	10.7	289	
End of surgery	1.08	13.1	265	1600 ml/180 min
1 day after surgery	1.65	15.0	195	3000
2 days after surgery	1.62	9.8	148	2300
3 days after surgery	1.01	11.6	170	2200
5 days after surgery	1.55	11.8	58	1600
7 days after surgery	1.42	11.9	52	1200

ECC, extracorporeal circulation; Pre. OP., preoperative; OP., operative.

function, countermeasures against susceptibility to infections, evaluation of adrenal dysfunction due to long-term steroid therapy, and the necessity for steroid supplement therapy become particularly important. Because post-kidney-transplant patients receive immunosuppressive agents, they are susceptible to infections. Among others, cytomegalovirus infection and pneumocystis carinii pneumonia are often fatal and require particular attention [5]. If the blood CYA level becomes too high, the incidence of these infections will increase. Therefore, it is essential to maintain an appropriate blood level of CYA and to monitor its blood level continuously. To prevent infections, it is also necessary to keep the operating room clean, to strictly sterilize the apparatus and tools for anesthesia, and to use aseptic techniques during eudotracheal intubation, urethral catheterization, gastric intubation, tracheal suction, and so on. It is also recommended to minimize the duration of the use of these catheters. Althogh the use of antibiotics are indispensable for the prevention of bacterial infection, those with renal toxicity should be avoided. In post-kidney-transplant patients, piperacillin and fosfomycin are safe and often used. Evaluation of the adrenal function following long-term steroid therapy is also important. Accurate assessment of the adrenal function is possible with the rapid ACTH test in the early morning. Based on the results of this test, the indication for steroid supplementation and its optimum dose can be determined [6].

In the present case, the preoperative rapid ACTH test revealed an apparent reduction in adrenal function. Therefore, steroid supplemental therapy, using hydrocortisone, was begun on the day of surgery, and the dosage was reduced to the preoperative level 1 week later. Immunosuppressive therapy should be continued to prevent rejection of the transplanted kidney; in the present case, we used three agents (CYA, mizoribine and methylprednisolone). In Japan, mizoribine is available only as an oral preparation. For this reason, mizoribine can not be used during surgery. CYA is the main immunosuppressive agent used after organ transplantation. This drug, however, has many adverse effects, complex pharmacokinetics, and a narrow range of effective blood concentrations. CYA is metabolized in the liver, by the cytochrome P450 enzymes. For this reason, blood CYA levels during surgery interact with drugs which are metabolized by the same mechanism, such as calcium antagonists, and with hematocrit, as 60% of CYA in blood is located in red blood cells. Serum CYA is also affected by hypothermia and blood dilution during ECC [7,8]. Previous reports have described oral administration of CYA. The perioperative repeated administration method was reported in only 1 case by Thomas et al. [1]. They orally administered CYA until the day before operation and intravenously administered 100 mg each at 4 and 16 h before surgery on the day of operation, 100 mg 2 h after the operation, and 100 mg at 12-h intervals for 3 days postoperatively. The blood CYA concentration during this period was sometimes below the preoperative trough level. They observed rejection at low CYA concentrations and renal toxicity such as tubulonecrosis at very high concentrations of CYA. Because of the risks associated with this method, the authors designed the continuous infusion method. In the present case, we aimed at maintaining the CYA level higher than the preoperative trough level throughout the perioperative period. For this purpose, CYA was continuously infused intravenously at a daily dose of 40 mg, which was about 30% of the oral dose level (120 mg/day). The finding that about 30% of the preoperative dose of CYA was absorbed via the intestinal tract was used to determine the intravenous dose level. No rejection of the transplanted kidney was observed in the perioperative period. With this method of CYA treatment, factors which can affect CYA during surgery did not adversely affect the therapeutic range of this drug.

In conclusion, analysis of the time course of blood creatinine and BUN level suggested that our method of continuous CYA infusion, and the use of dopamine, mannitol, and furosemide were appropriate. A rare experience with the anesthetic management of coronary artery bypass grafting in a post-kidney-transplant patient was presented in this paper.

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