Recurrent Cardiac Arrest during a Nontransplant Operation Due to Variant Angina in a Liver Transplantation Patient

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We report a case of recurrent cardiac arrest during a nontransplant operation in a liver transplant recipient with prior cardiac arrest during liver transplantation. A 45-year-old man who experienced cardiac arrest for 17 minutes during the preanhepatic phase of liver transplantation—which was performed 34 months ago—did not survive the recurrent cardiac arrest during portal venoplasty. Variant angina was not suspected for the first cardiac arrest; however, myocardial infarction by coronary vasospasm was revealed to be the cause of the second cardiac arrest.

Key Words: Liver transplantation, Heart arrest, Variant angina

INTRODUCTION

Liver transplantation (LT) is a high-risk procedure with possible perioperative and long-term morbidities and mortalities. Unfavorable preoperative conditions together with acute hemodynamic changes can result in acute cardiovascular events perioperatively. Even though various preoperative cardiac evaluations are performed, it is not easy to diagnose variant angina in LT recipients who do not have any history of heart disease. We report a case of unexpected recurrent cardiac arrest during a nontransplantation operation in a LT recipient who experienced cardiac arrest during LT but was not diagnosed with variant angina after the first cardiac arrest.

CASE REPORT

A 45-year-old man (body weight 83.2 kg, height 173 cm) with liver cirrhosis from a complication of hepatitis B virus infection was admitted for living-donor LT. His preoperative cardiac evaluation including electrocardiogram (ECG) and echocardiography were within the normal range (ejection fraction of 72%). His Model for End-Stage Liver Disease (MELD) score and Child class were 17 and C. After proper anesthetic and surgical preparations including pulmonary artery catheterization, the operation began without any event. The initial arterial blood gas analysis (ABGA) results were as follows: pH, 7.427; PaCO₂, 35.3 mmHg; PaO₂, 211.4 mmHg; HCO₃⁻, 22.7 mEq/L; base excess (BE), -1.2 mEq/L; hematocrit (Hct), 33%; Na⁺, 137 mmol/L; K⁺, 4.5 mmol/L; and Ca²⁺, 1.00 mmol/L. About one and a half hours into the surgery, the inferior vena cava (IVC) was partially clamped. An operator discovered an IVC injury and repaired it quickly without massive bleeding. Blood pressure and heart rate were maintained at around 100/50 mmHg and 70 beats per minute; however, ST segment of lead II decreased from -0.8 to -2.4 mm in ECG. Nitroglycerin infusion was
started at the rate of 1 μg/kg/min. On the ABGA measured 10 minutes prior to the cardiac arrest, pH, PaCO₂, HCO₃⁻, and BE had changed to 7.24 mmHg, 35.3 mmHg, 14.7 mEq/L, and −11.6 mmol/L, respectively, although the rest of the values had not significantly changed. Thirty minutes after the ST depression event, the patient’s blood pressure dropped to 60/40 mmHg. Within 30 seconds, sudden cardiac arrest accompanied by ventricular fibrillation and asystole occurred during dissection of the IVC for liver isolation. Chest compression was initiated immediately. His cardiac rhythm converted to a sinus rhythm after administration of 1 mg epinephrine five times, 0.5 mg atropine five times, 300 mg calcium chloride, and several 360 J defibrillations over 17 minutes of cardiopulmonary resuscitation (CPR). The patient’s blood pressure increased to 110/65 mmHg, and his heart rate was 70 beats per minute. The operation was completed without any other issues. On postoperative day 2, both ECG and echocardiography taken in the intensive care unit (ICU) were within the normal range and no regional wall motion abnormality (ejection fraction 64%) was reported. Troponin I and creatinine kinase (CK)-MB levels were also within the normal range. He was discharged on postoperative day 33 without any other complications.

Thirty-four months later, the patient was admitted due to elevated levels of total bilirubin. Stenosis of the portal vein was observed in abdominal computed tomography and ultrasonography, so we decided to perform portal venoplasty. His preoperative laboratory data, chest X-ray, and ECG were within the normal range. The operation began without any issues and his vital signs were stable. The initial ABGA results were as follows: pH, 7.459; PaCO₂, 32.9 mmHg; PaO₂, 176.5 mmHg; FiO₂, 0.53; HCO₃⁻, 22.0 mEq/L; BE, −0.3 mEq/L; Hct, 39%; Na⁺, 139 mmol/L; K⁺, 5.3 mmol/L; and Ca²⁺, 0.99 mmol/L. Blood pressure, heart rate, and ST segment level of lead II were approximately 100/60 mmHg, 70 beats/minute, and 0.3 mm, respectively. On the ABGA measured 30 minutes prior to the cardiac arrest, pH, PaCO₂, HCO₃⁻, and BE had changed to 7.3 mmHg, 45.7 mmHg, 22.0 mEq/L, and −4.5 mmol/L, respectively, but the rest of the values had not significantly changed. Four hours after the surgery began when balloon dilatation of the portal vein was performed, the patient’s blood pressure and heart rate dropped to 60/30 mmHg and 45 beats per minute. ST segment of lead II was depressed to −1.3 mm at the same time. Incremental ephedrine injections were not effective. Within 1 minute, ventricular fibrillation followed by asystole was observed and chest compression was started. A 100 mg lidocaine, 300 mg calcium chloride, 0.5 mg atropine, and 1 mg epinephrine were injected every 1 or 2 minutes. A 360 J defibrillation was applied regularly. Despite every effort for recovery, his cardiac rhythm did not recover. Extra-corporeal membrane oxygenation was applied after 60 minutes of CPR and the patient was transferred to the ICU. In the ICU, his blood pressure and heart rate were 140/90 mmHg and 140 beats per minute. Acute myocardial infarction was suspected based on postoperative laboratory

![Fig. 1. Postoperative right coronary angiography in the left anterior oblique view. (A) Baseline right coronary angiography. (B) Right coronary angiography after intracoronary ergonovine injection. The arrows indicate diffuse coronary spasm of the right coronary artery induced by ergonovine. (C) Coronary spasm of the right coronary artery was reversed by intracoronary nitroglycerine injection.](image-url)
data since troponin I (71.198 ng/mL; normal, <0.01 ng/mL), CK-MB (567.20 ng/mL; normal, 0–4.9 ng/mL), and lactate dehydrogenase (14,300 U/L; normal, 140 to 280 U/L) levels were all elevated. Acute coronary vasospasm in the left anterior descending artery and right coronary artery reversed by intracoronary nitroglycerin injection were observed in the coronary angiography taken in the ICU. He was diagnosed with acute myocardial infarction from acute intraoperative vasospasm (Fig. 1). Unfortunately, the patient expired on postoperative day 6.

DISCUSSION

The number of LT recipients who receive another non-transplant operation is expected to increase due to the growing number of LT cases and the improved survival rate of LT recipients. Patients who receive LT frequently have characteristic hyperdynamic hemodynamic patterns (1,2). Decreased systemic vascular resistance can increase cardiac output in these patients. As a result, their cardiac adaptation ability against physiologic stress is lower than normal. Although preoperative cardiovascular examinations are within the normal range, the possibility of cardiovascular events related to LT remains. If a patient experiences cardiac arrest during LT, it is certain that he or she will be allocated into the high-risk group for cardiovascular complications.

Variant angina was first described by Prinzmetal et al. (3) in 1959. He reported an atypical ischemic coronary syndrome that was not related with exercise, but rather associated with ST segment elevation on ECG. Even though the incidence of variant angina is 1% to 2.5% among patients with chest pain who receive a coronary angiogram, it is related with acute myocardial infarction, cardiac arrhythmias such as ventricular fibrillation, and ventricular tachycardia (4,5).

The typical clinical feature of variant angina is rest angina that responds well to nitrates. The chest pain can have a circadian pattern and is not exacerbated by physical exercise (6). Based on the criteria established by the Coronary Vasomotion Disorders International Study Group (COVADIS), variant angina can be diagnosed by three criteria: (1) nitrate-responsive angina; (2) ECG changes during a transient ischemic event; and (3) demonstration of coronary vasospasm (>90% constriction) spontaneously or in response to provocative stimulation (acetylcholine or ergonovine) (6).

The exact underlying mechanism of coronary vasospasm is still unknown; however, the imbalance between sympathetic-parasympathetic systems was suggested as a possible mechanism. Stimulation of the parasympathetic nervous system or acetylcholine could induce coronary vasospasm (7).

It has been shown that abnormalities in nitric oxide in the endothelium are related with coronary vasospasm (8). Enhanced phospholipase C enzyme activity has also been detected in smooth muscle in variant angina patients (9).

Smoking is a known predisposing factor for coronary vasospasm (10). Anesthesia can also trigger coronary vasospasm although this is rare (11-14). The cause of perioperative coronary vasospasm is still not known; however, several possible mechanisms have been suggested: an imbalance in vasoconstriction and vasodilatation forces (15), increased catecholamine level due to anesthesia and surgery (15), increased alpha adrenergic receptor activity (16), stimulation of the parasympathetic nervous system (17), and release of vasoconstrictive substances from platelets (18). An additional study found that ephedrine and inotropic drugs could lead to intraoperative coronary vasospasm during regional anesthesia (19).

There are many case reports suggesting that intraoperative manipulation of major vessels such as the carotid, coronary, iliac artery, and aorta can trigger coronary vasospasm by the previously mentioned mechanisms (20-24). Because it requires handling the major vessels, LT surgery can be stressful enough to trigger a sympathetic and parasympathetic imbalance.

There have been several case reports on coronary vasospasm related with renal and heart transplantation (25-27). Endothelial dysfunction has been suggested as a mechanism of coronary vasospasm in transplant recipients since immunosuppressive agents such as cyclosporine and tacrolimus are closely related with endothelial dysfunction (28,29), which is a strong triggering factor for coronary vasospasm (30). Liver transplant recipients also have a risk of coronary vasospasm associated with immunosuppressant therapy.

In this case, a cardiac evaluation for variant angina was not performed after the first cardiac arrest because variant
angina was not suspected. Even though ST depression was observed prior to cardiac arrest, it was difficult to diagnose variant angina because the cardiac arrest was accompanied with an IVC injury.

Uphrey et al.(31) reported that perioperative short-term cardiovascular complications could be expected in patients based on preoperative dobutamine stress echocardiography results and MELD scores. However current American Heart Association guidelines for perioperative cardiac evaluation do not recommend a routine coronary angiogram, the gold standard method to diagnose variant angina, for patients who do not have cardiac disease even in high risk non-cardiac surgery(32). Ripoll et al.(33) suggested that preoperative echocardiography was not statistically significant in its ability to predict perioperative cardiovascular events.

Matsusaki et al.(34) reported that the incidence of intraoperative cardiac arrest (ICA) during LT was 5.5%, and 90% of ICA occurred during the neohepatic phase. Most of the short-term cardiovascular events occur during anhepatic or reperfusion phases which are periods with significant hemodynamic changes(34).

During the first cardiac arrest, ST depression was detected prior to the cardiac event and nitroglycerin infusion was initiated. This may have aided in the relief of coronary vasospasm leading to an early recovery from cardiac arrest. The patient did not experience any cardiovascular symptoms until the second operation.

The progression of the second cardiac arrest was too abrupt and nitroglycerin was not immediately administered. Without nitroglycerin or calcium channel blockers, vasopressors were continuously injected for the cardiac resuscitation which may have exacerbated the coronary vasospasm during the second cardiac arrest.

In conclusion, the messages from this case are simple and clear. If a LT patient has a cardiac event at a relatively unexpected time such as during the preanhepatic phase, ICA such as variant angina should be suspected as the cause of the cardiac event even though it is rare. If ST segment change is detected, nitroglycerin infusion should be initiated early during LT surgery.

According to Ertel et al.(35) report, the reoperation rate within 90 days of LT is surprisingly high at 29.3%. Thorough preoperative cardiac evaluation and vigilant intraoperative monitoring are advised for liver transplant recipients who had intraoperative cardiac events and plan to undergo another surgery.

REFERENCES


