Clinical Case Report

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Intraoperative venesection and isosorbide dinitrate for postreperfusion syndrome during liver transplantation

A case report

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Abstract

Rationale: Postreperfusion syndrome is the most severe cardiovascular and metabolic alteration which typically occurs after the declamping of the portal vein of the grafted liver during liver transplantation, and it could affect the mortality and morbidity of the patient.

Patient concerns: We report the case of ischemic change in electrocardiogram with substantial increase of central venous pressure, from 6 to 16 mmHg, that developed immediately after reperfusion.

Diagnoses: Based on his hemodynamic parameters, it was suspected that this event was caused by sudden volume overload in the right ventricle after reperfusion rather than hypovolemic status, thromboembolism, or any other possibilities.

Interventions: He was treated with active venesection of 300 mL and isosorbide dinitrates infusion at the rate of 30 μg/min.

Outcomes: The parameter values were restored to normal within 15 to 20 minutes after treatment, and the patient was discharged postoperatively without any significant cardiac sequelae.

Lessons: Although ischemic ST change during reperfusion reported without any previous cardiac complication is limited, the patient could recover rapidly with careful identification of the cause of PRS and immediate treatment.

Abbreviations: BP = blood pressure, BT = body temperature, CI = cardiac index, CVP = central venous pressure, E/E' ratio = ratio of mitral peak velocity of early filling to early diastolic mitral annular velocity, ECG = electrocardiogram, HR = heart rate, IVC = inferior vena cava, LT = liver transplantation, PA = pulmonary arterial, PAP = pulmonary arterial pressure, PGE1 = prostaglandin E1, PRS = postreperfusion syndrome, QTc = corrected QT, RVEDA/LVEDA = right over left ventricular end-diastolic area ratio, RVSP = right ventricular systolic pressure, $ScvO_2$ = central venous oxygen saturation, SVR = systemic vascular resistance, SVV = stroke volume variation, TEE = transesophageal echocardiogram, TTE = transthoracic echocardiogram.

Keywords: isosorbide dinitrate, liver transplantation, postreperfusion syndrome, ST segment, venesection

1. Introduction

Since liver transplantation (LT) was first attempted by Starzl et al in 1963,[1] both surgical and anesthetic management have progressively improved. Although these advances increased the survival rate and supported LT to become a criterion standard for patients with end-stage liver disease,[2,3] LT remains a major surgical procedure involving significant fluid shifts often related with severe hemodynamic alterations. The greatest cardiovascular event which occurs during reperfusion of the grafted liver is called postreperfusion syndrome (PRS). Because Aggrawal et al[4] first described the definition of PRS in 1987, in general, it is defined when dramatic decrease in mean arterial pressure, ≥30% below the baseline, appears and lasts for at least 1 minute during the first 5 minutes after reperfusion. Throughout many years of research, the definition of PRS has evolved as well as its pathophysiology, risk factors and management which are still debatable.[5] For anesthesiologists, it is important to make an effort to stabilize these hemodynamic events. We report a case of change in electrocardiogram (ECG) with sudden increase in central venous pressure (CVP) that developed immediately after the reperfusion. This observation returned to normal range soon after we performed active venesection and isosorbide dinitrate infusion because we suspected that volume overload occurred after the reperfusion caused the event.

2. Case report

A 60-year-old man with multiple hepatocellular carcinoma and hepatitis B and C cirrhosis (Child-Turcotte-Pugh grade A and Model for End-Stage Liver Disease score, 4) was scheduled for

Editor: N/A.

The ethical approval was not necessary for this case report article under the institutional review board of the Kyungpook National University Hospital. The patient has provided informed consent for publication of this article.

The authors report no conflicts of interest.

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Medicine (2018) 97:34(e11893)

Received: 18 May 2018 / Accepted: 25 July 2018

http://dx.doi.org/10.1097/MD.0000000000011893

LT. He also had diabetes and a small nodule in the left lower lobe of the lung. His routine laboratory result was unremarkable showing normal electrolyte levels, without thrombocytopenia nor any other bleeding tendencies. Preoperative chest radiograph was unremarkable except for the small nodule described above. ECG showed normal sinus rhythm with heart rate (HR) of 93 bpm and corrected QT (QTc) interval 474 ms. Transthoracic echocardiogram (TTE) showed an ejection fraction of 58%, ratio of mitral peak velocity of early filling to early diastolic mitral annular velocity (E/E' ratio) of 6.79, right ventricular systolic pressure of 26 mmHg.

Induction and maintenance of general anesthesia were performed with propofol, remifentanil, cisatracurium, and desflurane. Besides standard monitoring which include ECG, noninvasive blood pressure (BP) device and oxymeter, a Vigileo monitor with FloTrac sensor and PreSep catheter (Edwards Lifesciences LLC; One Edwards Way, Irvine, CA) was applied through arterial and central catheterization because LT has a high possibility of profound hemodynamic alterations. Arterial catheters were inserted at both right radial and femoral arteries. Advanced venous access High Flow (AVA-HF, 9-French, Edwards Lifesciences LLC) and PreSep catheter were inserted at the right internal jugular vein. Insertion of pulmonary arterial (PA) catheter was not considered because the patient had no significant dysfunction at right heart and did not seem to have pulmonary hypertension during the preoperative checkup. Initial vital signs were stable, showing BP, HR, CVP, and body temperature (BT) of 142/82 mmHg, 71 bpm, 8 mmHg, and 35.5°C, respectively. A Vigileo monitor with FloTrac and PreSep continuously analyzed and informed the other hemodynamic values. Baseline results of the measurement showed cardiac index (CI), stroke volume variation (SVV), and central venous oxygen saturation ($ScvO_2$) of 2.3 L/min/m^2, 6%, and 87%, respectively (Table 1). During preanhepatic to anhepatic phase, no significant change was observed in the vital signs. Laboratory results were in the normal range. Although no significant change was observed in the QT interval compared to the preoperative QT interval, 1 g magnesium sulfate was replaced. Because the laboratory value of magnesium was checked in the low normal range, and the preoperative QTc interval was ≥440 ms, the incidence of arrhythmia could be higher.[6] We started the continuous infusion of calcium chloride at 450 mg/h since anhepatic phase to maintain ionized calcium concentration at approximately 1.0 mmol/L. Fluid replacement was mainly based on 5% albumin with crystalloid, and urine output was approximately 100 mL/h on average. Arterial blood gas analysis performed before reperfusion showed Hct of 38% and ionized sodium, potassium, and calcium concentrations were 130, 3.88, and 0.92 mmol/L respectively.

During reperfusion, neither vasopressor nor inotropic management was required to maintain BP because it did not drop significantly and recovered to its baseline within 1 min. However, CVP suddenly increased from 6 to 16 mmHg immediately after reperfusion and ST segment depression was also developed, which decreased to almost −5 mm (Fig. 1A, B). Hemodynamic values at this time showed CI, SVV, $ScvO_2$, and BT of 4.8 L/min/m^2, 10%, 90%, and 35.2°C, respectively (Table 1). Considering that BP was quite stable after reperfusion while significant changes were found in CVP and ST segment along with slight increase in CI and $ScvO_2$, we could assume that it was caused by sudden volume overload in the right ventricle after reperfusion rather than the possibility of thromboembolism or hypovolemia. Because CVP alone is not sufficient to reflect right ventricular preload accurately, we wanted to apply transesophageal echocardiogram (TEE) to check right ventricular volume or function. However, only TEE at our operating center was used in open heart surgery. The pulmonary arterial pressure (PAP) was not available because the PA catheter was not inserted in this case. We suspected that sudden increased preload from the grafted liver might became a profound burden which might led to right ventricular ischemia with the change of ST segment. Although we lacked of information from TEE or PA catheter, we immediately performed active venesection of 300 mL through one of the AVA-HF lumen and started to infuse isosorbide dinitrates at the rate of 30 μg/min. After this maneuver, both CVP and ST segment returned to baseline figure as they were before reperfusion within 15 to 20 minutes (Fig. 1A, B).

Postoperative ECG showed normal sinus rhythm with HR and QTc interval of 80 to 90 bpm and 420 to 440 ms without any abnormal signs of ST segment, respectively. Although laboratory tests performed immediately at the day of the surgery showed troponin I of 0.163 ng/mL, it tended to decrease and subsequently became normal. TTE showed no significant changes compared with preoperative values. At postoperative day 21, the patient was discharged without any surgical or cardiovascular sequelae,

Table 1

Hemodynamic parameters of the patient.

	Initial (before induction)	(10 min after)	Before reperfusion	After reperfusion	After recovery from PRS
NIBP, sys/dia (m)	142/82 (102)				
ABP, sys/dia m), mmHg					
Femoral		108/62 (76)	131/84 (99)	112/73 (86)	97/47 (63)
Radial		107/63 (77)	130/77 (94)	103/73 (83)	100/49 (66)
Heart rate, bpm	71	56	95	103	98
CVP, mmHg		8	6	16	9
CI, L/min/m^2		2.3	3.5	4.8	4.1
SVV (%)		6	9	10	5
$ScvO_2$ (%)		87	89	90	90
BT, °C	35.5	35.5	35.2	35.2	35.1
U/O, mL/h		135	95	95	155

ABP = arterial blood pressure, bpm = beats per minute, BT = body temperature, CI = cardiac index, CVP = central venous pressure, L/min/m^2 = liters per minute per square meter, ml/h = milliliters per hour, NIBP = noninvasive blood pressure, PRS = post reperfusion syndrome, $ScvO_2$ = central venous oxygen saturation, SVV = stroke volume variation, sys/dia (m) = systolic/diastolic (mean), U/O = urine output. U/O is the measurement of the average of 2 hours at each phase.

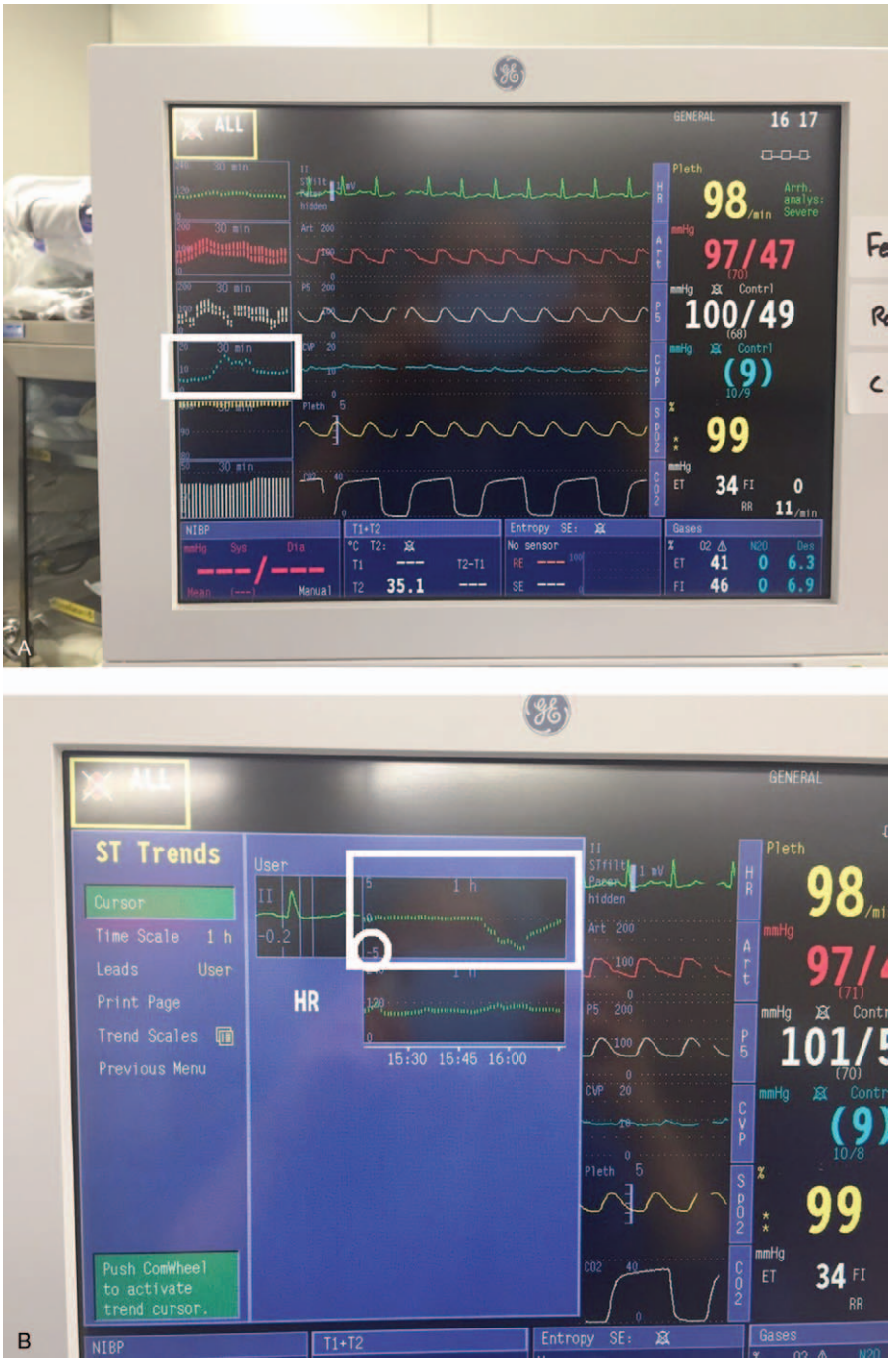

Figure 1. Screen captures of the monitoring device show sudden dramatic changes and recovery of both central venous pressure (A) and ST segment (B) at the reperfusion phase. The white square box of each figure (A) shows change of CVP 6 to 16 mmHg and recovery to 8–9 mmHg. Based on (B), we could detect the ST segment depression, which decreased almost approximately −5 mm (white circle) and restored to the baseline status within 15 to 20 minutes.

and he is still clinically stable with regular checkup for the last 7 months.

3. Discussion

Although the pathophysiology of PRS is not fully understood, sudden load of acidic, cold blood with electronic derangement, and release of vasoactive substances from the grafted liver are known to cause PRS.[5] As a result of cardiovascular disturbance, progressive bradycardia or other arrhythmias, decreased systemic vascular resistance (SVR), increased PAP, and CVP, and decreased mean arterial pressure could be detected. If ischemic changes in the ST segment occur because of decrease of coronary blood perfusion, we should identify the cause and manage it immediately. As Jeong reported,[3] we could consider vasopressor for decreased SVR, fluid challenge for hypovolemic status, and active venesection for volume overload. Considering active venesection of 200 to 300 mL is also recommended if CVP increases >15 mmHg after reperfusion and if CVP >15 mmHg is persistent with PAP >30 mmHg,

isosorbide dinitrate, prostaglandin E1 (PGE1) could be applied together with venesection.

In our case, a sudden dramatic increase of CVP 6 to 16 mmHg together with ST segment depression was observed during reperfusion. Meanwhile, vasopressor administration was not even needed because no severe and persistent decrease in both mean arterial blood pressure and systemic vascular resistance was found. ST segment depression seemed to be caused by volume overload based on those changes with other parameters, such as CI, SVV, and $ScvO_2$. During reperfusion, sudden increase in venous return would result in overloaded volume at right heart. Because this event increased oxygen consumption of the right ventricle, we should be aware that if it is poorly tolerated, it could possibly result in compromised right ventricular function, rare but eventually showing ECG changes similar to our case.[7] TEE would have been a very useful tool for monitoring cardiac performance and volume status by assessing parameters, such as right over left ventricular end-diastolic area ratio (RVEDA/LVEDA), cross-sectional area, and etc. There are some concerns regarding the potential risks such as variceal bleeding. However, esophageal varix is not an absolute contraindication for using TEE, and several reports showed that TEE is relatively safe with a low incidence of major hemorrhagic complication.[8] Therefore, as expected, benefits exceed the potential risks, and it would have been more accurate and reliable if we could use TEE in this case as we hoped. We also did not have chance to measure PAP. We understand that many centers routinely insert PA catheter to evaluate cardiac function. However, as Gwak et al[9] reported that PA catheterization during LT has high incidence of ventricular arrhythmia by irritation of the endocardium which could be severe sometimes, and we did not routinely insert the PA catheter unless the patient has any signs of pulmonary hypertension or any other underlying cardiac disease preoperatively. During the anhepatic phase, preload in the right ventricle decrease, which alleviates its work and also reduce PAP.[7] In contrast, during reperfusion, because of sudden increase of venous return, transient but, significant increase in PAP could develop as well as CVP occasionally. However, considering that ECG changes do not always appear in every volume overload cases, we assumed that increased preload in this patient was huge enough to be a severe burden for the right heart, and significant increase of PAP may be highly possible. Because high PAP has been noted as a negative implication, which could affect the perioperative mortality and morbidity,[10] although we lacked information from both TEE or PA catheter, we immediately performed venesection to reduce preload and administered isosorbide dinitrates to reduce afterload. Nitroglycerin, and prostacyclin are well-known treatments to control abrupt increase in patients with PAP with portopulmonary hypertension.[7] However, those medications induced not just vasodilation of pulmonary, but also of systemic vessels, and maintaining the BP could be difficult. Some other reports suggested the administration of sildenafil for its higher selectivity in pulmonary vasodilation and milrinone for its unique advantage of inotropic effect with vasodilating properties.[10,11] Further studies will be needed to compare those medications for deciding safer and more beneficial one.

By following both static and dynamic parameters such as CVP, SVV and urine output, we tried to maintain low normal range of volume status carefully at the anhepatic phase because it would be helpful to minimize the blood loss and avoid volume overload at reperfusion.[12,13] However, volume overload occurred regardless of those endeavors. In our center, modified right lobe graft technique is performed for adult living donor LT. It is one of the surgical techniques that clamp the inferior vena cava (IVC) partially. Looking back, femoral venous catheterization could have been helpful in patients undergoing LT. When the surgeons clamp IVC even partially, the femoral venous pressure would increase compare with CVP. This change results in the increase in renal venous pressure, reducing renal perfusion pressure consequently.[14] Therefore, we could prevent renal hypoperfusion by monitoring the femoral venous catheter, and we could also estimate how much IVC was clamped and could be more careful with circulatory volume as well. When the femoral venous pressure increases a lot, we could consider that a large amount of venous return would occur at reperfusion.

In summary, PRS is a serious cardiovascular events occurring during LT, which could affect the mortality and morbidity of the patients. Its incidence has not decreased significantly, still up to as high as 50%[15] despite improvement in management. Reports regarding ECG changes at reperfusion in patients without any previous cardiac event, similar to ours, are limited. In our case, when it occurred, rapid recover could be possible as we decided to perform active venesection with isosorbide dinitrate infusion immediately because we assumed the preload as the cause of the event based on other parameters, even without TEE or PA catheter. Therefore, identification of the cause and immediate active treatment are important when hemodynamic collapse occurs. Furthermore, because every center has different routine protocols of monitoring for LT, re-evaluating the benefits and risks of each would be helpful.

Author contributions

Conceptualization: Ji Hyun Kim.
Data curation: Ji Hyo Kim.
Investigation: Ji Hyun Kim, Ji Hyo Kim, Hyeon Jun Lee.
Writing – original draft: Ji Hyun Kim.
Writing – review & editing: Ji Hyun Kim.

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