



Case report

Anesthesia management of combined sequential heart–liver transplantation using a caval clamp without venovenous bypass: A case report

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ABSTRACT

Familial amyloid polyneuropathy, an autosomal-dominant disease due to mutations in the transthyretin gene, often affects the heart and liver, and is treated best with a combined heart–liver transplantation (CHLT). Although it remains an uncommonly performed procedure, the number of patients undergoing CHLT is increasing. Because of the complexity associated with dual pathophysiology, CHLT poses an extraordinary challenge for anesthesia management. Either both heart and liver transplantation are performed on cardiopulmonary bypass (CPB); or heart transplantation is performed on CPB, followed by liver transplantation with venovenous bypass. Recent reports suggested that liver transplantation can be performed without bypass using the inferior vena cava-sparing technique. However, both bypass and caval sparing technique have their own complications. Here, we present the anesthesia management in a case of sequential heart–liver transplantation using a routine caval cross-clamp technique without venovenous bypass. A 48-year-old man complaining of chest tightness, chest pain, and shortness of breath was diagnosed with amyloid cardiomyopathy. Cardiac ultrasonography revealed thickening of ventricular walls and left ventricular systolic insufficiency (ejection fraction decreased from 46% to ~20% in 6 months), which was refractory to medical therapy. Symptoms occurred repeatedly. Therefore, CHLT was planned. Heart transplantation was performed smoothly under general anesthesia and standard CPB. His heart functioned well with dobutamine and epinephrine infusion. Subsequently, the patient was weaned from CPB. Liver transplantation was planned using the piggyback procedure with the caval sparing technique. However, upon caval clamping, unexpected blood loss occurred. Clamping of the caval was tested followed by cross-clamping. Norepinephrine, epinephrine, and dobutamine were administered. After the hepatic vein was anastomosed, the clamp was released and nitroglycerin was administered. Hemodynamics was stable, and the patient was discharged after 37 days of hospitalization. The case indicates that CHLT could be performed using caval clamp without venovenous bypass in selected patients.

1. Introduction

Familial amyloid polyneuropathy is an autosomal-dominant disease due to mutations in the transthyretin (TTR) gene that can lead to decreased stability of the corresponding protein with subsequent extracellular deposition of amyloid in multiple tissue or organs. Because of the risk of sudden death due to rhythm disturbances related to cardiac autonomic dysfunction, patients with amyloidosis plus concurrent liver and cardiac involvement are treated best with a combined heart–liver transplantation (CHLT) [1]. Although CHLT remains an uncommonly performed procedure, the number of cases is increasing. It has been reported that in 2019 alone, there have been 45 cases of CHLT in the United

States [2]. Because of the complexity related to dual pathophysiology, CHLT presents an extraordinary challenge for anesthesia management. To maintain the hemodynamic stability and avoid the new grafted cardiac stress during caval clamp and hepatic reperfusion, the established management programs either involve performing both heart and liver transplantations on cardiopulmonary bypass (CPB), or performing heart transplantation on CPB, followed by liver transplantation with venovenous bypass (VVB) [3]. However, both CPB and VVB lead to additional difficulties for surgical manipulation, including vascular injury and surgical field bleeding [4]. Recent reports have suggested that after heart transplantation, liver transplantation could be performed without bypass using the caval sparing technique, which allows for uninterrupted blood

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flow from the inferior vena cava, thus reducing graft cardiac stress and hemodynamic instability during clamping and reperfusion [3]. However, the caval sparing technique requires surgical technique modifications, and is only available for piggyback procedures. CHLT using an inferior vena cava clamp without VVB is uncommon. We describe a case of sequential heart–liver transplantation using a conventional inferior vena cava cross-clamp without VVB, under optimized hemodynamics.

2. Case report

The case was reviewed by the Ethical Committee Board of our hospital. Informed consent was obtained from the patient for the publication of this case.

A 48-year-old man (height, 180 cm; weight, 57.5 kg) was diagnosed with familial myocardial amyloidosis (transthyretin amyloidosis type [ATTR]), due to progressive chest tightness, chest pain, and shortness of breath for 6 months. His parents and child were healthy. Tissue biopsy examination with Congo red staining of the abdominal adipose tissue was positive. He received multiple medical treatments after diagnosis, but they were largely ineffective. His heart function deteriorated progressively (with the ejection fraction decreasing from 46% to approximately 23%). His symptoms occurred repeatedly. After extensive consultation, the decision was made to perform CHLT.

On admission, his physical examination revealed a distant heart sound, and his blood pressure was 109/77 mmHg, heart rate was 83 beats/min, and respiratory rate was 20 times/min. No murmurs were heard, and no oedemas were perceived. Electrocardiography showed first-degree atrioventricular block, complete right bundle branch block, and high lateral wall abnormal Q waves. Cardiac ultrasonography revealed myocardial amyloidosis, thickening of the right ventricular wall, left ventricular systolic insufficiency (with the ejection fraction of approximately 20%), and pericardial effusion. The albumin and total bilirubin levels were 38.8 g/L and 16.8 $\mu\text{mol/L}$, respectively. His heart function status was classified as class III based on the New York Heart Association criteria.

CHLT was performed under general anesthesia. After standard monitoring, anesthesia was induced by etomidate (0.25 mg/kg) and fentanyl (5 $\mu\text{g/kg}$), with dobutamine infusion (3 $\mu\text{g/kg}\cdot\text{min}$). Tracheal intubation was facilitated by rocuronium (0.9 mg/kg). Central venous pressure was monitored. Anesthesia was maintained with propofol (300 mg/h), remifentanyl (0.8 mg/h), and cis-atracurium (5 mg/h). Blood gas and electrolyte analysis was performed intermittently to maintain homeostasis of the internal environment. The heart transplantation was performed using the bicaval technique under standard CPB. Milrinone (0.7 $\mu\text{g/kg}\cdot\text{min}$) was administered when aortic anastomosis began. Epinephrine (0.03 $\mu\text{g/kg}\cdot\text{min}$) and nitroglycerin (0.04 $\mu\text{g/kg}\cdot\text{min}$) were infused during the resumption of the heartbeat. After aggressive evaluation by the operation team, assisted with transesophageal ultrasound, the heart function and hemodynamics were considered stable under inotropic support with epinephrine (0.03 $\mu\text{g/kg}\cdot\text{min}$) and dobutamine (3 $\mu\text{g/kg}\cdot\text{min}$). Subsequently, the patient was weaned from CPB, and heparin was neutralized with protamine to achieve the activating clotting time of 172 s. The sternum was closed and draped in standard fashion, leaving drains in place. The liver transplant was planned with the piggyback procedure using the inferior vena cava-sparing technique. However, upon caval sparing clamp, uncontrollable blood loss occurred. Therefore, the caval was cross-clamped following a test clamp. Norepinephrine (0.04 $\mu\text{g/kg}\cdot\text{min}$) was administered, combined with epinephrine (0.05 $\mu\text{g/kg}\cdot\text{min}$) and dobutamine (3 $\mu\text{g/kg}\cdot\text{min}$). The clamp was released after the hepatic vein was anastomosed, and nitroglycerin was increased to 0.1 $\mu\text{g/kg}\cdot\text{min}$ to maintain stable hemodynamics. After portal vein unclamping and reperfusion, fibrinogen and prothrombin complex were administered according to laboratory testing.

The duration of the operation was 625 min; cardiopulmonary bypass, 95 min; and anhepatic phase, 32 min. The cold ischemia time of the heart and liver were 3 h and 8 h, respectively. A total of 15 units of packed

blood cell, 1940 mL of plasma, 1250 mL of crystalloid solution, 800 mL of albumin, 15 units of allogeneic platelets, and 10 units of cryoprecipitate coagulation factors were infused. In addition, fibrinogen (5 g), prothrombin complex (3000 units), and tranexamic acid (2.4 g) were administered. The total blood loss was estimated to be 4000 mL, and the urine volume was 2000 mL. At the end of the operation, his blood pressure was 116/45 mmHg and heart rate was 92 beats/min, and he received a dobutamine infusion (4 $\mu\text{g/kg}\cdot\text{min}$).

After the operation, the patient was transferred to the intensive care unit and became conscious 4 h after surgery. He was extubated 36 h postoperatively and transferred to the general ward after 21 days in the intensive care unit. He was discharged after 37 days of hospitalization and performed well at the 12-month follow-up examination.

3. Discussion

Since Thomas Starzl first described CHLT in 1984, the number of cases of CHLT has been increasing [5]. Indications include familial hypercholesterolemia, homozygous thalassemia, hereditary hemochromatosis, familial amyloidosis, alcoholic cardiomyopathy, cardiomyopathy with occult liver cirrhosis, and glycogen accumulation disease [1]. Reports have shown that the 1-year survival rate after CHLT exceeds 80%, which is similar to that after heart or liver transplantation alone [1, 6].

Transthyretin cardiac amyloidosis (ATTR-CA) is an invasive cardiomyopathy, which eventually develops to progressive heart failure [7]. Because of the amyloidogenic mutated transthyretin predominantly produced in liver, CHLT is considered to be the best treatment for familial amyloidosis if the heart has been involved [8]. However, due to the complexity of the recipients, CHLT makes intraoperative management a huge challenge to anesthesiologists. In order to avoid caval clamping and reperfusion stress to the newly implanted heart, several techniques have been used during liver transplant, including maintenance of the CPB to portal vein release, or temporary VVB [3]. CPB may support both heart and liver functions, help to avoid hemodynamic instability, and to avoid cardiac stresses in the newly planted heart during hepatic reperfusion [9]. However, heparinization and prolonged CPB duration lead to increased risks of coagulation dysfunction and blood loss during liver dissection and implantation [3]. While VVB is not without its own complications, namely vascular injury and embolization of debris [4]. Therefore, some centers may leave the superior vena cava cannula in place to be used for a potential VVB during the liver transplantation phase if a test inferior vena cava cross-clamp is not tolerated by the newly transplanted heart [10].

With the introduction of piggyback procedures, CHLT could be performed under the caval sparing technique, which may eliminate the need for VVB and can be safely performed in most cases. The caval-sparing technique allows uninterrupted blood flow in the inferior vena cava; therefore, dramatic fluctuations in hemodynamics during inferior vena cava clamp and release could be avoided to a large extent. A recent report showed that 48% of the cases of CHLT could be performed using the inferior vena cava-sparing technique without VVB during liver implantation [3]. However, the inferior vena cava-sparing technique requires changes to surgical skills, and adequate vascular cuffs must be prepared in advance. Meanwhile, this technique is only available in piggyback liver transplant procedures. In the case of orthotopic liver transplantation (caval interposition technique), or other unexpected situations in which the inferior vena cava have to be clamped, there is no opportunity to carry out the caval sparing technique. In the present case, the piggyback procedure with caval sparing technique was planned. However, uncontrollable blood loss occurred unexpectedly, and the vena cava was cross-clamped after a test clamping. Cross-clamp of the inferior vena cava presented extreme challenges to the anesthesia team. Meticulous inotropic and volume support successfully counteracted the hemodynamic fluctuation resulting from the caval clamp and subsequent release of the clamp. The case shows that orthotopic liver transplantation with caval interposition can be conducted in sequential CHLT without VVB or CPB.

4. Conclusions

CHLT presents extraordinary challenges in anesthesia management. The vena cava can be clamped without a venous bypass in selected patients. However, the merits of this technique require further observation.

Declarations

Author contribution statement

All authors listed have significantly contributed to the investigation, development, and writing of this article.

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The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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