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Case Report

Challenges and strategies in managing severe portopulmonary hypertension during living donor liver transplantation: A clinical case study

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ABSTRACT

Porto pulmonary hypertension (POPH) occurs in 2-10% of advanced liver disease cases. Preoperative screening and severity classification of POPH are crucial before liver transplantation. Living donor liver transplantation (LDLT) is recommended for patients who respond to medical therapy. Strategies to lower pulmonary artery pressure should begin at induction and continue through the postoperative period for successful management.

1. Introduction

Porto pulmonary hypertension is defined as the presence of pulmonary hypertension in a patient with portal hypertension. Porto pulmonary hypertension (POPH) occurs in 2-10% of advanced liver disease cases and presents significant challenges during intraoperative and immediate postoperative periods.[1]

Effective preoperative screening and severity classification of POPH are crucial before liver transplantation. Strategies to lower pulmonary artery pressure should begin at induction and continue through the postoperative period. Living donor liver transplantation (LDLT) is recommended for patients who respond to medical management.

2. Case Presentation

We describe a case of 64 year old diabetic male with Child Pugh class C cirrhosis, multi focal hepatocellular carcinoma, with recent trans arterial chemo embolisation (TACE), with no extra hepatic manifestations, and a history of Hepato renal syndrome, being worked up for LDLT.

On pre anaesthesia work up, he was found to have a recent onset of dyspnoea on exertion, with room air saturation 99 percent. Trans thoracic echocardiography was done and the right ventricular systolic pressure (RVSP) was found out to be 64mmHg. For assessing the severity of pulmonary hypertension, the patient underwent right heart catheterisation (RHC) which revealed severe Porto pulmonary hypertension (mean pulmonary artery pressure of 48mm Hg, PCWP 13 mm Hg, PVR 330 dyne.cm-5).

Patient was advised medical management for reduction of pulmonary artery pressure as surgery is contraindicated in cases of severe POPH.

He was started on Phosphodiesterase 5 (PDE 5) inhibitors thrice daily for reducing the pulmonary pressures and a plan was made to reassess after 2 month. All other investigations as a part of transplant work up was done and LDLT work up was completed.

After 2 months of medical therapy he was re assessed. Significant drop of pulmonary pressures were noted in the RHC. Mean pulmonary artery pressure 33mmHg, PVR 280 dyne.cm-5, PCWP of 12 (moderate POPHTN). A decision

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was made to proceed for LDLT with plan of continuing the therapy intra op and in the post op.

Anaesthetic induction was achieved with Propofol and fentanyl, Atracurium was used as the muscle relaxant, and was maintained with air 02 mix, isoflurane as per standard operating protocol for living donor liver transplant. Central lines and arterial lines were placed as per institutional protocol. Pulmonary artery pressures (PAP) were continuously monitored using a pulmonary artery catheter.

Intraoperative management included milrinone and prostaglandin E1 infusions to reduce pulmonary artery pressure.

Pulmonary artery catheter after induction showed a mean PAP of 32 mm Hg. Post induction vitals were stable and no episodes of hypotension or arrhythmias were noted. Infusion of Milrinone (0.5 μg/kg/min) was started to reduce the pulmonary artery pressures and was continued. An infusion of Prostaglandin E1 at a dose of 30 ng/kg/min was started with an aim of reducing the pulmonary pressures.

Standard surgical techniques were employed, with efforts to minimize the surgical duration. The reperfusion phase proceeded smoothly, requiring minimal inotropic support during the post-reperfusion period. The total anesthesia time was 11 hours, during which 7.5 liters of intravenous fluids were administered, including 2 units of packed red blood cells (PRBC), 2 units of cryoprecipitate, and 2 units of fresh frozen plasma (FFP). The hemodynamic values recorded at various stages of the procedure, as shown in (Table 1) and (Figure 1), remained stable throughout.

Inhaled nitric oxide (INO) therapy, administered using the INOMAX machine, was initiated in the post-transplant ICU to manage postoperative pulmonary hypertension, with a target dose of 20 ppm. Serial arterial blood gas analyses were performed in the postoperative period to monitor acid-base balance and prevent acidosis. Given the risk of methemoglobinemia, a known complication of INO therapy, serial measurements of blood methemoglobin levels were conducted, and the inhaled nitric oxide dose was adjusted accordingly.

Milrinone and PGE1 infusion was continued in the immediate post operative period.

Patient was extubated 8 hours post op. Milrinone was tapered off within 24 hour post op. Bioglandin infusion was continued till 48 hours post op. Inhaled nitric oxide was delivered through bi pap mask till 24 hours post extubation and was tapered off.

Restarting of the oral Phosphodiesterase 5 inhibitor was done on first post operative day. The post op pulmonary artery pressures showed a drastic reduction within 2 days.

He was shifted to the post operative ward after 7 days of ICU stay. The post operative graft function was found to be adequate and he was discharged from the hospital 22 days post surgery. Follow up ECHO showed a drastic reduction in pulmonary pressures. The patient is currently under follow up for the past 2 years without any major complications and an improvement in Pulmonary hypertension post LDLT.

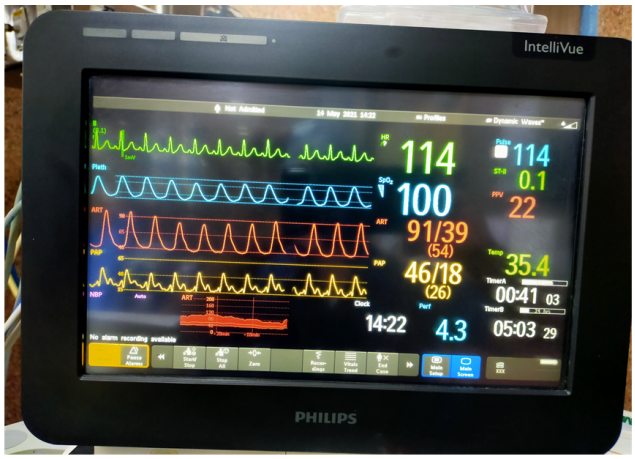

Figure 1: The reperfusion period

3. Discussion

Pulmonary arterial hypertension associated with portal hypertension (with or without cirrhosis) has been termed Porto pulmonary hypertension. Porto pulmonary hypertension is a serious condition with a high risk of post-transplant mortality. Effective preoperative medical management can significantly improve outcomes

Diagnostic criteria for PPHTN include:

(1) The presence of clinical portal hypertension, (2) a mean pulmonary artery pressure (mPAP) greater than 25 mm Hg, (3) a pulmonary artery occlusion pressure (PAOP) less than 15 mm Hg,(4) a pulmonary vascular resistance (PVR) greater than 240 dyne second/cm-5.

PPHTN is categorized as mild (mPAP 25-34 mm Hg), moderate (mPAP 35-44 mm Hg), severe (mPAP > 45 mm Hg). The prognosis of untreated PPHTN is generally poor, and the 5-year survival rate without any therapy is 14%.[2] Patients with moderate to severe PPHTN (mPAP 35 mm Hg) and a PVR greater than 250 dyne second/cm5 have a particularly poor prognosis and unacceptably high post transplant mortality.[3,4]

PAH-specific medications have been shown to improve pulmonary haemodynamics in patients with PPHTN. Pharmacological control of PPHTN before LT has been associated with post transplant survival rates similar to that of patients who undergo transplantation for other indications.[4] Phosphodiesterase 5 inhibitors, such as sildenafil, play a crucial role in the management of pulmonary hypertension by promoting vasodilation of the pulmonary vasculature. By inhibiting the degradation of cyclic guanosine monophosphate (cGMP), these drugs enhance nitric oxide-mediated relaxation of smooth

Table 1: The hemodynamic values recorded at various stages of the procedure

	Pre op	D-2	Intra op Dissection	An hepatic	Reperfusion	Post op 1 month	3 months
RVSP in mm Hg	64	52				40	41
Mean PAP in mm Hg	48	33	32	34	26	23	22
PVR in dynes/sec/cm5	330	280				210	180
PCWP in mm Hg	13	12				11	10

muscles, leading to reduced pulmonary arterial pressure.[5] Our case had severe Porto pulmonary hypertension, which was detected during evaluation. Patient was re assessed after 2 months of treatment with oral Phosphodiesterase 5 inhibitor (Sildenafil). Since there was a response to the medical management plan to proceed with LDLT was made.

PGE1 and inhaled nitric oxide are effective in managing POPH by dilating pulmonary and systemic vessels. Infusion of milrinone and PGE1 was done intra op to reduce the pulmonary artery pressures.[6] Infusion of milrinone has shown beneficial effects in treatment of of pulmonary hypertension as it reduces pulmonary vascular resistance rapidly. Its onset of action is rapid and is usually well tolerated Their use in this case was guided by their documented efficacy in improving pulmonary haemodynamics.

Post op use of inhaled nitric oxide was done for about 48 hours post surgery which was also helpful in reducing the pulm artery hypertension. Prostaglandin E1 (PGE1) is a potent vasodilator in both pulmonary and systemic arteries. Infusion of PGE1 have demonstrated significant reduction in pulmonary hypertension especially in neonates.[7]

The vasodilator and anti-proliferative actions of NO make it an attractive tool for pharmacological treatment of PAH.[8] Administration of NO gas by inhalation has been shown to be beneficial to patients with PAH. The usefulness of inhaled NO as a treatment is limited due cost, technical difficulties and the fact that not all patients respond to the therapy. The ability of NO to oxidise haemoglobin to form methaemoglobin, which has been shown to be related the cumulative exposure to the gas, may also limit its effectiveness.

4. Conclusion

Severe portopulmonary hypertension presents significant intraoperative and postoperative challenges. Effective preoperative screening, medical management, and intraoperative strategies are crucial for successful living donor liver transplantation. Efforts should be made to reduce the pulmonary artery pressure in cases of severe POPH. Living donor liver transplant should be offered to those cases which respond to medical management. Methods to reduce the pulmonary artery pressures should start from the induction of anaesthesia and should be continued throughout the post operative period.

5. Source of Funding

None.

6. Conflict of Interest

None.

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