Case Report

Anaesthetic Management of a Parturient with Severe Preeclampsia and a History of Liver Transplantation: A Case Report and Short Literature Review

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ABSTRACT

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Liver transplantation is becoming an increasingly common procedure, as the only viable treatment for liver failure. Many women recover from the acute event and lead mostly normal lives. With their fertility restored, many of them may wish to start their own family and will eventually come across the obstetric anaesthetist. Succesful pregnancies are the norm, but the reported rates of pre-eclampsia, IUGR, sepsis, preterm birth and operative delivery are higher than in the general population. We report the successful management of a post liver-transplant parturient requiring an urgent C-section due to preeclampsia with severe features. We review perioperative concerns and the relevant literature.

Keywords: Liver transplantation, Obstetric anaesthesia, Preeclampsia

INTRODUCTION

Orthotopic liver transplantation (OLT) has become a relatively safe procedure over the last decades, with reported 5-year survival rate of over 80%. Increasing numbers of patients will be transplated at a younger age and they will seek obstetric anaesthesia services, as their fertility is restored after succesful transplantation. In 1978, the first succesful pregnancy was

reported1. A recent metaanalysis shows favorable outcomes, but the pregnancies are considered high – risk seconda-ry to increased rates of complications (gestational hypertension spectrum, intrauteri-ne growth restriction [IUGR], gestational diabetes, among others). We report the successful management of a parturient, 8 years post OLT, whose pregnancy was complicated by pre-eclampsia with severe features. Additionally, we review anaesthetic manage-ment and hope to provide guidance based on the available evidence.

CASE REPORT

A 34 year old parturient, G1P0 (G: gravida, P: outcome of pregnancies) with a history of liver transplantation for biliary atresia 8 years ago, presented to the Emergency Department (ED) of our hospital at 33 weeks of gestation, complaining of malaise and generalized fatigue. She had been followed regularly on an outpatient basis as a high – risk pregnancy. There was documented IUGR and normal renal function (Cr 0.5/ BUN 33), her graft function was stable on cyclosporin 100mg bid and methylprednisolone 1mg qday , and she had been scheduled for an elective C – section at 36 weeks of gestation. Additional medications included aspirin 100mg daily and standard pregnancy supplements.

The first vitals recorded were heart Rate (HR) 70 bpm, non-invasive Blood Pressure (NIBP) 200/120mmHg and a normal temperature. Her urine was tested via a dipstick showing 2+ proteinuria, so a provisional diagnosis of pre-eclampsia was made. At this time the anaesthesia department was consulted for a possible urgent C-section.

In the ED, she was given a load of 4g Magnesium Sulphate IV and 60mg IV labetalol in divided doses. Furthermore, betamethasone was administered IV, as indicated for a premature delivery. Labs were drawn, which revealed normal liver function. An ECG showed sinus rhythm at 68bpm with no obvious abnormalities. Urinalysis confirmed significant proteinuria and grade 2 Acute Kidney Imjury (AKI) was diagnosed based on her creatinine value. The Complete Blood Count (CBC) was significant for low platelets (89.000). A peripheral blood smear inspection showed no schistocytes, and an actual platelet count of 100.000 (Table 1).

In view of her worsening renal function, platelet count and continued severe hypertension a diagnosis of pre-eclampsia with severe features was made and considering the way to optimally preserve her graft, she was transferred to the OR for an urgent C-section. Irradiated blood products (2 units pRBC) were crossmatched in anticipation of a possible complicated C- section. As soon as she was on the OR table, standard monitoring was attached, and her vitals were SpO_2 99% on room air, NIBP 180/90mmHg, HR 85bpm. Two peripheral cannulas (16G/18G) and a radial arterial line were inserted, and the decision was made to

proceed with neuraxial anaesthesia considering her platelet count and known benefits of neuraxial anaesthesia in obstetrics in general and pre-eclampsia in particular. A mixture of 14 mg of hyperbaric bupivacaine, 10 mcg of fentanyl and 100 mcg morphine was delivered via a subarachnoid injection at the L3/4 interspace, by the most experienced consultant anaesthetist using a 25g pencil-point needle under strict aseptic conditions. Ten minutes later, a sensory level to light touch was documented at the T6 dermotome bilaterally and surgery was allowed to proceed. ~150 ml of HES 130/0.6 were coloaded while performing the neuraxial procedure, and immediately thereafter a peripheral dilute norepinephrine infusion (8mcg/ml) was initiated to avoid precipitous drops in blood pressure, as per institutional protocol. The first BP measurement was 110/60 and the norepinephrine infusion was titrated to maintain it within 130-150 systolic. Additionally, 2g of cefoxitin was administered IV as SSI prophylaxis.

PARAMETERS	VALUES
White Blood Cell (WBC)/μL	10100
Hemoglobin (Hgb) mg/dl	11.9
Platelets (PLT) /μL (bood smear)	89000 (100.000)
Fibrinogen (Fg) mg/dl	6
International Normalized Ratio (INR)	0.91
Partial thromboplastin time (aPTT) sec	31.3
Albumin (Alb) g/dL	3.3
Sodium (Na^+) mmol/L	137
Potassium (K^+) mmol/L	4.2
Creatinine (Cr) mg/dL	1.2 (baseline 0.5)
Blood Urea Nitrogen (BUN) mg/dL	91 (baseline 33)

Table 1. Patient's laboratory results.

A Foley catherer was inserted for urine output monitoring, and the C-section proceeded uneventfully with delivery of a 1240g female neonate with an 1-minute APGAR score of 7. The newborn was immediately shifted to the Neonatal ICU, for assessment and further supportive care. The patient received 1g of paracetamol for post-op analgesia, 4mg of ondasetron for PONV prevention and 500ml of lactated ringer's for hydration. The norepi-

nephine infusion was downtitrated and soon discontinued. Surgery was completed within 45 minutes, and her urine output during the 1st hour was 200ml. She was transferred to the Post-Anesthesia Care Unit (PACU), where the motor block was documented to recede, and then to the High-Dependency Unit (HDU) for close monitoring of her blood pressure, renal and liver function. A 24hr urine collection was ordered, showing 7.500mg proteinuria, and her creatinine peaked at 1.28. Her antirejection regime was continued perioperatively, and she was discharged stable to the regular ward on the 2nd POD. The rest of her hospital stay was uneventful with resolution of her preeclampsia and improving renal function (Creatinine 1.1/ BUN 58). She was discharged to outpatient follow – up on the 4th POD.

DISCUSSION

This case presents the opportunity to consider multiple issues pertaining to pregnant post-OLT patients. These include: (a) complete assessment of graft function and designing an anesthesia plan that will not jeopardize it, (b) assessment of any comorbidities which most commonly are hypertension and renal dysfunction related to calcineurin inhibitors (CNI's), (c) potential pharmacologic interactions with the anti-rejection regime perioperatively, (d) status of the pregnancy and any pregnancy-specific complications, (e) optimization/stabilization of the patient preoperatively if needed, (f)planning for postoperative disposition. Generally, the recommended interval between OLT and pregnancy is at least 1 year, as outcomes are usually favorable for both mother & baby after this time period. However, both pregnancy - and patient-related complication rates may be increased. Marson EJ et al. presented 1496 pregnancies in 1073 women with 86.3% live birth rate and <1% congenital abnormalities. Gestational hypertension, pre-eclampsia & eclampsia, gestational diabetes, IUGR and preterm delivery rates were all increased compared to the general population. Acute graft rejection has been reported to be as high as 17%, but a clear correlation has not been established[2]. As a rule, the team managing these complex patients should be multidisciplinary and include the treating obstetrician, anaesthetist, transplant team following up the patient and possibly an intensivist.

Patient Assessment

The pre-anaesthetic assessment focuses on airway, cardiac and respiratory examination and sequlae of acute or chronic liver failure (Figure 1).

If regional anaesthesia is considered, any pre-existing paresthesias, common to chronic cyclosporin treatment should be documented. Relevant labs consist of a CBC, coagulation panel, metabolic and liver panel. In our case, the patient presented with severe hypertension, IUGR, thrombocytopenia, proteinuria, grade 1 acute kindey injury (AKI) and pre-

served liver function so a diagnosis of pre-eclampsia with severe features was made and an urgent C-section called (Table 2).

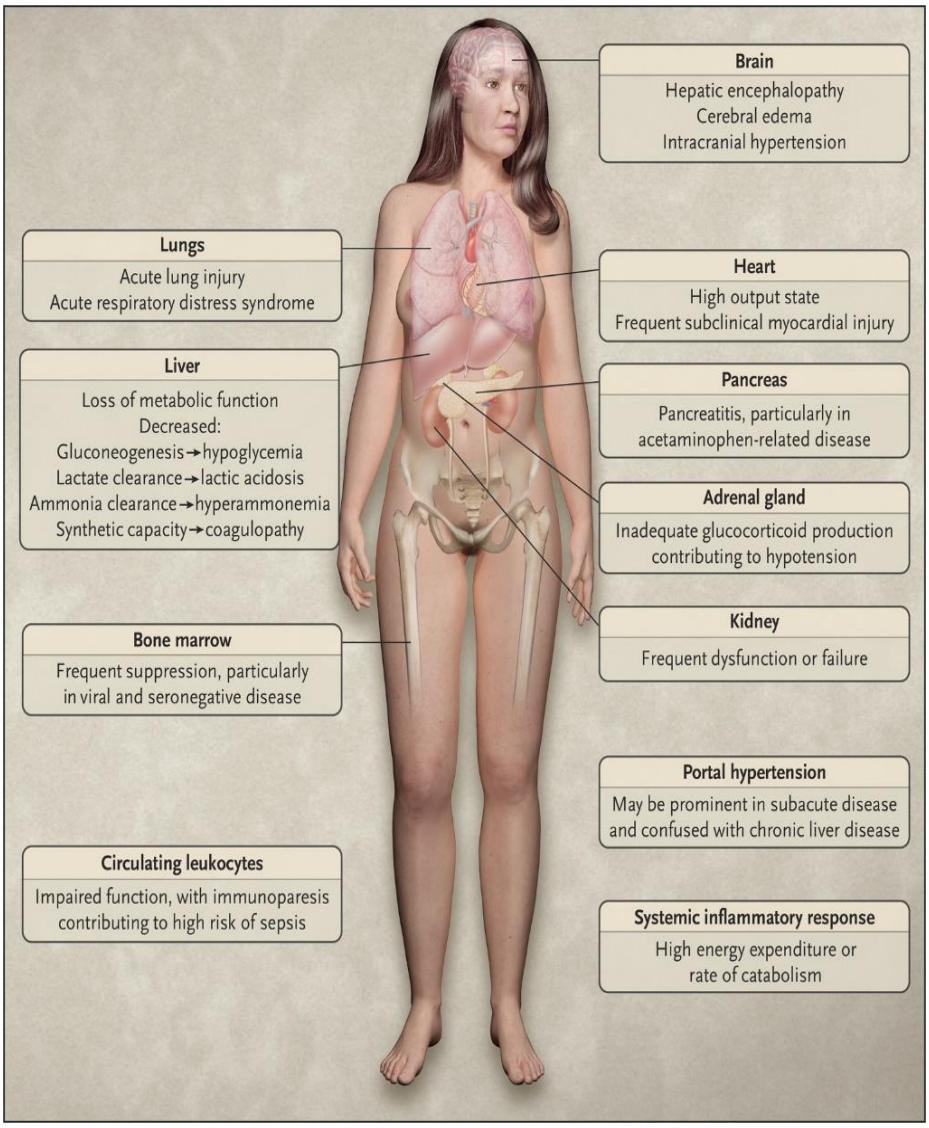

Figure 1. Sequelae of acute liver failure. *(Source: N Eng J Med 2013;369: 2525-34, reproduced with permission).*

It is an ominous disease process that may result in mortality because of intracranial hemorrhage, pulmonary edema, and hepatic failure/rupture. Additional complications include progression to eclampsia, placental abruption and disseminated intravascular coagulation/HELLP syndrome[3].However, one must be mindful that physiologic changes associated with OLT such as thrombocytopenia and hypertension/renal dysfunction related to immunosuppressants may mimic the presentation of pre-eclampsia. Assessment of graft function in a pre-eclamptic patient is initially via routine labs (γ-GT, ALP, AST, ALT, LDH, Albumin, Bilirubin, INR) and clinical signs of liver disease. If derangements are found, one should seek input from the transplant team regarding further diagnostics and management, as it may be very difficult to differentiate between acute graft failure and

complications of preeclampsia (e.g. HELLP syndrome, liver rupture) prior to delivery[4].

Severe features	CRITERIA
Severe Hypertension	• SBP >160 mmHg or • DBP >110 mmHg • Taken on 2 occasions at least 4h apart while on bed rest
CNS Symptoms	• Persistent headache not relieved by analgesics • Visual changes
Pulmonary Oedema	• Clinically diagnosed
Thrombocytopenia	• Platelet Count < 100.000/ml
Renal insufficiency	• Serum creatinine > 1,1 mg/dl
Liver Dysfunction	• Increase in liver enzymes to > twice the upper limits of normal
Severe Hypertension	• SBP >160 mmHg or • DBP >110 mmHg • Taken on 2 occasions at least 4h apart while on bed rest
CNS Symptoms	• Persistent headache not relieved by analgesics • Visual changes

Table 2. Preeclampsia. Clinical features and criteria. *(Source: UptoDate/Preeclampsia: Clinical Features and diagnosis).*

Patient Optimization

Optimization of the patient should start immediately with blood pressure management to a target of 140-150/80-100 mmHg (hydralazine, labetalol) and MgSO4 as seizure prophylaxis. Guidance regarding platelet transfusion usually sets a lower level of 50.000. Fluid resuscitation should be very careful as pulmonary edema is strongly associated with positive fluid balances in the context of pre-eclampsia and oliguria rarely resolves prior to delivery[3]. The anti-rejection regime should be continued perioperatively at a dose agreed with the transplant team, its levels checked (as toxicity is dose-related and subtherapeutic levels greatly increase rejection risk) and p.o. cyclosporin/tacrolimus should be taken at least 4 hours preoperatively to ensure adequate absorption. Documented side-effects (gingival hyperplasia, nephro-/hepato-/neuro-toxicity) should be sought to establish a baseline.

Patients on >10mg prednisone/day should receive additional stress-dose steroid. Blood products should be cross-matched in advance, as availability may be limited due to the patients' history of multiple transfusion and ac-

quired antibodies. Fresh frozen plasma and platelets may also be required if coagulation is deranged or in cases of massive hemorrhage. Irradiated and leukocyte poor blood products are preferred as these patients are susceptible to leukocyte related reactions such as GVHD[5].

Intraoperative Management

The above mentioned should be conducted in an expedient manner, as delays in delivery may threaten liver function, especially in the context of pre-eclampsia. In theater, central venous access should be considered on a case-by-case basis. The choice of anaesthesia depends on patient factors and anaesthetist preference, with a neuraxial block usually safe in stable patients without frank liver or coagulation abnormalities and a platelet count > 75.000/μL[6,7,3], and general anaesthesia reserved for patients in overt organ failure/extremis considering the need for extensive resuscitation and postoperative stabilization/ventilation. Depressed consciousness or a grossly altered mental state secondary to cerebral oedema due to either liver dysfunction or eclampsia present another indication for general anesthesia.

Irrespective of the mode of anaesthesia, blood pressure should be tightly controlled to avoid both intracerebral hemorrhage/stroke and hypoperfusion so a low threshold for instating invasive BP monitoring is recommended[3]. Consideration should be given to the fact that the transplanted liver is denervated, so the physiologic redistribution of blood in response to hypovolemia and the neurogenic autoregulation of hepatic blood flow are both absent[5,8]. Any commonly used drugs that could contribute to liver/kidney damage or that interfere with immunosuppressive regimens should be avoided (Table 3).

DRUG	EFFECT
Cimetidine, Omeprazole	↑ CNIs (cyclosporine, tacrolimus) levels
Metoclopramide	↑ CNIs levels
Carbamazepine	↓ CNIs levels
Succinylcholine	↑ risk of hyperkalemia in patients receiving CNIs
NSAID's	Risk of worsening renal function
NMB's	Prolonged duration on pts receiving CNI's

CNIs: Calcineurin inhibitors

Table 3. Common pharmacologic interactions[4].

Antibiotic prophylaxis according to the local protocol for C-sections and strict aseptic measures are especially important, as any infection can be catastrophic for patients on

immunosuppressants[8]. Left lateral tilt of 15° should be maintained until delivery of the fetus. If regional anaesthesia is chosen, the neuraxial block should be sited by the most experienced anaesthetist available, with careful risk benefit analysis as there is theoretically increased risk of peridural infection. Fluid coloading may be useful to avoid precipitous drops in blood pressure, and there should be a low threshold for peripheral vasopressors with the necessary precautions (dilute solutions, frequent inspection of IV site). If one opts for G.A., extreme attention should be paid to ablating the hypertensive response to laryngoscopy & intubation as it has been identified as a direct cause of maternal mortality[3]. Useful drugs include the synthetic opioids (especially remifentanil – fastest peak effect and shortest duration of action), esmolol and lidocaine). Gingival hyperplasia and pregnancy related changes to the airway may pose difficulties in airway management. Induction usually follows an appropriate dose of propofol or etomidate and isoflurane or desflurane are preferred for maintenance as they preserve hepatic artery blood flow and rely, the least, on hepatic biotransformation for their metabolism. Drugs with organ independent elimination such as remifentanil, cisatracurium are preferred if repeated doses of opioid/NMB are needed[9].

Postoperative Disposition/Management

Postoperatively, the patient should be closely monitored in an HDU or ICU with scrutiny on her coagulation status, blood pressure, liver and renal functions. The ICU setting is usually chosen for patients suffering from organ failure, with an expected need for a period of postoperative ventilation. Ergometrine cannot be used as it can induce a severe hypertensive crisis and stroke[3]. Avoidance of nephrotoxic medications and careful dosing of immunosuppressants is paramount to limit kidney injury in the setting of AKI. Analgesia should be provided as in any C-section but with avoidance of NSAID's and careful use of morphine in the setting of renal dysfunction. Thromboprophylaxis in the form of SCD's and prophylactic heparin is strongly recommended.

To summarize, the anaesthetist is commonly part of the multi-disciplinary team taking care of these patients and we believe is the best-suited to guide a holistic approach. A thorough assessment of the preoperative status, dilligent preparation, anaesthetic conduct ensuring splachnic perfusion and proper disposition to a higher level of care, if required, should be the cornerstones of proper management.

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REFERENCES

1. Walcott WO, Derick DE, Jolley JJ, et al. Successful pregnancy in a liver transplant patient. Am J Obstet Gynecol. 1978;132:340–1. doi: 10.1016/0002-9378(78)90906-7
2. Marson EJ, Kamarajah SK, Dyson JK, et al. Pregnancy outcomes in women with liver transplants: systematic review and meta-analysis. HPB 2020;22(8):1102-1111. doi: 10.1016/j.hpb.2020.05.001.
3. Dennis AT. Management of pre-eclampsia: issues for anaesthetists. Anaesthesia. 2012 Sep;67(9):1009-20. doi: 10.1111/j.1365-2044.2012.07195.
4. Orlikowski CE, Rocke DA, Murray WB, et al. Thrombelastography changes in pre-eclampsia and eclampsia. Br J Anaesth. 1996 Aug;77(2):157-61. doi: 10.1093/bja/77.2.157.
5. Agarwal A, Jha A, Baidya DK, et al. Anesthetic considerations in parturients with liver transplant. J Obstet Anaesth Crit Care 2014;4:4-11. doi: 10.4103/2249-4472.132812
6. Sharma SK, Philip J, Whitten CW, et al. Assessment of changes in coagulation in parturients with preeclampsia using thromboelastography. Anesthesiol 1999; 90: 385–90. doi: 10.1097/00000539-200105000-00033.
7. Dyer RA, Piercy JL, Reed AR, et al. Hemodynamic changes associated with spinal anesthesia for cesarean delivery in severe preeclampsia. Anesthesiol 2008; 108: 802–11. doi: 10.1097/01.anes.0000311153.84687.c7.
8. Toivonen, H.J. Anaesthesia for patients with a transplanted organ. Acta Anaesthesiol Scand. 2000;44(7):812-33. doi: 10.1034/j.1399-6576.2000.440708.x
9. Keegan MT, Plevak DJ. The transplant recipient for nontransplant surgery. Anesthesiol Clin North Am. 2004;22(4):827-61. doi: 10.1016/j.atc.2004.05.006.

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