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Neonatal Distant Transport for Liver Transplantation

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Abstract

A 36 weeks old baby boy was transferred interstate to the national paediatric liver transplant unit at the Children's Hospital, Westmead in Sydney for liver transplantation on Day 32 of life. Patient received liver transplantation at 41 weeks corrected age, which was three days after arrival to the transplant unit. This transfer involved road and aircraft ambulance utilization. We report this transport process in the setting of severe neonatal liver failure, complicated by persistent, uncorrectable coagulopathy, thrombocytopenia, ascites, hyperammonia and portal hypertension with particular reference to pre-transport preparations and the treatments undertaken during the difficult transport which spanned over eight hours.

Keywords: Neonatal; Transport; Liver; Transplantation

Abbreviations: FFP: fresh frozen plasma, PRBC: packed red blood cells, NICU: Neonatal Intensive Care Unit, PCH: Perth Children's Hospital, NETS WA: Newborn Emergency Transfer Service of Western Australia, IVIG: intravenous immunoglobulin, GALD: gestational alloimmune liver disease, IgG: immunoglobulin G

Case Summary

Patient was born at 36 weeks gestation to a G2P2 mother, by non-elective section for abnormal cardiotocography at a metropolitan hospital in Perth, Western Australia. This was on the perinatal background of oligohydramnios, intrauterine growth retardation and meconium stained liquor. His birth weight was 1. 4kg. Apgar was 9^1, 9^5.

There was no family history of liver disease.

Patient was first noted to have abnormal coagulation profile when he was screened for a couple of episodes of coffee ground aspirates on Day 3 of life. The initial management included an additional dose of Vit K, followed by blood products, which included multiple units of fresh frozen plasma (FFP), cryoprecipitate and packed red blood cells (PRBC), as well as intravenous antibiotics for suspected diagnosis of necrotizing enterocolitis.

The persistent coagulopathy and subsequent development of generalized edema, hypoglycaemia, conjugated bilirubinaemia, and elevated ferritin levels (2580 ug/L) suggested liver failure with possible diagnosis of neonatal

haemochromatosis. Patient was therefore transferred to the tertiary Neonatal Intensive Care Unit (NICU) at the Perth Children's Hospital (PCH) on Day 11 of life via Newborn Emergency Transfer Service of Western Australia (NETS WA).

The diagnosis of neonatal haemochromatosis was confirmed when MRI demonstrated iron deposits in the liver, pancreas and possibly in the myocardium on Day 16 of life.

On arrival to the PCH NICU, the patient received a double volume exchange transfusion and three doses of intravenous immunoglobulin (IVIG). This was followed by administration of FFP twice daily, cryoprecipitate daily, PRBC and platelet transfusion every second day, 20% Albumin infusions with regular diuretics, as well as 20% Dextrose infusion. However, patient continued to deteriorate with intractable coagulopathy, thrombocytopenia (platelet 32x10*9/L the lowest), hypoglycaemia, hyperammonia (highest of 318umol/L), conjugated hyperbilirubinemia, fluid retention, ascites, hypoalbuminemia and portal hypertension. A second opinion was sought from the paediatric liver unit team at Westmead children's hospital and a decision was made to transfer the baby to Sydney unit for potential definitive treatment with liver transplantation. Once the decision for transport was made, a stepwise approach was taken as detailed in **Table 1**.

Patient was electively intubated and ventilated 18 hours prior to the transport. Abdominal drain was inserted for generalised ascites at 15 hours before the transport. A plan of 8 hourly aspirations via the abdominal drain followed by 20% albumin replacement was made to prevent excessive fluid drainage en route.

Patient was transported by the NETS WA and Medical Air. He remained ventilated and on full cardiorespiratory monitoring and maintained stable observations throughout the transport. During the transport, he received a high concentration of maintenance fluid (25% Glucose), platelets, FFP, cryoprecipitate, PRBC, 20% albumin followed by frusemide for persistent coagulopathy and hypalbuminaemia, as well as potassium infusion for persistent hypokalaemia.

Patient was stable and required less oxygen (33% in flight compared to 40% at the start of the trip) during the transport. His in-flight blood gas showed mixed alkalosis, which was consistent with the results of diuretics use **[1]**. The patient had an indwelling urinary catheter to a urinary drainage bag as well as a nasal gastric tube which was kept on free-drainage. There was no aspiration of abdominal drain required during the transport.

The patient was assessed promptly after arriving at the national liver transplant unit at the Children's Hospital, Westmead in Sydney. His repeat blood gas at half an hour after arrival was normal. He was commenced on haemodialysis for hyperammonia within 3 hours of admission and was subsequently put on to the liver transplant list the following day. He underwent liver transplantation on Day 36 of life (41 weeks corrected age).

Our Perth to Sydney trip was estimated for 5 hours in total, 30 minutes by road ambulance, and 3.5 hours by air followed by another 1 hour on road. We experienced unexpected delay due to flight diversion from a fire at the Sydney airport control tower as well as the Friday afternoon traffic chaos in major freeways, all of which toughened the journey. Regular updates and discussions with the on call neonatologists at NETS WA for the logistic challenges were conducted successfully, as well as communication with the receiving hospitals staff. The parents of the patient were kept updated by text messages and photos throughout the retrieval.

Discussion

Liver transplantation in neonates

The survival rate for neonatal hemochromatosis is reported to be as low as 10-20% when treated with a combination of antioxidants and an iron chelator, which was based on the hypothesis of oxidative injury caused by iron overload in the past **[2-4]**.

Current evidence suggests that the most common cause of neonatal haemochromatosis is gestational alloimmune liver disease (GALD), which originates from the placental passage of maternal immunoglobulin G (IgG) antibodies that binds directly and only to the fetal hepatocyte cell surface antigens resulting in severe fetal liver injury, **[5-8]** leading to hepatocellular failure in the first few days of life **[9]**. GALD can present from 18 weeks gestation to 3 months post-delivery, which is likely undiagnosed antenatally **[10]**. To date, neonatal haemochromatosis is the most common cause

of neonatal liver failure and the commonest indication liver transplantation **[11-12]**. Successful liver transplantation in an infant with neonatal haemochromatosis at two months of age was reported in 2016 **[5-13]**.

To our knowledge, our patient was the youngest and the first neonate with severe liver failure who had successful, long distance air transport for liver transplantation in Australia.

Time prior to depart from NICU	Task 1	Task 2	Task 3	Task 4	Task 5	Task 6
12-24 hours	- Ventilation support: • Elective intubation • Transport ventilation set up plan • Prepare inhaled nitric oxide on board - Sedation • Fentanyl • Midazolam - Abdominal drain insertion - Indwellingurinary catheter for measuring urine output	Write up medications including inotropes, blood products and sedation medications orders for transport use • Dopamine • Noradrenaline • Frusemide • Pantoprazole • FFP • PRBC • Platelet • Cryoprecipitate • 20% Albumin • Fentanyl • Midazolam	• Contact blood bank to prepare blood products for transport use - Maintain patency of the central venous line - Insert IV cannula for emergency use	- Complete patient's summary - Collect digital images with all of patient's imaging - Hard copy of all investigation results	- Flight bookings for: • Patient and the transport team (Medical transport) • Parents (Commercial flight) - Accommodation bookings for: • Transport team • Parents	Email patient's summary and contact phone numbers of the transport team and the parents to all people who are involved in the transport, including • Referring Hospital: ○ NICU neonatologists ○ NICU nursing staff ○ Gastroenterologists • Receiving Hospital: ○ PICU intensivists ○ Hepatologists ○ PICU nursing co-ordinators
6-12 hours	Draw up a new set of medication for injection and infusion use during transport • Dopamine • Noradrenaline • Frusemide • KCL • Pantoprazole					
2 hours	Recheck blood tests: • FBE • Coagulation screen • UEC • Blood gas	Collect blood products from blood bank to be carried for transport • FFP • PRBC • Platelet • Cryoprecipitate • 20% Albumin				
1 hour	- Readjust management according to the latest blood results - Commence blood product infusion accordingly • FFP • PRBC • Platelet • Cryoprecipitate • 20% Albumin • Frusemide • KCL	- Abdominal drainage - Urinary catheter bag drainage	Recheck and ensure central line and peripheral iv access are working well	Transfer patient to the transport cot	Photocopy of observation charts, fluid orders, medication charts	

Table 1. Check list for multiple organ failure retrieval at 24 hours prior departure

Inter-state transports of sick neonates could pose a great challenge to transport teams, being usually time critical in nature. Therefore, we proposed a checklist at 12-24 hours prior departure from the referring NICU in **Table 1**, which covers most of the preparation needs for retrieving neonates with liver failure. In addition, the checklist will now be added to our protocol for complex distant transport.

Major concerns of transport a neonate with liver failure

Bleeding and hypotension

The main concerns for our patient during the air transport were oesophageal variceal bleeding and hypotension. This results from increase in portal pressure from expanded gas in the stomach due to incomplete pressurizing of the airplane's cabin (although there were no varices reported in the patient's imaging studies) **[14-16]**. Therefore, blood products including platelet, FFP, cryoprecipitate, packed red cells and 20% albumin were prepared and scheduled to be administered during the retrieval. Inotropes such as Dopamine and Noradrenaline infusion pumps were also prepared for the trip.

Respiratory deterioration

Respiratory compromise due to porto-pulmonary hypertension in neonatal hemochromatosis has been reported in literature. Hence, inhaled nitric oxide was prepared and carried through the retrieval **[11]**.

Unlike other neonates with respiratory illness, our patient required less rather than more oxygen support during the flight trip. His in-flight oxygenation came down from 40% to 33% without any alteration in the ventilation settings. This could be due to patient's hyperventilation state as a consequence from mixed alkalosis.

Worsening encephalopathy and raised intracranial pressure

Though the in-flight changes in intracranial pressure in patients with liver failure remain unknown, our patient was at risk of worsening hepatic encephalopathy as results of ammonia induced cytotoxic brain edema and intracranial hypertension **[16-18]**. Because hyperventilation can reduce intracranial pressure through cerebral vasoconstriction **[19-20]**, patient was kept hyperventilated with mixed alkalosis during the air transport.

Raised abdominal pressure

In an attempt to prevent increase in abdominal pressure during the air transport, regular abdominal drainage was commenced 15 hours prior to the retrieval. In particular, abdominal aspiration via the drain was done 1 hour prior to departure to decompress the abdominal pressure and minimise the likelihood of requiring drainage during the transport. Our patient did not develop abdominal distension and therefore, he did not require further aspiration during our eight-hour journey.

Sedation

There is la limited choice for sedation in patients with neonatal liver failure. As morphine lowers blood pressure, fentanyl and midazolam were chosen for transport. They were appropriately used in our patient during the retrieval.

Stress level of parents and staff

Decision makings on critical cases have never been easy. After multiple discussions among parents, neonatologists, gastroenterologists and interstate paediatric hepatologists, the decision was made to transfer patient for potential liver transplant when patient didn't respond to the medical treatment and continued to deteriorate in the tertiary NICU.

Because of the uncertainty of the outcomes of the distant retrieval and the assessment results in the interstate liver transplant unit, the level of stress of parents and the staff was incredibly high.

The national liver transplant unit at the Children's Hospital at Westmead in Sydney is the largest centre in Australia for children who require liver transplantation. Warm acceptance, prompt assessment, followed by commencement of haemodialysis and registration for the transplant list were very well received and not only reduced the stress, but also boosted the morale of the entire transport team.

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