An ABO-incompatible living donor liver transplant in an infant with acute liver failure in the Sri Lankan setting

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Abstract

Liver transplant (LT) is the standard therapy for medically refractory acute liver failure (ALF). Finding a deceased-donor graft in an emergency is challenging and often overcome by living-donation. Blood group matching is practised for LT though ABO-incompatible liver transplant (ABOi-LT) is performed inselected circumstances. We report an infant who underwent successful ABO-incompatible living donor LT for ALF of unknown aetiology. This being the country's first ABOi-LT, the youngest LT recipient to date and the youngest receiving emergency LT for ALF; we describe the novel experience at a resource-limited setting in Sri Lanka (SL).

Introduction

Emergency LT is the treatment of choice for progressive ALF [1,2]. Paediatric ALF is caused by various aetiologies. The exact cause of ALF is indeterminate in half of the cases and the reported survival in this group is 43% without LT [1,2]. Management of ALF of unknown aetiology include supportive care while waiting spontaneous liver recovery, or LT when indicated. Living donation predominates over deceased donation in Asia, due to the shortage of deceased donor grafts (DDG), increased prevalence of fatty grafts and lack of a system to improve the availability of DDG [3,4]. LT requires finding a blood group compatible donor. However, in an emergency, ABO-incompatible donor could be used [4,5]. The risk of ABOi-LT is antibody mediated rejection (AMR) [5,6,7]. This is minimised by plasmapheresis, increased immunosuppression, and splenectomy [5,6]. ABOi-LT has better results in younger children, especially less than two years due to immature immunity and less prior sensitization [7].

Escalating both donor and recipient to an emergency LT in a resource-limited setting is challenging, due to limited human resources, sorting out infrastructure and logistics. This case highlights the clinical, infrastructural, and social challenges faced in Sri Lankan setting in such a unique case, with discussions on the future perspectives to strengthen the paediatric LT programme in SL.

Case presentation

An eleven-month-old child (8.3kg) was referred due to progressive ALF. He was born to non-consanguineous parents with normal growth, immunization, and development without significant diseases in the family. The child was noted to have jaundice, and dark urine at 10-months of age preceded by an upper respiratory tract infection. Initially he was irritable and later became drowsy. Examination showed encephalopathy (lowest Glasgow coma score of 9/15), deep icterus and hepatomegaly of 2cm. Vital parameters including blood pressure were stable. The results of pre-LT investigations are stated in Table 1. Aetiology for ALF was unknown despite extensive evaluation as there was no history of drug ingestion and viral screening, autoimmune, inflammatory markers and basic metabolic screening being negative. Liver explant retrospectively showed massive hepatocyte necrosis due to ALF, however it was not delineating the aetiology (Figure 1).

The child was listed for emergency LT since he sustained progressive hepatic encephalopathy and coagulopathy despite supportive medical care. There were no contraindications for LT.

Both parents were assessed as donors. Child's, father's, and mother's blood groups were B, B and A

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respectively. Father (ABO-compatible) donor became ineligible for donation as he had grade 2 fatty liver and significant steatosis on elastography (body mass index-BMI of 24 kg/m^2). Hence, mother (ABO-incompatible, BMI 21kg/m^2) was assessed and found suitable for donation. Anti-A level in the child were assessed and IgM was 1/16, IgG was neat, which were safer to proceed with LT, without prior conditioning. Direct legal approval for living donor liver transplantation (LDLT) was obtained from Director General Health Services of Ministry of Health (MOH). The transplant team, operating theatres and intensive care were arranged. The surgery was performed at 36 hours from the referral, on 7th December 2022. Child received the left lateral segment of the donor liver (Figure 1).

Triple immunosuppression was used with steroids, tacrolimus and mycophenolate mofetil (MMF). Since the child developed cytopenia during immediate post-LT, MMF was changed to azathioprine. Liver function tests, anti-A levels were monitored and found to be normal (Table 1). There were no vascular, biliary, or other major complications during the first month post-LT.

Discussion

ALF demands super urgent LT before progression to severe encephalopathy and cerebral oedema [1]. Neurological outcome would be guarded if LT is performed late [1,2]. Further, ALF could set in multiorgan failure if waited longer, making the patient unstable for LT [1,2]. In the Sri Lankan context, emergency paediatric LT for ALF poses many logistical challenges. Shortage of DDG is a major limitation to perform timely LT as most DDG are fatty and available following a prolonged intensive care stay, where the graft quality is poor [3,4]. These grafts often do not fulfil splitable criteria as children requires splitting of the graft due to smaller body size. Finding a blood group compatible, splitable DDG on time is nearly

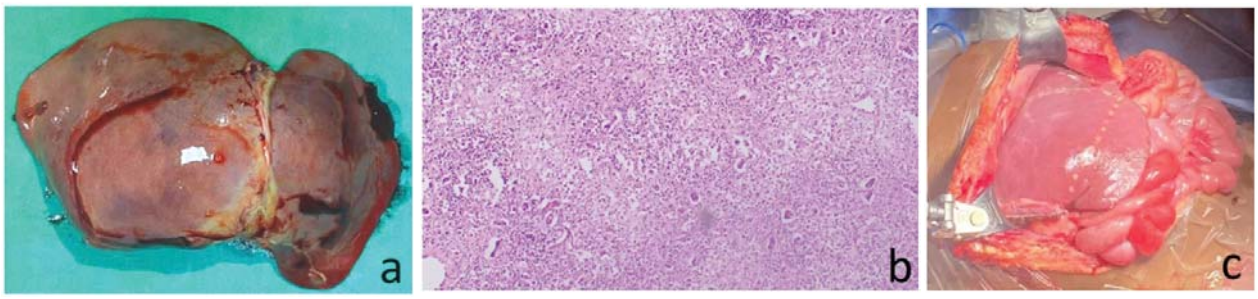

Figure 1. **a – Liver explant macroscopy; b – Liver explant histology showing extensive necrosis; c – Implanted donor liver.**

Table 1. Summary of investigation results pre and post liver transplant

Investigation and unit of measurement	*Pre-transplant*	*Post-transplant*			
		Day 1	Day 7	Day 14	Day 25 On discharge
INR	>10	4.86	1.47	1	1
AST (IU/L)	1316	653	29	26	24
ALT (IU/L)	1248	722	102	51	21
GGT (IU/L)	68	13	33	36	40
ALP (IU/L)	977	560	59	54	86
Bilirubin – total (micromol/L)	303.4	94.8	34.2	11.6	6.4
Bilirubin – direct (micromol/L)	225.3	66.8	23.9	7.4	3.0
Lactate (mmol/L)	5.5	1.0	0.9	0.9	0.8
	IgM – 1/16I		Not detected	Not detected	Not detected
Ant – A titre	IgG – Neat				

impossible in the Sri Lankan context. Therefore, LDLT is the most practical for paediatric ALF. In this case, the father, who had a matching blood group, was rejected due to the presence of lean, non-alcoholic fatty liver disease. ABO-incompatible mother became the donor ultimately.

Due to the lack of dedicated liver transplant facilities, completion of donor and recipient workup within a short period is challenging. Further, LDLT needs direct approval from MOH in emergency situations.

The rejection in ABOi-LT occurs due to the reaction between the antigens in the donor organ vascular endothelial cells and the corresponding AB antibodies in the recipient's serum [5,6,7]. This leads to a cascade of events resulting in hyperacute rejection, vascular thrombosis, biliary strictures, and hepatic necrosis [5,6,7]. The strategies to improve outcomes after ABOi-LT include reducing the AB antibodies in peri-transplant period by plasmapheresis and minimising the immune reaction by using extra immunosuppression with rituximab, immunoglobulins, and splenectomy [5,6,7]. Though splenectomy is a recognised method to minimise the rejection related to ABOi-LT, it was not performed in this child. As his anti-A levels were relatively low, risks associated with splenectomy such as infections, splenic vein thrombosis and the reduced portal venous flow outweighed the anticipated benefits of splenectomy [6,7].

Early outcomes in ABOi-LT have shown reasonable graft survival even in the absence of above measures, indicating that there are other mechanisms to develop immune tolerance in the liver [5,7]. Anti-AB isoagglutinin levels in infancy are relatively low and rise gradually with ageing. Therefore, rejection in ABOi-LT is lesser under one-year-olds.

In this case, there was no time for conditioning of ABOi-LT, pre-LT and anti-A level was safe to proceed. Post-LT, the child was given triple immunosuppression, and anti-A level remained low, hence did not required plasmapheresis. This was not complicated with immediate AMR, possibly due to the relatively low levels of anti-A Pre-LT and the child being younger and adequate immunosuppression post-LT [7]. However, he is being monitored for further short term and long-term outcomes.

Emergency liver transplant is the only rescue treatment in medically refractory ALF. Finding a suitable liver graft within 24 - 48 hours is essential to save life in such instances. Though there are well established deceased donor LT programmes in the West and America facilitating this prompt availability of grafts, it is challenging in Asian part of the world with limited DDG. Further, among living donors who are mostly the family members, it is not always possible to find a blood group matched donor. In such instances ABOi-LT becomes the only option to save life [3]. Nevertheless, it is demanding to manage more complicated ABOi-LT compared to standard matched LT in resource limited setting like Sri Lanka, due to the cost of additional immunosuppression and extended hospital stay.

Conclusion

ABO incompatible, LDLT is lifesaving in paediatric ALF, especially in a country without a good availability of DDG. Setting up dedicated liver transplant facilities would help to mitigate current logistical issues.

Authors contributions

All authors contributed the clinical management of the patient and manuscript writing. All authors read approved the final manuscript.

Competing interests

None declared.

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Ethical aspects

No ethics concerns identified.

Patient consent

Informed written consent obtained from the parents for publication.

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Abbreviations

LT - Liver transplant

ALF - Acute liver failure

ABOi-LT - ABO incompatible liver transplant

SL - Sri Lanka

DDG - Diseased donor grafts

AMR - Antibody mediated rejection

BMI - Body mass index

LDLT - Living donor liver transplant

MOH - Ministry of Health

MMF - Mycophenolate Mofetil

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