CASE REPORT

Auxiliary partial orthotopic liver transplant for Criggler-Najjar Syndrome: Report of 2 cases from Pakistan

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Abstract

Auxiliary partial orthotopic liver transplant (APOLT) is a treatment option for certain liver disorders where liver structure is preserved. It includes Criggler Najjar syndrome (CNS), urea cycle defects and familial hypercholesterolaemia. Liver transplant as a treatment modality has only recently become available in Pakistan. Here we report two paediatric cases of CNS type 1 where auxiliary liver transplant was performed to correct jaundice and prevent inevitable brain damage. Both recipients and their respective living donors had successful surgery and are doing well.

Keywords: Transplantation, Liver, Graft, Criggler Najjar Syndrome

Introduction

Criggler Najjar Syndrome (CNS) is characterized by unconjugated hyperbilirubinaemia in early neonatal age and can lead to irreversible neuro-developmental abnormalities and mortality if untreated. Conservative management with phototherapy is prone to failure as with growth of the child there is increase in body surface area which makes it less effective.[1] Since only 1-2% of total hepatocyte number is required to conjugate bilirubin and because OLT carries significant morbidity and mortality, auxiliary partial orthotopic liver transplant (APOLT) was proposed as an alternative treatment for CNS type 1. In this case usually only the left lateral segment of the recipient liver is removed and replaced with a similar sized donor graft. The APOLT has several advantages over complete OLT. It is associated with lower complications rate, in case of donor graft failure it can be removed and it offers a potential future option of liver directed gene therapy.[1,2]

For patients with liver failure in Pakistan, liver transplantation is a promising new development.[3] Here we report two paediatric cases of CNS type 1 who underwent successful auxiliary liver transplant at Shifa International Hospital in June 2014 from related living donors. Both patients are thriving well with near normal liver functions and no donor mortality.

Case One

A 6 year old child presented with a complaint of jaundice since birth. At birth patient was diagnosed with CNS type 1 and was subject to 8-10 hours of photo therapy daily but with static serum bilirubin levels of 15 to 18 mg/dl. She recently developed speech difficulty and mild ataxia. The child weighed 15 kg and was 104 cm tall. She was developmentally normal. On clinical examination, jaundice was the only positive finding. Cerebellar examination showed ataxic gait with a normal finger nose test. Parents opted for the liver transplant with complete knowledge of the fact that neurological functionality may not improve with transplant. Parents were first degree relatives and child's other three siblings were healthy.

Auxiliary transplant was performed with the left lateral segment of liver being donated by the mother. After left hepatectomy of the recipient, a left lateral segment graft from the donor was taken and transplanted orthotopically. Actual graft weighed 258 grams. Left hepatic artery (LHA) was anastomosed with common hepatic artery (CHA) of the recipient. Recipient's LHA was not used due to size mismatch and CHA was divided proximally to the origin of gastrodoudenal artery (GDA). Blood supply to the native right liver was preserved through pancreaticodoudenal branches of superior mesenteric artery (SMA) and GDA. Left hepatic vein (LHV) was anastomosed with inferior vena cava (IVC) of the recipient, left portal vein (left portal vein) with LPV and left hepatic duct (LHD) with LHD of the recipient.

Post-transplant recovery was uneventful. Patient was discharged on immunosuppressants including tacrolimus and steroids on day 10. She is doing well 1 year post transplant. Interestingly her speech and gait abnormality reversed with APOLT. Her liver function tests at 6 months post-transplant are shown in Table.

Case Two

A 6 year old boy presented with jaundice since birth. He was diagnosed with CNS type 1 at two weeks of age and

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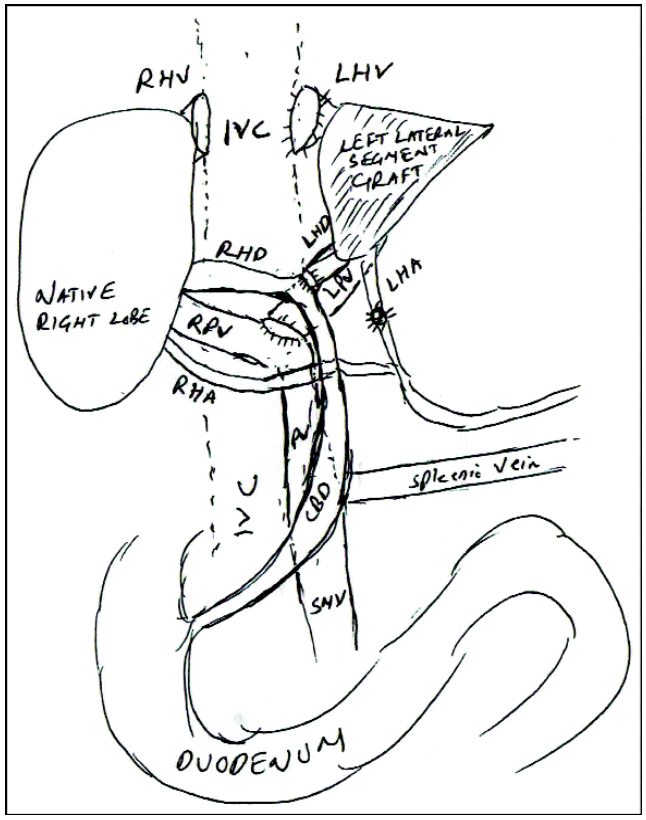
Table: Pre transplant and 6 months Post-transplant liver function tests.

Laboratory investigations	Child 1		Child 2		
Transplant	Pre transplant	6 months after transplant	Pre transplant	6	months after
Aspartate aminotransferase (AST)	52	28	996	28	
Alanine aminotransferase (ALT)	59	30	1004	38	
Total bilirubin	37.5	0.58	10	3.6	
Direct bilirubin	0.8	0.23	4	0.8	
INR	1.0	1.0	1.2	0.9	
Serum Albumin	4.3	4.1	2.0	3.5	

Acute liver failure (ALF)
Orthotropic liver transplant (OLT)
Criggler-Najjar syndrome (CNS)
Auxiliary partial orthotropic liver transplant (APOLT).



RHA:Right hepatic artery; LHA; Left hepatic artery;RPV:Right portal vein; LPV: Left portal vein; SMV: Superior mesenteric vein; CBD: Common bile duct; RHD: Right hepatic duct; LHD: Left hepatic duct; LHV:Left hepatic vein; RHV: Right hepatic vein; IVC: Inferior vena cava.

Figure: Diagram demonstrating technique of auxiliary partial orthotopic liver transplant.

since then was receiving photo therapy. There was no prior history of maelena, haematemesis or seizures. He was developmentally normal. On examination his height was 113cm and weight 20 kg. There was mild jaundice but no hepatosplenomegaly or signs of portal hypertension. Reflexes were brisk with down going plantars. Examination of all other systems was normal. His mother donated left lateral segment of liver. Figure highlights the surgical details in this patient. The weight of the graft was 324 grams. He is also doing well one year post transplant. His liver function tests are shown in Table. Liver function tests of both the donors returned to normal in 20 days.

Discussion

In conventional liver transplant, patient's whole liver is replaced with a liver from a brain dead or living donor. Auxiliary liver transplant is proposed for liver-based metabolic defects that do not structurally damage the liver such as CNS I, urea cycle defects, and familial hypercholesterolaemia. Patients with acute liver failure who fulfil transplant criteria but can have a complete morphological and functional recovery of their native liver in future are potential candidates for APOLT.

Studies show that only 1% to 2% of normal hepatocyte mass is required for bilirubin conjugation. In APOLT, since native liver is only partially replaced, metabolic defect can be corrected with preservation of the native liver. In case of graft failure, the patient still has a functional native liver. In the future, a suitable gene therapy may offer permanent cure to this metabolic abnormality and the patient can live with his own liver while the graft is allowed to atrophy by withdrawal of immunosuppression. Similarly in the setting of acute liver failure, APOLT leaves the possibility of regeneration of the native liver, in which case immunosuppression can be stopped and the graft allowed to atrophy.[1,2]

CNS is a rare inherited disorder. It can lead to severe disability and death from kernicterus due to unconjugated hyperbilirubinaemia. The underlying problem is impaired bilirubin conjugation and elimination due to a mutation in uridine 5'-diphosphate glucuronyl transferase. While CNS type 2 has partial

deficiency of enzyme and usually runs a benign course, type one has total deficiency of the enzyme manifesting in neonatal period and risk of mortality at a young age. Patients with CNS type 1 need10 to 12 hours of phototherapy to prevent kernicterus. Liver transplantation is the only permanent cure. Special phototherapy beds and bili-beds are also available to provide maximum body exposure for longer periods. The main aim of therapy is to prevent brain damage by keeping the levels of unconjugated bilirubin as low as possible.[4]

It is argued that liver transplantation is curative only if performed before the development of neurologic dysfunction and other urgent treatment options including plasmapheresis, exchange transfusion, phototherapy and liver transplantation may not reverse brain damage.[5] In our case the patient had initial signs of central nervous system involvement but after transplant the neurological symptoms reversed. This might be secondary to maintenance of lower bilirubin levels in the pre-transplant phase and transplantation at earlier stage of neuro-developmental involvement. Neurological improvement has been demonstrated in some other studies.[6,7] Transplantation at a younger age and early manifestation of neurological symptoms might produce better post-operative neurological outcomes. In 20 successful APOLT over a period of 19 years for various conditions, 17(85%) patients were alive on 113 months of follow up. When native liver regeneration was observed on CT volumetry and confirmed on liver biopsy, withdrawal of immunosuppression was commenced.[8]

Hepatocyte transplantation is being evaluated as an alternative to OLT in management of hepatic metabolic conditions for long-term, albeit partial, correction of the underlying metabolic defect.[9] Liver directed gene therapy is another potential alternative treatment and holds hope for the future whereby the patient's hepatocytes are transduced with the wild-type gene. This modality of treatment remains in its infancy primarily due to the fact that many liver diseases progress to a fibrotic stage with significant change of liver parenchyma, vasculature, and sinusoids.[10]

Conclusion

Auxiliary liver transplant provides adequate hepatocyte mass to correct the underlying metabolic abnormality in CNS type 1. It serves as a safety net in case of graft failure. It also keeps open the option for future liver directed gene therapy. Patients with CNS 1 should be referred early for liver transplantation in particular before the onset of neurological symptoms to achieve best outcomes.

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