The First Successful Pediatric Liver Transplant in the Armed Forces

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Introduction

Wilson's Disease (WD) is a rare, autosomal recessive disorder which affects copper metabolism and may present in childhood with liver dysfunction or rarely, as acute liver failure in childhood [1] when liver transplantation is a treatment option. We report an eleven-year old boy who was diagnosed to have Wilson's Disease with acute liver failure. He underwent the first successful pediatric liver transplant in the Armed Forces.

Case Report

A eleven-year old male child was referred to our hospital with history of fever of two months duration, jaundice, loss of appetite and lethargy, all of one month duration. Jaundice had progressed rapidly over the last ten days preceding admission. He had previously been investigated in a private hospital, treated on the lines of enteric fever, malaria and viral hepatitis. There was no history of jaundice in the sibling or other family members.

At admission, the child weighed 34.75 kg (50th centile 32.4 kg), had deep icterus, pallor and pedal edema. There were no stigmata of chronic liver disease. Higher mental functions were preserved, he had hepatomegaly of 2 cms, splenomegaly of 1 cm and ascites. Ophthalmic examination revealed bilateral Kayser Flescher (KF) rings.

Initial laboratory investigations revealed a serum bilirubin of 35.5 mg/dL (conjugated fraction 24.1 mg/dL), aspartate aminotransferase (AST) of 106 U/L, alanine aminotransferase (ALT) of 9 U/L, serum alkaline phosphatase (SAP) of 42 U/L, serum albumin of 2.4 g/dL and an International Normalized Ratio (INR) of 4.11. His haemoglobin was 4.0 g/dL, corrected reticulocyte count 4.2%. The total leukocyte count was 6400/cumm with a differential count of 65% polymorphs and 29% lymphocytes. Peripheral blood smear revealed haemolysis, Coombs test was negative. Serum ceruloplasmin was low –

0.143 g/L (normal 0.204 to 0.407 g/L). His 24-hour urinary copper excretion was elevated at 474.4 mcg/L (normal 20-40 mcg/L). Investigations for infective etiology including common viral agents that could present in this manner and markers for autoimmune and metabolic liver disease were negative. His blood group was A positive.

Based on the diagnosis of acute liver failure due to Wilson's disease and a Revised King's Score (Wilson Index) of 14 (Table 1), the family was counselled about the need for a living donor liver transplant (LDLT). The mother was willing and her blood group matched, but her liver anatomy precluded her from donating. The child's father, whose blood group is O positive also agreed to donate and was found suitable. His serum ceruloplasmin and urinary copper excretion (after penicillamine) were normal. A left lobe graft without caudate lobe and including middle hepatic vein was planned. Computed tomography (CT) angiography of the donor revealed replaced left hepatic artery arising from left gastric artery and segment IV artery from right hepatic artery. The recipient too had an accessory left hepatic artery arising from the left gastric artery in addition to the normal left hepatic artery arising from the common hepatic artery.

On 19 Aug 08, the child was transplanted with the father's left lobe. The graft was harvested without inflow occlusion. The graft weighed 500 g and was reperused in the donor via the portal vein. Both middle as well as left hepatic artery of the graft was anastomosed to the recipient's left hepatic artery and accessory left hepatic artery respectively. Biliary continuity was restored by duct to duct anastomosis without any stent (Fig. 1). The explanted liver was shrunken, nodular and green (Fig.2). The patient was given intravenous methylprednisolone at a dose of 10 mg/kg during the anhepatic phase followed by 2 mg/kg upon arrival in the transplant intensive care unit. The patient had an uneventful recovery following transplant and was switched to oral immunosuppression with Tacrolimus at a dose of 0.075 mg/

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Table 1
Revised King's score for liver transplantation in Wilson's disease

Score	Bilirubin ($\mu\text{mol/L}$)	INR	AST (IU/L)	White Cell Count ($10^9/\text{L}$)	Albumin (g/L)
0	0 - 100	0 - 1.29	0 - 100	0 - 6.7	> 45
1	101 - 150	1.3 - 1.6	101 - 150	6.8 - 8.3	34 - 44
2	151 - 200	1.7 - 1.9	151 - 300	8.4 - 10.3	25 - 33
3	201 - 300	2.0 - 2.4	301 - 400	10.4 - 15.3	21 - 24
4	> 300	> 2.5	> 401	> 15.4	< 20

Note: Bilirubin of 1 mg/dL = 17 $\mu\text{mol/L}$ [1]

Table 2
Post-transplant values of liver function tests

	26 Aug 2008 (1 week post-transplant)	15 Sep 2008 (4 weeks post-transplant)	20 Oct 2008 (2 months post-transplant)	24 Nov 2008 (3 months post-transplant)	13 Dec 2008 (4 months post-transplant)
Serum Bilirubin (mg/dL)	4.8	1.9	0.6	0.6	0.7
Aspartate aminotransferase (U/L)	58	33	31	37	36
Alanine aminotransferase (U/L)	125	84	31	46	44
Serum alkaline phosphatase (U/L)	69	161	87	72	101
Gamma glutamyl transpeptidase (U/L)	331	150	25	68	53
Serum albumin (g/dL)	3.2	4.0	4.7	4.0	4.4
International normalized ratio	1.25	1.10	1.2	1.10	1.09

Fig. 1 : The left lobe liver graft in situ in the recipient

Fig. 2 : The explanted liver shrunken and with visible nodules

kg/ dose twice a day. Upon achieving total oral immunosuppression by 4th post-operative day, tacrolimus dose was adjusted based on trough levels. The donor also had an uneventful recovery following surgery. Both were discharged on 19 Sep 08. Subsequent follow-up at four months post-transplant revealed an active and cheerful child with normal liver functions and acceptable tacrolimus levels. Hepatic blood flow and echotexture were normal on ultrasound. His serum ceruloplasmin levels had normalized (0.312 g/L). The child is on oral immunosuppression and regular follow-up. The results of serial liver function tests of the patient following transplant are depicted in Table 2.

Discussion

Wilson's disease was diagnosed in this patient based

on the clinical features, KF rings, low serum ceruloplasmin, elevated urinary copper excretion and a Coomb's negative haemolytic anaemia [1]. There is no dispute about liver transplantation for Wilson's disease presenting as fulminant hepatic failure with encephalopathy. However, transplant for a patient with deranged liver functions without encephalopathy, like our patient, is best decided by applying the Revised King's Score. A score of > 11 based on features at presentation predicts likely death without transplantation with a sensitivity of 93%, specificity of 98% and a positive predictive value of 88% [1]. Our patient qualified for a liver transplant as his score was 14.

Good results following liver transplantation in Wilson's disease have been reported recently from Poland [2] where 11 patients of WD were followed up for a median

of 2.47 years post-transplant with 100 % survival. In a longer median follow-up period of ten years, all 13 patients of WD who were transplanted survived with normal liver functions as reported from France [3]. Since the father was the donor, he could have been a carrier of the autosomal recessive gene. This however, does not preclude him from being a donor. Asonuma et al [4], have reported 11 transplants in children with WD where the donors were heterozygotes. At a mean follow-up of 31 months, all recipients were alive and well with the ceruloplasmin levels normalizing in all.

World over, acute liver failure due to any cause is an important indication for liver transplantation in adults as well as children [5-7]. The results of liver transplantation in children are very encouraging with one year survival of more than 90% and 10-year survivals in the range of 74-80% [8].

The first successful pediatric liver transplant in India was reported in 2001 [9]. The Liver Transplant Unit at Army Hospital (R & R) was established in Mar 07 and 30 transplants have been done to date of which 21 are cadaver donor organ and nine are living donor organ transplants. The first successful pediatric liver transplantation at this unit was done in Aug 2008 and a total of five pediatric patients (four survivors) have been transplanted including a 14 month old who received an in-situ split cadaver organ. Timely referrals of children with liver disorders could help provide them this therapeutic option with excellent results and near-normal quality of life.

Conflicts of Interest

None identified

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Book Review

Robert E, Marx DS. Oral & Maxillofacial Pathology: A rationale for diagnosis and treatment. Quintessence books, 2008 Edition, hard cover. Pages 908, Price-200/, ISBN Number-0-86715-390-3.

This clinically oriented text book of oral and maxillofacial pathology addresses the underlying mechanism of each disease, its clinical and radiographic presentation, differential diagnosis, specific treatment recommendations that are supposed to be most beneficial and the prognosis after treatment. The authors have challenged many long-held concepts that are no longer valid but have been passed down to succeeding generations of dental and medical students. The aim is to increase the knowledge and understanding of oral and maxillofacial surgeons and other entrusted with the care of these patients. This book features more than 2,100

photographs and covers more than 425 diseases and conditions that affect the oral, head and neck region. This book for sure will raise the standard of care in oral and maxillofacial surgery and pathology to a new level. Practicing oral and maxillofacial surgeons and pathologists, residents-in-training and allied specialists in medicine and dentistry will consider this book an indispensable addition to their library.

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