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Case Report

One Step at a Time: A Pediatric Case of Primary Two Staged Liver Transplantation in a Child with ESLD

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Abstract: Toxic liver syndrome is a rare condition with multiorgan failure in end-stage liver disease (ESLD), and a two-stage LT following hepatectomy with a prolonged anhepatic phase is an accepted approach to bridge to transplant. This primary approach has not been described for toxic liver syndrome in children with ESLD. We report a 6-year-old boy who developed toxic liver syndrome with multiorgan failure while awaiting LT for ESLD from biliary atresia and failed Kasai at the age of 2 years. Deemed too sick to transplant, he underwent full hepatectomy and portocaval shunt placement. The child was then transplanted hemodynamically stable after an anhepatic phase of 10 h and 30 min. Although his initial graft showed primary liver dysfunction and he needed re-transplantation after 14 days, he was able to leave the hospital 4 months following 2nd LT and is well with a fully working graft 5 years later. Primary two stage LT is feasible in children in dire situations.

Keywords: two stage liver transplantation 1; end-stage liver disease (ESLD) 2; biliary atresia 3; pediatric 4

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1. Introduction

Despite all advancements in the field of pediatric liver transplantation, due to severe organ shortage even today up to 15% of children die on the waiting list [1]. Toxic liver syndrome is defined as severe systemic inflammation in the setting of acute on chronic liver failure and necrosis leading to multiorgan systemic disease with renal and respiratory decompensation, as well as hemodynamic instability, and is usually fatal [2,3]. In 1988, Ringe and colleagues first described a two-step approach to transplant a liver in a patient with primary graft failure and toxic liver syndrome and in current AASLD guidelines a two-stage liver transplantation (LT) procedure is recognized as a bridge to transplantation in dire situations for adults [4,5]. For children, options for bridge to transplantation are limited, and the literature on two-stage LT is scarce. Although primary two stage LT has been described in children for trauma, to the best of our knowledge, it has not been described in children with toxic liver syndrome in the setting of acute on chronic liver failure.

2. Case Report

We report a boy with non-syndromic biliary atresia (BA) who underwent Kasai procedure at 57 days of life. Due to failing Kasai, he was listed for LT at the age of 7 months. His course was further complicated due to several episodes of culture negative sepsis, often requiring broad-spectrum antibiotic treatment making him temporarily unfit for transplantation. Immune phenotyping and whole exome sequencing was unremarkable. Additionally, no live donor was available and despite the application of exception points granted for BA in Germany, as well as considering an AB0-incompatible organ for transplantation, the child received insufficient offers for timely transplantation.

At the age of 2 years and five months, he presented with increasing ascites and suspected early hepato-renal syndrome with chronic kidney disease (HRS-CKD) and subsequently developed toxic liver syndrome. Despite intensive medical therapy, the boy deteriorated and became hemodynamically instable and anuric. In this condition, he received an organ offer of a 64-year-old female of marginal quality. The decision was made to accept this organ as part of a primary two-stage LT in the setting of suspected toxic liver syndrome. Critically ill on three pressors, intubated, anuric, and high inflammatory markers such as IL6 (59,040 pg/mL) the boy was brought to the OR and full hepatectomy was performed. A portocaval shunt was sown in place.

Post hepatectomy, a cytokine absorption filter (Cytosorb®, Berlin, Germany) was installed. Back in the ICU following the hepatectomy and during the anhepatic phase, the child stabilized. Hemodynamic support could be reduced significantly, and even some diuresis was seen. The inflammatory markers decreased significantly to an IL6 of 6000 pg/mL at time of transplantation. In total, the boy was anhepatic for 10 h and 30 min.

In the interim, the donor graft was airlifted to our center and was subsequently split to generate both a left lateral segment (LLS) and an extended right lobe (RL), both of which were to be transplanted in our center. The LT was complicated by repeated arterial thrombosis with a prolonged warm ischemia time. The child received a total of 150 mL/kg of red blood cells aside several other blood products.

Following the transplant, over the next few days the child stabilized significantly from a hemodynamic standpoint and further regained both kidney function and respiratory stability. He was extubated on postoperative day five and showed further clinical improvement thereafter.

Despite this significant clinical improvement and some synthetic activity by the new graft, overall, there was poor organ function and the child met criteria for primary non-function without any signs of technical or immunological problems. Consequently, he was relisted for LT. (Interestingly, the same was true for the patient who had received the extended RL of the same donor, who had also been transplanted in our center). Thirteen days after his first transplant, the boy was successfully re-transplanted, this time with a LLS from an ex vivo split from a 26-year-old donor. The second transplant, as well as the remaining postoperative course were uneventful. Today the child is well, attending primary school without limitations, 5 years following the transplant.

3. Discussion

To the best of our knowledge, this is the first reported case of a successful primary pediatric two-staged LT in the setting of toxic liver syndrome in a child with BA and acute on chronic liver failure.

So far, Ringe and colleagues in 1993 described the largest series of twelve patients undergoing primary or secondary two-stage LT including five children, two of which survived [3]. Overall, of the 12 patients who underwent primary hepatectomy, four patients died prior to LT and only 3, one after secondary two-stage procedure prior to re-LT, survived. Only one of these two children who survived underwent primary hepatectomy. However, this was a 14-year-old girl and the indication for primary hepatectomy was not toxic liver syndrome, but a traumatic liver injury. Therefore, this case is hard to compare to ours. Additionally, given that the girl was 14 years old, biology and physiology are more

comparable to that of an adult. Our child, on the other hand, at the time of transplant showed a body weight of 16 kg and can be considered a true pediatric transplant.

Table 1 summarizes children who were reported in literature with at least some available clinical details undergoing primary and, for the majority, secondary two-stage LT. None of these transplants was for toxic liver syndrome. Although the reason why most reported two stage LT cases are mainly post unsuccessful liver transplantation remains elusive, this is maybe due to its serious invasive manner and considering this approach as a last option, only in life threatening circumstances.

Despite the general poor survival rates with regard to two-stage LT described by Ringe et al., in a more recent case series of 6 adults undergoing primary hepatectomy prior to liver transplantation, who remained anhepatic from 330 up to 2640 min, only one patient died [6].

Table 1. Summary of available literature.

Age	Gender	Indication for LT	Primary vs. Secondary Hepatectomy	Indication	Anhepatic Duration	Survival	Reference
14 years	Female	Liver Trauma	Primary Hepatectomy		14 h 45 min	46 months	Ringe [3]
12 years	Female	Budd Chiari	Secondary Hepatectomy	(1) ACR after LT for acute Budd Chiari (2) ACR	(1) 17 h 43 min then re-LT (2) 9 h then re-LT	yes	Ringe [3]
19 months	Male	Acute liver failure	Secondary Hepatectomy	Primary non-function	163 h then re-LT	Yes	Ringe [7]
3.5 years	Male	Giant Cell Hepatitis	Secondary Hepatectomy	Primary non-function	66 h then re-LT	yes	Hammer [8]
Not available	Not available	Not available	Secondary Hepatectomy	Primary non-function	26 h	Not available	So [9]
Not available	Not available	Not available	Secondary Hepatectomy	Primary non-function	48 h	Not available	So [9]

(h) hours; (min) minutes.

In our case, it remains uncertain how much the cytokine hemadsorption device post hepatectomy influenced the sharp decrease in inflammatory markers, stabilization in hemodynamics, and improvement of renal function, but we consider the prolonged anhepatic phase crucial for stabilizing this patient and to allow liver transplantation.

We are in full accordance with the current AASLD guidelines, which clearly state that a two-stage procedure "can only be advocated as a last resort with a suitable liver graft en route" [5].

This case, however, also illustrates that if the unfortunate situation of toxic liver syndrome does arise for whatever reason, primary two-stage LT can be carried out as bridge to transplantation even in a small child.

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