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Case Report



# Domino Liver Transplantation for Familial Amyloidosis Polyneuropathy: Case Report and Review of Literature

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## Abstract

Liver transplantation remains the gold standard therapy for end stage liver disease. Limitations to this therapy are based around graft availability. Domino liver transplantation (DLT) is an emerging strategy by increasing the number of liver grafts available. Livers that appear normal in structure but come from donors with metabolic diseases can be used for certain patient profiles. Familial Amyloidotic Polyneuropathy (FAP) is the most common indication for DLT. These patients constitute a potential cohort of living donors, whose native explanted livers may be viable for transplantation into another recipient. This strategy has proven to expand the donor pool and has been validated with excellent results.

**Keywords:** Domino liver transplant, Amyloidosis, liver transplant, FAP

## Introduction

Familial Amyloidotic Polyneuropathy (FAP) is an autosomal dominant disorder (linked to chromosome 18). The liver produces a variant pre albumin that is deposited along nerves, leading to progressive and fetal neuropathy. A point mutation in protein Transthyretin (TTR). More than 80 amyloidogenic TTR variants have been described [1-3]. The most common form leading to transplantation is a point mutation of Methionine substituting Valine at position 30." TTRval30met" and TTRval 122 Ile is carried by approximately 3.9% in Afro Americans [4]. Liver transplant has been the only successful treatment to date.

The first symptoms usually occur during the third decade of life (*Andrade, et al and Coutinho, et al.*) The patients subsequently develop a progressive sensor motor neuropathy with autonomic dysfunction, gastrointestinal disorder, orthostatic hypotension, weight loss, and frequent cardiac and renal involvement leading to death within a mean of 10.8 years (*Coutinho, et al.*)

Recently, liver transplantation has been proposed as a means of treating this condition as the liver is the main source of TTR, as shown by in situ hybridization *Jacobson, et al.*, by the dramatic reduction of abnormal serum TTR levels in the first patients who have been operated on *Holmgren, et al.*, The favorable clinical results in the first four patients *Holmgren, et al.*, prompted several centers to perform liver transplantation in FAP patients (*Steen, et al*)

Three other kinds of domino liver grafts for metabolic disorders have also been reported, including:

i. Primary hyperoxaluria

ii. Homozygos Familial Hypercholesteremia (HFH)

iii. Maple Syrup Urine Disorder (MSUD)

iv. Protein C deficiency

## Case Report

The patient is a 66-year-old Caucasian with a history of progressive polyneuropathy particularly in his lower extremity, refractory diarrhea, and orthostatic hypotension for 2years. He underwent extensive work out including small bowel biopsy spectroscopy shown amyloid and DNA sequencing Valine 30 methionine mutation consistent with Familial systemic amyloidosis. The patient underwent liver transplant evaluation in our center and successfully completes all the requirement. He also consented to donate his liver for someone else on the list as a" Domino". The recipient of the domino liver was 50 years old gentleman with the history of end stage liver disease secondary to hepatitis C, alcoholic cirrhosis and Hepatocellular carcinoma which was out of Milan criteria who underwent Radiofrequency ablation for down staging to meet Milan criteria for liver transplantation. He also consented to receive a liver graft from patient who has familial amyloidosis polyneuropathy, and he understands risk and benefit and chance of developing systemic amyloidosis in the future that may need another liver transplant.

## Surgical Technique

A cadaveric graft from a 43-year-old woman who progress to brain death due to intracerebral bleeding became available and was harvested with standard multi visceral organ retrieval technique. The native hepatectomy in FAP patient performed with standard fashion we were able to get good length in the supra hepatic vein without piggyback technique (Figure 1).

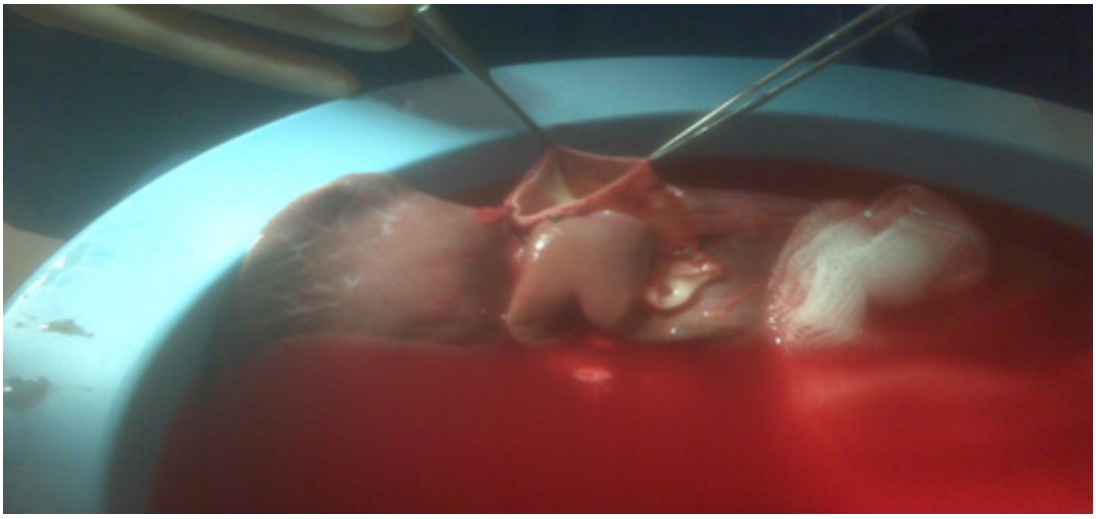

**Figure 1:** It showed length of supra hepatic vein after hepatectomy.

The Tru cut needle biopsy from the FAP liver showed less than 5% macro and micro vesicular fat, no fibrosis.

Then proceed with standard Hepatectomy while coordinating with FAP recipient surgeon on the other room. We divide the hepatic artery at the bifurcation of proper hepatic artery and Gastro duodenal artery. Figure 2 Portal vein divided 1cm below the bifurcation and bile duct divided below the cystic duct.

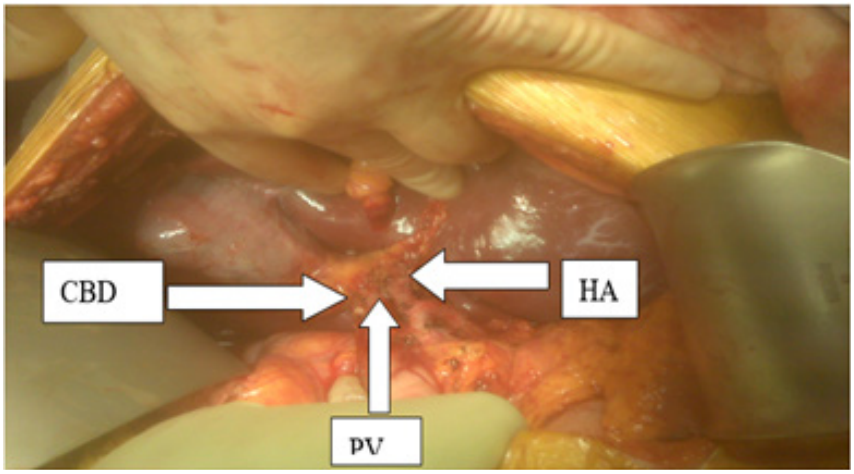


**Figure 2:** FAP liver, showed transaction line for HA (hepatic artery), Portal vein (PV) and CBD (Common Bile Duct).

The liver flushed in the back table with two liters of University of Wisconsin, UW, solution through the portal and hepatic artery. The gallbladder flushed with UW solution as well. The FAP liver put in ice back and transport to the recipient room. The cadaveric allograft transplanted with standard fashion without piggyback, or venovenous bypass to the patient with FAP. Biliary anastomosis was performed duct to duct without T-Tube. Total operating time was recorded 240min and no blood and blood products required. Figure 3. Pt extubated in the operating room.

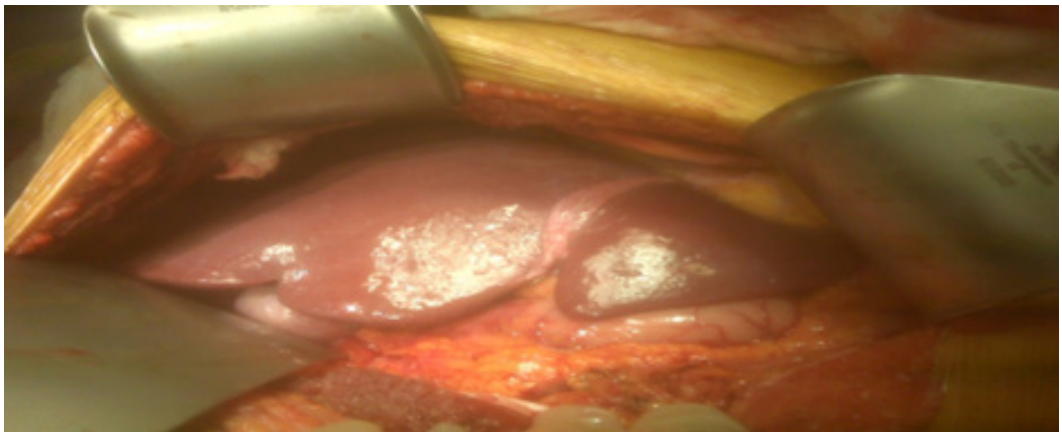

**Figure 3:** Post perfusion view.

At the same time in the other room, the recipient of the FAP liver was explored by another surgeon. No extra hepatic metastasis noticed and sample lymphadenectomy from hepatic artery and common bile duct send for frozen that showed negative for malignancy. Then proceed with native hepatectomy with standard fashion without Piggyback or venovenous bypass. The hepatic artery, portal vein and CBD divided close to the hilum to get enough length. The supra hepatic vein divided close to the Rt, Middle and Lt hepatic veins.

All anastomoses done in standard fashion, no piggyback or venovenous bypass (VVB) required. Biliary anastomosis performed as a duct to duct without T-Tube. No blood transfusion required. Patient extubated in the OR. Total operating time recorded 240min. total cold ischemic time was less than 15min. total warm ischemic time was less than 30min. Peak AST level post op was 290.

## Discussion

Orthotopic liver transplantation has evolved to be an established treatment for end stage liver diseases, but the ongoing shortage of suitable livers, together with progressively longer waiting lists, prevents many patients from being transplanted [5]. Because of this, many patients die while being on the waiting list [6,7]. The use of livers from living donors is one way to increase the supply of liver grafts that can be used for transplantation [8,9]. One group of potential living liver donors consists of some selected liver recipients whose own native explanted liver, in turn, can be considered for transplantation into another patient. This technique has been named "Domino Liver Transplantation (DLT)" and was first carried out in Portugal on October 26, 1995. The domino approach can be considered in patients with some genetic or biochemical disorders that today are treated by liver transplantation. The rationale behind this is that such livers ultimately cause severe systemic disease but are otherwise normal. The primary and main indication until now has been Familial Amyloidotic Polyneuropathy (FAP) [10-12].

FAP is debilitating disease that progress to fetal neuropathy and death in relatively young age. The diseases started in the 3rd decade of life; the minimum time that required the disease to affect the patient is 20 years.

The disease is endemic in Portugal, Sweden, and Japan [3,12,13]. Liver transplantation, which suppresses the main source of the amyloidogenic mutated TTR, is widely recommended for treatment of FAP. The first liver transplantation for hereditary TTR amyloidosis was performed in Sweden in 1990 on a patient with ATTR Val30Met. Today, liver transplantation for TTR amyloidosis is an established treatment. However, the disease is rarely seen except in a few endemic areas. But there is sporadic case has been reported in Brazil, France, UK, USA10. The first domino liver transplant done by Furtado on October 26, 1995, By December 31, 2006, a total of 579 domino liver transplantations done in 569 patients had been recorded in the Domino Liver Transplant Registry' DLTR' most are done in endemic area, there is a male predominance of 75% 13. In the United state up to now more than 50 domino liver transplants performed.

The advantages of domino liver transplant are:

i. Expanding the donor pool,

ii. Short cold ischemic time,

iii. Transplant patient with poor prognosis, and short window.

The main disadvantage is that the domino liver transplant can transfer the metabolic disease of the donor to recipient. There is no advantage in proceeding to liver transplantation in patients with severe sensor motor neuropathy/urinary incontinence or severe cardiac conduction disturbances as survival rate at five years after liver transplantation is like a control group.

In summary, domino liver transplantation for FAP has proven to be technically possible and expands the donor pool. It has been safe

for both the FAP liver donor and recipient. It is indicated in patients whose age or prognosis would delay or even preclude their receiving cadaver liver transplant. Longer term follow-up is required for final evaluation of the use and indications of this approach [14-17].

## Acknowledgements

None.

## Conflict of Interest

None.

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