Case Report

En-Bloc Liver-Pancreas Transplant in Iran

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Abstract

Liver transplant can be challenging in cirrhotic patients with diabetes mellitus. In chronic liver disease, the glucose metabolism is altered; uncontrolled diabetes negatively influences the outcome of liver transplantation and poses difficulty in the management of immediate post transplantation period. Simultaneous liver-pancreas transplantation is an option to prevent early complications due to diabetes and also to improve the quality of life after transplantation in patients with Insulin-Dependent Diabetes Mellitus (IDDM) and chronic liver disease. We report the first en-bloc liver-pancreas transplant done in the transplant history of Iran. We describe the technical details of the procedure as well as the short term outcome after transplantation. In this case report, we also discuss in some details, the surgical, medical and immunological advantages of combined liver-pancreas transplantation as opposed to separate implantation of both organs.

Keywords: Cirrhosis, diabetes mellitus, en-bloc, liver-pancreas, transplantation

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Introduction

ombined liver-pancreas transplantation was formerly used as a salvage procedure for non-resectable upper abdominal malignancies, but the procedure was almost abandoned due to poor outcome. 1,2 Recently, the indication for combined liver-pancreas transplantation has been changed and transplant surgeons have started using this technique for patients with IDDM who are candidates for liver transplantation at the same time. There are several advantages to using simultaneous liver-pancreas transplant such as insulin independence after transplantation, improving patient management and decreasing the risk of post transplant cardiovascular diseases.3 Diabetic patients who receive only liver graft are not only at increased risk of developing cardiovascular diseases but also remain diabetic after transplantation which may itself negatively affect the long-term graft survival.⁴⁻⁶ Though there are so many advantages to combined liverpancreas transplantation, surprisingly only few cases have been reported in the literature.⁷

Case Report

A 25-year old male (64 Kg in weight) with a history of IDDM since age 11, presented with intractable pruritis and jaundice at 19 years of age. His laboratory findings revealed elevated cholestatic enzymes and ERCP showed multiple bile duct strictures consistent with primary sclerosing cholangitis (P.S.C) which was later

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confirmed on liver biopsy.

In June 2012, the patient referred with advanced liver disease. He had intractable and refractory pruritis, was deeply jaundiced and anemic. He was on insulin therapy (90 units/day) and had a history of recurrent hypoglycemic episodes recently. His examination revealed no signs of diabetic neuropathy or retinopathy. At the time of admission, the laboratory parameters were as follows: total bilirubin 18.2 mg/dL, AST 106 U/L, ALT 73 U/L, Alkaline Phosphatase 3919 U/L, BUN 19 mg/dL, Serum creatinine 0.8 mg/ dL and Hemoglobin 7.7 g/dL. Bleeding profile was within normal

He received en-bloc liver-pancreas graft from an ABO identical deceased donor aged 15 years. Liver biopsy of the graft showed no macro- or microsteatosis.

Operative procedure started with a classic Mercedes incision. Hepatectomy was performed in standard fashion with caval cross clamping. The liver, along with the en-bloc duodenopancreatic graft, was then transplanted orthotopically. First, supra and infra hepatic caval anastomoses were done. Inflow was established by anastomosing the recipient's portal vein to the infrapancreatic superior mesenteric vein of the graft. Arterial anastomosis was performed between inferior orifice of the donor's aorta (including both celiac and the superior mesenteric arteries) to infra renal aorta of the recipient in end-to-side fashion. Finally, a Roux-en-y enteroenteric anastomosis was performed between the recipient's jejunum and graft duodenum for exocrine pancreatic and biliary drainage. Total duration of the operation was 360 minutes and 3 units of packed cell were transfused. Total cold ischemia time was 9 hours while warm ischemia time was 80 minutes. Post operative recovery was uneventful and the patient was discharged on the 15th post operative day with normal liver function tests and free of insulin therapy. Initial immunosuppression included induction with Alemtuzumab (Campath 1H) and maintenance therapy with Tacrolimus (target trough level 12 - 15 ng/mL) and mycophenolate mofetil (MMF) 2 g/day. Steroids were tapered down and completely withdrawn within 6 months post transplantation. The patient is insulin free, 10 months after transplantation and the hemoglobin A1C level and fasting C-peptide levels are also within normal range.

Discussion

The concept of multiorgan transplantation was first developed by Thomas E Starzl and his colleagues. They performed multiorgan transplants as salvage procedure in patients who had unresectable abdominal malignancies, but the procedure was largely abandoned due to poor outcome and disease recurrence.^{8,9}

The most accepted indication for combined liver-pancreas transplantation is chronic liver disease in patients who concomitantly suffer from IDDM. This approach not only corrects liver disease but at the same time allows the patient to have insulin independence.¹⁰

Certain liver diseases have strong association with diabetes mellitus; P.S.C is one of the diseases which has been described in association with diabetes mellitus type 1. 11,12 Other diseases of the liver which have direct association with diabetes mellitus are NASH, 13,14 and cystic fibrosis. 15 In selected cases, these diseases justify combined liver-pancreas transplantation.

As well as those previously mentioned benefits of combined liver-pancreas transplantation, it may have an immunologic advantage. Unlike liver, pancreas is considered a highly immunogenic organ¹⁶ and when liver transplant combines with other organ transplants such as pancreas or multiple organs, the liver can protect these organs from severe rejection episodes.^{17,18} Despite the advantages of combined liver-pancreas transplantation, only few centers have reported this kind of transplantation and only in limited numbers.⁷

In conclusion, en-bloc liver-pancreas transplantation may have some advantages over separate implantation of both organs in patients having IDDM and end-stage liver disease, including better long-term survival and better quality of life after transplantation. Moreover, combined transplant can prevent more serious rejection episodes due to the immunotolerant effect of liver allograft.

References

 Mieles L, Todo S, Tzakis A, Starzl TE. Treatment of upper abdominal malignancies with organ cluster procedures. Clin Transplant. 1990;

- **4**: 63 67
- Abu-Elmagd K, Bond G, Reyes J, Fung J. Intestinal transplantation: a coming of age. Adv Surg. 2002; 36: 65 – 101.
- 3. Aguirrezabalaga J, Gomez M, Novas S, Fernandez C, Corbal G, Fraguela J, et al. Combined liver-pancreas transplantation: contribution of five cases. *Transplant Proc.* 2002; **34:** 211 212.
- Haydon G, Neuberger J. Liver transplantation in cirrhotic patients with diabetes mellitus. *Liver Transpl.* 2001; 7: 234 – 237.
- Shields PL, Tang H, Neuberger JM, Gunson BK, McMaster P, Pirenne J. Poor outcome in patients with diabetes mellitus undergoing liver transplantation. Transplantation. 1999; 68: 530 – 535.
- Yoo HY, Thuluvath PJ. The effect of insulin-dependent diabetes mellitus on outcome of liver transplantation. *Transplantation*. 2002; 74: 1007 1012.
- Trotter JF, Bak TE, Wachs ME, Everson GT, Kam I. Combined liverpancreas transplantation in a patient with primary sclerosing cholangitis and insulin-dependent diabetes mellitus. *Transplantation*. 2000; 70: 1469 – 1471.
- Alessiani M, Tzakis A, Todo S, Demetris AJ, Fung JJ, Starzl TE. Assessment of five-year experience with abdominal organ cluster transplantation. *J Am Coll Surg.* 1995; 180: 1 9.
- Starzl TE, Todo S, Tzakis A, Podesta L, Mieles L, Demetris A, et al. Abdominal organ cluster transplantation for the treatment of upper abdominal malignancies. *Ann Surg.* 1989; 210: 374 – 85; discussion 85 – 86.
- Pirenne J, Deloose K, Coosemans W, Aerts R, Van Gelder F, Kuypers D, et al. Combined 'en bloc' liver and pancreas transplantation in patients with liver disease and type 1 diabetes mellitus. *Am J Transplant*. 2004: 4: 1921 1927.
- Thompson HH, Pitt HA, Tompkins RK, Longmire WP, Jr. Primary sclerosing cholangitis: a heterogenous disease. *Ann Surg.* 1982; 196: 127 – 136.
- Kay M, Wyllie R, Michener W, Caulfield M, Steffen R. Associated ulcerative colitis, sclerosing cholangitis, and insulin-dependent diabetes mellitus. Cleve Clin J Med. 1993; 60: 473 – 478.
- James O, Day C. Non-alcoholic steatohepatitis: another disease of affluence. *Lancet*. 1999; 353: 1634 – 1636.
- Day CP. Non-alcoholic steatohepatitis (NASH): where are we now and where are we going? Gut. 2002; 50: 585 – 588.
- Stern RC, Mayes JT, Weber FL, Jr., Blades EW, Schulak JA. Restoration of exocrine pancreatic function following pancreas-liver-kidney transplantation in a cystic fibrosis patient. *Clin Transplant*. 1994; 8:
- Humar A, Khwaja K, Ramcharan T, Asolati M, Kandaswamy R, Gruessner RW, et al. Chronic rejection: the next major challenge for pancreas transplant recipients. *Transplantation*. 2003; 76: 918 – 923.
- Calne RY, Sells RA, Pena JR, Davis DR, Millard PR, Herbertson BM, et al. Induction of immunological tolerance by porcine liver allografts. *Nature*. 1969; 223: 472 – 476.
- Benedetti E, Pirenne J, Troppmann C, Hakim N, Moon C, Gruessner RW, et al. Combined liver and kidney transplantation. *Transpl Int*. 1996; 9: 486 491.