# Case Report of an ABO-Incompatible Living-Donor Liver Transplant for a Familial Amyloid Polyneuropathy Patient



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## Abstract

**Liver transplant is a treatment for familial amyloid polyneuropathy. Few cases of ABO-incompatible living-donor liver transplant for familial amyloid polyneuropathy exist. The outcome of an ABO-incompatible living-donor liver transplant has improved recently, using local infusion therapy and rituximab prophylaxis. Here, we describe a successful ABO-incompatible living-donor liver transplant in a patient with familial amyloid polyneuropathy in whom disease progression ceased at 2 years' follow-up. Additionally, no evidence of acute or chronic rejection, or adverse events of the immuno-suppressive therapy, was seen. As a postoperative complication, fatty changes in the grafted liver because of malnutrition or adverse events of corticosteroids were confirmed by a liver biopsy taken early after transplant. The main cause of malnutrition was considered to be gastrointestinal dysfunction caused by familial amyloid poly-neuropathy. Therefore, before deterioration of digestive function, liver transplants should be considered for familial amyloid polyneuropathy. This case suggests that an ABO-incompatible living-donor liver transplant may provide greater opportunities for familial amyloid polyneuropathy patients.**

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## Introduction

Familial amyloid polyneuropathy (FAP) is an inherited form of systemic amyloidosis characterized by peripheral somatic and autonomic neuropathy associated with various involvement of visceral organs. Liver transplant is the treatment for FAP and is associated with favorable outcomes.[1] However, FAP is rare, and only 2 cases have been reported of ABO-incompatible (ABO-I) living-donor liver transplant (LDLT) for FAP patients.[2,3] Therefore, clinical features and treatment of FAP with ABO-I LDLT have not been studied in detail. Here, we describe an FAP patient who underwent an ABO-I LDLT.

## Case Report

The patient was a 35-year-old man, with a body mass index of 22.2 kg/m$^2$. He was impotent at 24 years of age, owing to erectile dysfunction. He had diarrhea and hypohidrosis at 32 years of age. Orthostatic hypotension was noted at 33 years of age. He had frequent diarrhea, anorexia, languor, fatigue, and paresthesia of the planta pedis from the age of 34 years onward. Because amyloid deposits were detected in the skin and large intestinal mucosal biopsy specimens by Congo red staining, his disease was diagnosed as FAP at 34 years of age. He underwent vitreous surgery to treat a vitreous opacity in his right eye at 30 years of age and in his left eye at 33 years of age. His father was diagnosed



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as having FAP and died at 43 years of age. Additionally, his grandmother was diagnosed as having FAP.

He was referred to our Department of Gastroenterologic Surgery at Kanazawa University for LDLT. The donor was his healthy mother. The recipient's blood type was A (+), which differed from the donor type of B (+). Although ABO-I LDLT was avoided, there was no candidate donor. Before the ABO-I LDLT, he underwent preoperative plasma exchange twice with fresh frozen plasma and was administered rituximab (375 mg/m$^2$) twice. These treatments effectively reduced his serum anti-B antibody level from 1:16 to 1:1 immediately before transplant. We performed an ABO-I LDLT using a right lobe graft without the middle hepatic vein (645 g), with splenectomy and intraportal catheterization. The graft recipient body weight ratio was 0.82 and comprised 49% of his standard liver volume. Immunosuppressants consisted of tacrolimus, mycophenolate mofetil, and a corticosteroid. Prostaglandin E1, methylprednisolone, and heparin were administered via the portal vein for 2 weeks. The target trough level of tacrolimus was 10 to 15 ng/mL for the first 2 weeks and was decreased gradually afterwards.

A slight increase in biliary tract enzyme levels was observed approximately 2 weeks after the LDLT. A liver biopsy was performed on postoperative day 23 for pathological investigation. Ten percent fatty changes in the graft were confirmed by histopathology. Fatty changes in the liver worsened on postoperative day 42, and a liver biopsy specimen revealed 70% to 80% macrovesicular steatosis (Figure 1). Color Doppler ultrasonography showed no abnormalities. Computed tomography (CT) scans revealed severe fatty changes in the grafted liver (Figure 2A) but neither vascular stenosis nor thrombosis. 99m-Tc galactosyl human serum albumin liver dynamic single-photon emission computed tomography did not reveal any deterioration in hepatic function. We suspected that either malnutrition resulting from the digestive disorder or adverse events of corticosteroid administration were associated with fatty liver. The patient had continued diarrhea and reduced dietary intake after the LDLT. We thought that mycophenolate mofetil administration was the precipitating factor for diarrhea, and reduced the dosage. We also tapered the dosage of corticosteroids. Computed tomography scans revealed marked improvement in fatty changes in the liver on postoperative day 144 (Figure 2B). As with other complications, *cytomegalovirus* antigen-positive status or cholangitis were often observed and treated with medication. No evidence of acute and chronic rejection or adverse events of the immunosuppressive therapy were observed at 2 years' follow-up. No abnormalities were reported in cardiac or renal function; however, treatment of diarrhea and orthostatic hypotension continued.

**Figure 1.** Liver Biopsy Specimen Revealed 70% to 80% Macrovesicular Steatosis

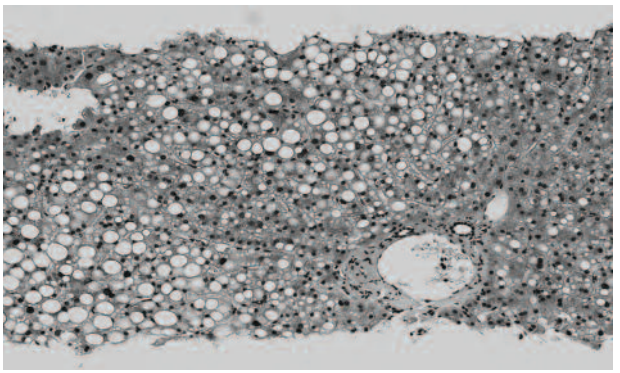
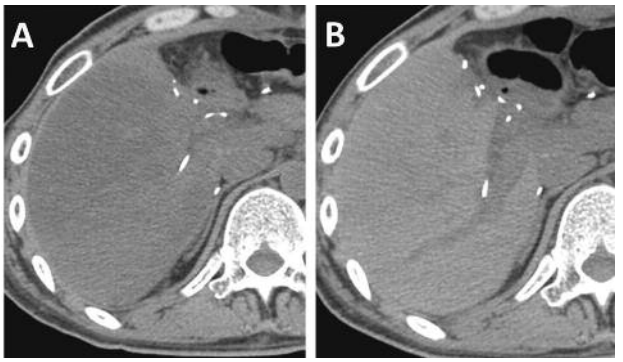


**Figure 2.** A Plain Computed Tomography Scan of the Grafted Liver Showed Severe Fatty Changes




**(A)** Postoperative day 42 and **(B)** marked improvement in fatty changes in the liver on postoperative day 144.

## Discussion

The outcome of an ABO-I LDLT has improved recently by using local infusion therapy and rituximab prophylaxis.[4] The number of deceased donors is limited in Japan, and living relatives are the main source of donors. The indications for liver transplant in our department have been extended to ABO-I. According to the Japanese Liver Transplantation Society, 3872 adult patients until 2010 underwent an LDLT. Three hundred forty-seven

(8.96%) had undergone an ABO-I LDLT; 72 of which (1.85%) had FAP.[5]

Two previous cases of an ABO-I LDLT for FAP have been reported.[2,3] Case No. 1 was a patient with late-onset FAP who underwent an auxiliary partial orthotopic liver transplant from an ABO-I living related donor showing marked clinical improvement.[2] Case No. 2 also had a favorable outcome.[3] We described a successful ABO-I LDLT for an FAP patient in whom progression of FAP had been stopped at 2 years' follow-up. These cases suggest that an ABO-I LDLT provides greater opportunities to FAP patients.

Fatty changes in the grafted liver were confirmed pathologically in this case. Previous studies described an 18% incidence of de novo nonalcoholic fatty liver disease and 9% for de novo nonalcoholic steatohepatitis after liver transplant after an average 28 months' follow-up.[6] The use of tacrolimus, posttransplant obesity, diabetes mellitus, hypertension, hyperlipidemia, steatosis in the donor liver, and alcoholic liver disease as primary indications for liver transplant are predictors after a liver transplant of nonalcoholic fatty liver disease.[7] Early fatty changes in the liver within 1 month of an LDLT because of vascular complications (eg, thrombosis of the portal system) also have been reported.[8] Our case developed fatty liver in the early posttransplant period; however, neither vascular complications nor the predictors of nonalcoholic fatty liver disease described previously were observed. We could not identify a specific cause for fatty changes in the liver. However, the effectiveness of relieving the diarrhea and reducing the dosage of corticosteroids suggest that a combination of malnutrition from the gastrointestinal dysfunction because of FAP and drug adverse events may have contributed to development of fatty liver. Malnutrition has been shown to lead to fatty liver because of an overproduction of triglyceride deposits in the liver after an increase in free fatty acid beyond the ability of liver lipoprotein metabolism.[8] Such a low nutritional status may have occurred in our case because of continued diarrhea and reduced intake food. As suggested previously,[9] before deterioration of digestive function, liver transplant should be considered.

Long-term survival after liver transplant in FAP patients is good[10]; however, there are no studies of FAP patients alone after an ABO-I LT or an LDLT. The accumulation of more cases and further follow-up are warranted to examine whether survival rates and clinical symptoms of FAP patients after an ABO-I liver transplant are similar to those of an ABO-identical/compatible liver transplant.

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