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Idiopathic Fulminant Graft Failure Rescued by Urgent ABO-Incompatible Liver Transplantation

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Introduction

Seventh-day syndrome (7DS) is a rare but fatal acute complication of liver transplantation. It is characterized by an abrupt rise in liver enzymes and massive hepatocyte necrosis at around a week post-transplant, leading to fulminant hepatic failure in a previously well-functioning graft.[1-3] We describe a recipient with 7DS, successfully managed with emergent ABO-incompatible (ABOi) retransplant. The patient provided informed consent to publish case.

Case

A 47-year-old man with well-compensated cirrhosis (Na-MELD 18) and hepatoma secondary to autoimmune hepatitis underwent uncomplicated liver transplant with a brain-dead donor liver. Immunosuppressive induction was methylprednisone. Tacrolimus was introduced on postoperative day (POD) 1.

He had a routine recovery until POD 6 (with tacrolimus level 9.4 ug/L), when the liver enzymes abruptly increased (AST > ALT) (Table 1). Doppler ultrasound and computerized tomograph with contrast revealed patent vasculature and no clear abnormalities. Viral serologies/PCRs were negative. He developed encephalopathy and acidosis, requiring listing for urgent retransplantation. On POD 7, the enzymes climbed further (Table 1). He was intubated for airway management. Liver biopsy revealed coagulative geographic necrosis with no viral cytopathic effect (Figure 1A and B).

An ABOi offer (donor blood group-B, recipient blood group-O) was accepted due to rapid deterioration and lack of blood group matched offers. His clinical condition continued to worsen, requiring inotropic support, initiation of hemodialysis and operative devascularization of the graft with temporary portocaval shunt. On POD 8, retransplant was performed with simultaneous splenectomy.

Prior to ABOi transplant, 2 sessions of plasmapheresis were completed. Induction therapy was thymoglobulin and methylprednisone. He received 5 sessions of plasmapheresis and IV Immunoglobulin G on alternate days. Surveillance biopsies on PODs 10 and 21 were unremarkable. At 10 months posttransplant, he was doing well with no evidence of rejection and normal graft function.

Discussion

Seventh-day Syndrome is an uncommon transplant complication, with incidence between 0.5% to 1.68% and male preponderance.[2,3] There has been no demonstrated association with age, wait time, etiology, MELD score, type of allograft or surgical factors.[2,3] Massive coagulative necrosis without major inflammation is the most prominent histological feature. The postulated pathogenesis involves an undefined immune response and activation of apoptosis pathways,[3] as supported by mice models demonstrating

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Table 1. Laboratory Trend Showing Renal and Liver Functions of Patient Before and After Transplant.

Date & time	INR	Creatinine (μmol/L)	Bilirubin (μmol/L)	AST (IU/L)	ALT (IU/L)	ALP (IU/L)
Pre OP	1.5	49	87	63	49	216
POD-0 4:27	1.6	108	102	754	360	100
POD-4 8:19	1.1	61	34	70	130	79
POD-5 7:54	1.1	58	44	137	177	77
POD-6 8:28	1.4	67	83	865	746	124
POD-6 16:27	1.8		146	3311	2313	137
POD-7 2:29	3.4	66	179	6098	3929	116
POD-7 21:01	8.8	179	278	10385	5699	178
POD-0 5:29	2.3	227	144	6006	2145	126
POD-1 8:03	1.3	85	53	384	327	85
POD-3 7:41	1.0	179	24	102	152	90
POD-10 5:26	1.2	57	14	28	44	57

Abbreviations: INR, International normalized ratio; AST, aspartate aminotransferase; ALT, alanine transaminase; ALP, alkaline phosphatase.

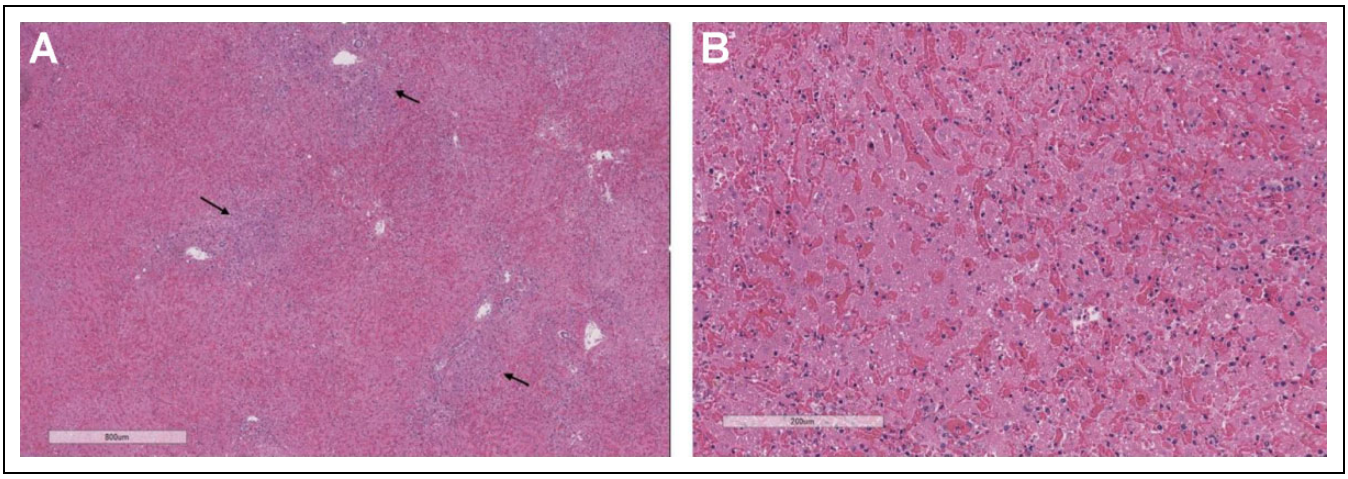

Figure 1. Graft hepatectomy histology from recipient with fulminant transplant liver failure. A, Severe sinusoidal congestion and hemorrhage as well as marked coagulative geographic necrosis. Note the scattered islands of viable hepatocytes at zone 1 (arrows) (hematoxylin and eosin). B, Higher power view of (A), showed severe sinusoidal congestion and coagulative necrosis with almost no inflammation and no obvious apoptotic bodies (hematoxylin and eosin).

increased hepatocyte expression of Fas receptor and induction of hepatocyte apoptosis by systemic injection of monoclonal antibody to Fas receptor.[4] The mortality rate is above 80%,[2,3] and retransplantation is the only curative option with 80% 1-year survival.[1]

In North America, ABOi transplant has largely been reserved for patients with fulminant hepatic failure in the absence of a blood group-compatible organ. Intensive desensitization using IVIG, plasmapheresis, and rituximab vs splenectomy has improved graft and patient survival after ABOi transplantation.[5]

Our case describes the rare entity of 7DS, characterized by sudden graft necrosis and failure. This represents a posttransplant emergency, highlighting the need to urgently act upon development of markedly abnormal liver biochemistry and evidence of liver failure, despite initial normal graft function and in the absence of vascular thrombosis. Fortunately, certain mortality was avoided with the successful application of emergent ABOi transplantation.

Abbreviations

7DS	Seventh Day Syndrome
ABOi	ABO incompatible
ALT	Alanine Transaminase
AST	Aspartate Transaminase
INR	International Normalizing Ratio
IVIG	Intravenous immunoglobulin
Na-MELD	Sodium—Model for End Stage Liver Disease
POD	Post-Operative Day; PCR: Polymerase Chain Reaction.

Authors' Note

Participated in research design: FQ, RU, AL, ZG, BS, MB. Participated in the writing of the paper: FQ, RU, AL, ZG, MM, MC, KT, BS,

MB. Critical revision for important intellectual content: FQ, BS, MB. All authors approved the final version and are accountable for all aspects of the work. Permissions: An informed consent was provided by the patient for publication.

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