Graft-versus-Host Disease After Liver Transplantation

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INTRODUCTION

Graft-versus-host disease (GvHD) is a rare but serious complication after liver transplantation (LT). GvHD occurs when the immunocompetent donor T lymphocytes attack the recipient's tissue such as skin, intestine and bone marrow. GvHD is diagnosed based on clinical symptoms, evidence of donor chimerism and histopathological findings of affected tissue. The incidence is estimated to be 0.2%–2%, but the mortality rate can be up to 60%-85%. Addressing potential risk factors for GvHD in liver transplantation is important for the field.

PATIENT CLINICAL HISTORY

In this case, a 59-year-old blood group O-negative male with a history of alcohol-related (ETOH) cirrhosis underwent liver transplantation. Following transplantation, the patient developed a systemic inflammatory response consistent with infection/sepsis and experienced clinical concerns for GvHD.

The patient has a history of red blood cell (RBC) transfusions. Given the post-transplant clinical course and sensitization history, immunologic monitoring was performed to evaluate for the presence of alloantibodies and their potential role in graft dysfunction.

METHODS

The case utilized multiple histocompatibility laboratory methods, including rSSO (Reverse Sequence-Specific Oligonucleotide) testing for HLA typing, Luminex Single Antigen Bead (SAB) testing for HLA antibody identification and characterization, and Short Tandem Repeat (STR) analysis for chimerism monitoring and assessment of donor-recipient cell populations after transplantation.

RESULTS

The patient has a history of chronic liver failure secondary to alcohol-related cirrhosis complicated by bleeding esophageal varices status post banding. He was undergoing orthotopic liver transplant (OLT) evaluation. The patient's single antigen bead (SAB) testing performed on pre-transplant serum dated 9/9/2025 showed negative results for both HLA Class I and Class II antibodies (cPRA 0%; **Table 1**).

Table 1. SAB history for the patient

	09/09/25 AR1097136
NEGATIVE	-

The patient received a liver transplant from a 39-year-old male deceased donor. The donor and recipient HLA typing are shown in **Table 2**. The donor was 9/12 HLA antigen mismatched with patient. Pre-transplant CDC crossmatches and T and B cell flow crossmatches were negative (**Table 3**).

Table 2. HLA typing of the patient and donor

	A	B	Bw	C	DRB1	DRB345	DQB1	DQA1	DPB1	DPA1
Patient	2	8	6	7	17	52	2	05	401	01
	31	39	6	7	14	52	7	05	402	01
Donor	11	37	4	6	15	52	6	01	401	01
	26	51	4	14	11	51	7	05	402	01

Table 3. Physical crossmatch using pre-transplant serum. The serum was tested both with and without DTT (dithiothreitol) treatment using the CDC (complement-dependent cytotoxicity) crossmatch. Pronase-treated donor T and B cells were used in flow crossmatches.

Physical crossmatch (Pre-transplant)

Treatment	Cell	Method	Result
NONE	T	CDC	Neg
DTT	T	CDC	Neg
NONE	B	CDC	Neg
DTT	B	CDC	Neg
Pronase	T	FLOW	Neg
Pronase	B	FLOW	Neg

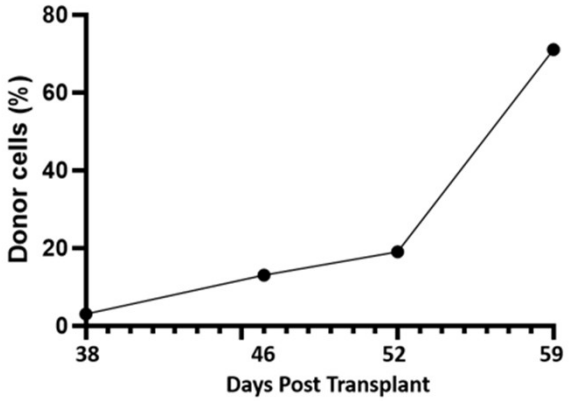


Figure 1. STR testing to monitor the percentage of donor cells in post-transplant samples

On post-transplant day 16, the patient developed acute hypoxic respiratory failure accompanied by rash, diarrhea, and nausea, raising concern for GvHD. Donor chimerism testing using STR methodology on post-transplant day 38 demonstrates 3% of donor cells in unfractionated PBMCs, which increased to 71% over the following three weeks (**Figure 1**) and the patient died at post-transplant day 61.

Reported Risk Factors for GvHD in This Case

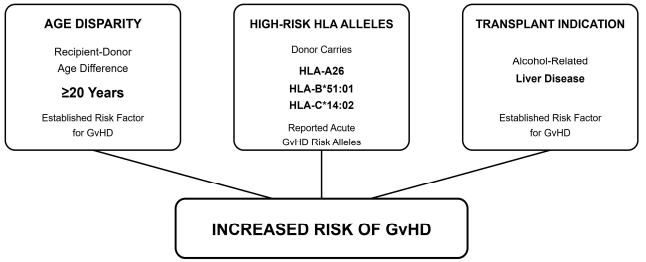


Figure 2. Multiple reported risk factors for GvHD were present

Age difference of greater than 20 years between recipient and donor, mismatched HLA risk alleles, and the underlying disease for transplant indication (alcohol related liver disease, hepatocellular carcinoma) are considered risk factors for GvHD development.

In hematopoietic stem cell transplantation, HLA-A26 in HLA-matched sibling donor transplants, HLA-B*51:01 in HLA-matched unrelated transplants, and HLA-C*14:02 mismatch in unrelated donor transplants have been reported as high risk alleles associated with incidence of acute GvHD.

Interestingly, in this case, the donor–recipient age disparity is ≥20 year, and the donor carries HLA-A26, B*51:01, C*14:02 and the underlying disease is alcohol related liver disease (**Figure 2**).

DISCUSSION

Multiple risk factors contribute to the development of post liver transplant GvHD. Identifying high-risk factors for GvHD may allow risk assessment at the time of transplant and improve transplant outcome.

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