When the Liver Doesn't Absorb: Class I DSA Driving AMR

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PURPOSE

Evidence suggests that liver transplants have a natural ability to protect against donor-specific antibodies (DSA), particularly those directed against HLA class I targets. This ability often leads to the lack of post-transplant DSA monitoring in liver transplantation when DSA is crossed. We present the case of a patient who received a liver transplant in the presence of pre-existing HLA class I DSA that mounted a robust B cell memory response leading to acute antibody-mediated rejection (AMR).

METHODS

A 44 y/o female presented for transplant due to metabolic dysfunction and alcohol-related liver cirrhosis. The patient's sensitization history included pregnancy. The patient was transplanted with a deceased donor liver across moderate levels of HLA-B7 and Cw2 DSA. In addition, weak levels of DSA to A68 and Cw15 were also present (Table 1).

Table 1. Pre-Transplant DSA Levels and Specificities

DSA Specificity	MFI (Neat)	MFI (1:64 Dilution)
B7	24135	2563
Cw2	10546	177
A68	3078	x
Cw15	2827	x

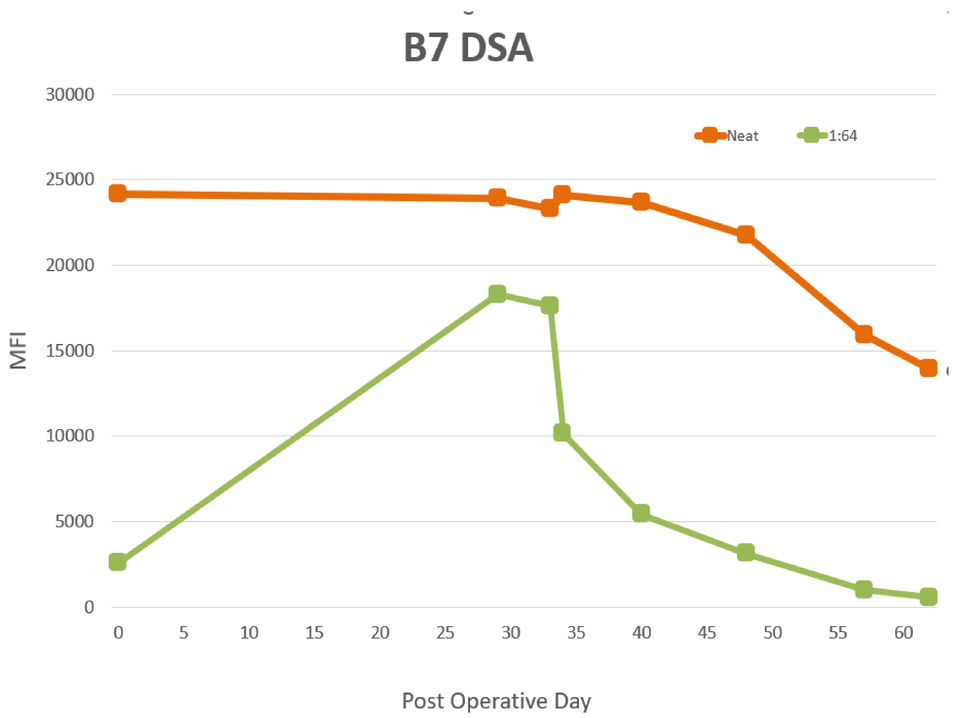


Figure 1 - MFI levels of B7 DSA for neat (orange line) and 1:64 dilution (green line) in patient serum.

RESULTS

Post-transplant, the course was quickly complicated by ischemic cholangiopathy and acute AMR. DSA was first measured one-month post-transplant to evaluate the severity of the AMR. Although most of the DSAs decreased, the B7 DSA showed a substantial increase rather than the expected absorption by the liver allograft. MFI values for the neat sera suggested saturation of the single antigen beads, so the DSA trends were monitored at 1:64 dilutions (Figure 1). Diluted sera showed an increase in B7 DSA from 2,563 MFI to 18,270 MFI at one month. Additional dilutions of the post-transplant B7 DSA showed an MFI of 11,519 at 1:1024, demonstrating the high levels of DSA generated by this memory response.

The patient was treated with three rounds of plasmapheresis and IVIG, leading to a decrease in DSA that became non-detectable at a 1:64 dilution. After only two months, the liver transplant proceeded to fail primarily due to ischemic cholangiopathy.

CONCLUSION

Our case challenges the belief that pre-formed HLA class I DSAs are always absorbed by the liver without impacting graft function. The case also highlights that some memory B cell responses can generate DSA levels capable of overwhelming the ability of the liver to absorb the DSA and lead to AMR. Although it is unclear how much the DSA and resulting AMR contributed to the graft loss, we have changed our protocols for HLA antibody monitoring for liver transplant patients, where we now utilize an admission serum for flow crossmatching.

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