Predictive value of C1q-binding assay in allo-antibody IVIg desensitization for pediatric heart transplant candidate

Lin Wang[1], Marcelo Fernández-Viña[2], Alin Girnita[1]

1. Department of Pathology and Laboratory Medicine, UC Irvine, Orange, CA | 2. Department of Pathology, Stanford University, Palo Alto, CA, United States.

Background

Highly sensitized pediatric patients awaiting heart transplantation—particularly those supported with ventricular assist devices (VADs) and exposed to multiple blood transfusions—face significant barriers due to preformed human leukocyte antigen (HLA) antibodies. Intravenous immunoglobulin (IVIG) is a well-established desensitization strategy; however, accurate monitoring of treatment response is essential to determine whether donor-specific antibodies (DSAs) have decreased to acceptable levels for transplantation.

Case Report

To investigate the clinical utility of integrating Single Antigen Bead (SAB)-IgG and SAB-biotinylated-C1q (Bio-C1q) assays for predicting and monitoring the efficacy of high-dose intravenous immunoglobulin (IVIG) desensitization in a highly sensitized pediatric heart transplant candidate.

A 2-year-old Hispanic male supported by a ventricular assist device (VAD) presented with a calculated panel-reactive antibody (cPRA) of 100%. Baseline profiling at Month -7 revealed high-titer HLA antibodies (MFI 35,000 SAB-IgG; 40,000 SAB-BioC1q). In vitro IVIG inhibition testing (1:2serum dilution with 10% IVIG versus buffer) showed >50% suppression of C1q binding, supporting initiation of clinical desensitization.

Results

The patient received a two-phase IVIG protocol. Phase I consisted of 11 doses (2g/kg) over four months, and Phase II included 4 consolidation doses prior to transplant. Serial antibody monitoring at Month –3, Day 0, and post-transplant used SAB-IgG and SAB-BioC1q assays to track HLA antibody levels before transplantation and monitor donor-specific antibodies (DSAs) after transplant. At Month –3, SAB-IgG showed partial Class I reduction (HLA-A3: –60%, HLA-B82: –32%), whereasSAB-BioC1q demonstrated 87–92% clearance (HLA-A3: –94.7%) (Table 1).

Class II antibodies (DR51, DQ6) were detectable by SAB-IgG but cleared by SAB-BioC1q. By the current pre transplant serum, SAB-BioC1q remained negative, while SAB-IgG showed residual HLA-B82 (1.8K MFI) and HLA-DQ6 (2K MFI) (Figure 1).

Prospective flow crossmatch using the current pre transplant serum was negative, contrasting with a positive crossmatch using historical peak serum.

Figure 1

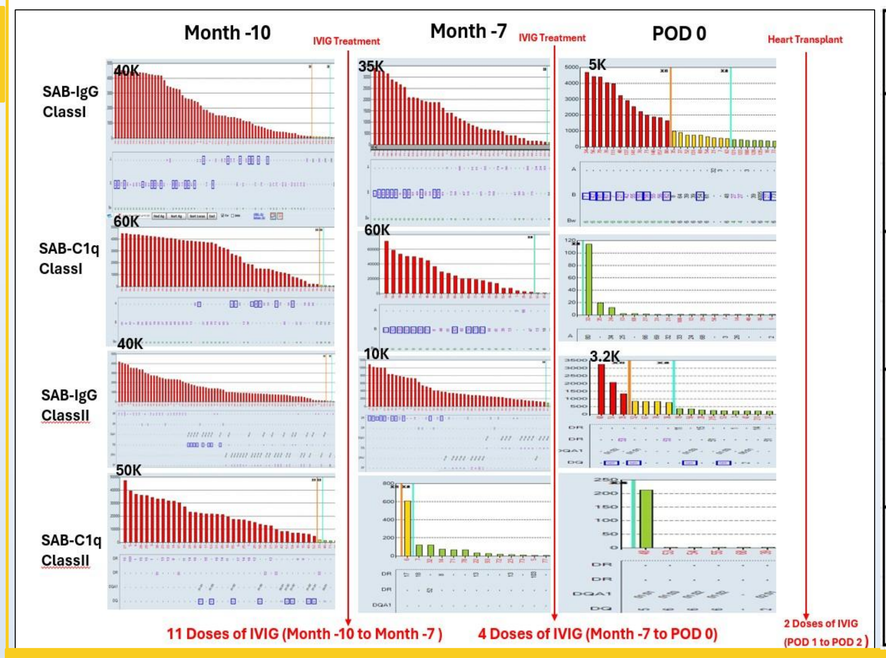


Table 1

Test Type	Levels of Patient's HLA Abs	Month -7	Month -3 (% Drop from M-7)	POD 0 (% Drop from M-3)	Total % Drop (Overall)
HLA Class I SAB-IgG	HLA-A3 (Median Level HLA Abs)	35K	14K (-60.0%)	Negative (-100%)	-100%
	HLA-B82 (Strong Level HLA Abs)	31K	21K (-32.3%)	1.8K (-91.4%)	-94.20%
HLA Class I SAB-C1Q	HLA-A3 (Median Level HLA Abs)	38K	2K (-94.7%)	Negative (-100%)	-100%
	HLA-B82 (Strong Level HLA Abs)	40K	22K (-45.0%)	Negative (-100%)	-100%
HLA Class II SAB-IgG	HLA-DQ6 (Median Level HLA Abs)	20K	2K (-90.0%)	2K (0%)	-90%
	HLA-DR51 (Strong Level HLA Abs)	35K	5K (-85.7%)	Negative (-100%)	-100%
HLA Class II SAB-C1Q	HLA-DQ6 (Median Level HLA Abs)	20K	Negative (-100%)	Negative	-100%
	HLA-DR51 (Strong Level HLA Abs)	32K	Negative (-100%)	Negative	-100%

Conclusion

This pediatric heart transplant case demonstrates that high-dose IVIG differentially modulates HLA antibodies, blocking and/or suppressing complement-binding activity (C1q) more rapidly than total IgG. SAB-BioC1q enables accurate monitoring when exogenous IgG confounds SAB-IgG. The shift from 100% CPRA to a negative prospective crossmatch identified a viable transplant window. Nine-month follow-up showed no DSAs or rejection, confirming durable desensitization