SARS-CoV2 Infection Post-Transplantation Induces Transient HLA Antibodies in Pediatric Heart Recipients

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INTRODUCTION

Pediatric heart transplant (HTx) recipients with donor-specific HLA antibodies are at higher risk of cardiac allograft vasculopathy, chronic rejection, and graft dysfunction. Both infection and vaccination are often cited as potential drivers for pre-transplant HLA antibody sensitization, but their consequence post-transplant within an immunocompromised host is unclear.

Paradoxically, use of immunosuppression to reduce HLA antibodies also increases risk of infection, a potential trigger for an HLA antibody response. Here we report a retrospective study on HLA antibody formation, exacerbation, and persistence following either SARS-CoV2 infection or vaccination in a cohort of pediatric HTx patients.

METHODS/DEMOGRAPHICS

We performed a longitudinal review of 77 pediatric post-HTx cases who later tested positive for SARS-CoV2 (n=31) or were vaccinated against SARS-CoV2 (n=46). HLA ab were assessed by flow PRA bead and SAB assays on sera prior to initial positive test for SARS-CoV2 (or prior to any dose for the vaccination group), and then again at 6m-,1y-, and 3y-post.

Sex, n (%)	
Male	49 (63.6)
Age, years (IQR)	
at txp	9.1 (1.3-15.4)
POY to Infection	5.3 (0.5-8.8)
POY to Vaccination	12.9 (3.3-15.6)
Race, n (%)	
Black	11 (14.3)
Caucasian	31 (40.3)
Hispanic	21 (27.3)
Not Reported	14 (18.2)

RESULTS

Fig 1A

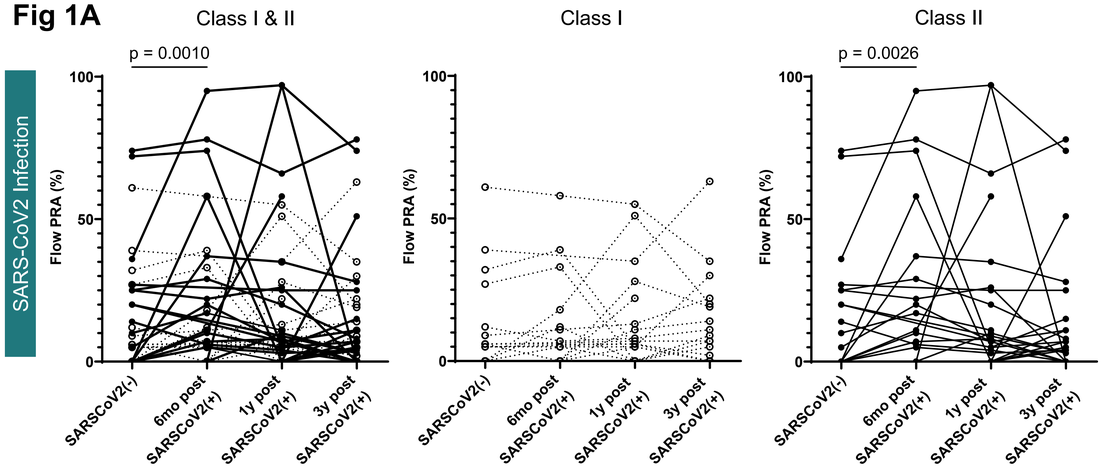

Fig 1B

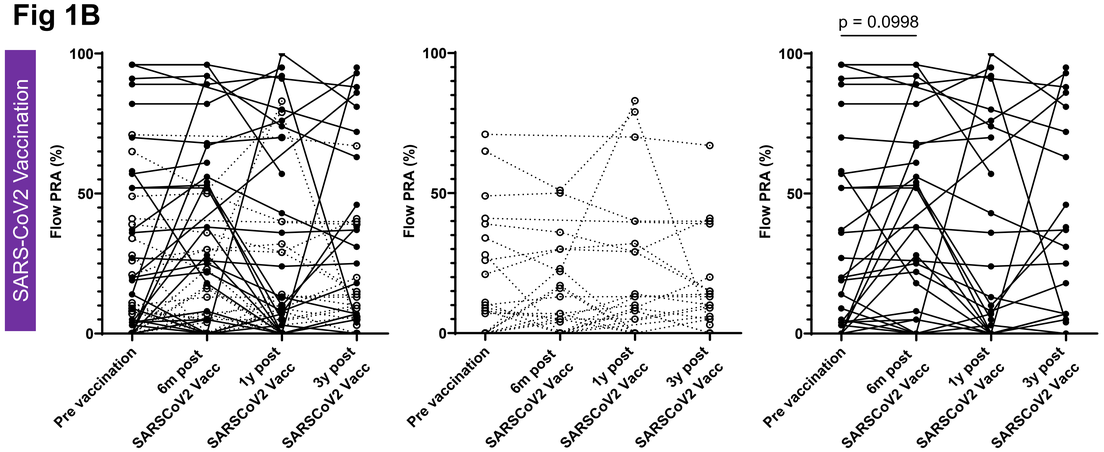

Figure 1. HLA Class I and II antibody levels by flow PRA following (A) infection or (B) vaccination against SARS-CoV2. Significance by Wilcoxon rank-sum, p>0.05.

Figure 2. HLA Ab by SAB in post-Htx SARS-CoV2 pts

		Pre,n	6m-post,n	p-val
Infection	HLA Ab (+)	25	30	0.04
	DSA increase			
	pre-existing	6	1	0.29
	no prior	25	5	0.02
Vaccination	HLA Ab (+)	35	37	0.61
	DSA increase			
	pre-existing	10	2	0.14
	no prior	36	8	0.003

SARS-CoV2 infection led to an increase in HLA antibodies out to 6 months when measured by PRA or SAB (**Fig 1A** and **Fig 2**) but not sustained at 1 and 3 years follow up. In comparison, no significant increase in HLA antibodies was observed following a full vaccine regimen. Neither infection nor vaccination caused an increase in cumulative MFI of pre-existing DSA. However, 5/25 infection and 8/36 vaccination cases developed *de novo* DSA afterwards (**Fig 2**).

RESULTS

Fig 3

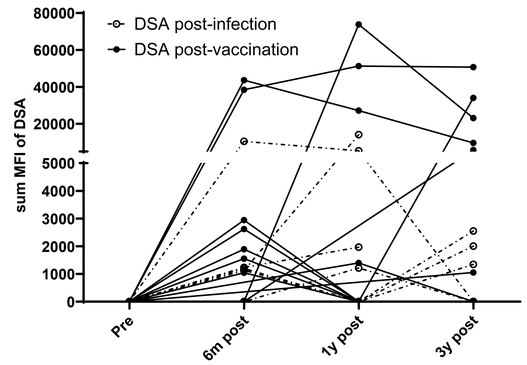

Figure 3. Tracking cumulative MFI levels of *de novo* DSA following infection (dashed line) or vaccination (solid line)

Of the patients who formed *de novo* DSA following either infection or vaccination, 7/13 were low level (cumulative MFI of DSA <3000) and were negative at 1 year.

CONCLUSIONS

Our findings show that post-HTx patients may develop HLA antibodies after infection with or vaccination against SARS-CoV2. A significant proportion of patients with no prior DSA subsequently formed DSA after infection/vaccination. However, as the response was not durable, it is unlikely that these antibodies pose an immunological threat to the allograft.

The mechanism by which infection or vaccination leads to development of HLA antibodies is unclear. Our data demonstrate a predilection towards Class II, but no association was found with a particular HLA loci (data not shown). Possibly, these antibodies arise due to molecular mimicry with SARS-CoV2 or inadvertently with general immune activation.