Spontaneous allosensitization in pediatric adenosine deaminase 2 deficiency: a histocompatibility laboratory case series

Moshe Israeli, *Abigail Rosengarten, Larisa Bachmatov, Ronit Elchasid, Amit Dotan*
Tissue Typing Laboratory, Rabin Medical Center, Petah Tikva, Israel; Tel Aviv Medical Center, Tel Aviv, Israel

BACKGROUND

- Anti-HLA antibodies are a major barrier to successful HSCT, typically developing after transfusion or pregnancy exposure
- ADA2 deficiency (DADA2) is a rare inherited disease, causing vasculitis, stroke, bone marrow failure, and immunodeficiency
- HSCT is the definitive curative treatment for DADA2
- The occurrence and clinical significance of anti-HLA antibodies in DADA2 have not been systematically evaluated

OBJECTIVE: To characterize anti-HLA antibodies in a series of pediatric DADA2 patients undergoing HSCT and assess their impact on transplant outcomes.

KEY FINDING: All three transfusion-naive DADA2 patients developed extraordinarily high anti-HLA antibody levels (7,200-20,000+ MFI) without prior known alloantigen exposure

Case	Age/ Sex	Donor	Peak Anti-HLA (MFI)	DSA (MFI)	Outcome
1 (Y.F.)	3.5y F	9/10 MUD	Class I: 15,900 Class II: 4,500	11,400	Poor graft function Autologous rescue
2 (S.H.)	22m M	MSD (CB) then Haplo	Class I: 17,300 Class II: 18,700	7,400 (refers to the haploi donor)	Primary graft failure (both) Fatal outcome
3 (A.L.)	9.5y F	9/10 MUD	Multiple high-level	7,200	DSA reduced successfully Fatal post-BMT complications

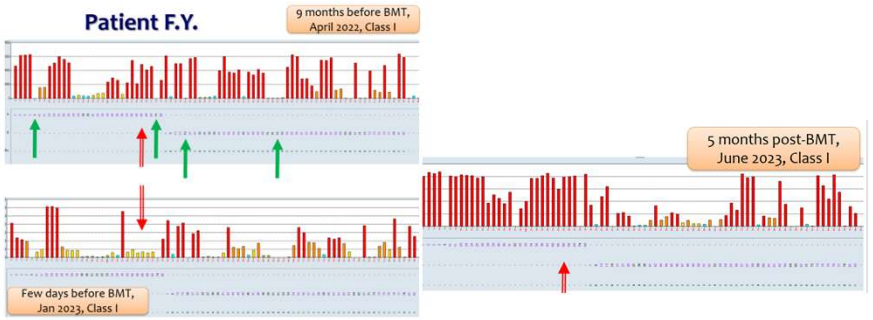
MATERIALS & METHODS

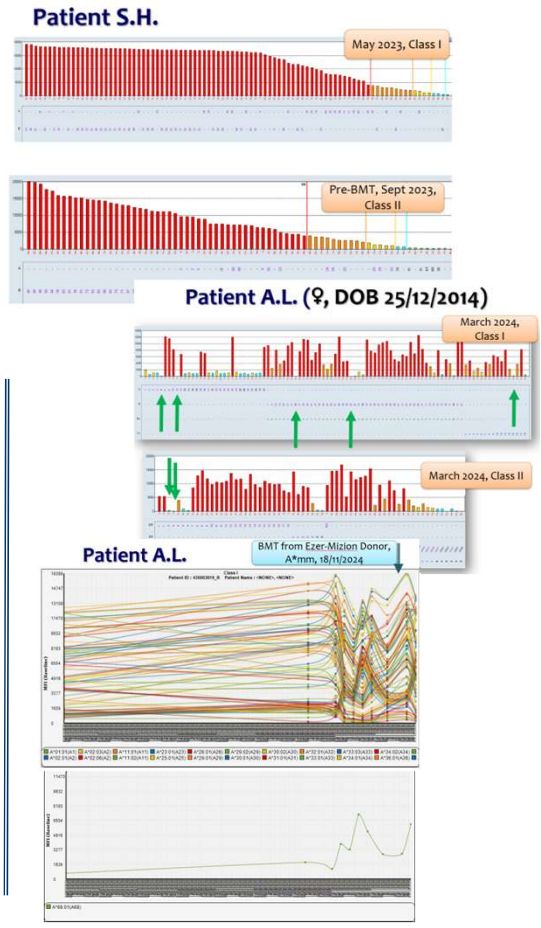
Study Design: Retrospective case series of 3 consecutive pediatric DADA2 patients
HLA Antibody Testing:

- Luminex single antigen bead assays (LABScreen, One Lambda)
- Serial monitoring: pre-transplant, post-desensitization, and post-HSCT
- MFI threshold for positivity: >1000

Desensitization Protocols: Bortezomib, IVIG, Plasmapheresis, Rituximab
Transplant Characteristics:

- All patients: Bu-Flu-ATG conditioning
- GVHD prophylaxis: CsA-based regimens





DISCUSSION

→ Unprecedented Finding: Spontaneous development of extremely high-level anti-HLA antibodies in transfusion-naive DADA2 patients. To our knowledge, this phenomenon has not previously been reported in DADA2.

→ We hypothesize: ADA2-related immune dysregulation may drive spontaneous HLA allosensitization

→ Possible mechanisms:

- Molecular mimicry
- Autoimmune cross-reactivity with HLA molecules
- Enhanced B-cell activation from chronic inflammation

→ Clinical significance:

- High-level non-DSA antibodies persisted despite successful DSA reduction
- Persistent broad HLA sensitization may contribute to graft failure independently of donor-specific antibodies.
- Outcomes highlight the potential clinical impact of unrecognized anti-HLA antibodies

→ Comparison to published data:

- Our series highlights challenges not commonly reported in the literature
- Suggests anti-HLA antibodies represent an underrecognized barrier in DADA2 transplantation

Contact: israelimoshe@yahoo.com
Disclosure of Interest: None
Clinical outcomes from these cases were previously presented as a poster at the 4th Emirates Pediatric BMT Congress, Abu Dhabi, November 2025.

SCAN ME

Conclusion

DADA2 is associated with spontaneous HLA allosensitization in transfusion-naive children, posing a unique immunogenetic challenge to the histocompatibility laboratory.
The laboratory plays a central role in risk stratification, donor selection, and treatment monitoring in this setting.
Mandatory HLA antibody screening and serial Luminex testing are recommended for all DADA2 HSCT candidates.