A New Perspective on Disseminated Adenovirus Infection and Its Outcomes in Pediatric Solid Organ Transplantation

Coralee Del Valle Mojica, MD, MPH[1]; Sharon F Chen, MD[1]; Hayley A. Gans, MD[1]
Department of Pediatrics, Stanford University School of Medicine, Stanford, CA

Background

- Adenovirus (AdV) is increasingly recognized in pediatric solid organ transplants (SOT).
- There are no standardized definitions for *dissemination* to assess which infections progress into severe disease.
- Detection of AdV at ≥ 2 sites is predictive of disseminated disease in other immunocompromised populations, however data is lacking for SOT.
- Advances in post-transplant management with tacrolimus-based immunosuppressive regimens, use of PCR for early detection of infection and cidofovir (CDV) use have led to improved outcomes in SOT recipients.

Objectives

- To evaluate the host and viral risk factors associated with disseminated AdV infection in a large pediatric SOT population

Methods

Retrospective cohort design Jan 2005-Jun 2017 → Children ≤ 18 years of age at time of SOT → Recipients with AdV isolated from 1 or more sites

- **AdV infection**: The first positive clinical specimen from any site
- **Time to Infection (TTI)**: The time between the transplant date and the first positive specimen (days)
- **Biopsy-proven infection**: Those that tested positive via immunohistochemistry or viral culture
- **Dissemination**: Biopsy-proven infection, or ≥ 2 positive sites (aside from DNAemia).

- Descriptive statistics and univariate correlational analyses using Fisher's exact, $\chi 2$, or Mann–Whitney *U* test were performed.

Results

Figure 1. SOT Cohort and Infected Recipients

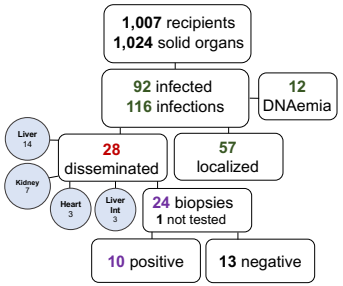


Figure 2. Role of Supportive Care in Dissemination

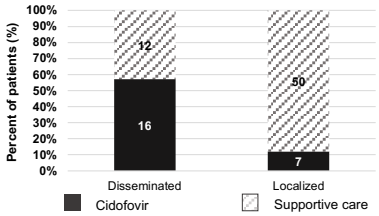


Table 1. Impact of TTI and Initial Viral Load of Management

		Cidofovir	Supportive Care	p value
Median TTI (days)	Disseminated	31	371.5	0.25
	Localized	43	558.5	0.006*
Initial viral load (log10)	Disseminated	4.27	2.74	0.04*
	Localized	4.15	1.93	0.02*
	Biopsy +	5.44	2.15	0.05*
	Biopsy -	3.61	1.94	0.09

Figure 3. Age at Infection Impact on Dissemination

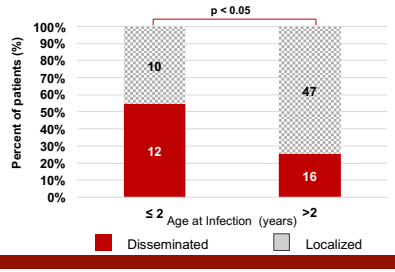


Figure 4. Time to Infection Impact on Dissemination

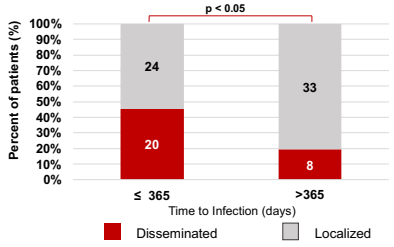


Figure 5. Significance of Initial Serum Viral Load on Dissemination

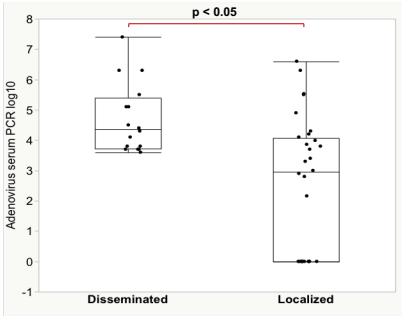
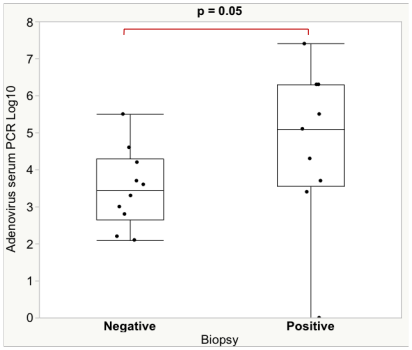


Figure 6. Significance of Initial Serum Viral Load on Biopsy-Proven Infections



Summary

- Twenty-eight recipients (30%) had disseminated disease (biopsy proven disease or ≥2 sites) and 57 (62%) tested positive from only 1 site, excluding DNAemia only patients (12, 13%) (Figure 1).
- Dissemination was more common in liver (14, 15%) and kidney (7, 8%), followed by liver-intestine (3, 3%) and heart (3, 3%) (Figure 1).
- Fifty-seven percent of disseminated infections were treated with cidofovir. The remaining 43% were treated with supportive care (Figure 2).
- In the localized infection group, 7 (12%) of recipients were treated with cidofovir.
- Amongst these 7, TTI (median 43 days, IQR 3-960 days) and the initial viral load (mean log10 4.2, IQR 2.1-6.3) influenced decision to treat (Table 1).
- Children ≤ 2 years were *significantly* more likely to have disseminated disease (Figure 3).
- Infections occurring within the first year post-transplant were *significantly* more likely to be disseminated (Figure 4).
- Initial serum viral load is *significantly* higher in disseminated disease, including biopsy proven infections.

Conclusions

- In this pediatric cohort, there is a broader spectrum of disease than previously recognized.
- Younger age at infection, shorter TTI and initial viral load are risk factors for disseminated AdV infection in pediatric SOT patients.
- Even disseminated infections can be managed supportively with good outcomes.

Future Directions

- Investigate the host and viral factors' role on rejection episodes.

References

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