

4<sup>th</sup> International Congress on

# Infectious Diseases

May 11-12, 2017 Barcelona, Spain

## Adenovirus-rough and tough: Successful treatment of disseminated adenovirus infection in two solid organ transplant recipients

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Adenovirus is a DNA virus that causes infections of the respiratory tract, gastrointestinal tract, conjunctiva and rarely urinary or neurological systems. Disease caused by adenovirus is usually self-limiting but it can cause disseminated infection with high morbidity and mortality. We presented two cases of transplant recipients who developed disseminated adenovirus infection and were successfully treated on a compassionate basis with the investigational drug brincidofovir. The first patient was a 47 year old female with kidney/pancreas transplant done six months prior to presentation who was admitted with hematuria for nine days, fever and acute kidney injury. A cystoscopy was done which revealed erythema in the bladder and transplant ureter. Biopsy of transplanted kidney was PCR positive for adenovirus and had changes consistent with adenovirus tubulo-interstitial nephritis. Due to pancytopenia, she underwent a bone marrow biopsy which was PCR positive for adenovirus. She was started on cidofovir but quickly developed worsening renal failure; hence she was switched to brincidofovir. Within three weeks of starting treatment, her symptoms resolved and adenovirus PCR was negative in urine. Unfortunately, her renal function did not improve and she remained on hemodialysis. The second patient was a 46 year old African American female who underwent deceased donor kidney transplant (DDKT) four months prior to presentation. She presented with fever for two days, abdominal pain and non-bloody watery diarrhea. Temperature was 103 F and she had pancytopenia. On labs, pertinent negatives included urine culture, blood culture, serum PCR for CMV and EBV and stool studies. Adenovirus was detectable by PCR in urine and was positive in blood with 11,571 copies detected. Due to pancytopenia, she had a bone marrow biopsy which was PCR positive for adenovirus. She was diagnosed with disseminated adenovirus infection and was initiated on brincidofovir with improvement in fever and diarrhea. Due to our experience with the first patient, we were hesitant to initiate cidofovir. At one month follow up, blood cell counts had improved and adenovirus PCR in blood and urine were both undetectable. Brincidofovir is an investigational drug that is an oral lipid formulation of cidofovir and is less nephrotoxic. Our center has had positive experiences with the compassionate use of this agent. Polymerase chain reaction testing (PCR) is useful for diagnosis as it is highly sensitive and specific. Due to significant morbidity and mortality as well as limited data on prevention and treatment, it is important to consider adenovirus as a causative infectious agent in solid organ transplant patients who present with fever of unknown origin, pancytopenia and hemorrhagic cystitis. It is critical to rule out disseminated adenovirus disease, reduce immunosuppression where possible, and consider starting anti-viral therapy early. Brincidofovir is currently in phase three clinical trial for adenovirus infections.

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