ADENOVIRUS NEPHROPATHY [HAdVN]

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INTRODUCTION

- HAdV in the healthy population to be associated with self-limited respiratory, gastroenteritis, and conjunctivitis illness.
- In kidney transplant recipients :ranges from asymptomatic viremia to hemorrhagic cystitis to allograft loss and mortality
- HAdV in kidney transplant recipients may be secondary to reactivation of latent disease, *de novo* from environmental sources or from endogenous transmission through a donor organ.
- Clinically symptomatic patients with HAdV viremia and 2 or more organ systems involved is considered disseminated disease.

SIGNS AND SYMPTOMS

- The most frequent signs and symptoms at presentation include dysuria, fever, hematuria, sterile (bacterial) pyuria , hemorrhagic cystitis, obstructive uropathy and acute kidney injury.

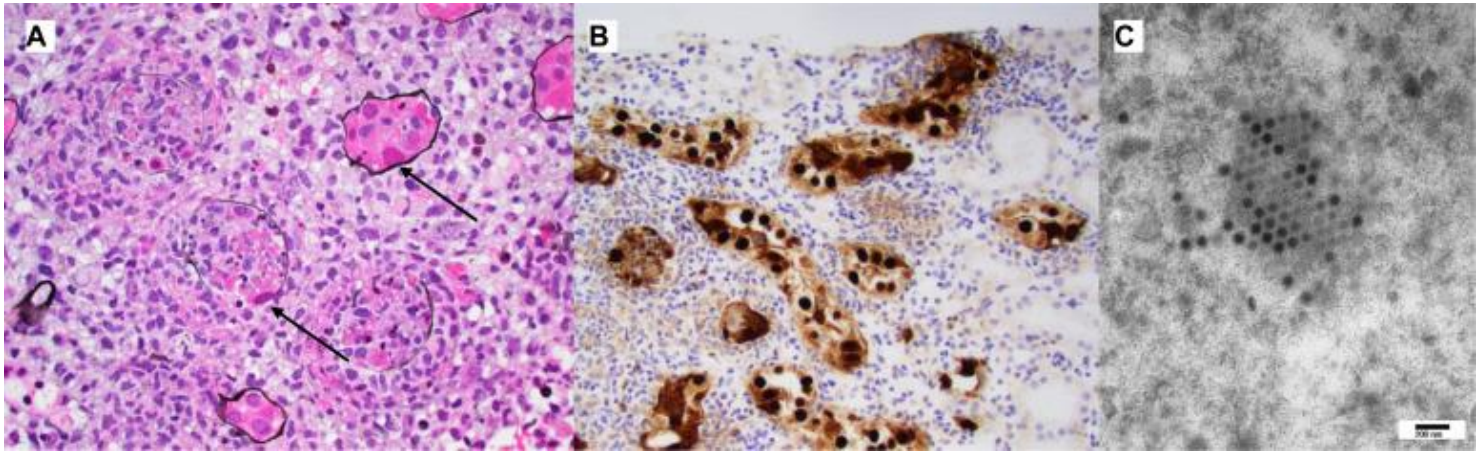
- Common extrarenal manifestations among kidney transplant recipients with disseminated disease include orchitis, lymphopenia, gastroenteritis, and pneumonitis.

- A 10-year review of 170 kidney transplant recipients reported an incidence of 4.7% for hemorrhagic cystitis with median time to onset of 1 year.

INVESTIGATION

- HAdV PCR quantification.
- Allograft biopsy.
- The most common histologic manifestations included granulomas (82%), tubulocentric inflammation (73%), and tubular degenerative changes consistent with acute tubular necrosis (73%).
- Viral inclusions - smudgy basophilic intranuclear inclusions with enlarged nuclei of infected cells. Distal tubules are more commonly involved than proximal tubules
- Viral culture. [In some cases.]
- PCR is sensitive to all known serotypes of HAdV, and has the benefit of serial monitoring for response to treatment.

Renal biopsy



Kidney biopsy findings. (A) Diffuse tubulointerstitial inflammation with a vaguely granulomatous appearance, associated tubular rupture, and nuclear viral inclusions (arrows) (400×; Jones Silver Stain). (B) Adenovirus immunohistochemical stain (200×). (C) Electron micrograph demonstrating adenovirus virions (59,500×).

The Pathologic Spectrum of Adenovirus Nephritis in the Kidney Allograft

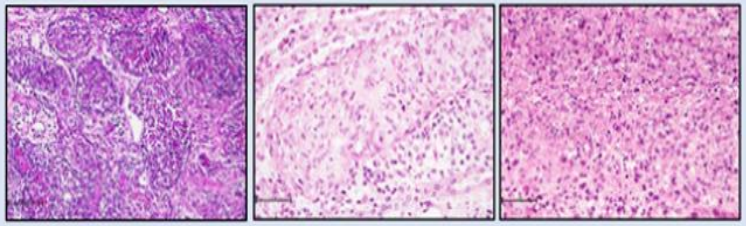
Kidney allograft biopsies

11 cases of adenovirus nephritis (ADVN) of the kidney allograft

Control biopsies

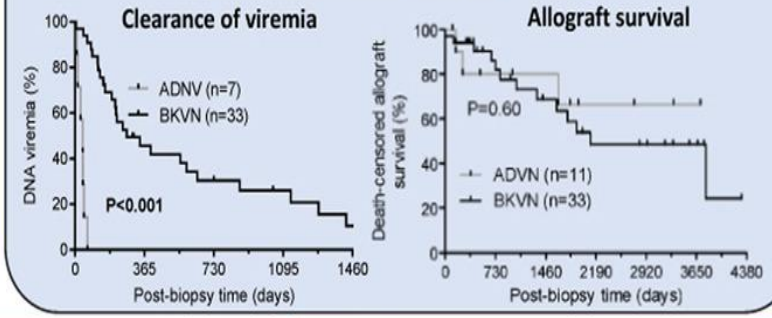
33 cases of BK virus nephropathy (BKVN) of the kidney allograft

Histopathological patterns of ADVN

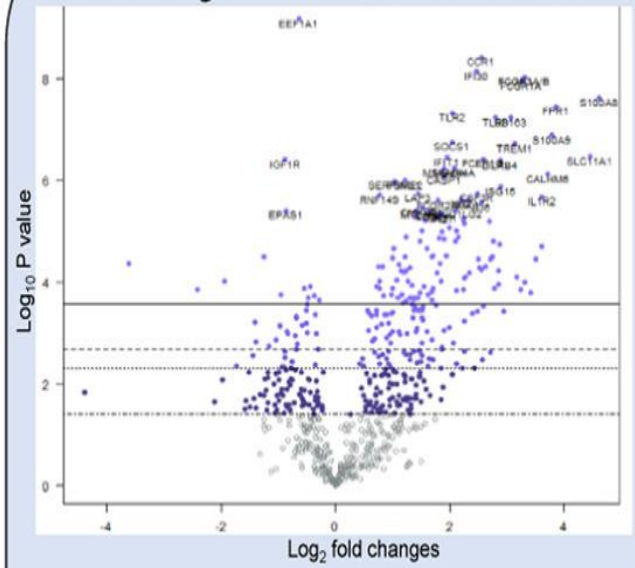


Tubulocentric inflammation | **Granulomas** | **Necrotizing lesions**

Clinical outcome: ADVN vs BKVN



Nanostring BHOT Panel: ADVN vs BKVN



ADVN showed increased expression of proinflammatory transcripts (several related to innate immunity) and a few anti-inflammatory transcripts

Jagannathan et al, 2022

CONCLUSION:

Compared to BKVN, ADVN is associated with more aggressive inflammation, enrichment with neutrophils, increased expression of innate immunity related transcripts and faster viral clearance but similar allograft survival

TREATMENT

- First step :-Reduction of the immunosuppressive regimen.

- A PCR quantification of 1 log reduction within 2 to 3 weeks is considered a therapeutic response.

Antiviral therapies in kidney transplant recipients include:

- cidofovir [s/e-hematological and nephrotoxicity],
- ganciclovir,
- ribavirin,
- brincidofovir and
- i.v. Ig.

TREATMENT

- Intravenous Ig is proposed to promote antiviral activity and to provide passive immunotherapy.
- Intravenous Ig has been used in combination with cidofovir.
- Brincidofovir (formally CMX101) is a new lipid derivative of cidofovir.[AdVise Study].
- The lipid formulation allows increased intracellular penetration that minimizes proximal tubular accumulation, and reduce the risk of nephrotoxicity.