Test Your Knowledge: Polyomavirus-Associated Nephropathy

Polyomavirus-associated nephropathy (PVAN) is common in kidney transplant patients, but infrequent following hematopoietic stem cell transplantation (HSCT). Aside from reduction of immunosuppression, few therapeutic options exist for treatment of PVAN. In the May issue of AJKD, Papanicolaou et al report a case of PVAN in a severely immunocompromised allogeneic HSCT recipient treated with brincidofovir without reduction of immunosuppression. Brincidofovir is an orally bioavailable lipid acyclic nucleoside phosphonate that undergoes intracellular conversion to cidofovir-diphosphate. The following questions based on the article will test your knowledge on PVAN.

1. Numerous factors can reduce glomerular filtration rate following HSCT. Which of the following is least likely?

   A. Radiation therapy
   B. Calcineurin inhibitors (CNIs)
   C. Bacterial infections
   D. PVAN

2. The SUPPRESS trial is an ongoing trial to demonstrate efficacy and safety of brincidofovir against which of the following viruses?

   A. Prevention of cytomegalovirus (CMV)
   B. Prevention of PVAN
   C. Prevention of adenovirus
   D. Prevention of herpes simplex virus

3. Which of the following biopsy features are seen in BK virus nephropathy? (select all that apply)

   A. Interstitial fibrosis and tubular atrophy
   B. Arterial intimal thickening and hyaline arteriosclerosis
   C. Tubular inflammation with marked neutrophilic infiltrate
   D. Intranuclear inclusion bodies which stain positive for large T antigen

4. Which of the following agents has been disproven to prevent PVAN in kidney transplant recipients?

   A. High dose cidofovir
   B. Leflunamide
   C. Rapamycin
   D. Levofloxacin

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Solutions to AJKD Blog’s Test Your Knowledge: Polyomavirus-Associated Nephropathy

Based on Papanicolaou et al AJKD Case Report

1. D. PVAN

Common causes of glomerular filtration rate loss following HSCT include radiation therapy, medication toxicity (CNIs), and bacterial infections. While CNIs can cause both AKI and CKD, medications like amphotericin B, aminoglycosides, and acyclovir, which are commonly used in HSCT patients with sepsis, primarily induce AKI. A hepatorenal-like syndrome due to hepatic sinusoidal obstruction is another frequent cause of AKI in HSCT patients. PVAN is thought to be relatively uncommon cause of AKI after HSCT. Instead, hemorrhagic cystitis is the most common presentations of BK infection following HSCT.

2. A. Prevention of Cytomegalovirus (CMV)

SUPPRESS is an ongoing phase 3 trial designed to demonstrate the efficacy and safety of brincidofovir for the prevention of CMV infection. Brincidofovir is an orally bioavailable lipid acyclic nucleoside phosphonate with broad-spectrum antiviral activity against all five families of dsDNA viruses that affect humans, including herpes viruses such as CMV, adenoviruses, polyomaviruses such as BK virus, papillomaviruses, and orthopoxviruses. As explained by Papanicolaou et al, brincidofovir has been shown to have activity against BK virus in renal tubular cells, but is not associated with the renal toxicity of cidofovir.

3. A, B, & D. Interstitial fibrosis and tubular atrophy; Arterial intimal thickening and hyaline arteriosclerosis; Intranuclear inclusion bodies which stain positive for large T antigen

Kidney biopsy is the gold standard for the diagnosis of BK virus nephropathy. The histology of BK virus nephropathy is characterized by tubular atrophy and fibrosis with an inflammatory lymphocytic infiltrate that can be mistaken for acute cellular rejection. The presence of intranuclear inclusion bodies which stain positive for the large T antigen is pathognomonic for BK virus nephropathy (Papanicolaou et al). Owing to patchy involvement, a negative biopsy cannot rule out early BK virus nephropathy. Most important prognostic parameters in determining the outcome of BK virus nephropathy is the degree of Interstitial fibrosis and tubular atrophy.

4. D. Levofloxacin

A reduction of immunosuppression is the mainstay of PVAN treatment. Management approaches differ and can include discontinuation of the anti-metabolite, dose reduction of the CNI, and conversion of tacrolimus to cyclosporine. Other treatment options include
leflunomide, low dose cidofovir, ciprofloxacin, rapamycin, or intravenous immunoglobulin. Quinolone antibiotics have antiviral properties against BK virus, but efficacy at preventing this infection has not been shown in prospective controlled studies. In a randomized, controlled trial published in *JAMA*, early treatment of kidney transplant recipients with a 3-month course of levofloxacin did not prevent BK viruria. Levofloxacin was associated with an increased risk of adverse events such as bacterial resistance. These findings made it evident that the use of levofloxacin to prevent posttransplant BK virus infection was without any benefit but some harm.