Management of BK Polyomavirus Infection in Kidney and Kidney-Pancreas Transplant Recipients

A Review Article

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KEYWORDS

• Kidney transplantation • BK virus • BKV-associated nephropathy (BKVAN)
• Polyomavirus

KEY POINTS

- BK virus (BKV) infection is common in kidney transplant recipients.
- BKV-associated nephropathy can cause premature graft loss in severe cases.
- Preventive strategy with active surveillance has improved outcomes of BKV infection but optimal management and specific therapy remain unclear and variable.
- Judicious immunosuppression adjustment is warranted in case of significant BK viremia and nephropathy.
- Currently, there is a limited role of use of antiviral agents either as prophylaxis or active treatment.

HISTORY AND BACKGROUND

BK virus (BKV) belongs to a large family called Polyomaviruses. Polyma in the Greek language means many (-poly) tumors (-oma). There are 77 recognized species in this family. Of these, 13 species, which are ubiquitous and usually asymptomatic, are known to infect humans.[1] However, 4 species of polyomaviruses are associated

Disclosure of Interest: None.
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Infect Dis Clin N Am 32 (2018) 599–613
https://doi.org/10.1016/j.idc.2018.04.009
id.theclinics.com

with human diseases: BKV[2]; JC virus (JCV)[3]; Merkel cell virus[4]; and, most recently, New Jersey polyomavirus.[5]

JCV and BKV are 70% related in their genome sequence. JCV was first discovered in 1959[6] but it was not until 1971 that it was isolated from a brain of a patient with Hodgkin disease diagnosed with progressive multifocal leukoencephalopathy.[7] The same year and in the same issue of the *Lancet*, BKV was first described.[8]

BK Virus is named after a Sudanese patient who suffered from endstage renal disease secondary to chronic pyelonephritis and underwent a living-related kidney transplant. Postoperative course was complicated with 2 mild rejections. Five months after transplant, the patient was admitted with graft dysfunction and ureteric obstruction. Tissue culture from the donor's ureter revealed a virus with unique cytopathic effect that distinguished the newly discovered virus from the rest of the polyoma viruses.[8]

EPIDEMIOLOGY AND ROUTE OF TRANSMISSION

There have been 4 genotypes identified for BKV (I to IV). BKV type I has the higher prevalence in the 4 groups. Baksh and colleagues[9] described 19 cases of renal allograft viral interstitial nephritis due to BKV. Eleven out of the 19 grafts (58%) corresponded to genotype I. Interestingly, in addition to BKV, JCV was seen in 7 interstitial nephritis grafts (37%), suggesting that both JCV and BKV can be isolated from renal tissue. This is consistent with some case reports linking JCV with a milder form of nephropathy seen in renal transplant patients.[10–12]

BKV is ubiquitous, with a worldwide seroprevalence in adults of 75% (range 46%–94%)[13] and of 30% to 90%.in the United States and Europe.[14,15] In several anecdotal reports, 60% to 100% of children are seropositive to BKV by the age of 10 years, indicating that infection occurs early in life and is usually asymptomatic.[16] The antibodies then decline to around 70% as age advances[17]; this observation suggests the role of maternal fetal antibodies transmission, which is supported by the identification of BKV IgM in newborns[18] and BKV genome in aborted fetuses.[19] However, there is no evidence in the literature suggesting teratogenicity or adverse fetal events secondary to BKV prenatal transmission. Following primary infection, the virus remains latent in the renal epithelium (tubular, transitional, and parietal epithelium) due to its tropism to the urinary tract.

The route of BKV transmission is believed to be human-to-human with no animal reservoir identified. To date, there is no specific route of transmission that has been identified. Some reports have identified BKV in stool[20,21] and sewage,[22] suggesting a possible fecal-oral route. Other studies detected BKV in tonsillar tissues,[23] which suggests either an oral or a respiratory route of transmission might be possible, with the latter the most important.

CLINICAL SIGNIFICANCE AND PREVALENCE AFTER KIDNEY AND KIDNEY-PANCREAS TRANSPLANTATION

BK Virus in Immunocompetent Population

As previously mentioned, BKV is highly seroprevalent in the healthy immunocompetent population, mostly presenting as asymptomatic low-grade viruria with no data suggesting clinical significance. Coleman and colleagues[24] showed evidence of high incidence of asymptomatic BKV viruria among 1235 pregnant women, which was attributed to impaired cell-mediated immunity, with no evidence of subsequent complications or fetal transmission.