Recurrent Nephropathy among Immunocompromised Persons could Warrant BK Polyomavirus Testing

Dear Editor,

BK virus (BKV) is a naked DNA virus, which belongs to the *Polyomaviridae* family. BK and JC polyomaviruses were the first human polyomaviruses isolated from immunosuppressed patients.[1,2] BKV was first isolated in 1971 from the urine of an immunocompromised renal transplant patient with the initials B.K.[2] BKV causes interstitial nephritis in kidney transplant patients but has also been reported to cause renal diseases in nonrenal transplant patients and bone marrow transplant recipients.[3] The BKV seroprevalence stood as high as 81%, with the virus in latent/dormant stage embedded in the urothelium.[4] Intermittent reactivation with low-level viruria (10^6 virus copies/mL of urine) has been noted in approximately 5% of immunocompromised patients without clinical consequence.[5] Due to the detection of viral DNA in tonsillar tissue, BKV transmission is thought to occur via a respiratory route.[6] There is also evidence for other possible routes of transmission such as fecal-oral, urino-oral, transplacental, and blood transfusion.[6]

There are four BKV genotypes: designated I, II, III, and IV. After primary infection, BKV enters a latency phase and tends to persist indefinitely.[7] Autopsy studies have detected BKV mainly in kidney parenchyma, renal pelvis, ureter, and urinary bladder of immunocompetent individuals.[7] Reactivation of BKV replication is observed in states of relative or absolute immunodeficiency such as transplantation, pregnancy, diabetes, cancer, HIV infection, and systemic lupus erythematosus. Unchecked BKV replication can then lead to BKV nephropathy (BKVN) and other organ diseases.

Pathologically, BKV infection manifests by BK viruria, BK viremia, and BKVN. BK viruria precedes BK viremia by a median of 4 weeks and BKVN by an average of 6.5 months.[8] One of the earlier methods to detect BKV infection was by the detection of "decoy" cells in the urine. Decoy cells originate from infected renal tubular cells with nuclei altered by BKV inclusions.[8] They can be observed on urine cytology using Papanicolaou stains (Pap) or on phase-contrast microscopy. The urine Pap smear, though sensitive for the diagnosis of BKVN, has a positive predictive value of only 29%.[8] The measurement of BK viral load by polymerase chain reaction in the urine is another method used to monitor BKV infection.[9] Low levels of viruria may reflect asymptomatic shedding during the latent phase, and increasing viral load is indicative of active BKV replication.

In two clinical studies on BKV pathology, 35% of kidney transplant recipients develop BK viruria, 11.1% develop BK viremia, and 6.4% develop BKVN.[8,10] Although rarely tested in time, it is thought that BK reactivation in kidney transplant recipients occurred very infrequently in the 1970s–1980s. The increased prevalence in recent times is attributed, in part, to the use of a more potent calcineurin inhibitor (CNI)-based immunosuppressive regimens. It is important to acknowledge that better understanding of BKV infection has led to screening protocols in kidney transplantation that has resulted in the increased recognition of asymptomatic BKV infections.[11]

The definitive diagnosis of BKVN requires a kidney biopsy where intranuclear polyomavirus inclusion bodies in tubular epithelial and/or glomerular parietal cells can be identified.[11] Inclusion bodies are basophilic structures seen on light microscopy.[8] The cytopathic changes are often associated with epithelial cell necrosis resulting in denudation of tubular basement membranes and acute tubular injury.[8]

BKV reactivation following kidney transplant should be considered in the differential diagnosis of acute kidney injury (AKI) or chronic kidney disease. Other common causes of AKI in kidney transplant recipients are CNI nephrotoxicity and allograft rejection. A kidney biopsy is necessary to definitively differentiate these, although the specific clinical scenario can raise suspicion for BKVN. With the rising cases of recurrent kidney diseases among kidney transplant recipients and other immunocompromised persons, it is recommended that BKV viremia level and histological grading be considered to promptly ameliorate complication associated with BKVN.

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Conflicts of interest

There are no conflicts of interest.

Idris Abdullahi Nasir[1,2], Halima Ali Shuwa[3], Hafsat Saidu Isiaka[2]

[1]Department of Medical Laboratory Services, University of Abuja Teaching Hospital, Gwagwalada, FCT Abuja, [2]Department of Medical Microbiology and Parasitology, College of Health Sciences, University of Ilorin, Ilorin, [3]Department of Immunology, School of Medical Laboratory Science, Usmanu Danfodiyo University, Sokoto, Nigeria

Address for correspondence:
Mr. Idris Abdullahi Nasir,
Department of Medical Laboratory Services, University of Abuja Teaching Hospital, Gwagwalada, FCT Abuja, Nigeria.
E-mail: eedris888@yahoo.com

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