Cytomegalovirus and BK polyomavirus co-infection nephropathy after kidney transplantation

Florian Lacave[1], Nada Kanaan[1], Arnaud Devresse[1]

Affiliations : [1]Division of Nephrology, Cliniques universitaires Saint-Luc, Brussels, Belgium

Correspondence: Florian Lacave, MD, Division of Nephrology, cliniques universitaires Saint-Luc, Brussels, Belgium, florian.lacave@saintluc.uclouvain.be

Funding: none

Disclosures: none to declare

Running head: cytomegalovirus and BK polyomavirus co-infection

A 62-year-old man with diabetic nephropathy was transplanted with a kidney from a deceased donor. His immunosuppressive regimen included tacrolimus, mycophenolate mofetil and steroids. No induction therapy was administered. Cytomegalovirus (CMV) serology was negative in both donor and recipient. He was discharged quickly with normal kidney function.

Nine months later, the patient reported loss of appetite and nausea. Laboratory tests revealed acute kidney injury (doubling of serum creatinine), hepatic cytolysis (3-fold increase in serum alanine and aspartate aminotransferase levels), the absence of *de novo* HLA antibody, leukocyturia or proteinuria.

Urine cytology showed decoy cells with simian virus 40 (SV40) immunoassay. BK polyomavirus (BKPyV) quantitative plasma polymerase chain reaction (PCR) viral load was high (10,128,020 IU/mL). Concomitantly, CMV quantitative plasma PCR revealed 2,173,546 IU/mL. An allograft biopsy showed an interstitial lymphoplasmocytic infiltrate with tubulitis. Immunochemistery analysis confirmed CMV and BKPyV renal co-infection (Figure 1). Gangiclovir was started and mycophenolate mofetil was discontinued. Six weeks later, kidney function has stabilized; CMV and BK polyomavirus viral loads have decreased considerably but have not yet normalized.

Co-infection with BKPyV and CMV in kidney transplant recipients are uncommon and poorly reported, although some data have suggested that plasma BKPyV positivity is highly associated with co-infection of CMV, suggesting possible risk factors for one another.[1] Outcomes of patients infected by both virus are not well defined as only limited data are available, emerging from small retrospective case series.[2-3] Jehn et al[2] compared the outcomes of kidney transplant recipients presented both BKPyV viremia and CMV viremia (n=59), CMV viremia alone (n= 182) and BKPyV viremia alone (n= 102). They found a strong

association between co-infection and occurrence of acute rejection. However, although patients with co-infection had lower graft function, there was no difference between groups regarding graft and patient survival. Kaul et al[3] also compared the outcomes of 6 patients with co-infection to those of 10 and 4 patients with CMV viremia alone or BKPyV viremia alone, respectively. Co-infection was not associated with increased risk of acute rejection or patient and graft death-censored graft survival. Treatment of co-infection is not well defined either. However it seems logical to apply recommendations for CMV infection[4] alone and BKPyV infection[5] alone, namely (val)ganciclovir and reduction of immunosuppression.

The patient signed informed consent for the publication of this clinical image.

Bulleted teaching points:

- Co-infection with BKPyV and CMV in kidney transplant recipients are uncommon.

-Outcomes of patients co-infected by both virus is not well defined.

-Optimal management is not known and is based on recommendations for the treatment of each virus individually.

References

1. Toyoda M, Puliyanda DP, Amet N, et al. Co-infection of polyomavirus-BK and cytomegalovirus in renal transplant recipients. *Transplantation.* 2005;80:198-205.
2. Jehn U, Schütte-Nütgen K, Bautz J, et al. Clinical features of BK-polyomavirus and cytomegalovirus co-infection after kidney transplantation. Scientific Reports. 2020;10,22406.
3. Kaul A, Kumar S, Bhaduaria D, et al. Outcome of renal transplant recipients with cytomegalovirus and BK polyomavirus co-infection nephropathy, Saudi J Kidney Dis Tranplant. 2018,29:101-106.
4. Razonable RR, Humar A. Cytomegalovirus in solid organ transplant recipients-Guidelines of the American Society of Transplantation Infectious Diseases Community of Practice. *Clin Transplant.* 2019;33:e13512.
5. Hirsch HH, Randhawa PS, AST Infectious Diseases Community of Practice. BK polyomavirus in solid organ transplantation-Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. *Clin Transplant.* 2019;33:e13528.

Figure legend

Figure 1: Renal allograft biopsy (A, hematoxylin and eosin staining, magnification x 20; B, Periodic acid Schiff staining, magnification x 16) shows interstitial lymphoplasmocytic infiltrate with few neutrophiles surrounding infected tubules. These are infiltrated by lymphocytes (A and B, black arrows) and infected tubular epithelial cells are characterized by an homogenous intranuclear inclusion of BK polyomavirus (A and B, red arrows). This infection was confirmed by SV40 immunohistochemistry which reveal by nuclear labeling the infected cells close to other healthy ones (C, arrows, magnification x 15). The patient had a simultaneous infection by cytomegalovirus, proven by immunohistochemistry revealing rare nuclear positivity in glomerular cell (D, arrow, magnification x 33).