Kidney Transplantation

진행성 BK 바이러스 신병증 환자에서 최선의 치료전략

경북대학교 의학전문대학원 내과학교실

김 찬 덕

Best Strategy in Progressive BK Virus Nephropathy

Chan-Duck Kim, M.D., Ph.D.

Division of Nephrology, Department of Internal Medicine, School of Medicine, Kyungpook National University, Daegu, Korea

During the last decade, the BK virus (BKV) has emerged as a common post-transplant infection among kidney recipients, with detection rates from 20% to 60% in the urine or blood. The progression to the specific BKV-associated nephropathy (BKVAN) is reported in 1-10% of cases and is a leading cause of graft dysfunction, permanent graft injury, and even graft loss in approximately 50% of cases. With the lack of effective antiviral therapy, intensive monitoring for BKV replication by testing urine for high-level BKV viruria/decoy cells or by testing plasma for BKV viremia in combination with a reduction of immunosuppressive therapy are advocated to detect and prevent BKV reactivation and BKVAN, respectively. Screening for BKV replication should be performed at least every 3 months during the first 2 years post-transplant and then annually until the fifth year posttransplant. The following pre-emptive reduction strategies of immunosuppressive therapy and their combinations have been reported: Strategy 1. First dose reduction of the calcineurin inhibitor by 25-50% in one or two steps; followed by reducing the anti-proliferative drug by 50%; followed by discontinuing the latter. Strategy 2. First reducing the anti-proliferative drug by 50% followed by reducing calcineurin inhibitors by 25-50% followed by discontinuing the anti-proliferative drug. This intervention allows for increasing BKV-specific cellular immune responses, diminishing of BKV replication in the graft, and clearance of BKV viremia in 70-90% patients.

Failure to achieve BKV plasma clearance through reduction of immunosuppressive therapy alone and/or occurrence of allograft dysfunction should prompt performance of a renal biopsy in order to exclude BKVAN. For established BKVAN, the mainstay of therapy in kidney transplant patients without concurrent acute rejection is reducing or discontinuing immunosuppressive drugs as outlined above. Reduction of immunosuppressive therapy alone is associated with a reduction in pooled death-censored graft failure rate to eight per 100 patient-years. Additional strategies have been switching from tacrolimus to low-dose cyclosporine, or switching from the calcineurin inhibitor to low-dose sirolimus, or switching from mycophenolic acid to leflunomide or to low-dose sirolimus. Successful outcomes have been reported using each of these different interventions in small case series, but there is to date no randomized controlled trial recommending one over the other strategy.

Adjuvant therapy with cidofovir, leflunomide, intravenous immunoglobulin, or fluoroquinolones can be attempted in individual cases of BKVAN where adequate reduction of immunosuppressive therapy alone fails to clear BKVAN, but adverse effects should be weighed against the insufficient proof of benefit. Moreover, there are no randomized controlled trials providing evidence what kind of adjunctive use of these agents is best strategy in progressive BKVAN. None of

the available drugs yet tested as adjuvant therapies for BKVAN have unequivocally demonstrated an additional clinically relevant antiviral effect. Finally, adequately powered randomized trials and in vitro studies for novel compounds against BKV are urgently needed to better guide best strategy and improve outcomes for kidney transplant patients with BKVAN.