BK Nephropathy: Clinical Decision Making in the Face of Uncertainty

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In the past decade, most transplant centers have experienced an increased number of patients with BK nephropathy. A historical review of archival renal allograft biopsies by Dr. Nickeleit and colleagues in this volume indicate that this is a true increased incidence rather than the result of recent improved diagnostic techniques. Although much needs to be learned about the pathogenesis and therapy of BK nephropathy, sick patients must be treated based on the best available current information, incomplete as it is. In that regard, this issue of *Graft* provides a valuable resource for physicians. The guest editor has also invited articles by experts in basic virology; the juxtaposition of these and clinical articles may stimulate studies that will result in a more profound understanding of this disease and provide diagnostic and therapeutic approaches that will prevent the current high incidence of allograft loss after BK nephropathy.

After an overview by Dr. Ahsan and colleagues, two articles by Dr. Randhawa and colleagues and Drs. Cubitt and Stoner summarize what is currently known of the virology and epidemiology of BK infection and nephropathy. This is followed by a series of clinical articles. Dr. Nickeleit and associates report the experience of 29 renal allograft recipients with 89 renal biopsies. This clinical pathological study suggests a sequence of events within the kidney that follows viral activation and progresses to viremia and renal failure. In addition, the study suggests morphologic distinctions between BK nephropathy and rejection, as well as a clinical algorithm for the diagnosis and treatment of the disease. Drs. Agha and Brennan review their approach to BK nephropathy at Washington University; remarkably, they found no difference in the incidence of BK nephropathy in patients receiving a cyclosporine- versus tacrolimus-based immunosuppression. They suggest that intensity of immunosuppression rather than the quality of immunosuppression predisposes some patients to develop BK nephropathy. These larger experiences with BK nephropathy are complemented by several detailed case reports by Dr. Constantinescu and colleagues and Dr. Sakoulas and colleagues; these report patients with fatal cardiovascular collapse due to BK virus infection of capillary endothelial cells, as well as parenchymal and extraparenchymal disease.

In addition to causing illness in renal transplant patients, BK virus also causes other diseases. Drs. Haririan and Klassen review the result of BK virus infections in nonrenal transplant recipients. Drs. Rekvig and Moens discuss the potential contribution of polyoma viruses such as BK to autoimmunity, and Drs. Lee and Langhoff discuss the potential contribution of polyoma viruses to malignancy.

Pharmacologic treatment of BK nephropathy is in its infancy. Dr. Roskopf and colleagues review the possible agents. Dr. Scantlebury and colleagues discuss a protocol using cidofovir.

As guest editor, Dr. Ahsan has gathered, in one place, the current understanding of BK nephropathy. This is a major contribution. However, a large percentage of patients with BK nephropathy continue to lose their allografts. Many questions remain. Why is BK nephropathy a relatively recent clinical problem? Is it the quality or quantity of the immunosuppression, or is it mutations in the virus? What are the contributions of CMV and JC viral infections that are often associated with BK virus? Why is the regulatory domain of the BK genome highly mutated in the kidney but archetypical in the urine? Does this reflect viral adaptation to the kidney that results in viral proliferation and disease?

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What are the mechanisms of reactivation, tropism, and viral replication? Why does BK usually afflict the renal allograft but not the bladder in renal transplant recipients and the bladder but not the native kidneys in bone marrow recipients? What is the nature of the host defense against BK; what are the roles of T cells, natural killer cells, and so on? Why does BK, unlike CMV, often not induce an inflammatory response or MHC Class II expression on infected renal tubule cells? As these questions and others are answered, we may see improved approaches to the diagnosis and treatment of BK nephropathy, as well as improved clinical outcomes. By gathering together the current state of the art in one place, it is hoped that this volume will not only be a resource for the clinician but also stimulate needed research in this area.